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Nitroxide radicals formed *in situ* as the regulators of polymer chain propagation

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Abstract. The literature data on the controlled synthesis of macromolecules using nitroxide radicals formed *in situ* in the course of polymerization as the regulators of polymer chain propagation are systematized and generalized. Attention is focused on the mechanism of control over the polymer chain propagation in the radical homopolymerization under conditions of the reversible inhibition and on the effect of the structure of precursors and regulating additives on the polymerization kinetics of different monomers and the molecular-weight characteristics of the synthesized high-molecular-weight compounds. The main methods for the *in situ* generation of stable nitroxide radicals are considered. The prospects for the development and practical application of the mentioned approaches to the synthesis of new polymeric materials are assessed. The bibliography includes 238 references.

I. Introduction

Production of polymers is one of the most rapidly advancing fields of chemical industry. Therefore, the perfection of the methods for the synthesis of polymeric materials and the quest for effective ways of controlling and regulating the chain propagation aimed at the synthesis of macromolecules with the desired properties pertain to the challenges of chemistry and technology of high-molecular compounds.

A possible route for the solution of these problems is associated with a concept of the controlled ('pseudo-living') radical polymerization (CRP) that opens up wide and sometimes unique prospects in regulating the polymer chain propagation under the conditions of radical initiation. The name 'pseudo-living' (or 'quasi-living') CRP was given by analogy with a similar process of 'living' anionic polymerization discovered by M Szwarc.[1, 2] This method allows one to synthesize macromolecules with intricate architectures thus solving many problems of macromolecular design. Particularly, CRP methods make it possible to control the polymer topology (comb-like, star and dendritic high-molecular compounds), deliberately design the composite structures (random, gradient and block co-polymers), carry out functionalization of polymeric materials (introduction of strictly specified functional end or side groups) and also prepare nanostructured polymeric materials.

The past two decades were marked by the rapid progress in this research field. Today, the CRP methods and approaches are being quickly upgraded and perfected, which is clearly reflected in numerous original papers and reviews published on this subject in the Russian and foreign journals.[3 – 20]

The key principle of the CRP is the establishment of the dynamic equilibrium between the 'dormant' and 'active' states of the propagating radicals by introducing functional additives into the system. In contrast to the classical radical processes, here, the irreversible decay of propagating radicals as a result of bimolecular disproportionation or recombination reactions of two propagating macroradicals should be eliminated.

Depending on the nature of additives chosen as the chain propagation regulators, the activation – deactivation of a propagating chain can occur by different mechanisms. Traditionally, the following three key types of CRP are considered:[3 – 19] stable free-radical polymerization (SFRP), atom-transfer radical polymerization (ATRP) and degenerative transfer processes (DTP).

II. The main methods for the *in situ* generation of stable radicals

Among methods employed for conducting CRP, a special place belongs to those involving stable radicals. These methods are topical, first of all, because varying the structures of the stable radicals opens up prospects for the synthesis of macromolecules with desired properties by SFRP.

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On the whole, depending on the way of generation of stable radicals, the SFRP processes can be divided into two main types:

1) the use of extraneous stable radicals introduced into a polymerization system (*i.e.*, the use of stable radicals synthesized *ex situ*);

2) generation (*in situ*) of stable radicals, *i.e.*, chain propagation regulators, directly in the polymerization system during the synthesis of macromolecules.

To date, the former processes have been studied in most details, being analyzed in hundreds of papers and many reviews.[3–6,8–10,13,14] At the same time, it is the latter approach to SFRP that is being actively developed in recent years. This is due to the availability and low cost of the precursors, which as a rule are represented by stable organic (less often, inorganic) compounds and also to the ease of realization of this approach and the high efficiency of the corresponding CRP processes.

As a whole, the following major methods for the *in situ* formation of stable radicals deserve mention:

1) the formation of stable radicals directly by homolytic dissociation of a relatively labile covalent bond in organic compounds, *i.e.*, by a monomolecular reaction that occurs as a result of thermal energy absorption, UV irradiation and other impacts on molecules (*e.g.*, the use of different types of iniferters and alkoxyamines);

2) the formation of stable radicals upon homolytic decomposition of a molecule induced by another reactive species (for example, hydroxylamines, phenols, and metal-containing compounds);

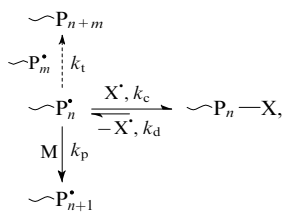
3) generation of stable radicals by quenching of free radicals by different 'spin traps' (*e.g.*, by nitrones, nitroso and nitro compounds, nitrogen oxide, sterically hindered quinones, *etc.*);

4) synthesis of stable radicals in the course of a redox process in the polymerization system, *e.g.*, the oxidation of compounds containing a nitrogen atom in a relatively low oxidation state (amines, hydroxylamines); the use of binary systems based on hydroxytriazenes and oxidants (lead or silver oxides, organic oxidants); the reduction of nitrogen-containing compounds (nitro compounds, nitriles, *etc.*).

It should be noted that despite a certain similarity in the methods of formation of stable radicals, the polymerization processes that involve these radicals are characterized by substantial differences and peculiarities associated with the nature of the additive used. Hence, in this review, the literature data on the use of active additives in the controlled synthesis of polymers are systematized according to the structure of precursors and stable radicals.

III. High-molecular nitroxide radicals as the regulators of radical polymerization

The SFRP mechanism is based on the reversible coupling of propagating radicals with stable radicals, as shown by the following scheme.[3–19]



(1)

Here, $\sim P_n^{\bullet}$ is a polymer radical; $X^{\bullet}$ is a stable radical; M is a monomer; k_c, k_d, k_p, k_t are the rate constants for recombination, dissociation, chain propagation and chain termination, respectively.

A broad range of additives are used as scavengers of macroradicals, in particular, different stable radicals [nitroxide (aminoxyl), verdazyl, triazolyl, arylazoxyl, boroxyl, organometallic radicals, *etc.*]. Nitroxide radicals were studied most comprehensively (the corresponding polymerization type was called nitroxide-mediated radical polymerization, NMRP), which is due to the commercial availability of the corresponding reagents including 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) and its analogues as well as several other nitroxide radicals with different structure.

The practical implementation of NMRP faces difficulties due to inherent drawbacks. Thiese include low rate, the possibility of control over the chain propagation, as a rule, only at high temperature, the problem of compatibility of regulators with the monomers, the relatively high cost of the regulators, *etc*. This is why the development of new methods that would provide solution to these problems is of undeniable interest and quite topical.

Since the mid-1990s, a new version of CRP, *viz.*, reaction in the presence of different precursors of chain propagation regulators, has been actively developed. The following well-known commercially available compounds were used as the precursors: nitrones, nitroso compounds, hydroxylamines, amines, hydroxytriazenes, and also sodium nitrite, nitrogen oxides, *etc*. It deserves mention that for years, many of these compounds were known as only inhibitors of radical polymerization processes[21–28] and it is only recently that they have found new application as the efficient regulators of not only chain termination, but also its propagation.

The topicality and significance of the new and actively developed trend, namely, the regulation of the polymer chain propagation by stable radicals formed *in situ*, is evident from the keen attention paid to the mentioned problem by different research groups both in Russia and abroad.[7,8,17,18]

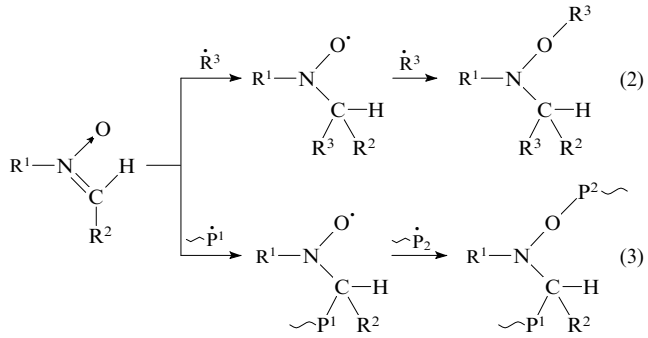
The main pathways of formation of nitroxide radicals from various precursors are illustrated by reactions (2)–(10).

Reactions (2)–(5) are scavenge of short-lived radicals by spin traps (nitrones or nitroso compounds). Depending on conditions, it is possible to obtain either low-molecular-weight [reactions (2), (4)] or macromolecular nitroxides [reactions (3), (5)] and also the corresponding alkoxyamines.

A different method of the *in situ* generation of nitroxide radicals and alkoxyamines is the oxidation of *N*-hydroxytriazenes to the corresponding nitroso compounds by single-electron transfer [reaction (6)]. The latter compounds can further react to form spin adducts [reactions (4) and (5)]. In contrast to nitrones and nitroso compounds, the hydroxytriazene–oxidant systems represent unique bifunctional iniferters. The decomposition of hydroxytriazenes affords not only nitroso compounds capable of control over the chain propagation, but also active radicals that initiate polymerization.

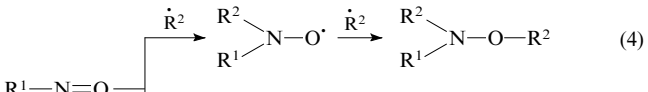
Yet another method of synthesis of nitroxide radicals is the reduction of nitro compounds [reactions (7), (8)]. However, this results in a large number of components that in turn can react with the active propagating radicals, thus increasing the number of undesired side reactions.

The four-step mechanism of alkoxyamine synthesis from sodium nitrite is illustrated by reactions (9), (10). First, sodium nitrite is reduced to nitrogen oxide, a paramagnetic molecule capable of scavenging active radicals, including macroradicals to form nitroso compounds. Alkoxyamines are obtained analogously from a mixture of nitrogen oxide and nitrogen dioxide.

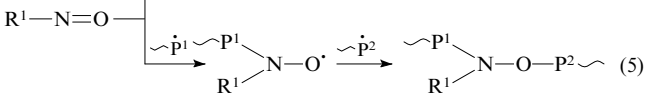


(2)

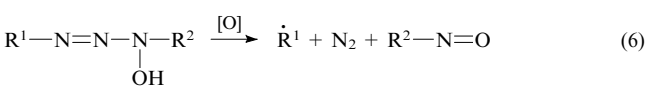
(3)



(4)

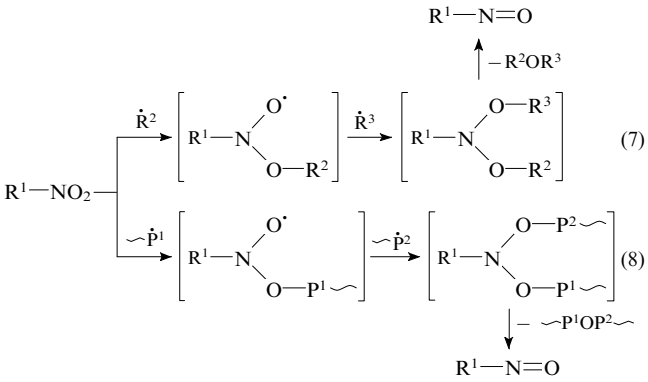


(5)



(6)

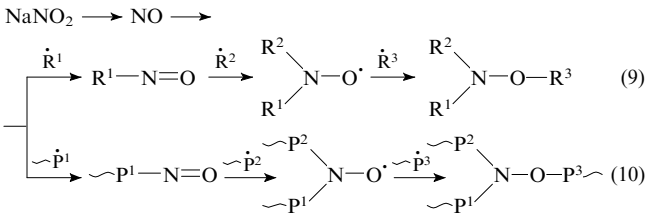
[the chain propagation is controlled according to reactions (4), (5)].



(7)

(8)

[and the further chain propagation occurs according to reactions (4), (5)].



(9)

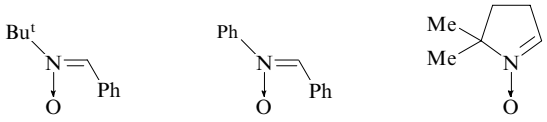
(10)

$\sim\dot{P}$ is a propagating macroradical; $R^{\bullet}$ is an initiator radical.

Depending on conditions, these processes can produce low- or high-molecular-weight nitroxides and alkoxyamines.

1. The use of nitrones as the source of stable nitroxide radicals

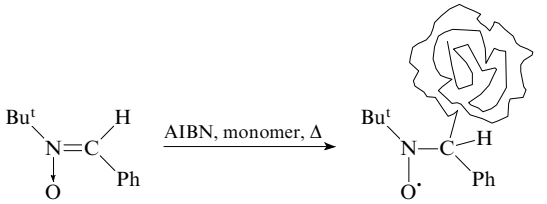
In organic chemistry, nitrones are the best known 'spin traps' usually applied in the quenching of short-lived radicals for their subsequent identification by EPR.[29] These compounds are efficient acceptors of free radicals including macroradicals formed in the course of polymer chain propagation (the corresponding accepting rate constants were usually $\geqslant 1 \times 10^3$ litre mol^{-1} s^{-1}).[29] In the excess of propagating free radicals, alkoxyamines can be formed to act later as the effective chain propagation regulators. Certain nitrones [*C*-phenyl-*N*-*tert*-butylnitrone (PBN), *C*,*N*-diphenylnitrone (DPN) and 5,5-dimethylpyrroline 1-oxide (DMPO)] are widely known commercial products.



PBN DPN DMPO

Other nitrones can be prepared by simple synthetic procedures.[30, 31]

The first mention [32] of the use of this class of compounds as the polymer chain propagation regulators in CRP dates back to 1998. In this and the subsequent publication,[33] by the example of polymerization of methyl methacrylate (MMA) in the presence of PBN, a fundamentally new concept of the *in situ* formation of high-molecular-weight nitroxide radicals was put forward. In the first step, the initiator dissociates to active radicals that could either be captured by the nitrone present in the system or initiate the polymerization to afford oligomeric propagating radicals. High-molecular-weight nitroxides appeared as a result of quenching of these oligomeric radicals by the nitrone.



(11)

AIBN is azobisisobutyronitrile.

In the second step, high-molecular-weight nitroxides reversibly react with propagating radicals to form the corresponding alkoxyamines, as in the classical CRP scheme involving low-molecular-weight nitroxides and alkoxyamines [see mechanism (1)].

By the example of polymerization of MMA in the presence of PBN, the effect of the nature of initiators [azobisisobutyronitrile (AIBN) and dicyclohexyl peroxydicarbonate (CHPC)] on the formation of high-molecular-weight nitroxides and the chain propagation mechanism was assessed.[34] The polymerization was carried out at 50–65 °C, *i.e.*, in the temperature range as close as possible to the conditions of industrial synthesis of polymers. It was shown that in the presence of these initiators, identical trends in the chain propagation were observed, namely, the suppression of the gel effect, the linear increase in the

molecular weight (MW), a shift of the molecular-weight distribution (MWD) to higher MW with conversion and the lower polydispersity indices as compared with the processes in the absence of the nitrone. At the same time, the noticeably different effects of these initiators on both the initial polymerization rate and the molecular-weight characteristics of synthesized polymers deserve attention. Thus for CHPC, the initial polymerization rate slows down with the increase in the additive concentration as compared with the analogous process in the presence of AIBN and, conversely, the polydispersity index increased with the monomer conversion (Table 1). Presumably, these differences are associated with the following factors, *viz*., different rate constants for nitrone reactions with the radicals formed in the decomposition of the initiators and the oligomeric radicals; the ratio of rate constants of radical quenching by the trap and the radical addition to the monomer multiple bond; the contribution of side reactions determined by the different half-lives of the initiators; and also possible reaction of the nitrone with the peroxide initiator. These side reactions can successfully compete with the main CRP route; hence, the CRP contribution to the overall process is not always decisive. Actually, the polydispersity index of poly(methyl methacrylate) (PMMA) synthesized in the presence of PBN exceeded 1.5 for deep conversion; at the same time, MMA polymerization in the presence of low-molecular alkoxyamines occurs at lower rates and higher temperatures, but the polymers produced have the polydispersity index of 1.35.[55]

Table 1. The main characteristics of radical polymerization of vinyl monomers in the presence of alkoxyamines synthesized *in situ* from nitrones.

Nitrone [a]	Alkoxyamine and conditions of its formation [b]	Polymer [c]	Initiator [d]	T/°C	Ratio initiator : nitrone	Time /h	Conversion (%)	$10^{-3} M_n$	M_w/M_n	Ref.
PBN	A	PMMA	AIBN	50	1 : 8	~1	2	309	1.8	32, 33
		PMMA	AIBN	50	1 : 8	~17	74	727	1.7	32, 33
		PMMA	CHPC	50	1 : 4	~0.4	3	103	1.6	34
		PMMA	CHPC	50	1 : 4	~8	82	302	2.5	34
		PMMA	AIBN	30 [e]	1 : 7	~7	61	121	2.2	35
		PMMA	BP	120	1 : 10	–	55	20	2.3	36
		PBMA	AIBN	50	1 : 2	~25	79	6500 [f]	–	37
		POMA	AIBN	65	1 : 2	~6	75	740	1.8	38
		POMA	BP	100	1 : 2	~1	82	35	2.1	38
		PCMA	AIBN	65	1 : 2	~6	80	–	–	38
		PBA	AIBN	65	1 : 0.2	~7	64	671	1.7	37
		PBA	AIBN	85	0.5 : 1	~3	70	25	3.0	39
		PS	AIBN	70	1 : 0.1	~9	80	45	1.5	40, 41
		PS	BP	90	1 : 2	~96	94	82	1.6	42
		PS	BP	120	1 : 0.7	~24	98	47	2.3	42
		PS	AP	90	–	~1	98	7	2.8	43
		PVS	CHPC	50	1 : 0.1	~2	89	44	2.2	44, 45
		PVP	AIBN	60	1 : 0.25	~20	60	69 [f]	–	46
DPN	A	PMMA	AIBN	50	1 : 15	~12	81	2900 [f]	–	47
1	A	PS	AIBN	120	1 : 1.5	~5	78	13	2.4	48
2	A	PS	AIBN	120	1 : 1.5	~46	67	9	3.0	48
3	A	PS	AIBN	120	1 : 1.5	~40	99	6	1.5	49
4	B	PBA	AIBN	130	1 : 1	~2.5	83	~7	2.0	50, 51
PBN	B	PS	peroxide mixture	120	–	~7.5	85	–	1.6	52
5	B (see [g])	PS	BP	110	0.5 : 1	~25	50	60	1.25	53
	C	PS	AIBN	110	0.5 : 1	~15	37	33	>2	54
6	C	PS	AIBN	110	0.5 : 1	~20	36	44	1.7	54
7	C	PS	AIBN	110	0.5 : 1	~30	80	~23	1.35	54
8	C	PS	AIBN	110	0.5 : 1	~25	60	~27	1.35	54
9	C	PS	AIBN	110	0.5 : 1	~25	60	~23	1.35	54
10	C	PS	AIBN	110	0.5 : 1	~25	70	~23	1.35	54
PBN	C	PS	AIBN	110	0.5 : 1	~25	56	20	1.3	54
		PBA	AIBN	110	0.5 : 1	~7	80	~50	1.5	39
DPN	C	PS	AIBN	110	0.5 : 1	~15	26	8	>4.5	54
DMPO	C	PS	AIBN	110	0.5 : 1	~30	22	~4	1.5	54

[a] For the nitrone structure, see text. [b] A is a high-molecular-weight species, formed *in situ* in a single step in the medium of the monomer; B is an oligomeric species formed *in situ* in two steps with initial heating at lower temperature in the medium of the monomer; C is a low-molecular-weight species, formed *in situ* in two steps with initial heating at lower temperature in toluene. [c] PMMA is poly(methyl methacrylate), PBMA is poly(butyl methacrylate), POMA is poly(octyl methacrylate), PCMA is poly(cetyl methacrylate), PBA is poly(butyl acrylate), PS is polystyrene, PVC is poly(vinyl chloride), PVP is poly(vinylpyrrolidone). [d] BP is benzoyl peroxide, AP is ammonium peroxydisulfate. [e] Under irradiation. [f] Viscosity-average MW. [g] Here, alkoxyamines of different structures.

In a series of studies,[37, 38, 40, 41, 44–46, 56, 57] the mechanism of polymerization was explored for a wide diversity of monomers in the presence of both PBN as the source of stable radicals and different conventional radical initiators. It was shown that CRP occurs for the following vinyl and (meth)acrylic monomers: butyl methacrylate (BMA), butyl acrylate (BA),[37] octyl methacrylate (OMA), cetyl methacrylate (CMA),[38] styrene (St),[40, 41] acrylonitrile (AN),[41] vinyl chloride (VC),[44, 45, 56] *N*-vinylpyrrolidone (VP).[46, 57] In all these cases, the *in situ* formation of nitroxide radicals was confirmed by EPR. With these systems, it was shown that PBN and, correspondingly, nitroxide radicals formed directly in the polymerization system are efficient chain propagation regulators at temperatures as close as possible to conditions of industrial syntheses of polymers. It was found that with the addition of PBN to the mentioned monomeric systems in amounts commensurable with the initiator concentration, the following characteristics of CRP were observed:

— polymerization of vinyl and (meth)acrylic monomers proceeded without any pronounced self-acceleration; in most cases, polymerization of these monomers in the presence of high-molecular-weight nitroxide radicals formed *in situ*, as opposed to their low-molecular-weight analogues, had no substantial inhibiting effect on the polymerization initial rate and the overall time of this process;

— the linear increase in the number-average and viscosity-average MW of the synthesized polymers with the increase in the monomer conversion. The MW *vs*. conversion dependence for CRP processes in the presence of nitroxides generated *in situ* in the medium of the monomer differed from those observed for processes carried out in the presence of low-molecular stable radicals. The MW value did not tend to zero at zero conversion and the *y*-intercept corresponded to the average MW of the polymeric adduct formed by a macromolecular nixtroxide and a propagating radical. This MW value was reached in the period from the chain initiation up to its termination as a result of quenching of the radical with a nitrone molecule to form a high-molecular-weight nitroxide, which was followed by the loss of another propagating radical upon its recombination with the high-molecular-weight nitroxide;

— MWD curves of polymers uniformly shifted to higher MW with conversion;

— polydispersity indices of samples slightly decreased with the monomer conversion. Polydispersity indices of polymers synthesized in the presence of high-molecular-weight nitroxide radicals were somewhat higher as compared with the corresponding M_w/M_n values for polymerization in the presence of low-molecular-weight alkoxyamines (see Table 1). However, this parameter was substantially smaller than that of polymers synthesized in the presence of conventional initiators under industrial conditions in the absence of mentioned additives (the polydispersity indices were 3–5);

— polymers synthesized in the presence of PBN were intrinsically capable of acting as macroinitiators, which is direct and most important evidence of the CRP mechanism.[45, 48, 57, 58]

An advantage of the proposed system is the possibility of homo- and co-polymerization of a wide spectrum of monomers. Particularly, CRP can be carried out for not only styrene, but also acrylic monomers, which was a challenge of polymer chemistry over the past decades.[5–10] A PBN-based system made it possible to perform co-polymerization of styrene with AN for their azeotropic composition (60 mol.% St and 40 mol.% AN) at 70 °C.[41] The synthesized co-polymers had polydispersity indices that varied in the range of 1.5–2.3 depending on the concentration and the initiator-to-regulator ratio. These values were far smaller than analogous parameters of co-polymers synthesized in the absence of chain propagation regulators for which $M_w/M_n > 3.5$.

In several studies,[48, 57, 58] the ability of high-molecular-weight alkoxyamines formed *in situ* on the basis of PBN to act as macroinitiators was experimentally confirmed. Bulk polystyrenes (PS) synthesized in the presence of different PBN : initiator ratios in the temperature range of 70–120 °C were tested as the initial macroinitiators for post-polymerization. The initiating polymers were isolated at 30% conversion, at which the polydispersity index was the smallest. In the case of macroinitiators synthesized under conditions described in our studies,[40, 41] the MWD of the reaction products shifted to the high-molecular-weight region with respect to the distribution of the original polystyrene. This suggests that the molecular weight of the original polymer increased as a result of post-polymerization due to the 'insertion' of new monomeric units into the labile alkoxyamine bond. At the same time, the mentioned MWD of post-polymers were bimodal, which pointed to certain contributions of chains formed under conditions of uncontrolled polymerization.

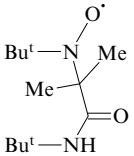
The ability of high-molecular-weight alkoxyamines to re-initiate polymerization was also experimentally confirmed by studying block co-polymerization.[48] In block co-polymerization of PS with MMA, PS was used with $M_n = 16\,800$, which was prepared in the presence of 0.8 mol.% AIBN and 0.08 mol.% PBN at 70 °C, *i.e*., under the conditions similar to those used earlier.[40, 41] The isolated PS–PMMA block co-polymer was characterized by IR spectroscopy and GPC (gel-permeation chromatography). With conversion, the MWD curves of block co-polymer samples shifted to higher molecular weights with respect to the original polymer. Moreover, the block co-polymer MW noticeably increased as compared with the original polymer. Thus for the degree of conversion of MMA to a block co-polymer of 60%, the M_n of the PS–PMMA product was 740 000. The amounts of active ('living') and passive ('dead') polymer in the macroinitiator were calculated. It was shown that the majority of chains (~87%) involved in the macroinitiator contained active groups capable of re-initiating the polymerization process and responsible for the formation of post- and block co-polymers.[48]

The proposed method pioneered the polymerization of VC in the presence of PBN as the source of nitroxide radicals at a temperature (50 °C) optimal from the technological standpoint.[44, 45, 56] The polymerization of VC carried out in the presence of *in situ* generated high-molecular-weight alkoxyamines demonstrated the main features typical of CRP, particularly, the linear increase in MW with conversion, which is of fundamental importance as a confirmation that 'pseudo-living' polymerization occurs in the presence of PBN. It is the polymeric chain propagation by the 'pseudo-living' mechanism that is responsible for gradual increase in the molecular weight of poly(vinyl chloride) (PVC), whereas in the conventional polymerization of vinyl chloride, the MW of the polymer remained unchanged up to high degrees of monomer conversion, which was due to the

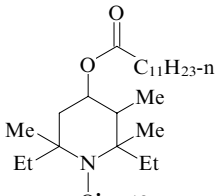
high constants for the chain transfer to the monomer.[59] The polydispersity index of PVC varied insignificantly, being equal to 2.2 for deep conversion (see Table 1).

The mechanism of control over the radical polymerization of VC in the presence of PBN was proved by performing additional post- and block co-polymerization of VC.[45, 58] A new portion of VC was added to PVC samples synthesized in the presence of PBN for the conversion of 52% and 58%; the process was continued at 50 °C. As a result, M_n of the post-polymer increased and fitted the extended linear dependence of M_n on conversion for PVC prepared in the presence of PBN. In a similar way, block co-polymers of VC with methyl acrylate were synthesized.[58] The MWD of a block co-polymer following its separation from homo-polymers was unimodal and shifted to higher MW with respect to the original homo-polymer, which is typical of polymerization processes that occur in the 'living' chain mode.

It deserves mentioning that no information on the 'pseudo-living' radical polymerization in the presence of nitroxide radicals is available so far. It is only since 2002 that the publications and patents [60–63] have appeared on the suspension homo- and co-polymerization of VC at 40–90 °C and elevated pressures in the presence of low-molecular-weight stable radicals [di-*tert*-butylnitroxide (DBN) and also radicals **11** and **12**].



11



12

It was shown that in contrast to common polymerization of VC where MW strongly depends of the temperature and decreases with its increase, CRP with nitroxide radicals affords PVC with relatively high MW at elevated temperatures. The polydispersity index of PVC decreased with the degree of polymerization, which pointed to the controlled process. Block co-polymerization of PVC with various monomers (styrene, BA, butadiene, *etc.*) also pointed to the presence of 'living' chains in the synthesized polymer. However, the polydispersity index substantially increased in the course of block co-polymerization, being > 2.5 for the majority of polymers.

Among high-molecular-weight compounds, special place belongs to water-soluble polymers, for example, poly(*N*-vinylamides), that serve as the models of natural polymers with amide groups (protein molecules). This type of polymer, namely, poly(*N*-vinylpyrrolidone) (PVP), has found wide application in different fields of science, technology and, especially, medicine. From the standpoint of demands imposed on PVP for medical applications, the NMRP seems to be the most suitable for its preparation by CRP. It was found that at temperatures above 100 °C, stable radicals such as TEMPO did not act as reversible inhibitors of VP polymerization.[64, 65] Nonetheless, it was noted that at lower temperatures (60 °C) an effect of secondary inhibition appeared in the polymerization system in the presence of TEMPO after the end of the induction period. This method allowed preparation of PVP with definite MW somewhat lower than in the classical system; however, the polydispersity index of PVP synthesized in the presence of TEMPO was rather high (3.2).

An original procedure for the controlled synthesis of PVP in the presence of alkoxyamines formed *in situ* in the course of PBN-mediated polymerization has been developed.[46, 57] This method affords PVP with controlled molecular-weight characteristics over the whole range of conversion. Radical polymerization of VP is known to be characterized by the high activity of the monomer in the chain transfer reaction.[66] This is why, for ordinary initiation, the polymer MW depended little on the conversion up to high degrees of transformation. For PVP synthesized in the presence of PBN, the viscosity-average MW increased 60-fold with conversion. Moreover, addition of the nitrone had a substantial effect on the molecular-weight characteristics of PVP, namely, polymers with the lower molecular weight [MW $\approx (1-6)\times 10^4$] were obtained as compared with common (uncontrolled) radical polymerization [MW $\approx (15-20)\times 10^4$]. It should be noted that it is polymeric materials with the first-mentioned MW that are demanded by medicine.[67, 68]

Peculiarities of the PBN effect on the kinetic characteristics of co-polymerization of VP with MMA and of VP with St and also on the molecular-weight parameters of co-polymers were studied for the polymerization of these monomers in the molar ratios of 50 : 50 and 80 : 20, respectively.[46, 69] The co-polymerization was carried out in the bulk at 60 and 80 °C. It was shown that the introduction of PBN into the polymerization system leads to a linear increase in the intrinsic viscosity of the VP–MMA and VP–St co-polymers with conversion. For the VP–MMA co-polymers synthesized in the presence of an excess of PBN (1.0 mol.%), the intrinsic viscosity virtually did not change with conversion, remaining constant throughout the process. These co-polymers exhibited unimodal MWD in contrast to polymers synthesized in the presence of AIBN without PBN; with the increase in the co-polymerization time, the MWD peak gradually shifted to higher MW. Polydispersity indices of co-polymers increased somewhat with conversion ($M_w/M_n = 1.8-2.0$), but remained far below the polydispersity indices of co-polymers synthesized in the presence of AIBN without PBN ($M_w/M_n = 4.3$).

To make certain that the 'pseudo-living' mechanism indeed occurs in the co-polymerization of VP with MMA and VP with St in the presence of PBN, the PVP–PS and PS–PVP block co-polymers were synthesized.[57, 69] PVP and PS obtained by controlled polymerization in the presence of PBN and AIBN were employed. The MWD of the block co-polymerization products was unimodal and gradually shifted to higher molecular weights as compared with the original macroinitiator, which suggests that under the mentioned conditions, the propagating radicals could be reinitiated. The polydispersity indices of synthesized block co-polymers PVP–PS and PS–PVP were 2.1 and 1.4, respectively.

As was shown above, the use of high-molecular-weight nitroxides generated *in situ* made it possible to substantially lower the temperature of controlled synthesis of macromolecules as compared with the analogous schemes based on TEMPO and its low-molecular-weight analogues, which is of exceptional practical importance. However, this gain is counter-balanced by a certain increase in the polydispersity of synthesized polymers. From the viewpoint of classical radical polymerization in the 'living'-chain mode, this is a serious drawback of the processes under study.

To extend the temperature interval that allows one to exert control over the polymer chain propagation using spin traps, a new efficient method for regulation of the polymer chain propagation under conditions of radical photoinitiation has been developed.[35] MMA polymerization initiated by near UV light (UV-A, $\lambda_{max} = 365$ nm) was studied in the presence of AIBN as the photoinitiater at 30 °C. PBN was chosen as the source of nitroxide spin adducts, because it lacks absorption at 365 nm ($\lambda_{max} = 295$ nm in benzene[29]).

Photoinduced polymerization in the presence of PBN, as in the case of thermal initiation, considerably decreased self-acceleration of the process. It was found that at the nitrone concentration of 0.7 mol.%, the gel effect was virtually absent; at the same time, as for thermal initiation, PBN did not have any significant effect on the total duration of polymerization.

In the presence of PBN, under photoinitiation conditions, the linear increase in MW with conversion was observed. Gradual increase in the PBN concentration in the system led to a decrease in the molecular weight of the polymer formed. At the PBN concentration >0.7 mol.%, the MWD was unimodal. The polydispersity index was relatively high in the beginning of the process and decreased with conversion.[35] Nonetheless, even for deep conversion, the polydispersity of synthesized samples (see Table 1) was somewhat higher than the analogous parameter of PMMA synthesized in the presence of PBN with thermal initiation ($M_w/M_n \approx 1.8$).[32,33] Yet, it was substantially lower than that of PMMA synthesized under the same conditions, but in the absence of the nitrone (4.0).

This approach to the *in situ* formation of high-molecular-weight nitroxides and alkoxyamines was later tested for emulsion polymerization.[43,48] Polymerization in disperse media is characterized by the presence of at least two phases, which gives rise to certain peculiarities as compared with the block polymerization and solution polymerization.[70] It was shown that the introduction of PBN reduces the average molecular weight of PS as compared with that of samples obtained in the absence of additives. The MWD curves of polymers synthesized in the presence of nitrones were unimodal with MW increasing up to the maximum conversions. However, the polydispersity indices of samples remained high and increased with the monomer conversion (see Table 1). The optimum temperature of the polymerization process was 90 °C. The 'pseudo-living' nature of this process was confirmed by post-polymerization of styrene with a macroinitiator obtained in emulsion in the presence of PBN.[48,58]

Studies of polymerization of various monomers in the presence of PBN-based high-molecular-weight nitroxide radicals convincingly demonstrated that the conditions for the reversible inhibition mechanism depend on the nature of both the monomer and the propagating radical.[32–35,37,38,40,41,43–46,48,56–58,69] It was found that the electronic and steric characteristics of high-molecular-weight nitroxides play the crucial role in their reversible recombination with propagating radicals. The structures of propagating radicals also have a considerable effect on the reversible dissociation process.

Thus the polymerization of methacrylic monomers (MMA, BMA, OMA, CMA) that form bulky tertiary propagating radicals occurs with an insignificant induction period in the presence of PBN, while the main features of a controlled mechanism are observed at PBN concentrations higher than the AIBN concentration. With the introduction of PBN, the polymerization of BA, styrene, VC, AN, VP, *i.e.*, monomers that form secondary propagating macroradicals, was accompanied by a substantial induction period; moreover, the controlled process occurred at substantially lower concentration of the additive and, in some cases, at higher temperatures (see Table 1, Refs 32–34, 37, 38, 40, 41, 44–46, 56, 57 and 69). These peculiarities can be explained by several factors. First, from the viewpoint of thermodynamics, sterically hindered tertiary macroradicals form weaker and, hence, more labile bonds with nitroxide radicals as propagation regulators [reaction (3)]. In the case of polymerization of monomers that generate secondary propagating radicals, the bonds in the 'high-molecular-weight' alkoxyamines are stronger and less prone to dissociation. Moreover, depending on the nature of both the monomer and the propagating radical, a certain role is played by conjugation of the radical's unpaired electron, for instance, with the aromatic ring in the case of a propagating styrene radical or with a carbonyl group in the case of acrylates. Second, from the viewpoint of kinetics, the structures of nitroxide radicals and propagating macroradicals also often have a dominating effect on the reversibility of the recombination process. The spatial and electronic characteristics of nitroxides and propagating radicals have a substantial effect on the rate constants for the recombination of these radicals and the disproportionation of the corresponding alkoxyamines.[71–73] Third, for the *in situ* formation of high-molecular-weight nitroxides and alkoxyamines, one must bear in mind a fact that the rate constants for the quenching of short-lived propagating radicals by a 'spin trap' (PBN) differ almost by an order of magnitude for secondary and tertiary radicals.[29] Probably, this explains both the appearance of a long induction period and the fact that the polymerization of monomers that form secondary radicals requires the use of lower nitrone concentrations as the propagation regulators in the chain propagation step in order to obtain high-molecular-weight nitroxide spin adducts.

It should be noted[74] that no indications of CRP typical of (meth)acrylic monomers, styrene and VC were observed for vinyl acetate (VA). At 65 °C, the 'spin trap' (PBN) acts as a conventional inhibitor of polymerization. In the initial moment of polymerization, an induction period proportional to the PBN concentration was observed. Further, the process proceeded at the same rate as with a conventional initiator with no gel-effect degeneration. The addition of PBN did not exert any substantial controlling effect on the molecular-weight characteristics of poly(vinyl acetate) (PVA), decreasing the MW only insignificantly. The polydispersity index of PVA substantially increased with conversion for both conventional radical polymerization and in the presence of PBN.

The attempts to carry out the controlled synthesis of PVA failed even when the temperature was increased to 120 °C. For the ratio initiator : PBN = 1 : 1, the polymerization of VA at 120 °C proceeded at a very low rate, *viz.*, the monomer was converted only by ~30% after 65 h. The polydispersity indices of samples sharply increased with conversion (to 4.4) and substantially surpass the analogous parameters of PVA synthesized in the presence of AIBN without the nitrone (for the conversion of 72%, $M_w/M_n = 3.3$). The MWD profile of a polymer synthesized in the presence of PBN is bimodal, which gives the grounds for assuming that two mechanisms of chain propagation occurred (traditional radical polymerization and inhibition

of chain propagation by the nitrone). Probably, the reaction of propagating radicals with nitroxides produced a sufficiently strong C–ON≺ bond so that no reversible inhibition occurred. It should be noted that only scarce information is available on CRP of vinyl acetate in the presence of agents of reversible chain transfer and organoaluminium compounds.[75,76] No reliable data could be found on the 'pseudo-living' chain mechanism for the polymerization of VA in the presence of TEMPO or other nitroxide radicals. However, it cannot be ruled out that the observed features of polymerization of VA were associated with the high constant of chain transfer to this monomer.[77]

A possible reason for the high activity of PBN as the CRP agent is the formation of a weaker (more labile than in the case of TEMPO) bond between the propagating radical and the high-molecular-weight nitroxide [reaction (3)]. Unfortunately, the possibility of direct experimental studies of the propagating chain in the processes of 'pseudo-living' radical polymerization involving high-molecular nitroxides is very limited as regards both instrumentation and methods.

This is why in another study[74] these processes were explored by modern methods of quantum chemistry. The structure and the energy stability of the labile bond between a propagating macroradical and a stable PBN-based nitroxide spin adduct were studied. Moreover, factors determining the lability of this bond were revealed. The effect of steric hindrance on the energy of the C–ON≺ bond between the methyl methacrylate radical $Me_2C^{\bullet}CO_2Me$ and nitroxide radicals formed upon addition of different alkyl radicals to PBN was assessed. It was found that the increase in steric hindrance in the alkyl radical led to a substantial decrease in the energy and enthalpy of the C–ON≺ bond cleavage.

For high-molecular-weight nitroxides, the C–ON≺ bond energy was also shown to substantially depend on the structure of the stable nitroxide radical.[74] Thus according to the results of quantum chemical simulation, the energy of the C–ON≺ bond between the propagating macroradical of (meth)acrylic monomers (MMA, BMA and BA) and 2,2,6,6-tetramethyl-4-oxopiperidine-1-oxyl (TEMOPO) is in the range from 89 to 104 kJ mol^{-1} depending on the macroradical structure (Table 2). For the same (meth)acryl monomers and the PBN-based high-molecular-weight nitroxide spin adducts [reaction (11)], the bond energy between a propagating macroradical and a stable nitroxide was only 43–74 kJ mol^{-1}. Hence, the polymerization of these monomers in the presence of PBN resulted in a weaker and, hence, labile C–ON≺ bond capable of reversible dissociation at lower temperatures as compared with the bond in adducts formed by TEMPO and its analogues.

Table 2. Energies of C–ON≺ bonds (kJ mol^{-1}) in the macroradical–nitroxide adducts [$\sim P_n \cdots A$], calculated by the PM3 method [in the parentheses, the results of B3LYP/6-31G(d) calculations with the geometry found by the PM3 method are given].[74]

Monomer in $\sim\dot{P}_n$	A$^{\bullet}$		
	$\sim P_n$—CH(Ph)—N(O$^{\bullet}$)—Bu^t	$\sim P_n$—N(O$^{\bullet}$)—Bu^t	TEMOPO
MMA	40 (28)	47 (80)	64 (89)
BMA	40	57	66
BA	90 (74)	111 (123)	98 (104)
St	45 (64)	65 (110)	66 (128)
VC	96 (138)	123 (209)	107 (176)
VA	114 (147)	126 (175)	116 (144)

The propagating radical structure directly affects the mechanism of chain propagation under the conditions of 'pseudo-living' radical polymerization. Thus for the sterically hindered tertiary radicals ($\sim$PMMA$^{\bullet}$ and $\sim$PBMA$^{\bullet}$), the C–ON≺ bond energies were substantially lower than those of secondary end radicals ($\sim$PBA$^{\bullet}$, $\sim$PVC$^{\bullet}$ or $\sim$PVA$^{\bullet}$), where both PBN and 2-methyl-2-nitrosopropane (MNP) were used (see Table 2). For styrene, the C–ON≺ bond energy took the intermediate value (between the secondary acrylate and tertiary methacrylate macroradicals), which was associated with the presence of a benzene ring in the styrene macroradical, which affected the macroradical reactivity and hence the lability of the C–ON≺ bond. These results were well consistent with the experimental data on the PBN effect on the chain propagation under the conditions of radical polymerization (Refs 32–35, 37, 38, 40, 41, 44–46, 56, 57 and 69) and explained the observed differences in the polymerization of (meth)acrylic monomers and vinyl acetate. Particularly, for VA, the C–ON≺ bond energy was considerably higher with both PBN and TEMOPO, being equal to $\sim$147 kJ mol^{-1} (see Table 2). This forms a sufficiently high energy barrier. It is not by accident that PBN did not exert any substantial effect on the mechanism of the chain propagation in the VA radical polymerization.

Despite all advantages mentioned above, the PBN-based systems have several drawbacks as compared with low-molecular-weight alkoxyamines. It should be noted that as a rule, the polydispersity indices of polymers synthesized in the presence of high-molecular-weight alkoxyamines were $\geqslant$1.5. Moreover, the increase in the polymer MW with conversion was not so pronounced as for low-molecular-weight alkoxyamines, although here the apparent gain in MW could be 'masked' by the high MW values of the high-molecular-weight alkoxyamine. A certain deviation of the proposed systems from the 'ideal' CRP criteria could be associated with insufficiently high concentration of re-initiated 'living' chains and a substantial contribution of the uncontrolled radical polymerization due to the presence of a conventional radical initiator in the system. This undeniably led to the undesired increase in the polydispersity of the synthesized polymers. At the same time, the results of post- and block co-polymerization involving macromolecular nitroxides confirmed the presence of 'living' chains in the considered systems.

Block polymerization of styrene with the PBN–benzoyl peroxide (BP) system was carried out[36,42] for different ratios of components (from 0.7 : 1 to 10 : 1) in the temperature range of 90–120 °C. Presumably, such an approach would optimize the CRP conditions. Insofar as at elevated temperatures the half-life of the initiator was short, virtually all initiator present could be decomposed in a short time, which allowed rather 'quick' synthesis of alkoxyamines. At low temperatures, the initiation proceeded throughout the polymerization process and, correspondingly, formed new polymeric chains, which resulted in broader MWD. Indeed, it was found that the MW of polystyrene synthesized with either excess or deficiency of PBN with respect to initiator increased linearly with the monomer conversion. For the

equimolar PBN : BP ratio, high-molecular-weight nitroxides were formed that contained about 40 monomeric styrene units. For the tenfold excess of PBN, nitroxide formed in the beginning of reaction included only few monomeric units. However, the polydispersity indices of samples synthesized at 120 °C were on average 2.1–2.3 (see Table 1). At 90 °C in the presence of excess of PBN, the polymerization proceeded for several days and the polydispersity indices did not exceed 1.6. The increase in the polydispersity of samples at higher temperatures pointed to a substantial contribution of side processes. The equilibrium constant of the reversible radical dissociation was assessed [36,42] to be $K \approx 4 \times 10^{-11}$ mol litre^{-1} at 90 °C and $K \approx 4 \times 10^{-10}$ mol litre^{-1} at 120 °C. These values are an order of magnitude higher than for 'pseudo-living' polymerization of styrene in the presence of TEMPO,[13] which eventually determines the higher rate of polymerization in the presence of high-molecular-weight alkoxyamines.

However, the attempts to carry out controlled polymerization of butyl acrylate to high degrees of conversion under the chosen conditions failed. The process ceased at 30% conversion of the monomer to the polymer.[36,42] For MMA,[36] polymerization involving PBN-based high-molecular-weight nitroxide proceeded up to 55% conversion under similar conditions, but the resulting homo-polymer was characterized by polydispersity index not lower than 2.3 (see Table 1).

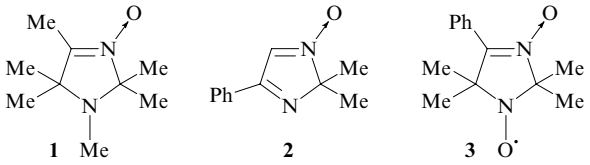
To confirm the 'living' mechanism of styrene polymerization involving high-molecular-weight alkoxyamines, post-polymerization of styrene using PS with $M_n = 12\,300$ as the macroinitiator was carried out as well as its block co-polymerization with BA. The resulting St–BA block co-polymers were characterized by a broad bimodal MWD.[36,42]

Macromolecular nitroxides based on PBN were also used under the given conditions in carrying out the gradient co-polymerization of St–VA [36,78] and the random co-polymerization of St with MMA.[36] For the St–VA co-polymerization with the tenfold excess of PBN, the co-polymer yield was ~30%. As the PBN content dropped to the threefold excess, the conversion increased to 54%; however, in both cases, this approach led to the formation of co-polymers with broad MWD ($M_w/M_n = 2.2–3.0$). According to certain data,[36] the effective equilibrium constant for the St–VA co-polymerization was higher as compared with the TEMPO-mediated reaction by 1.5 orders of magnitude and the process could occur at 100 °C. In contrast to co-polymerization of styrene with VA, co-polymerization of styrene with MMA [36] at 120 °C proceeded up to high conversion (98%). This was characterized by the steady increase in the MW of co-polymers and relatively high polydispersity indices ($M_w/M_n = 2.6$).

The K values and activation energies for the decomposition of a high-molecular-weight alkoxyamine based on PBN and PS (116 kJ mol^{-1}) [36,79] pointed to the possibility of performing the process at temperature lower than that necessary for TEMPO. Thus it was noted [80] that the decrease in the activation energy of dissociation of a sterically hindered low-molecular-weight alkoxyamine from 122 to 116 kJ mol^{-1} allowed the styrene polymerization to be conducted in the 'living' chain mode at 70 °C, *i.e.*, in the same temperature range as for high-molecular-weight nitroxide radicals based on PBN.

The relationships analogous to those described above were also observed for polymerization of vinylic monomers in the presence of DPN as the source of stable radicals.[47]

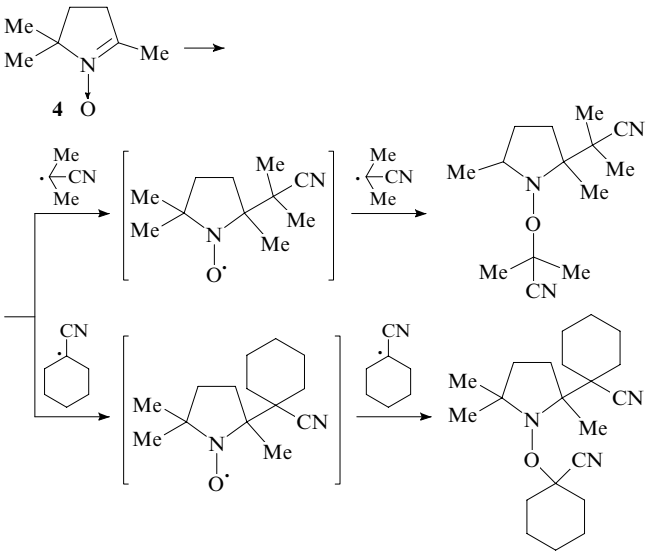
A cycle of studies on the use of nitrones **1**–**3** of the imidazole series as the source of high-molecular-weight nitroxide radicals capable of acting as the regulators of chain propagation was carried out.[48,49]



Compounds **1** and **2** generate high-molecular-weight nitroxides upon addition of propagating radicals. Compound **3** represents a nitroxide radical that also contains a nitrone group that can react with active radicals; at sufficiently high rate constants for the capture of propagating radicals, biradicals (including high-molecular) can be formed to take part in further steps of chain propagation.

The regularitites of polymerization of styrene in the presence of nitrones of the imidazole series were studied [48] for the ratio intiator : nitrone = 1 : 1.5 in the temperature range of 70–120 °C. The styrene polymerization in the presence of nitrone **2** and nitroxide radical **3** proceeded at much similar rates but much slower than the polymerization of the same monomer in the presence of compound **1** (at the same temperatures). At high temperatures, the MW of polystyrene synthesized in the presence of nitrones **1**–**3** depended linearly on the monomer conversion. However, in the presence of nitrones **1** and **2,** high polydispersity indices of polymers (~3) (see Table 1) and bimodal MWD profiles were observed. The presence of two modes can be associated with different mechanisms of chain initiation and termination in the initial stages of the process and for high conversions as well as with the possibility of side processes in the presence of nitrones (to be discussed below). Thus it was found [81] that nitrones of this type are sufficiently weak acceptors of free radicals and inhibitors of polymerization, which was demonstrated especially clearly for styrene polymerization in the presence of nitrone **1**. Compound **3** was the most efficient reversible inihibitor; however, its efficiency appears to be associated with the presence of a nitroxide radical in its structure rather than with the nitrone group, because all the main relationships of the styrene polymerization in the presence of this compound were virtually identical to those of polymerization of vinyl monomers in the presence of nitroxides of the imidazole series.[48,49,82,83] On the whole, cyclic nitrones of the imidazole series were less efficient as the chain propagation regulators as compared with their acyclic counterparts.

Almost simultaneously with the aforementioned studies by Russian scientists, Swiss researchers [50,51,84] also developed the concept of CRP in the presence of nitroxides formed *in situ*. The authors of the latter studies pioneered the use of two original methods of nitroxide radical synthesis based on nitrones. The first method included the synthesis of low-molecular-weight alkoxyamines upon direct interaction of nitrone **4** with free radicals generated by classical initiators [AIBN or 1,1′-azobis(cyclohexanecarbonitrile) (ACHC)].

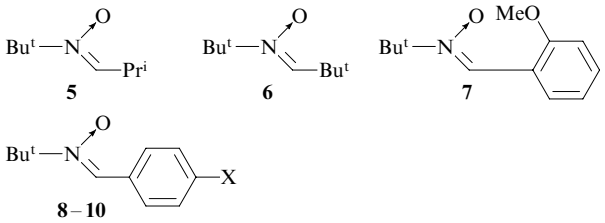


After purification, the alkoxyamines were used as the source of nitroxide radicals in homopolymerization of styrene and different acrylates and also in the random and block co-polymerization of these monomers at 100–145 °C. It was shown that alkoxyamines of similar structure make it possible to prepare low-molecular-weight polymers more or less quickly (1–6 h), *i.e.*, faster than with alkoxyamines based on TEMPO and other low-molecular-weight nitroxide radicals.[50, 51, 84] All the main relationships of the 'pseudo-living' radical polymerization were observed. However, in this case, the polydispersity indices of polymers varied in a rather wide interval (from $1.18 \leqslant M_w/M_n \leqslant 1.24$ for St to $1.59 \leqslant M_w/M_n \leqslant 2.1$ for BA).

According to the second method proposed by Swiss scientists, nitroxide radicals based on nitrones were synthesized *in situ*. However, in contrast to numerous studies,[32–35, 37, 38, 40, 41, 44–46, 48, 56–58] the synthesis of these alkoxyamines was originally conducted at 60–80 °C for a short time (from 15 min to 2 h) either directly in the monomer medium or with sequential addition of the monomer without isolation of the alkoxyamine. As a result, sterically hindered alkoxyamines were formed in the system. The subsequent synthesis of polymers was carried out at 130 °C. It was found that in the presence of the proposed sterically hindered alkoxyamines, the BA polymerization proceeded much faster than in the presence of alkoxyamines such as TEMPO. However, the polydispersity index of samples turned out to be larger than for low-molecular-weight alkoxyamines of similar structure (see Table 1).[50, 51]

Later, Japanese scientists have patented [52] an analogous method of styrene polymerization in the presence of nitrones (mainly PBN) and a mixture of substituted benzoyl peroxides. As in the above studies,[50, 51] the mixture of peroxide initiators and PBN with styrene were heated at 95 °C for 3.5 h. The polymerization itself proceeded at 120 °C at a high rate to afford PS samples with rather large polydispersity indices (see Table 1).

To improve the molecular-weight characteristics of polymers synthesized by the CRP method involving the *in situ* nitroxide generation and also to get insight into the difference between the mechanisms of nitrone-based nitroxide radical formation in the monomer medium and in the absence of monomer, a series of studies was carried out.[39, 53, 54, 85] By the example of styrene polymerization in the presence of nitrone **5** and AIBN, it was shown that the one-step synthesis of nitroxide radicals at high temperature (120 °C) gives no way for controlled polymerization.[53] Polymerization with thermal initiation in the presence of nitrone **5** produced PS with high molecular weight (M_n = 310 000) and sufficiently wide MWD (M_w/M_n = 1.9). The use of the nitrone **5**–AIBN system led to yet more heterogeneous polystyrene samples as regards the MW (M_n = 58 000, M_w/M_n = 4.0). Lowering the polymerization temperature to 85 or 76 °C in the nitrone **5**–AIBN system made it possible to lower the polydispersity index of PS to 1.6; moreover, the polymerization process proceeded at a sufficiently high rate, but was not accompanied by any substantial increase in MW with conversion. The best control over the chain propagation was achieved using a two-step method similar to that described earlier.[50, 51, 84] By the example of the nitrone **5**–BP system with the component ratio of 1 : 0.5, a 'pre-reaction' was initially carried out in the presence of styrene at 85 °C for 4 h, where no polymer formed. Subsequent polymerization was carried out at 110 °C.[53] In the primary reaction, only ~20% of the nitrone transformed into the nitroxide radical. After the 'pre-reaction' at 110 °C, a long induction period was observed (~10 h), which was attributed to the formation of nitroxide radicals during the 'pre-reaction'. The addition of a free-radical initiator (AIBN) at the end of the 'pre-reaction' made it possible to eliminate the induction period. Under the chosen conditions, narrow-distribution PS was synthesized (see Table 1). However, as in many other studies,[32–34, 37, 38, 40, 41, 44, 45] the specific structure of nitroxide radicals and alkoxyamines, responsible for the controlled synthesis of macromolecules, was not established.

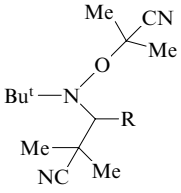


X = OMe (**8**), Cl (**9**), CF_3 (**10**).

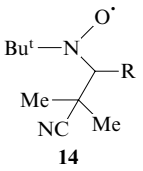
In the presence of the nitrone **5**–BP system, the co-polymerization of styrene with AN (molar ratio 60 : 40, M_n = 50 000, M_w/M_n = 1.4 for conversion of 45%) was systematically studied as well as the block co-polymers P(St–AN)–PS ($M_n \approx 100\,000$, M_w/M_n = 1.4) [where P(St–AN) was a random co-polymer of styrene and AN].[53] Although this system turned out to be less efficient in homopolymerization of BA and isoprene, it allowed the successful synthesis of block co-polymers on the basis of these monomers (PS–PBA, PS–PI; PI is polyisoprene).[53]

The efficiency of certain nitrone–AIBN systems (involving PBN, DPN, DMPO, compounds **5**–**10**) in the controlled radical polymerization of styrene was studied.[54] To exclude the contribution of uncontrolled styrene polymerization that occurs for the *in situ* two-step CRP method and also to study in more detail how the nitrone structure affects the mechanism of chain propagation, the synthesis of alkoxyamines was carried out in toluene. Styrene was added after the end of the 'pre-reaction' of the nitrone with the initiator, the polymerization was conducted at 110 °C. Under these conditions, alkoxyamines and nitroxide radi-

cals **13** and **14**, respectively, were formed from nitrones **5**–**10**.



13



14

R = Pr^i, Bu^t, 2-MeOC$_6$H$_4$, 4-MeOC$_6$H$_4$, 4-ClC$_6$H$_4$, 4-CF$_3$C$_6$H$_4$.

Systematic studies of polymerization of styrene in the presence of alkoxyamines based on the chosen nitrones have shown that the PBN–AIBN pair is the most efficient (the main molecular-weight characteristics of PS are listed in Table 1).[54] The introduction of electron-donating (nitrones **7**, **8**) and electron-withdrawing (nitrones **9**, **10**) groups in the phenyl ring of PBN had only insignificant impact on the polymerization kinetics. With the substitution of alkyl (Pr^i, Bu^t) groups for the phenyl group at the carbon atom in the nitrone, the major CRP parameters were slightly impaired. DPN proved to be the least efficient of all nitrones under consideration. In all the cases, experimental MW values were much higher that those theoretically calculated. It was shown that in the one-step CRP *in situ* (simultaneous heating of the nitrone + initiator + monomer system) at high temperature (110 °C), these systems appeared to be less efficient as regards their influence on polydispersity.[54]

The polymerization of styrene in the presence of the PBN–AIBN pair was studied in more detail.[85] The molecular-weight characteristics of PS were found to depend on the concentration of the alkoxyamine formed in the first step as a result of the 'pre-reaction'. EPR measurements confirmed that the nitroxide radicals (compound **14**, R = Ph) indeed formed under the chosen conditions (g = 2.00549, a_N = 14.33, a_H = 3.13 G).[85] Polystyrene synthesis was studied in the temperature range of 90–100 °C; however, it was shown that the controlled polymerization in the presence of low-molecular-weight alkoxyamines could also proceed at lower temperatures. The equilibrium constant (K) between the 'dormant' and 'active' states was determined for low-molecular-weight alkoxyamine **13** (R = Ph) obtained as a result of the 'pre-reaction' of PBN with AIBN at 85 °C in toluene. The rate constants for dissociation (k_d) and recombination (k_c), of this alkoxyamine and the activation energy of dissociation of sterically hindered alkoxyamine **13** (R = Ph) (~125 kJ mol^{-1}) were also determined.[85]

T/°C	K/mol litre^{-1}	k_d/s^{-1}	k_c/litre mol^{-1} s^{-1}
90	2.9×10^{-10}	4.4×10^{-4}	1.5×10^{6}
120	2.3×10^{-9}	7.2×10^{-3}	3.1×10^{6}

The equilibrium constant and the rate constant for dissociation of this sterically hindered amine turned out to be higher than those of analogous amines based on TEMPO and other low-molecular-weight nitroxides,[13] as opposed to the rate constant for recombination that decreased with the introduction of sterically hindered groups into the alkoxyamine molecule.

In a joint study by Belgian and French scientists[39] on polymerization of BA in the presence of PBN, different methods for alkoxyamine *in situ* synthesis were used [for the molecular-weight characteristics of synthesized poly(butyl acrylate) (PBA), see Table 1]. Using the EPR method, it was shown that if the nitroxide radicals were formed in the monomer medium, PBN added the propagating radicals along with the initiator radicals. This was proved by analyzing the hyperfine splitting constants (a_N = 14.67, a_H = 3.40 G) and also by comparing with alkoxyamine **13** (R = Ph) obtained from PBN upon addition of radicals resulting from AIBN decomposition (see above).[39] For this system in the medium of BA, the main kinetic parameters were also found ($K = 1.6\times10^{-12}$ mol litre^{-1}, $k_d = 1.9\times10^{-3}$ s^{-1}, $k_c = 1.2\times10^{9}$ litre mol^{-1} s^{-1} at 110 °C; the dissociation energy of the C–ON< bond was 122 ± 15 kJ mol^{-1}). The 'pseudo-living' mechanism of the BA polymerization was substantiated by carrying out the post-polymerization (the polydispersity index for post polymer decreased to 1.35 as opposed to 1.55 for the macroinitiator). Block co-polymers PBA–PS with the definite molecular-weight characteristics were synthesized; however, the polydispersity indices of samples were somewhat higher as compared with the macroinitiator (M_w/M_n = 1.7).

In 2005, a method of controlled radical co-polymerization of vinyl monomers in the presence of nitrones containing long-chain alkyl groups (C_8–C_{36}) was patented.[86] Alkoxyamines were synthesized in a single step; the nitrone + monomer + BP mixture was heated at 130 °C for 24 h. This method was employed in the synthesis of high-molecular-weight PS (MW from 98 000 to 146 000); however, the polydispersity of PS was not specified. In the presence of nitrones containing long-chain alkyl substituents, the PS–PBA block co-polymers with polydispersity indices of 2.3–2.6 were synthesized.

Yet another method of controlled synthesis of polymers using high-molecular-weight alkoxyamines was proposed.[87,88] These were synthesized at low temperatures (20–60 °C) directly in the monomer medium (styrene, BA, *N*-isopropylacrylamide). PBN, *C*-phenyl-*N*-methylnitrone and *C*-(4-bromophenyl)-*N*-methylnitrone were used as the precursors. It was shown that varying the nitrone : initiator ratio in the interval from 2 : 1 to 8 : 1 reduced the MW of alkoxyamines. Moreover, their MW remained constant throughout the interval of conversion of the chosen monomers. The resulting high-molecular-weight PS-alkoxyamines (M_w/M_n = 1.7) were used in the syntheses of a styrene post-polymer (M_w/M_n = 2.2) and a PS–PBA block co-polymer (M_w/M_n = 2.3) at 110 °C.[87] The results obtained allowed calculations of the constants of quenching of macroradicals by the nitrones over a wide temperature interval.[88]

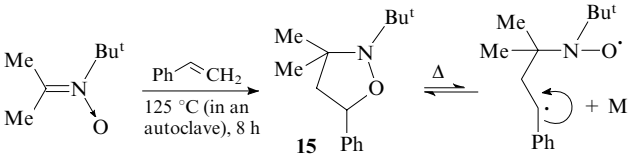
Thus, nitrones are very promising polymer chain propagation regulators. They make possible polymerization of a wide spectrum of monomers with no gel-effect and with the MW of polymers increasing linearly with conversion. Synthesis of di- and tri-block co-polymers can be effected under relatively mild temperature conditions. It is of the processes that occur in the 'living' chain mode that these features are typical.

At the same time, it should be noted that the experimental MW of polymers synthesized in the presence of different nitrones were, as a rule, higher than the theoretically calculated ones. Certainly, for the chain propagation controlled by the nitroxide radials formed *in situ* as a result of reactions of the nitrone with the propagating radicals, one can only speak of a certain share of the 'pseudo-living'

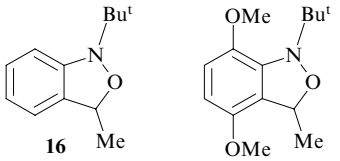
mechanism that contributes to the process and the overall polymer characteristics. Polymerization carried out in the presence of high-molecular-weight nitroxides, as for low-molecular-weight alkoxyamines, may involve several side reactions, namely, the ordinary bimolecular termination of the propagating radicals, the disproportionation of a nitroxide and a propagating radical to afford hydroxylamine,[8] the secondary catalytic inhibition.[89–91] Moreover, reactions directly associated with the destruction of the nitroxide radicals can occur in the system. These reactions were discussed in most details in a recent review.[92] The reactions that exclude the nitroxide radicals from the 'pseudo-living' equilibrium include the nitroxide oxidation to *N*-oxoammonium derivatives, the decomposition of the nitroxide radicals at high temperatures and UV radiation, the addition of several iminoxyl radicals and TEMPO derived radicals to alkenes, the reversible formation of diamagnetic dimers of nitroxide radicals, the dimer decomposition through disproportionation and some other processes.

It should be noted that in contrast to low-molecular-weight alkoxyamines, nitrones undergo 1,3-dipolar cycloaddition to the monomer multiple bond to form five-membered heterocyclic compounds (isoxazolidines) at low temperature (~60 °C).[30,93,94] This reaction can considerably contribute to the polymerization process. Isoxazolidines are sufficiently stable compounds that can be isolated from the reaction mixture. Monosubstituted alkenes (styrene, AN, acrylates and isoprene) produced 5-substituted isoxazolidines,[93] which can be considered as the cyclic analogues of alkoxyamines. The C–ON< bond in isoxazolidines was shown to be labile at high temperature. Its cleavage liberated a carbon-centred radical that induces polymerization and a nitroxide fragment of the molecule. Such a peculiarity of isoxazolidines made it possible to use them as the CRP controlling agents.

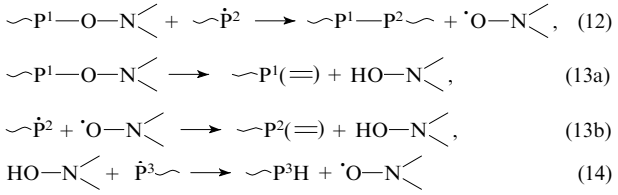
Indeed, the use of isoxazolidines as the initiators-regulators of radical polymerization of various monomers in the temperature range of 100–130 °C was patented.[95] Thus isoxazolidine **15** prepared from a nitrone and styrene was used in the radical polymerization of styrene and synthesis of a PS–P(St–AN) block co-polymer at 110 and 125 °C. It took short time (4.5–6 h) for polymerization to proceed to deep degrees of conversion. Unfortunately, no detailed information was given on the MWD of PS samples and also on the structure and composition of block co-polymers.



The same authors studied the activity of benzoisoxazolidines **16** and **17** in the syntheses of PS and PS–P(St–AN). Polymers with sufficiently high MW (> 100 000) were synthesized over a relatively short time interval. However, the MW of samples was virtually independent of the degree of polymer conversion. It cannot be ruled out that isoxazolidine formation contributes to one-step *in situ* polymerization in the presence of nitrones, especially at elevated temperatures.



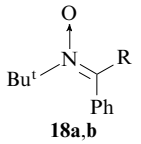
At the same time, the secondary catalytic inhibition is one of irreversible processes that lead to a 'dead' polymer, impairing its molecular-weight characteristics. The mechanism of inhibition in the presence of nitroxide radicals at 60 °C was studied.[89–91] The following two possible pathways of the catalytic recovery of the nitroxide radicals were inferred, *viz.*, chain-transfer radical substitution upon reaction of an alkoxyamine with a propagating radical [reaction (12)]; and intramolecular disproportionation of an alkoxyamine [reaction (13a)] or intermolecular disproportionation between a nitroxide and an active radical (reaction (13b) to afford a 'dead' chain and a hydroxylamine followed by the hydrogen atom transfer from the hydroxylamine and the recovery of the nitroxide [reaction (14)].



P(=) is a polymer with a terminal multiple bond.

However, the mechanism of secondary inhibition cannot be considered proved unambiguously. Thus the mechanism (12) was proposed[89] by analogy with the known processes of peroxide decomposition by the chain mechanism. The possibility of the TEMPO-mediated secondary inhibition by the mechanisms of reactions (13), (14) was discussed in detail in a review.[8] In a later study,[96] the kinetics of 'living' radical polymerization of styrene in the presence of low-molecular-weight TEMPO-based alkoxyamine at 120 °C was interpreted within the framework of a hypothesis of secondary inhibition. However, the mechanism of styrene polymerization in the presence of alkoxyamines formed *in situ* at the 100-fold variation of the initial TEMPO concentration did not receive any unambiguous explanation.

Based on the ^{1}H NMR studies, it was found[92] that the substituent at the nitrone carbon atom (PBN, **18a**,**b**) affects the rate of nitrone thermolysis in the temperature range of 70–110 °C.



18a,**b**

R = Et (**a**), Pr^i (**b**).

The rate of nitrone decomposition was shown to increase with the increase in steric hindrance due to substituents R. Thus PBN is thermally stable up to 80 °C. With an increase in the temperature to 110 °C, it decomposed

quite insignificantly (by 8% in 2 h). A similar situation was observed for nitrone **18a** with a somewhat higher decomposition rate. For compound **18b**, an almost sixfold increase in the extent of nitrone decomposition was observed with temperature. Thus at 110 °C nitrone **18b** decomposed by 91% in 2 h. With an increase in steric hindrance in the nitrone, the conjugation of the benzene ring with the π-system is violated to enhance the possibility of the Bu^t group elimination and to form a planar oxime. Similar trends were also observed for the nitroxide radicals of similar structure.[92] The obtained results[92] made it possible to assume that high-molecular-weight nitroxides decompose at high temperature, which substantially decreases their concentration and, hence, augments the uncontrolled component of radical polymerization.

As a whole, these side processes favour the formation of a 'dead' polymer in the system thus increasing the polydispersity of the polymers. The overall contribution of the side reactions was determined by several parameters, namely, the chosen method of the alkoxyamine synthesis *in situ*, the nature of the nitrone, the monomer structure, *etc*. Thus, from the viewpoint of synthesis of narrow-distribution homo- and co-polymers, the high-molecular-weight alkoxyamines formed *in situ* rank slightly below their low-molecular-weight analogues.

At the same time, the polymerization methods considered in this section that involve nitroxides and alkoxyamines derived from different nitrones had the following advantages as compared with analogous processes involving low-molecular-weight alkoxyamines:

— the introduction of nitrones as the chain propagation regulators makes it possible to control the kinetic parameters of polymerization and the molecular-weight characteristics of a wide range of polymers. Polymerization involving nitrone-based systems proceeds up to high degrees of conversion (80% – 90%) and at higher rates as compared with low-molecular-weight alkoxyamines, which is an important advantage from the applied standpoint;

— varying the ratio nitrone : initiator : monomer makes it possible to regulate the structure of high-molecular-weight nitroxides obtained *in situ*. Nitroxides synthesized from nitrones contain two substituents, one of them is only determined by the nature of the starting nitrone, while the nature and the spatial structure of the second substituent depend on the method of nitroxide synthesis. In the case of one-step method, this is determined by the number and the nature of the monomer units that have time enough to add to the initiating radical before the latter reacts with the nitrone [reactions (2), (3)]. Modifying the structure of the nitroxide radical, in particular, varying its steric factors and the length of the polymeric substituent, affected the lability of its end group;

— for block co-polymerization, the use of high-molecular-weight nitroxides based on nitrones allows preparation of a tri-block co-polymer ABA, in contrast to low-molecular-weight nitroxides that can lead to di-block co-polymers of the AB type;

— the majority of proposed additives are thermally stable commercial products, they can efficiently operate at temperatures corresponding to the conditions of industrial syntheses of polymers (50 – 100 °C), which determines their potential for practical applications.

2. Nitroso compounds as the precursors of nitroxide spin adducts

The regularities of polymerization of vinyl monomers in the presence of nitrones as the sources of stable nitroxide radicals considered in the previous section suggest that alkoxyamines prepared from nitrones are sufficiently promising chain propagation regulators. In addition to nitrones, aliphatic and aromatic nitroso compounds of which some pertain to commercially available products and substances that can easily be synthesized are also used as 'spin traps' and hence nitroxide radical sources. The main methods of synthesis of nitroso compounds are documented in original papers, reviews and monographs (*e.g.*, see Refs 30 and 97). Nitroso compounds can capture short-lived chain propagation radicals to transform then into stable nitroxide radicals, *i.e.*, act as the precursors of chain propagation regulators [reactions (4), (5)].

R in R–N=O	Name	Designation
Bu^t	2-methyl-2-nitrosopropane	MNP
2,4,6-$Bu^t_3C_6H_2$	tri-*tert*-butylnitrosobenzene	TTNB
Ph	nitrosobenzene	NB
$Bu^tCH_2Me_2C$	2,4,4-trimethyl-2-nitroso-pentane (nitroso-*tert*-octane)	NTO
2,3,5,6-Me_4C_6H	nitrosodurene	ND
2,4,6-$Br_3C_6H_2$	tribromonitrosobenzene	TBNB

The first mention of the possibility of using MNP and TTNB as the sources of stable nitroxide radicals in the MMA polymerization at 80 °C and a constant nitroso compound : AIBN ratio dates back to 1995.[98] However, this publication was largely devoted to the effect of nitroso compounds on the rate of MMA polymerization.

In further studies, nitrosobenzene was used[99] as the precursor of low-molecular-weight alkoxyamines. The alkoxyamine prepared from NB and AIBN was purified and used as an additive for the polymerization of styrene, MMA and BA at 120 – 140 °C in the presence of camphorsulfonic acid as an agent increasing the polymerization rate.[99] The major molecular-weight characteristics of the synthesized polymers can be found in Table 3.

Swiss scientists have patented and published the use of nitroso compounds as the regulators of radical polymerization of vinyl monomers.[50, 51, 84] Two versions of alkoxyamine synthesis are feasible, namely, a classical version (*i.e.*, directed synthesis of alkoxyamines followed by their isolation from the reaction mixture) and the *in situ* formation of alkoxyamines from nitroso compounds without isolation. The latter version involves mixing of a nitroso compound with the radical polymerization initiator (AIBN, ABCN) and heating this mixture at 80 °C in solution or in the medium of a monomer. The activity of alkoxyamines synthesized by the former version as the CRP regulators was tested for several monomer systems (styrene, BA, MMA, 2,2-diaminoethyl and glycidyl methacrylates) and also in the random and block co-polymerization of these monomers in the temperature range of 110 – 145 °C. Various polymeric materials were synthesized up to deep degrees of conversion, with the polydispersity indices varying in the range of 1.3 – 3.5 depending on the nature of monomers and alkoxyamines.[50, 51, 84]

Polymerization of styrene in the presence of low-molecular-weight alkoxyamines prepared from nitroso-*tert*-octane exhibited the major features typical of 'pseudo-

Table 3. The main characteristics of polymerization of different monomers in the presence of alkoxyamines synthesized from nitroso compounds and *N*-hydroxytriazenes.

Additive	Alkoxyamine and conditions of its formation [a]	Polymer	Initiator	T/°C	Ratio initiator : additive	Time /h	Conversion (%)	$10^{-3} M_n$	M_w/M_n	Ref.
NB	A	PS		140		6	97	30	2.2	99
		PMMA		140		6	77	14	1.9	99
		PBA		120		6	44	53	4.7	99
NTO	A	PBA		120–145		~0.5	95	3.4	1.8	50, 51
	B	PBA	AIBN	130	1 : 1	2.5	21	1.2	1.4	50, 51
	B	PBA	ACHC	130	1 : 1	2.5	38	2.8	2.0	50, 51
MNP	B	PS	peroxide mixture	130	—	~ 7.5	70	—	1.25	52
MNP	C	PMMA	AIBN	50	1 : 0.2	4.5	4	78	1.6	100
		PMMA	AIBN	50	1 : 0.2	24	72	579	2.2	100
		PS	BP	100	1 : 0.8	2.5	17	18	1.4	40, 101
		PS	BP	100	1 : 0.8	23.5	74	22	1.3	40, 101
		PS	BP [b]	120	1 : 0.8	24	91	98	1.8	36
		PS	BP [c]	120	1 : 0.8	24	89	47	1.4	36
		P(St–AN)	BP	100	1 : 0.9	4	78	56	2.3	102
		POMA	AIBN	65	1 : 0.2	~13	75	240	2.2	38
		POMA	BP	100	1 : 0.6	~0.25	4	6	1.7	38
		POMA	BP	100	1 : 0.6	~0.7	65	18	2.3	38
		PCMA	AIBN	65	1 : 0.2	~12	58	460	2.5	38
NB	C	PMMA	DPC [d]	50	1 : 0.6	6	8	126	2.4	103
		PMMA	DPC	50	1 : 0.6	20	89	428	2.9	103
		PMMA	AIBN	70	1 : 0.3	9	93	174	2.0	104
		PS	BP	100	1 : 0.4	0.5	31	19	1.5	105
		PS	BP	100	1 : 0.4	1.5	70	26	2.2	105
		PS	BP	100	1 : 0.5	0.5	19	18	1.5	105
		PS	BP	100	1 : 0.5	3	57	22	2.0	105
ND	C	PMMA	AIBN	70	1 : 0.25	2.5	51	201	2.0	104, 106
		PS	AIBN	70	1 : 0.25	13.5	75	58	1.8	40, 106
		P(St–MMA)	AIBN	70	1 : 0.25	6	65	32	1.7	106, 107
		P(St–BA)	AIBN	70	1 : 0.25	12	83	51	1.8	107
		P(St–AN)	AIBN	70	1 : 0.3	4	70	69	1.8	57
		PVA	AIBN	90	1 : 1	12	17	2	1.2	108
		PVA	AIBN	90	1 : 1	55	85	12.5	3.0	108
TBNB	C	PMMA	AIBN	70	1 : 0.3	5	96	234	1.9	104
NTO	C	PS	AIBN	90	1 : 1	30	45	~90	—	109
		PS	AIBN	110	1 : 1	12	55	~90	—	109
BPT	C	PMMA	DPC	50	1 : 0.6	1	12	96	1.5	110, 111
		PMMA	DPC	50	1 : 0.6	8	70	170	1.8	110, 111
		PBMA	DPC	50	1 : 0.75	2	15	230	1.5	111, 112
		PBMA	DPC	50	1 : 0.75	10	66	232	1.9	111, 112
		PS	BP	100	1 : 0.5	0.5	26	13	1.5	111
		PS	BP	100	1 : 0.5	7	67	23	1.6	111
DPT	C	PMMA	DPC	50	1 : 2	1	10	72	1.8	103, 112
		PMMA	DPC	50	1 : 2	34	76	75	1.5	103, 112
		PS	BP	100	1 : 0.5	0.25	7	22	1.5	105
		PS	BP	100	1 : 0.5	2.5	79	37	1.8	105

[a] A is a low-molecular-weight species, preliminarily obtained from a nitroso compound and AIBN; B is an oligomeric species, formed *in situ* in two steps with preliminary heating at a certain temperature in the medium of the monomer; C is a high-molecular-weight species, formed *in situ* in a single step in the medium of the monomer; [b] 5 mmol litre^{-1}; [c] 20 mmol litre^{-1}; [d] DPC is dicetyl peroxydicarbonate.

living' processes, namely, the absence of the gel-effect, the linear MW increase with conversion (where the M_n values were comparable with those theoretically calculated), low polydispersity indices (1.15–1.27). In the case of butyl acrylate, the MW of the polymer also increased linearly with conversion; however, the MW values substantially exceeded the theoretical M_n. Despite decreasing with the monomer conversion, the polydispersity index remained high (>2).[84]

The *in situ* radical polymerization was studied [50, 51] only for BA. As in the case of nitrones, the results of the polymerization in the presence of NTO were comparable irrespective of the chosen strategy; PBA samples had low

molecular weights, but sufficiently high polydispersity indices (see Table 3).[50, 51]

Systems based on mixtures of *m*-toluyl and benzoyl peroxides with MNP to be used in homo- and co-polymerization of styrene were patented.[52] The polymerization was carried out in two steps, which included the initial 'pre-reaction' of MNP with the mixture of initiators in styrene at 95 °C for 3.5 h. Subsequent process was carried out at 130 °C up to high degrees of conversion. The MW of polystyrene linearly increased with the monomer conversion. As a result, a polymer with low M_w/M_n ratio was obtained (see Table 3). The one-step polymerization of styrene proceeded in the controlled mode, but the polydispersity index was somewhat higher (1.35 – 1.40).

A one-step version of the synthesis of high-molecular-weight alkoxyamines based on nitroso compounds was considered also in a different study.[100] As in the case of nitrones, the process of polymerization of MMA in the presence of MNP and AIBN was carried out at 50 – 65 °C to afford nitroxide radicals with sufficiently high MW. This approach produced polymeric chains with high MW but with polydispersity indices varying from 1.6 to 2.2 and increasing with the monomer conversion (see Table 3). It was found that the polymerization of MMA in the presence of MNP exhibits the features typical of CRP, namely, the absence of gel-effect, the linear growth of MW and the shift of unimodal MWD with conversion. The relatively high polydispersity is associated with the possibility of side reactions, particularly, a reaction of secondary catalytic inhibition,[89 – 91] which was considered in detail in the previous Section. On the whole by the example of polymerization of MMA, it was shown [100] that the use of MNP led to similar effects as the use of PNB, but the polymer chain regulation could be achieved at lower concentrations of additives (0.01 mol.% – 0.05 mol.%). Probably, this fact can be explained by higher constants of capture of macroradicals by nitroso compounds as compared with nitrones.[29] According to quantum chemical calculations,[74] the C – ON< bond energy of an alkoxyamine derived from MNP and a PMMA radical, was much lower as compared with low-molecular-weight analogues (see Table 2), which in principle allows one to carry out CRP at lower temperature. Similar pattern was observed in the polymerization of other methacrylic monomers (OMA and CMA) in the presence of MNP and BP. Table 3 shows the molecular-weight characteristics of polymers obtained from higher alkyl methacrylates.[38]

The activity of MNP as the precursor of high-molecular-weight nitroxide radicals was studied by the example of synthesis of polystyrene.[40, 101] The quantum chemical analysis of lability of the C – ON< bond in an alkoxyamine formed by a MNP-based high-molecular-weight nitroxide and a propagating PS radical has shown that the energy of this bond is comparable with that in the case of low-molecular-weight alkoxyamines (see Table 2).[74] Hence, the controlled polymerization of styrene may occur at higher temperature (100 °C).

It was found that MNP affects the kinetics of bulk polymerization of styrene. Thus at temperatures relatively low for CRP (60 °C), the introduction of MNP into the polymerization system gave rise to a long induction period (more than 6 h). The polymerization of styrene at 100 °C proceeded at a sufficiently high rate and involved no gel-effect. The addition of MNP affords PS with a constant MW and a low polydispersity index throughout the conversion; the polydispersity index remained unchanged with conversion, being equal to 1.3 – 1.4 (Table 3). However, it should be noted that the proposed scheme does not match the main criteria of 'pseudo-living' radical polymerization, one of the most important conditions, namely, the linear increase in MW with conversion is not fulfilled, which points to the fragmentary chain propagation typical of 'pseudo-living' processes. Thus in the polymerization of styrene under the chosen conditions, MNP acts as an efficient regulator of the kinetic and molecular-weight characteristics rather than a 'pseudo-living' polymerization agent. The independence of the polystyrene MW of conversion was probably caused by the fact that under the chosen conditions, throughout the process, the termination of two propagating radicals on a 'spin trap' was observed, which ruled out further involvement of the products in the chain propagation step.

By the example of a monomeric pair St – AN, the effect of MNP on the mechanism of radical co-polymerization was studied.[102] It should be noted that co-polymers of styrene with AN are among the most important large-scale polymeric products and find much wider application as compared with their homopolymers. This system is characterized by linear growth in M_n of co-polymers with conversion and a pronounced shift of MWD to the high-molecular-weight range, the MWD being sufficiently wide (see Table 3). Moreover, the MWD of co-polymers with low degrees of conversion clearly demonstrated a diffuse low-molecular-weight 'shoulder' corresponding to the oligomeric fraction. Contribution of the latter to MWD decreased with conversion and disappeared at the maximum conversion.

'Pseudo-living' polymerization of styrene was carried out [36] in the presence of MNP under conditions slightly different from those reported:[40, 101] the process was carried out at 120 °C and at lower concentrations of BP and MNP. It was shown that the steady-state mode in a wide conversion range was realized only for MNP : BP ≈ (0.6 – 0.8) : 1; for the larger content of MNP (MNP : BP = 1 : 1), this reaction had a long induction period. Varying the MNP : BP ratio also affected the molecular-weight characteristics of alkoxyamines. In the deficiency of MNP, the primary adduct included ~300 monomeric units; correspondingly, a macromolecular nitroxide would contain ~150 units. The increase in the MNP concentration to its equimolar ratio with BP reduced the number of styrene units in the alkoxyamine to just a few. Such structures are typical of low-molecular-weight analogues. Polymerization of styrene under conditions where high-molecular-weight nitroxides are formed afforded, PS with the polydispersity index varying from 1.4 to 2.9 at the maximum conversion as a function of the BP : MNP ratio (see Table 3). It was shown that the constant of the 'pseudo-living' equilibrium in the polymerization of styrene involving the MNP-based macromolecular nitroxides was 1.4×10^{-10} mol litre^{-1}, *i.e.*, three times smaller than in the case of PBN.[36]

The 'pseudo-living' nature of polymerization of styrene in the presence of MNP was proved by the possibility of its re-initiation at 105 °C and block co-polymerization of PS with MA, *tert*-butyl acrylate (tBA), acrylamide, *N*-isopropylacrylamide, VA, VP.[36] The mechanism of this process and the nature of the co-polymer depended on the nature of the second monomer. The homo-polymerization of MA and tBA in the presence of MNP could not be carried out in the

controlled mode under these conditions. It was noted that at the equimolar MNP : initiator ratio, the process proceeded with uncontrolled acceleration, while with the excess of the 'trap', the polymerization ceased even at low conversion. For MA, the block co-polymerization proceeded to high degrees of conversion, with the polydispersity index of PS – PMA (for conversion of 85% – 87%) equal to 2.2 – 2.4.[36] The most important parameters of a 'pseudo-living' process (equilibrium constants, rates constants for re-initiation and reversible termination) that involved the propagating polymethacrylate radicals and the MNP-based PS-macronitroxide radicals were determined,[36, 113] which suggests the efficient block co-polymerization involving PS-macronitroxides and MA.

Studying the polymerization of VC initiated by dicetyl peroxydicarbonate (DPC) (0.1 mol.%) and MNP (up to 0.1 mol.%) at 50 °C has shown[45] that, in contrast to PBN capable of sufficiently effective control other chain propagation in the synthesis of PVC, no catalytic chain propagation was observed in the presence of catalytic amounts of this nitroso compound. Thus MNP acted as an ordinary inhibitor of polymerization of VC, demonstrating, first of all, an induction period followed by the kinetic process that obeyed the same mechanism as the polymerization of VC in the absence of additive up to high degrees of conversion, with the polymer MW remaining constant throughout the process.

Virtually at the same time, French scientists studied the radical polymerization of styrene in the presence of NTO at 90 and 110 °C by a one-step version of *in situ* polymerization.[109] The presence of a high-molecular-weight fragment in the nitroxide was confirmed by EPR measurements. Based on kinetic data and EPR spectra, it was shown that the polymerization occurs in the controlled mode up to conversions of 50% (see Table 3). Regretfully, no data were shown on the polydispersity of the synthesized PS.[109]

In certain studies, a comparative analysis of the efficiency of different aliphatic and aromatic nitroso compounds (NB,[103 – 105] ND,[40, 104, 106] TBNB[104]) in radical polymerization was carried out.

By the example of MMA,[103, 104, 106] it was shown that polymerization in the presence of NB, ND and TBNB with AIBN as the radical initiator at 70 °C had features of a controlled process, namely, the linear increase in MW with conversion, the suppression of gel-effect, *etc*. However, the polydispersity indices of samples synthesized in the presence of aromatic nitroso compounds were sufficiently high (~2). Studies of polymerization of styrene[40, 105, 106] in the presence of nitroso compounds (NB and ND) have revealed analogous regularities (see Table 3).

The effect of aromatic nitroso compounds on the processes of co-polymerization of styrene with different acrylic monomers (MMA, BA and AN) in the azeotropic ratios was studied.[57, 106, 107] It was shown that ND affects the kinetic features and molecular-weight characteristics of the co-polymers. Although the polydispersity indices somewhat increased with conversion (see Table 3), they remained substantially lower than for co-polymers synthesized with the use of AIBN without ND (2.6 – 3.9).

The relative activity of the monomer pair St – MMA was assessed by IR and UV spectroscopy and the composition of random co-polymers of styrene with MMA and BA synthesized in the presence of ND was studied. The numerical values of co-polymerization constants of the St – MMA pair in the presence of ND were found to virtually ideally coincide with the constants of conventional radical co-polymerization of styrene with MMA. It was shown that for the molar ratios St : MMA = 53 : 47 and St : BA = 77 : 23 the co-polymer composition approached that of the original mixture throughout the monomer conversion range.[107] With the addition of ND into the polymerization system, the azeotropic conditions were retained up to high degrees of conversion of co-monomers. Block co-polymers PS – PMMA and PS – PBA were synthesized using PS macroinitiators prepared in the presence of ND at 70 °C.[57]

Aromatic nitroso compounds, particularly, ND (in contrast to PBN and MNP) can be employed for the regulation of the kinetic parameters of polymerization of VA and the MW of the synthesized PVA.[108] The synthesis of PVA in the presence of ND at 90 – 100 °C was characterized by the constant rate throughout the interval of monomer-to-polymer conversion and also by the linear increase in the polymer M_n with conversion. However, the polydispersity indices of polymers increased with conversion, though they remained much lower than those of the polymers synthesized in the absence of ND (M_w/M_n = 6.2). The presence of 'living' chains in the synthesized PVA was confirmed by post-polymerization of the monomer.

It should be noted that, except for few examples (St + MNP), the polydispersity indices of polymers synthesized in the presence of high-molecular-weight nitroxides generated *in situ* from nitroso compounds were relatively high, which was attributed to deviation of the polymerization process from the ideal CRP conditions. This was associated with several factors.

— A substantial contribution of the conventional (uncontrolled) radical polymerization that leads to the formation of a 'dead' polymer and, as a consequence, the broadening of MWD and the increase in the polydispersity index.

— The majority of nitroso compounds in the solid state exist as dimers.[29] For polymerization in the presence of aromatic nitroso compounds, the time of attainment of the equilibrium concentration of a nitroso compound plays a very important role: slow dissociation will preclude suppression of the active monomer molecules. As a result, the monomeric form of the nitroso compound that captures the propagating radicals will virtually extinguish, which should have a substantial effect on the kinetics of polymerization and the molecular-weight characteristics of the synthesized polymers.

— In addition to the 'pseudo-living' mechanism, other processes can be involved in the polymerization in the presence of nitroso compounds, which results in the removal of the nitroxide radical from the reaction. Thus a hydrogen atom can be abstracted by the nitroxide radical from either MMA or (for ND) the methyl groups linked to the aromatic ring. As a result, hydroxylamine is formed, which further affects the chain propagation by the mechanism of secondary catalytic inhibition.[89 – 91] This process demonstrates many features typical of 'pseudo-living' polymerization.

— For nitroxides with unsubstituted aromatic rings, side processes involving the benzene ring can occur. The high degree of the unpaired electron delocalization in the aromatic system is assumed to be the reason for the relative instability of diaryl- and arylalkylnitroxides. The introduction of substituents into the benzene ring stabilizes the radical due to the violation of co-planarity and the appropriate decrease in the spin density of the aromatic system.[114]

Thus for polymerization of MMA and styrene in the presence of NB (see Table 3), in contrast to other nitroso compounds, the polydipersity index was observed to increase with conversion, which indirectly confirms the possibility of side reactions involving the benzene ring.

It is quite obvious that the efficiency of high-molecular-weight radicals based on nitroso compounds in the CRP is determined by the degree of unpaired electron delocalization along the substituent bonds (thermodynamic factor) and the steric hindrance (kinetic factor), which blocks the main reaction centre, thus reducing the radical reactivity. Possibly, side reactions can involve the structures of the nitroxide radical centres.

Thus, some studies in Russia and abroad demonstrated the possibility of using nitroso compounds as sources of stable nitroxide radicals, the chain propagation regulators. However, it should be noted that the efficiency of nitroso compounds in CRP processes is somewhat lower than of nitrones. Particularly, in certain cases, the rate of polymerization in the presence of alkoxyamines formed from nitroso compounds was lower than that in the presence of nitrones, whereas the polydispersity indices of polymers synthesized in the presence of alkoxyamines formed from nitroso compounds were relatively high and increased in the course of macromolecular synthesis. This fact was due to the substantial contribution of side processes discussed above. Moreover, nitroso compounds rank below nitrones as regards the thermal and photo-stability, which is a substantial limitation for their industrial use. However, this class of compounds were actively used in the synthesis of various alkoxyamines. For example, 2,2-dimethyl-3-(1-phenylethoxy)-4-phenyl-3-azapentane was synthesized from MNP.[115] This alkoxyamine was obtained by the addition of the 1-phenylethyl radical formed from 1-bromoethylbenzene in the presence of the $CuBr-Cu^0$–pentamethyldiethylenetriamine catalytic system to MNP. The efficiency of the isolated alkoxyamine was tested in the polymerization of styrene, isoprene and BA.[115,116] Based on this alkoxyamine, low-molecular-weight polymers with low polydispersity indices (1.14 for PS; 1.28 for polyisoprene; 1.39 for PBA) were obtained, which is comparable with the best results of CRP conducted in the presence of TEMPO and its low-molecular-weight analogues.

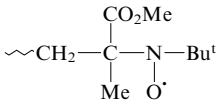
3. Redox-type binary iniferters based on *N*-hydroxytriazenes

In the 1970s it was shown[117] that in the presence of inorganic oxidants, *e.g.*, lead or silver oxides, phenylhydroxytriazenes decompose to aryl radicals, molecular nitrogen and nitroso compounds [see reaction (6)]. These results served the basis for studies on the search for a new type of initiators-regulators.

For example, novel binary initiators-regulators of the polymeric chain propagation were proposed[40,45,103,105,110–112] based on hydroxytriazenes [1-*tert*-butyl-3-phenyl- (BPT) and 1,3-diphenyl-1-hydroxytriazene (DPT)] and oxidants (metal oxides, organic peroxides, *etc.*).



By the example of MMA, it was found[110] that the introduction of a pair BPT + oxidant (PbO_2 or Ag_2O, BP, DPC) into the monomer results in the appearance, in the EPR spectra, of a triplet with the splitting constant on the nitrogen atom a_N = 15.2 G, which belonged to the nitroxide spin adduct formed by a poly(methyl methacrylate) radical with MNP by reaction (6).



When inorganic oxides were used as oxidants, the reaction proceeded at relatively low temperature (50 °C); however, the rate of the process and the maximum conversion of MMA were low. The ineffectiveness of such compositions was associated with the heterogeneous nature of systems due to the limited solubility of metal oxides in the monomer.[110]

At the same time, systems based of hydroxytriazene and diacyl peroxides (or peroxy esters) exhibit high efficiency. These compositions can simultaneously initiate polymerization of vinyl monomers and generate nitroxide radicals in the system. In the presence of organic peroxides, the polymerization proceeds up to high conversions.[40,45,103,105,110–112]

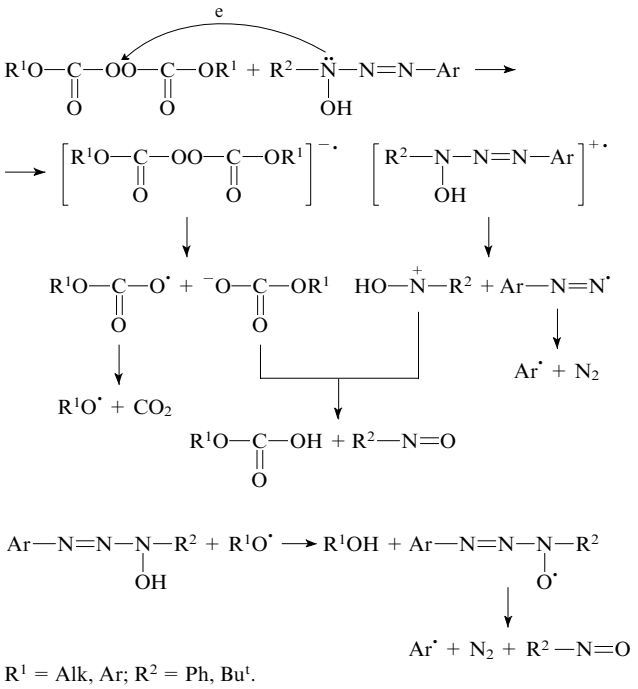
The regularites of the polymerization in the presence of compositions based on BPT and DPT were studied in the temperature range of 50–100 °C.[40,45,103,105,110–112] Studies of radical polymerization of MMA,[110–112] BA,[111,112] BMA[111,112] and styrene[40,111] in the presence of BPT and of MMA[103,112] and styrene[105] in the presence of DPT have shown that, depending on the structures of the hydroxytriazene and the monomer and the hydroxytriazene : initiator-oxidant ratios, the control over molecular-weight characteristics and kinetic parameters of polymerization was observed in different temperature intervals. At the same time, all analyzed systems demonstrated the general features, namely, the gel-effect degeneration with an increase in the hydroxytriazene concentration, the linear MW *vs.* conversion dependence, the relatively low polydispersity (see Table 3).

In the case of methacrylic monomers that form tertiary carbon-centred radicals in the propagation step, the introduction of hydroxytriazenes allows the control over the kinetics and molecular-weight characteristics in the temperature interval of 50–65 °C at the comparable amounts of hydroxytriazene and the oxidant. Moreover, the initial polymerization rate changed insignificantly as compared with the process without additives. Polymerization of BA and styrene that form secondary radicals in the chain propagation step proceeded in a somewhat different manner, namely, the considerable reduction of the gel-effect and the control over the molecular-weight characteristics (see Table 3) were observed at higher hydroxytriazene concentrations (as compared with MMA and BMA polymers).[40,103,105,110–112] At the same time, in the case of BA, the initial rate substantially decreased with the increase in the BPT content; moreover, in contrast to common radicals, the polymerization of BA in the presence of hydroxytriazene was characterized by an induction period that increased with the additive concentration.[111,112]

In the DPC-initiated polymerization of VC, BPT acted as a conventional radical inhibitor:[45] the initial induction period is followed by slow acceleration of the reaction up to 30% conversion. Kinetics of subsequent reaction was similar to that in the absence of the additive up to high conversion. These regularities are similar to those observed

for the polymerization of VC in the presence of MNP, described in Section III.2. However, the addition of BPT decreased the induction period from 4 to 1 h, because the formation of MNP in this process (Scheme 1) is accompanied by liberation of active radicals that are involved in the initiation stage. The molecular weight of PVC was constant irrespective of conversion, which is typical of common radical polymerization of VC.[59]

Scheme 1



R^1 = Alk, Ar; R^2 = Ph, Bu^t.

When comparing the regularities of polymerization of vinyl monomers in the presence of DPT[103, 105, 112] and BPT,[40, 45, 110–112] mention should be made that, despite good correlation between the results for these two hydroxytriazenes, from the standpoint of practice, the latter is a more efficient regulator of chain propagation. Thus MNP and NB formed in the decomposition of BPT and DPN, respectively, and acting as radical propagation mediators are characterized by different constants of scavenging with respect to active radicals and form nitroxide radicals with somewhat different stabilities, which has a direct effect on the polymerization process. It cannot be ruled out that the processes of photo- and thermal decomposition of nitroso compounds under the polymerization conditions make a certain contribution.[29] Thus the synthesis of PMMA in the presence of DPT was characterized by an unusual temperature effect. It was shown[103] that in the polymerization of MMA at 50 °C, the gel-effect was suppressed for the DPT concentration of 0.2 mol.%; however, when the temperature was increased to 70 °C, degeneration of the gel-effect was not complete at this concentration. The disturbance of the chain propagation control in the presence of DPT as the temperature increased to 70 °C was also reflected in the dependence of MW on conversion, namely, the polymer MW increased with conversion stepwise, as in common radical processes. This fact points to the thermal decomposition of NB formed upon oxidation of DPT and to its removal from the controlled chain propagation step. It deserves mention that the polymerization of MMA in the presence of DPT at 50 °C afforded PMMA with a constant MW regardless the conversion, which may point to the inhibiting role of DPT.[103]

By and large, the kinetic features of polymerization of vinyl monomers in the presence of hydroxytriazenes and the analysis of molecular-weight characteristics of synthesized polymers pointed to the direct involvement of these additives in the elementary steps of this process, including the chain initiation, propagation and transfer.

In the first step, hydroxytriazene is oxidized with a peroxide by a reaction of single-electron transfer (see Scheme 1). The subsequent decomposition of the radical ions formed afforded radicals that initiate polymerization in the system. In parallel with the mentioned process, active radicals are also formed as a result of thermal decomposition of the initiator. Moreover, the secondary reactions that involve alkyl and alkoxyl radicals and hydroxytriazenes and lead to decomposition of the latter to nitroso compounds cannot be ruled out (see Scheme 1). As was noted above, the short-lived carbon- and oxygen-centred radicals can later initiate polymerization by reacting with the monomer. The resulting nitroso compound that represents a 'spin trap' reacts with the radical centres present in the system to generate stable nitroxide spin adducts that act as chain propagation regulators [see reactions (4) and (5)].

Thus, hydroxytriazenes in combination with organic peroxides can be considered as novel binary iniferters (initiators-regulators of radical polymerization) that allow generation of stable radicals *in situ*, thus controlling the kinetic parameters and the molecular-weight characteristics of the product.

One of advantages of systems based on hydroxytriazenes is that their decomposition proceeds under mild conditions. This favourably distinguishes these systems among the other known iniferters that efficiently operate only at 90–140 °C.[6, 8, 10, 13, 14] A sufficiently high rate of polymer synthesis is observed throughout the process. The possibility of using different hydroxytriazenes allows one to control the chain propagation in polymerization of different monomers and, correspondingly, modify the properties of polymeric materials by using such procedures as random and block co-polymerization.

4. Nitro compounds as the sources of nitroxide radicals

It is well known that nitro compounds are widely used in inhibition of polymerization and, in certain cases, as chain propagation regulators in the synthesis of high-molecular-weight compounds.[118] Depending on their structure, nitro compounds may act as both strong and weak inhibitors.[119] In addition, stable radicals formed during the radical polymerization in the presence of nitro compounds can be involved in the CRP mechanism. The reactions of nitro compounds with active radicals [reactions (7) and (8)] have been studied since the 1950s.[119–122]

The starting nitro compound is reduced in the reaction medium to nitroso compounds [see reactions (7), (8)], their subsequent reduction to a nitroxide radical makes it possible to infer the feasibility of CRP. It should be noted that this route of the nitro compound reduction to a nitroxide radical is accompanied by several side reactions and affords numerous species that can react themselves with active propagating radicals.

The possibility of the *in situ* reduction of aliphatic and aromatic nitro compounds to high-molecular-weight nitroxide radicals and their effect on the polymerization of styrene were studied.[101] Thus it was shown that the introduction of Bu^{t}NO$_2$ into the St + 1.0% BP (initiator) system at 100 °C and the gradual increase in the nitro compound concentration to 8 mol.% results in a gradual decrease in

the polymerization rate in the self-acceleration step. At the same time, the addition of Bu^tNO_2 did not have any substantial effect on the polymer molecular-weight characteristics. The dependence of MW of PS samples synthesized in the presence of different concentrations of a nitro compound had the same pattern as for usual initiation. Particularly, the introduction Bu^tNO_2 into the system does not result in the linear increase in MW with conversion, which is typical of controlled radical polymerization, and, hence, precludes the preparation of polymers with the preset MW. Nonetheless, the polydispersity indices of polymers synthesized in the presence of the Bu^tNO_2 + BP system were somewhat lower (1.7–1.8 for high conversion) as compared with those of polymers synthesized in the absence of nitro compounds. The described features of the polymerization are typical of processes that occur in the presence of weak inhibitors.

The use of *p*-nitroaniline (NA) containing both amino and nitro groups as the regulator did not exert any substantial effect on the initial polymerization rate, while its additions decreased the limiting degree of styrene conversion.[57] Apparently, this is associated with the reactions of NA with BP and active propagating radicals to yield nonradical products; thus, the initiating and propagating radicals are eliminated from the polymerization process. It should be noted that NA, like Bu^tNO_2, did not have any substantial effect on the molecular-weight characteristics of polymers. In particular, the dependence of polystyrene MW on conversion is S-shaped, which is typical of common radical polymerization.

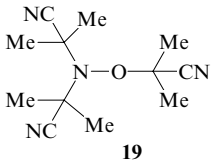
Thus, as follows from the analysis of data shown in certain publications[57, 101], the method of synthesizing the chain propagation regulators in one step directly in the medium of the monomer from different 'spin traps' proved to be virtually inefficient in the case of nitro compounds. This is associated with numerous side processes involving nitro compounds and the fact that different radicals are formed in the course of the synthesis of macromolecules.

Using the EPR method, the structures of stable radicals formed in the autopolymerization of styrene in an inert solvent in the presence of nitrophenols, nitroanisoles and nitronaphthols was studied.[123, 124] It was shown that the ratio and the concentration of nitroxide radicals and also of alkoxynitroxide, iminoxyl and phenoxyl radicals depend on several factors. First, this is the structure of a nitro compound, because the radical structure is directly associated with the possible side processes involving the nitro compound (such as disproportionation and oxidation) and, second, it is conditions of the experiment and the time factor.

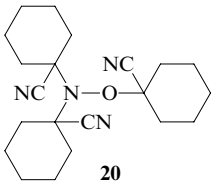
Presumably,[123, 124] these additives can be involved in CRP processes. It was assumed that their efficiency should depend on the fulfilment of several 'necessary' requirements namely, the stability of nitro compounds under experimental conditions, the persistence of apparent and equilibrium concentrations of free radicals during the polymerization, the absence of side reactions, *etc*. So far, no reliable evidence for the efficacy of the use of such systems in CRP has been presented.

5. Nitrogen oxides and nitrites in the synthesis of polymers

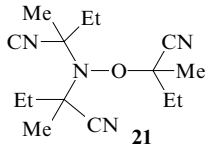
In 1998, a new method of synthesis of different low-molecular-weight alkoxyamines (compounds **19**, **20**, **21**) by the reaction of gaseous nitrogen(II) oxide with active radicals formed in the decomposition of conventional radical initiators was proposed.[99]



19



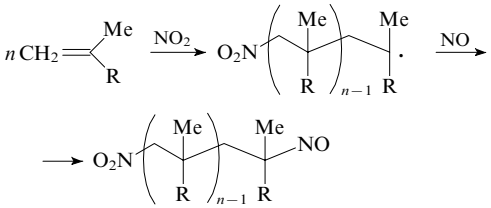
20



21

The efficiency of synthesized alkoxyamines as the CRP regulators was tested with different monomers (styrene, MMA, BA and isoprene). In the presence of camphorsulfonic acid, these alkoxyamines were very efficient chain propagation regulators at 120–140 °C. The polymerization proceeded at a high rate to reach high degrees of conversion in less than 6 h. However, the polydispersity of most polymers was 1.5–3.3; for PBA, the polydispersity index was even higher (2.4–8.6). Virtually simultaneously with the above-mentioned study, an identical method of synthesis of alkoxyamine initiators **19** and **20** was patented[125] and their use in polymerization of different monomers was described. However, an example is given only for BA and alkoxyamine **20**. The polymerization proceeded at a high rate at 140–145 °C (to 96% in ~35 min), the polydispersity index of the synthesized polymer was 2.4.

Later, it was proposed to use a mixture of NO and NO_2 for the synthesis of α-nitroso-ω-nitro adducts to be applied as the regulators of polymerization of alkyl methacrylates.[126, 127] This method is based on different reactivities of nitrogen oxides in different oxidation states with respect to the alkene double bond. Nitrogen monoxide and dioxide are paramagnetic species capable of capturing the propagating chains to form nitroso and nitro compounds, respectively. As was mentioned in Section III.4, nitro compounds can later transform into nitroso compounds in the reaction with an excess radical. It should be noted that although nitrogen(II) oxide is a paramagnetic species, this, unlike NO_2, does not add to alkenes containing electron-withdrawing or donating substituents to form β-nitrosoalkyl radicals. Nitrogen dioxide does add to the less sterically hindered carbon atom of a double bond to form β-nitroalkyl radicals. Hence, passage of a mixture of NO and NO_2 through a monomer (MMA or BMA) at room temperature affords a polymeric α-nitroso-ω-nitro-adduct.



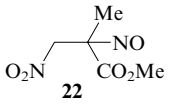
α-Nitroso-ω-nitro-adduct

R = CO_2Bu^t, CO_2Me.

The thus formed polymeric adducts (α-nitroso-ω-nitro-PMMA and α-nitroso-ω-nitro-PBMA) were used as regulators of the AIBN-induced polymerization under temper-

ature conditions close to those used in industry (60 °C).[126,127] These compounds affected the kinetics of polymerization of alkyl methacrylate; the polydispersity indices of samples noticeably increased in the course of the process, namely, from 1.15 in the initial steps of conversion to 1.8–1.95 for the conversion of ~90%. In addition, random polymerization of MMA and 2-hydroxyethyl methacrylate was carried out based on the primary adduct (α-nitroso-ω-nitro-PMMA).[127]

Similar regulating ability was demonstrated[127,128] for low-molecular-weight α-nitroso-ω-nitro-adduct **22**.



22

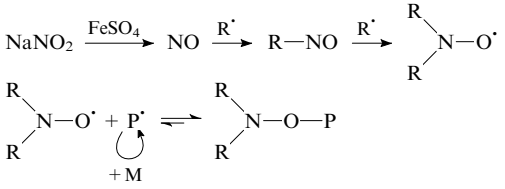
Compound **22** was synthesized by the reaction of MMA with the $NO + NO_2$ mixture formed *in situ* in the sodium nitrite–sulfuric acid system. The purified compound **22** was tested in polymerization of MMA and BMA at 60 °C in the presence of AIBN. The regularities for the controlled process were comparable with those for polymerization involving the polymeric adduct: the polydispersity gradually increased to 1.95.[127,128] The possibility of chain re-initiation in the presence of compound **22** was illustrated by successful synthesis of a PMMA–PBMA block co-polymer with relatively low polydispersity index (1.4).[128] Presumably,[126–128] the complicated nature of proposed systems was first of all associated with the formation of both low- and high-molecular-weight α-nitroso-ω-nitro compounds. Correspondingly, with the introduction of these adducts, various alkoxyamines and nitroxide radicals that are involved in CRP are formed in the system.

Yet another approach to the *in situ* formation of nitroxide radicals consists of using sodium nitrite, a widely known polymerization inhibitor of water-soluble monomers at room temperature. The first mention of the use of $NaNO_2$ as the regulator in the polymerization of sodium methacrylate was made in 1998.[129] The process was carried out in water at 90 °C in the presence of ammonium peroxydisulfate (AP) as the initiator. $NaNO_2$ exerted weak inhibitory effect on the polymerization rate. M_n slightly increased with time; however, the polydispersity indices of synthesized polymers were extremely high ($M_w/M_n > 6.5$). It was assumed that sodium nitrite reversibly decomposes in an aqueous medium.

$$2\,NaNO_2 + H_2O \rightleftharpoons NO + NO_2 + 2\,NaOH.$$

The evolved nitrogen oxides served as the sources of nitroxide radicals that act as the CRP regulators. However, no data on the structures of these nitroxide radicals were presented.

Later, radical polymerization of BMA in an aqueous medium at 80 °C (initiator: AIBN or $K_2S_2O_8$) in the presence of the $NaNO_2–FeSO_4$ system was studied.[126,128,130] The molecular weight of PBMA increased linearly with conversion; however, as with nitrogen oxides, the initially low polydispersity ($M_w/M_n = 1.1–1.2$) increased to 1.9–2.4 at the end of polymerization. The involvement of parallel processes, *i.e.*, the violation of the CRP ideal mode, was inferred based on the deviation from the linear dependence of the logarithm of the reduced monomer concentration. The MW of the polymer directly depended on the amount of $NaNO_2$ rather than of $FeSO_4$. However, the addition of even small amount of $FeSO_4$ substantially improved the main parameters of CRP. The following four-step mechanism of polymerization involving the $NaNO_2–FeSO_4$ system was assumed. In the first step, $NaNO_2$ was reduced with iron(II) sulfate to produce NO. In the second step, NO reacted with the propagating or initiating radicals to form nitroso compounds (RNO). Next, the nitroso compound was transformed into low- and/or high-molecular-weight nitroxide radicals ($R_2NO^{\bullet}$). In the last step, the latter radicals were directly involved in the reversible inhibition of propagating radicals ($P^{\bullet}$).



The simultaneous formation of NO and NO_2 in the reduction of $NaNO_2$ with iron(II) sulfate was stressed.[128,130] It was shown that this system gives rise to alkoxyamines differing in structures, reactivities and stabilities (low- and high-molecular-weight and alkoxyamines based on α-nitroso-ω-nitro-PBMA formed from the NO and NO_2 mixture). The exact concentration of alkoxyamines is difficult to assess, because their yield and the efficiency of initiation depend strongly on several factors, such as reactant concentrations, solvent, temperature, reactor free volume, *etc*.[126,128,130] Contamination of polymers with iron is a serious drawback of the $NaNO_2–FeSO_4$ system. In connection with this, the search for non-metal activators of $NaNO_2$ decomposition was undertaken; ascorbic,[131] acetic, formic, hydrochloric and sulfuric acids[17] were successfully used.

Another method of the *in situ* formation of NO and the corresponding alkoxyamines from an organic precursor was patented.[126] Bu^tONO was chosen as the precursor. Complex systems containing Bu^tONO, $HSCH_2CH_2OH$ and $K_2S_2O_8$, which served as the initiator, could exert a partial control over polymerization of BMA in water at 80 °C. Polydispersity of PBMA increased in the course of polymerization from 1.2 to 1.7. Nitrogen(II) oxide was formed upon thermal decomposition of an *S*-nitrosothiol, an intermediate of the reaction of Bu^tONO with $HSCH_2CH_2OH$. The main drawback of this kind of systems is the use of malodorous thiols that colour the polymers. Also, no individual mechanisms of the control over the polymerization can be traced in the proposed system. For example, thiols and disulfides formed in the decomposition of *S*-nitrosothiols (thionitrites) could themselves, along with NO, act as the polymerization regulators.

The main advantage of the systems discussed in this Section is the commercial accessibility and the low cost of the required reagents. This approach allows also CRP of alkyl methacrylates under relatively mild temperature conditions, which, undeniably, is yet another advantage of these systems over the classical low-molecular-weight alkoxyamines used in CRP. However, in addition to apparent advantages, these systems possess several serious drawbacks that shift the polymerization parameters such as

polydispersity index and polymerization rate away from the ideal conditions of 'pseudo-living' processes. These include the heterogeneous nature of the system, the contamination of polymers with iron if iron(II) sulfate is used, multistep mechanism of polymerization leading to the formation of alkoxyamines different in the structure and reactivity. Special attention should be paid to the problem of toxicity and corrosivity of NO and NO_2. Therefore, it is the *in situ* formation of this mixture upon decomposition of $NaNO_2$ that presents a promising alternative.

IV. Nitrogen-containing compounds as the precursors of low-molecular-weight stable nitroxide radicals, chain propagation regulators

The survey of the main methods for the *in situ* formation of nitroxide radicals and alkoxyamines presented in Section III suggests that commercial accessibility of regulators is among the most important factors determining the prospects of the application of CRP on the industrial scale. Therefore, the search for accessible and relatively cheap polymer chain propagation regulators is a challenge of modern polymer chemistry. In this Section, possible alternative routes to solve this problem are analyzed.

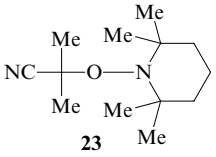
1. The use of binary systems 'sterically hindered amine – oxidant'

One of the most accessible and experimentally simple methods of synthesis of nitroxide radicals in high yields is the oxidation of amines.[132] It is well known [132, 133] that, in the presence of oxidants, primary and secondary amines, in contrast to tertiary amines, are oxidized to nitroxide radicals. In this type of reactions, the conventional oxidants are represented by oxides of certain transition metals as well as hydrogen peroxide, peroxy acids and some other oxidants.[132–134] It is this approach to the synthesis of nitroxide radicals and alkoxyamines from secondary amines that has been patented. [135–139]

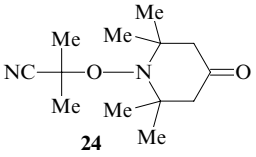
$$\begin{array}{l} RNH_2 \xrightarrow{[O]} [RNHOH] \xrightarrow{[O]} [RN{=}O] \begin{array}{l} \xrightarrow{[O]} RNO_2 \\ \rightarrow [R_2N{-}O^{\bullet}] \end{array} \\ R_2NH \xrightarrow{[O]} R_2N{-}O^{\bullet} \end{array} \qquad (15)$$

Thus it was proposed to use 2,2,6,6-tetramethylpiperidine (TEMP) as the precursor of nitroxide radicals.[135] TEMP was initially oxidized with *m*-chloroperoxybenzoic acid at room temperature for 5 h to TEMPO. Then, a mixture of styrene, TEMPO and BP in a specified proportion was heated to 95 °C for 3.5 h to give an alkoxyamine; no polymer was formed in this stage. Alkoxyamines were not isolated; instead, the mixture was heated at 123 °C for 69 h to produce PS with low polydispersity (Table 4).

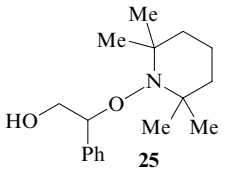
In studies by another research group, a two-step one-pot synthesis of low-molecular-weight alkoxyamines **23**–**26** was developed.[136–139]



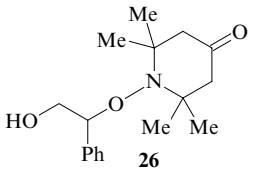
23



24



25



26

In the first step, cyclic amines TEMP and 2,2,6,6-tetramethyl-4-oxopiperidine (TEMOP) were oxidized to the corresponding nitroxides by different oxidants [peracetic acid or oxone ($KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$)]. After removal of the excess of the reactants, alkoxyamines **23** and **24** were prepared by introducing AIBN into the reactor and heating the reaction mixture at 60 °C.[136, 137] Heating of nitroxides with a mixture of styrene, H_2O_2 and $FeSO_4$ afforded compounds **25** and **26**.[138, 139] Polymerization was carried out in the presence of both isolated and purified alkoxyamines and alkoxyamines formed *in situ* without recourse to purification. The syntheses of PS and a St – AN co-polymer were conducted at sufficiently high temperatures (> 100 °C). It was shown that the CRP mechanism was realized in all the cases irrespective of purity of the alkoxyamine. The maximum degrees of monomer conversion were reached in a short period (7–24 h). The MW value increased with conversion while the polydispersity indices remained relatively low (see Table 4). Based on these systems, diblock co-polymers PAN – PBA with MW = 69 000 and polydispersity of ~1.7 were synthesized.[136–139]

Two research groups independently proposed an approach to the *in situ* synthesis of stable nitroxide radicals in a polymerization system based on commercially accessible amines.[101, 140–146]

Thus patents [140, 141] report the use of acyclic amines (TEMP and TEMOP) as the nitroxide radical precursors and organic peroxy acids (peracetic and *m*-chloroperoxybenzoic acids) as oxidants without addition of special initiators of polymerization. Initially, a mixture of monomers, an amine and an oxidant were exposed at room temperature for a certain period, while subsequent polymerization was carried out at a temperature > 100 °C. This approach made it possible to obtain the St – AN and St – BA co-polymers with relatively low polydispersity indices (see Table 4). It was shown that when BP was additionally introduced into the polymerization mixture as the initiator, the polymerization rate substantially increased, but the control over the molecular-weight characteristics loosened ($M_w/M_n \approx 2$).

A different method of the *in situ* generation of nitroxide radicals based on binary systems amine – oxidant was tested.[142–146] In contrast to the procedure described above, the process was carried out in a single step using acyl peroxides, peroxy esters or hydroperoxides as the polymerization initiators and amine oxidants. Different amines, *e.g.*, primary (*tert*-butylamine, TBA) and secondary (di-*tert*-butylamine, DBA), TEMP and TEMOP were studied.

The direct proof of the nitroxide radical formation from the secondary amines and the peroxide initiators in the polymerization systems under study was obtained by EPR. As expected, with AIBN as the initiator, no nitroxide radicals were observed in the polymerization in the presence of amines.[142–145]

By the example of polymerization of MMA in the presence of the DBA – DPC system, the formation of nitro-

Table 4. The main characteristics of polymerization of vinyl monomers in the presence of amines as the precursors of stable nitroxide radicals.

Amine	Conditions of alkoxyamine synthesis [a]	Polymer	Oxidant	T/°C	Ratio initiator : amine	Time/h	Conversion (%)	$10^{-3} M_n$	M_w/M_n	Ref.
TEMP	A	PS	*m*-chloroperoxybenzoic acid	123	see [b]	69	90	~9	1.26	135
	B (**23**)	PS	peracetic acid	125		14	81	41	1.35	136, 137
	B (**23**)	P(St–AN)	peracetic acid	boiling		24	82	54	1.40	136, 137
TEMOP	B (**24**)	PS	peracetic acid	125		14	93	50	1.48	136, 137
TEMP	B (**25**)	PS	$KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$	125		7.5	81	23	1.42	138, 139
		P(St–AN)	$KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$	boiling		9	45	53	1.93	138, 139
TEMOP	B (**26**)	PS	$KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$	125		12	88	34	1.61	138, 139
		P(St–AN)	$KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$	boiling		24	95	56	1.59	138, 139
TEMP	A	P(St–BA)	peracetic acid	70–150		33	65	27	1.40	140, 141
		PS	*m*-chloroperoxybenzoic acid	123		44	85	11	1.44	140, 141
TEMOP	A	P(St–BA)	peracetic acid	110–140		6	48	42	1.97	140, 141
TBA	C	PS	BP	100	1 : 1	–	17	28	1.3	101, 142
		PS	BP	100	1 : 1	2	86	56	1.7	101, 142
		PS	BP	100	1 : 4	–	25	20	1.7	101, 142
		PS	BP	100	1 : 4	5	66	37	3.4	101, 142
		PS	BP	100	1 : 8	–	11	36	1.4	101, 142
		PS	BP	100	1 : 8	10	70	92	2.9	101, 142
DBA	C	PMMA	DPC	65	1 : 1.25	–	13	46	1.6	143
		PMMA	DPC	65	1 : 1.25	~3	77	133	3.5	143
		PS	BP	100	1 : 2	–	10	12	1.4	142
		PS	BP	100	1 : 2	9	68	25	2.2	142
		PS	TBHP	100	1 : 1	–	28	26	1.4	144
		PS	TBHP	100	1 : 1	~4	89	45	2.5	144
TEMP	C	PS	BP	100	1 : 2	–	10	13	1.5	145
		PS	BP	100	1 : 2	14	76	38	1.7	145
		PS	BP	120	1 : 2	5	74	33	2.2	145
		PS	BP	130	1 : 2	3	73	28	2.2	145
		P(St–AN)	BP	100	1 : 2	–	9	31	1.6	145
		P(St–AN)	BP	100	1 : 2	1	80	79	3.9	145
TEMOP	C	PS	BP	100	1 : 2	–	10	10	1.5	145
		PS	BP	100	1 : 2	1.5	82	17	2.3	145
		PS	BP	100	1 : 4	–	4	7	1.7	145
		PS	BP	100	1 : 4	2.3	73	12	2.3	145

[a] A is *in situ* synthesis of alkoxyamine in two steps with preliminary heating at a certain temperature in the medium of the monomer, B is preliminary synthesis of alkoxyamine (compound number is shown in parentheses), C is *in situ* synthesis of alkoxyamine in a single step in the medium of the monomer, where oxidant acts as the initiator. [b] Initiator is BP.

xide radicals under the chosen conditions was demonstrated and their direct involvement in the chain propagation control at 65 °C was proved.[143] It was found that the introduction of DBA into the polymerization system leads to degeneration of the gel-effect and the linear growth of MW with conversion. The best control over the chain propagation in a binary system DBA–DPC was observed with a small excess of DBA with respect to DPC. However, the use of this system was associated with a substantial broadening of MWD and the increase in the polydispersity indices in the course of the process (see Table 4), although for high conversions, the M_w/M_n values were larger for PMMA synthesized in the presence of DPC than in the presence of DBA. This fact suggests that in the polymerization of MMA in the presence of DBA and DPC, only a part of polymeric chains propagated by the mechanism of reversible inhibition. The high polydispersity of PMMA was due to several side processes (chain transfer to amine, reactions of secondary catalytic inhibition most typical of methacrylic monomers, bimolecular termination of propagating chains, homolytic decomposition of peroxides in the presence of amines), as evidenced by the increase in the primary polymerization rate in the presence of DBA.[143]

The analysis of kinetic regularities of polymerization of styrene in the presence of different secondary amines confirmed that DBA and TEMP affected the overall polymerization rate more strongly than TEMOP. In addition, these amines differ in the effect on the molecular-weight characteristics of the products. When DBA or TEMP were introduced into the polymerization system, a linear dependence of MW on conversion was observed, which served as an indication of the controlled radical polymerization mechanism. However, the polydispersity of PS samples synthesized in the presence of TEMP and, the more so, DBA was relatively high and considerably increased with conversion (see Table 4). It is probable that the increase in the polydispersity during the polymerization is associated with the involvement of the amine in several side processes listed above.[142, 145] For the polymerization of styrene in the presence of the TEMOP–BP system,[145] the classical

dependences of the MW and the polydispersity index on conversion, typical of conventional radical initiators, were observed. Under the chosen conditions, TEMPO exerted control on neither the kinetic parameters of polymerization nor the molecular-weight characteristics. It is reasonable to assume that in this case the elimination of the gel-effect was associated with the reaction of chain transfer to TEMPO because the latter has a labile hydrogen atom at the nitrogen atom. Analyzing the processes of PS synthesis in the presence of the most efficient regulators, namely, an aliphatic amine DBA and a cyclic amine TEMP, it can be noted that in the presence of TEMP the polymerization rate to high degrees of conversion was lower than in the presence of DBA. However, from the standpoint of the control over the PS molecular-weight characteristics, TEMP should be preferred (see Table 4).

The effect of temperature on styrene homo-polymerization was studied by the example of the most efficient cyclic amine, TEMP.[145] At 120 and 130 °C, the effect of TEMP on the parameters of styrene polymerization was the same as at 100 °C. As expected, with the increase in the temperature, the overall styrene polymerization rate in the presence of TEMP increased. The absolute values of viscosity-average and number-average MW of polymers depended to the lesser extent on temperature of polymerization; a linear increase in the MW with conversion was also observed. However, the polydispersity of PS samples became more pronounced in the course of polymerization (see Table 4). The increase in the polydispersity index with the elevation of the polymerization temperature became more distinct as evidenced from a substantial contribution of side reactions, which resulted in broadening of the molecular-weight distribution of the polymers.

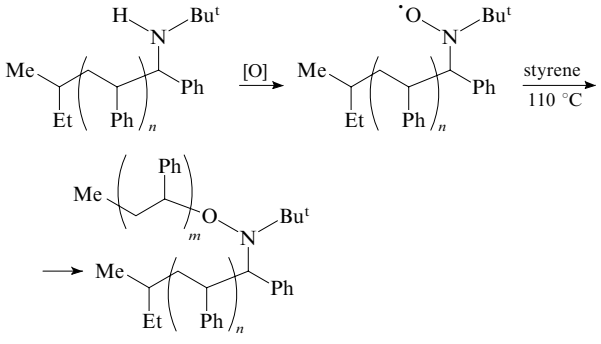
Synthesis of block co-polymers PS–PMMA in the presence of secondary amines DBA and TEMP was undertaken with the aim of proving that, in the presence of binary amine–oxidant systems, the polymer chain propagation is controlled by the 'pseudo-living' mechanism.[142, 145] However, block co-polymers possessed high polydispersity indices, especially those obtained in the presence of DBA.

It was found [145] that TEMP is a weak chain propagation regulator in the co-polymerization of styrene with AN, in contrast to the homo-polymerization of styrene. The effect of this amine on the kinetic regularities of co-polymerization manifested itself at its relatively high concentrations. However, even in this case, its presence in the polymerization system had virtually no effect on the molecular-weight characteristics of co-polymers. The polydispersity indices of samples substantially increased with conversion (see Table 4), which points to the uncontrolled nature of co-polymerization of styrene with AN in the presence of the binary TEMP–BP system.

By the example of styrene and an aliphatic amine (DBA), the efficiency of another oxidation agent, Bu^tOOH (TBHP), was studied.[144] The latter was used as both the oxidant and the polymerization initiator. The addition of DBA increased the initial rate of polymerization of styrene. In the presence of the TBHP–DBA system, no gel-effect was observed. For all the polystyrene samples obtained, the MWD curves were unimodal irrespective of the amine concentration and the monomer conversion. The mechanism of reversible inhibition was the most pronounced at the amine concentration of 1.0 mol.%. Here, the M_n values increased linearly with the conversion. However, being small for low degrees of conversion, the polydispersity indices of samples substantially increased in the course of the process (see Table 4).[144]

As mentioned above, primary amines can also generate nitroxide radicals in one of the oxidation steps [reaction (15)]. The effect of primary amines on the polymerization of styrene in the presence of BP as the oxidant and polymerization initiator was studied by the example of TBA.[101, 142] In contrast to secondary amines, the addition of TBA to the system had a far less positive effect on the kinetic parameters of polymerization and, particularly, on the molecular-weight characteristics of polymers. The most pronounced inhibitory effect of TBA was observed at its concentration of 8.0 mol.%. The effect of TBA on MW, MWD and polydispersity indices of polymers also depended on its concentration. In the presence of 8.0 mol.% of amine, the linear increase in the viscosity-average MW with conversion was observed. However, for lower amine concentrations (2 mol.%), the contribution of the uncontrolled process increased and, as a consequence, the MW *vs.* conversion dependence acquired a break typical of polymerization processes accompanied by the gel-effect. For even smaller amine concentration (1.0 mol.%), the polydispersity index of the synthesized PS was relatively low (see Table 4) at a unimodal MWD. With an increase in amine concentration, the MWD curves considerably broadened starting from 40% conversion and took the bimodal form. The polydispersity indices of samples synthesized in the presence of 2 mol.%–8 mol.% TBA (see Table 4) were relatively large ($M_w/M_n = 2.1$) for high degrees of conversion. The peculiarities of the polymerization of styrene in the presence of the TBA–BP system were probably caused by the considerable contribution of several side processes (chain transfer, amine oxidation to form non-radical products, *etc.*), which led to the higher polydispersity of samples. It cannot be ruled out that the accumulation of Bu^tNO_2 upon oxidation of the amine with benzoyl peroxide [reaction (15)] and its subsequent involvement in the polymerization process took place. The specific features of the polymerization of styrene in the presence of Bu^tNO_2 are considered in Section III.4.

Special attention should be paid to studies [147, 148] that pioneered the method of *in situ* polymerization involving oligomeric and polymeric amines with MW in the range from 650 to 2795.



It was shown that the oligomeric substituent in the secondary amine exerts a substantial effect on the kinetic parameters of polymerization and the molecular-weight characteristics of PS and St–AN and BA–St–AN co-polymers. As is the case of low-molecular-weight amines (TEMP and TEMOP), peracetic acid was employed as the oxidant, no additional inducer of radical polymerization was needed. The oxidation of high-molecular-weight amines was carried out directly in the amine–oxidant–monomer

mixture at room temperature for 0.5–1 h. Further, polymerization of styrene and co-polymerization of St with AN and of BA with St and AN were conducted at elevated temperatures (95–110 °C).

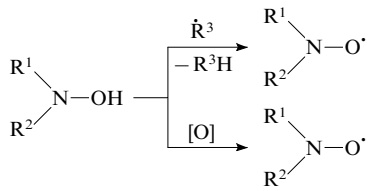
A distinguishing feature of the systems based on oligomeric (polymeric) amines is the high CRP rate as compared with their low-molecular-weight analogues and low-molecular-weight alkoxyamines considered above. It took 9.5 h for the homo-polymerization of styrene at 110 °C to reach high degrees of conversion (80%), whereas the degree of random co-polymerization of styrene with AN reached 90% as soon as in 2.3 h. The polydispersity of the synthesized polymers, even if somewhat increased during the polymerization, remained low, for example, the polydispersity of PS varied from 1.25 to 1.5 with conversion, whereas for the co-polymer BA–St–AN, it varied from 1.56 to 1.75. For St–AN co-polymers, at high degrees of conversion, the ratios M_w/M_n varied from 1.44 to 1.88 depending on the MW of the oligomeric amine.

With the same system, post-polymerization of styrene was carried out at 110 °C using a pre-synthesized macro-initiator with $M_n = 30\,000$ and $M_w/M_n = 1.33$. The post-polymerization proceeded at a high rate (with conversion of 64% in 4 h), and the experimental MW of polystyrene ($M_n = 68\,000$) increased, being in good agreement with the theoretically calculated value. The polydispersity index, even if increased somewhat during the process, nonetheless remained low (~ 1.45).[147, 148]

Low-molecular-weight amines considered in this Section as the precursors of stable nitroxide radicals demonstrated substantial advantages over the low-molecular-weight alkoxyamines as regards their cost and commercial accessibility, which are very important factors for the practical application of this process. However, as a whole, the critical analysis of the polymerization peculiarities in the presence of amine–oxidant systems makes it possible to conclude that although the chosen additives can act as the CRP agents, the substantial contribution of various side processes may lead to an increase in the sample polydispersity in the course of polymerization, being a serious drawback of this system.

2. Hydroxylamines in the controlled synthesis of polymers

Hydroxylamines are among the effective sources of nitroxide radicals. On the one hand, *N*,*N*-disubstituted hydroxylamines can generate nitroxide spin adducts in the reaction with active radicals by the S_R2 mechanism [reaction (16a)]. On the other hand, compounds of this type can easily be oxidized to form stable nitroxide radicals in air or in the reactions with different oxidants [reaction (16b)].



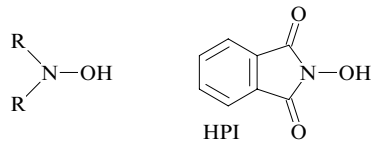
It is of note that since the 1970s hydroxylamines have been widely used as the inhibitors of polymerization of vinyl monomers and as polymer stabilizers.[149–152] Today as well, the interest in them as the emulsion polymerization regulators did not cease. Thus *N*,*N*-dialkyl- and *N*,*N*-diarylhydroxylamines were studied as the inhibitors of radical polymerization.[153]

Japanese scientists patented controlled polymerization of vinyl monomers in the presence of cyclic and aliphatic hydroxylamines using different radical polymerization initiators (organic peroxides and hydroperoxides, azo compounds).[154, 155] As an example, the polymerization of styrene in the presence of *N*,*N*-diethylhydroxylamine (DEHA) and *N*-hydroxyphthalimide (HPI) with BP was described. A 'pre-reaction' at 95 °C for 3.5 h followed by polymerization at 130 °C afforded narrow-distribution PS (Table 5).

Table 5. The main characteristics of polymerization of vinyl monomers as the precursors of stable nitroxide radicals.

Hydroxyl-amine	Conditions of synthesis of alkoxyamines [a]	Polymer	Initiator	T/°C	Ratio initiator : hydroxylamine	Time /h	Conver-sion (%)	$10^{-3} M_n$	M_w/M_n	Ref.
DEHA	A	PS	BP	130	1 : 0.5	2	21	40	1.53	154, 155
		PS	BP	130	1 : 0.5	8	75	78	1.30	154, 155
	B	PS	BP	130	1 : 0.5	1	12	24	2.01	154, 155
		PS	BP	130	1 : 0.5	6	89	77	1.64	154, 155
		PS	BP	95	1 : 0.3	1	31	34	1.52	154, 155
		PS	BP	95	1 : 0.3	3	70	53	1.51	154, 155
HPI	A	PS	BP	130	1 : 0.5	2	10	56	1.82	154, 155
		PS	BP	130	1 : 0.5	8	56	152	1.71	154, 155
DBHA	B	PMMA	DPC	50	1 : 0.15	2	10	137	1.7	156
		PMMA	DPC	50	1 : 0.15	6	85	400	2.9	156
		PS	BP	100	1 : 0.4	0.5	18	6	1.9	156
		PS	BP	100	1 : 0.4	2.5	77	16	1.5	156
		PS	AIBN	70	1 : 0.6	5	13	17	1.5	156
		PS	AIBN	70	1 : 0.6	10	76	27	1.9	156
DOHA	B	PS–PBA [b]	BP	130	1 : 0.5	6	98	139	2.3	86
		PS–PBA	BP	130	1 : 2	6	63	85	1.9	86

[a] A is *in situ* synthesis of alkoxyamine in two steps with preliminary heating at 95 °C in the medium of the monomer, B is *in situ* synthesis of alkoxyamine in a single step in the medium of the monomer; [b] block co-polymer.



HPI

R = Et (DEHA), Bu^t (DBHA), n-$C_{18}H_{37}$ (DOHA).

One-step polymerization [154, 155] at 130°C provided less efficient control over the molecular-weight characteristics, and the PS polydispersity slightly increased (see Table 5). Hence, several competitive processes occurred in this system, namely, the initiation of polymerization by benzoyl peroxide, oxidation of hydroxylamine with peroxides and the abstraction of a hydrogen atom from hydroxylamine by active radicals. It should be noted that the formation of PS could also be observed at 95 °C. This confirms the possibility of analogous processes at lower temperatures. However, a two-step approach proved to be the most effective to produce polymers with narrow MWD. This involved the initial oxidation of hydroxylamine to the nitroxide radical at lower temperature, followed by CRP at higher temperature, which enabled the reversible recombination of propagating radicals and nitroxides. Presumably, in the presence of hydroxylamines, a controlled process took place, although no clear evidence was given to substantiate this mechanism, particularly, no data on the post- and block co-polymerization.

The efficacy of DBHA as the source of nitroxide radicals and chain propagation regulators in the polymerization of MMA and styrene with various oxidants was assessed.[146, 156] It was shown that in the polymerization of MMA at 50 °C in the presence of DPC as the initiator hydroxylamine had a substantial effect on the polymerization rate in the autoacceleration step and substantially eliminated the gel-effect. With the addition of DBHA, the dependence of the polymer MW on the conversion was linear; however, starting from 30% conversion, the polydispersity indices of polymers considerably increased in the course of the process (see Table 5).

Similar results were obtained for the polymerization of styrene at 100 °C in the presence of DBHA and BP as the initiator.[156] The formation of the $Bu^t_2NO^{\bullet}$ (DBN) radical upon oxidation of DBHA with benzoyl peroxide was confirmed by EPR data. The EPR spectrum demonstrated a triplet of this radical with the splitting constant on the nitrogen atom a_N = 15.5 G. It is this radical that played the role of the chain propagation regulator. In contrast to PMMA, polystyrene synthesized under the same conditions was characterized by a smaller polydispersity index, M_w/M_n being decreased with the degree of polymerization (see Table 5).

In addition to oxidation [reaction (16b)], a possible mechanism of the *in situ* formation of stable nitroxide radicals from hydroxylamines involves the abstraction of a hydrogen atom from the OH group [reaction (16a)]. The features of this process were studied by the example of DBHA for the polymerization of styrene at 70 °C in the presence of AIBN.[156] The main regularities typical of CRP were observed, including elimination of the gel-effect and the linear increase in MW with conversion. Although at high degrees of conversion, the polydispersity of polymers synthesized in the presence of DBHA was lower than of polymers synthesized in the presence of AIBN without DBHA (M_w/M_n = 3.2) it increased with conversion unlike that for polymers obtained in the presence of the BP – DNHA system (see Table 5). The observed differences suggest that for the polymerization carried out in the presence of hydroxylamines, peroxides are more efficient oxidants than azo compounds.

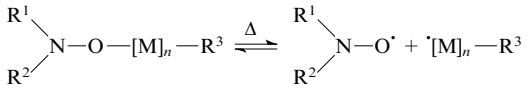
Based on the available data it was suggested that the PBHA-mediated CRP of ethyl methacrylate and styrene is feasible.[156] However, as in the previous studies by Japanese scientists,[154, 155] no direct evidence (*e.g.*, synthesis of post- and block co-polymers) was presented that would unambiguously interpret the polymerization mechanism.

It was also proposed [86] to use hydroxylamines containing long (oligomeric) alkyl chains as the regulators of polymerization. Particularly, *N*,*N*-dioctadecylhydroxylamine (DOHA) was used as the source of stable nitroxide radicals. The synthesis of PS was carried out at 130 °C for 24 h and BP simultaneouly played the roles of initiator and oxidant. However, this patent did not specify other characteristics of the process and the parameters of the synthesized polymers. It was shown that PS synthesized under these conditions acts as the macroinitiator of polymerization of BA. The synthesis of block co-polymers was carried out at the same temperature (130 °C). Table 5 shows the molecular-weight characteristics of polymers.

Hydroxylamines discussed in this Section are very promising precursors of stable nitroxide radicals. Exhibiting the same virtues as amines (commercially accessible compounds or compounds that can easily be synthesized), they have an important advantage, namely, the ability of *in situ* transformation into the nitroxide radicals not only under the action of oxidants, but also in reaction with conventional non-peroxide initiators of radical polymerization, which substantially extends the field of industrial application of these additives.

3. Alkoxyamines as monomolecular chain propagation initiators and regulators

One of the ways of *in situ* generation of the nitroxide radicals is the thermal decomposition of alkoxyamines as described in sufficient detail in several reviews.[6, 8, 10, 13, 157, 158] The C–O bond in alkoxyamine derivatives is thermally unstable and cleaves on heating to form an initiating radical and a nitroxide spin adduct in the stoichiometric ratio 1 : 1.



M is the monomer residue.

An advantage of these systems over those described above and bimolecular compositions based on nitroxides is the unambiguously specified nature and concentration of the initiator. This allows the mathematical apparatus to be invoked to provide a clearer description of kinetic regularities of polymerization and to predict the molecular-weight characteristics of polymers. Alkoxyamines make it possible to reach high degree of control over the polymer structure by suppressing side reactions that increase the polydispersity.

The use of nitroxides as the radical polymerization regulators stems from the pioneering studies on the mechanism of radical initiation and the development of efficient 'traps' for carbon-centred radicals. In the early 1980s, it was shown that at relatively low temperatures (40 – 60 °C) the

nitroxide radicals of the TEMPO type can react with polymeric radicals,[159,160] substantially affecting the polymerization kinetics and molecular-weight characteristics of the polymers. In Russia, analogous studies have been initiated even somewhat earlier. Thus it was proposed[161] to use different nitroxide mono- and biradicals as the initiators of radical polymerization. The inhibitory effect of different nitroxide radicals on the radical polymerization of styrene and (meth)acrylic monomers was studied in the temperature range of 60–80 °C.[162–165] These reactions afforded alkoxyamines sufficiently stable at the temperatures mentioned and not involved in further reactions. The method of polymerization inhibition by the nitroxide radicals was improved,[166] and for the first time the 'living' mechanism of radical polymerization of styrene in the presence of TEMPO at 130 °C was reported.

To date, a wide spectrum of methods of the synthesis of alkoxyamines were proposed that include both specific approaches and traditional procedures of decomposition of radical initiators in the presence of different nitroxides.[10,167] It deserves mention that so far the polymerization involving alkoxyamines represents the best explored direction of CRP. The substantiation of kinetic regularities of these processes and the detailed description of practical applications of 'pseudo-living' radical polymerization to afford block and graft co-polymers, dendrimers and star-like polymers is documented.[6,8,10,13,157,158]

Along with substantial progress in the synthesis of polymers with narrow MWD, several problems may be mentioned. The main problem is the necessity of using high temperatures of polymerization (120–145 °C) and the low rate of the process. Thus polymerization of styrene should be carried out for more than 2 days at 120 °C to reach high conversion. It should be noted that the number of monomers the polymerization of which can be regulated by TEMPO derivatives is very limited and includes homopolymerization of styrene and its analogues and also its random co-polymerization or the synthesis of styrene block co-polymers with some other monomers.

The following approaches allow the increase in the polymerization rate:

— an increase in the concentration of active radicals that initiate the polymerization by introducing high-temperature initiators (*e.g.*, cumene peroxide, TBHP, *etc.*) into the system;

— reduciton of the steady-state concentration of stable radicals by introducing special additives that can react with the radicals (sugars, aldehydes and acetic anhydride proved to be the most efficient in this respect).

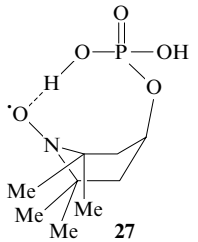
The quest for new chain propagation mediators based on sterically hindered alkoxyamines characterized by higher rate constants for dissociation as compared with TEMPO derivatives is carried out.

The former two approaches discussed in several reviews[8,10,13,158] make it possible to reduce the polymerization time and increase the molecular weight of the polymer. However, as a whole, the potentials of these methods of increasing the CRP rate are very limited, because any interference into the process of re-initiation–propagation–reversible termination inevitably leads to the MWD broadening. Naturally, the incorporation of an additional reaction disturbs the steady state as a result of irreversible removal of the nitroxide from the system and, correspondingly, increases the probability of quadratic termination (*i.e.*, the appearance of additional 'dead' chains and the removal of some propagating chains).

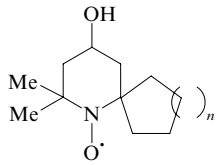
Obviously, the most efficient way to overcome these drawbacks observed in the TEMPO-mediated polymerization is the modification of the structure of the used nitroxide spin adducts as the components of the alkoxyamines. In contrast to the initiating radical involved only in the initial polymerization steps, the regulating radical takes part in many reactions of reversible termination and re-initiation and, hence, the changes in its structure will have a substantial effect on the propagation step and the polymerization process as a whole.

The initial attempts to develop new polymer chain propagation regulators were connected with the use of various TEMPO derivatives.[168–170] Thus the introduction of polymeric[171] or dendrimeric[172] fragments in position 4 of TEMPO, or the use of a nitroxide-containing monomer[173] which would afford macromolecular nitroxide radicals on polymerization made it possible to somewhat reduce the temperature of synthesis of polystyrene (from 140 to 120 °C). It was proposed[98] to use a TEMPO derivative (compound **27**) with a phosphate group in position 4. Intramolecular hydrogen bonds formed in these radicals stabilize them, which weakens the C–ON< bond and accelerates the polymerization of styrene.

However, an approach that consists of the introduction of sterically hindered groups in positions 2 and 6 of piperidine nitroxides proved to be the most efficient. Thus Japanese scientists[174–176] carried out 'low-temperature' polymerization of styrene (70–110 °C) in the presence of sterically hindered TEMPO analogues and the corresponding alkoxyamines. Steric hindrance in TEMPO was achieved by the introduction of bulky substituents, particularly, spiro structures, into α-positions relative to the >N–O· group. Nitroxide radicals **28–33** and the corresponding alkoxyamines were used as the propagation regulators. In the presence of these sterically hindered nitroxide radicals and alkoxyamines, the main regularities of 'pseudo-living' radical polymerization were observed as low as at 70 °C.

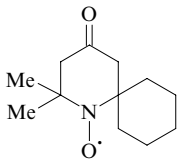


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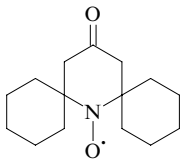


28–30

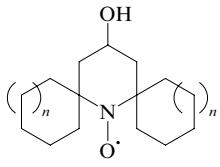
n = 1 (**28**), 2 (**29**), 3 (**30**).



31



32



33, **34**

n = 1 (**33**), 2 (**34**).

Later, polymerization of styrene was studied in the presence of even more sterically hindered nitroxide radical **34** and various alkoxyamines obtained therefrom.[177] The 'pseudo-living' mechanism of polymerization of styrene was observed at 70 °C and the resulting PS possessed low polydispersity (Table 6). As the temperature increased, the

Table 6. The main characteristics of 'pseudo-living' polymerization of different monomers in the presence of nitroxides and alkoxyamines.

Monomer	Nitroxide and(or) alkoxyamine [a]	T/°C	Time/h	Conversion (%)	$10^{-3} M_n$	M_w/M_n	Ref.
Styrene	R-**33**, R = MePhCH	80	400	~70	–	1.22	174
	R-**34**, R = Me($MeCO_2$)CH	70	800	~70	60	1.25	177
	R-**35**, R = MePhCH	105	15	85	10	1.12	178
	R-**36**, R = MePhCH	70	26	56	7	1.16	80
	R-**37**, R = MePhCH	70	6	59	10	1.39	80
	R-**38**, R = MePhCH	123	18	~90	22	1.14	179
	R-**39**, R = MePhCH	90	28	55	10	1.17	180
	MONAMS	90	49	65	13	1.55	180
	MONAMS	120	4	75	14	1.31	180
	BlocBuilder®	90	65	58	11	1.23	180
	BlocBuilder®	120	4	90	25	1.12	180
	R-**40**, R = $BzOCH_2$(Ph)CH	104	7	34	14	1.10	181
	R_2-**41**, R = MePhCH	70	264	65	46	1.18	182
Chloromethylstyrene	TEMPO	130	–	80	24	1.33	183
Methylstyrene	4-MeO-TEMPO	125	171	98	5	1.24	168
4-Vinylpyridine	TEMPO	138	9	56	40	1.38	184
	R-**39**, R = MePhCH	110	1.3	54	61	1.15	185
Isoprene	R-TEMPO, R = MePhCH	145	4	25	21	1.33	186
	R-**38**, R = MePhCH	120	36	~75	20	1.08	187
BA	R-TEMPO, R = MePhCH	145	5	65	46	1.55	186
	R-**38**, R = MePhCH	123	2	90	27	1.44	179
	R-**42a**, R = MePhCH [b]	125	6	41	8	1.20	188
	MONAMS [b]	90	87	64	10	1.26	180
	MONAMS [b]	120	4	65	12	1.36	180
	BlocBuilder®	120	1.5	92	20	1.3	180
	R-**42b**, R = MePhCH [b]	90	72	56	10	1.16	188
	R-**42c**, R = Pr^iPhCH [b]	125	6	49	14	1.18	188
	R-**35**, R = MePhCH	70	96	34	6	2.12	80
	R-**36**, R = MePhCH	70	87	88	11	1.16	80
	R-**37**, R = MePhCH	70	3	82	13	1.38	80
	R-**40**, R = $BzOCH_2$(Ph)CH	124	5	50	7	1.56	181
	R-**43**, R = MePhCH, Me(4-$MeO_2CC_6H_4$)CH	90	–	60	60	1.3	189
tBA	DBN	120	–	30	6	1.42	190
	R_2-**41**, R = MePhCH	70	264	24	22	1.64	182
Ethyl acrylate	R-**43**,R = MePhCH, Me(4-$MeO_2CC_6H_4$)CH	90	–	–	–	1.5	189
AN	R-**38**, R = MePhCH [b]	120	–	–	55	1.13	179
N,*N*-Dimethylacrylamide	R-**38**, R = MePhCH [b]	120	–	–	48	1.21	179
	R-**39**, R = MePhCH	110	33	64	16	1.54	185
	R_2-**41**, R = MePhCH	70	216	69	24	1.47	182
Acrylic acid	MONAMS	120	5	90	9	1.4	191
MMA	TEMPO	120	0.3	15	12	2.4	192
	BlocBuilder® (see [c])	90	1.5	56	24	1.21	193
	BlocBuilder®	45	0.5	9	22	1.39	71
	R-**44**, R = $PhOC(O)CMe_2$, (4-$O_2NC_6H_4$)$OC(O)CMe_2$	100	8	65	17	1.35	55

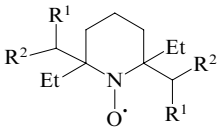
[a] Alkoxyamines are presented as nitroxide derivatives R–O–N< or their designations are given; for the structure of all compounds, see text; [b] in the presence of small amounts of a nitroxide with the analogous structure; [c] polymerization was carried out in the presence of a small amount of styrene (4.4%–8.8%).

equilibrium shifted to the decomposition of either adducts of propagating radicals with the nitroxide or the corresponding alkoxyamines, and hence the contribution of the 'pseudo-living' polymerization mode decreased. Thus polymerization at 120 °C produced PS with the polydispersity index > 1.7 at conversion of 75%. As a whole, according to the studies on the polymerization of styrene in the presence of nitroxides with the spiro structure,[174–177] the latter can be arranged in the following order as regards their efficiency in the low-temperature CRP:

34 > **33** ≈ **30** ≈ **32** > **31** ≈ **29** > **28** > TEMPO.

The low-temperature polymerization of styrene in the presence of 2,6-disubstituted nitroxides of the piperidine series (compounds **35**–**37**) was carried out.[80, 178] The 'living' process of polymerization of styrene in the presence of either nitroxides containing siloxyalkyl groups and or derived alkoxyamines was observed in the temperature

range of 70–105 °C to afford PS with narrow MWD (see Table 6). It was shown that the introduction of these sterically hindered groups into the nitroxide fragments of alkoxyamines is largely manifested in the reduction of the rate constant for recombination of the stable nitroxide with the propagating macroradical rather than in the decrease in the rate constant for dissociation of the corresponding alkoxyamines.

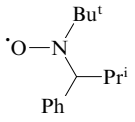


35–37

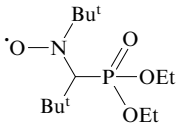
$R^1 = OSiBu^n_3$, $R^2 = H$ (**35**); $R^1 = OSiMe_3$: $R^2 = Me$ (**36**), Pr^i (**37**).

A more efficient approach to the controlled synthesis of macromolecules might be the use of new nitroxides and alkoxyamines that lack any structural similarity with TEMPO. Thus the use of DBN and the corresponding alkoxyamines enables the controlled synthesis of polymers at 90–100 °C.[194]

The most spectacular breakthrough in this direction was the use of aliphatic nitroxides **38** and **39** (SG1). An essential feature of nitroxides **38** and **39** is the presence of a hydrogen atom at one of α-carbon atoms, which is absent in TEMPO and all nitroxides considered above. Examples of such new polymer chain propagation regulators are documented.[72, 179, 195–197] Thus the use of radicals **38** and **39** increased the polymerization efficiency considerably and extended the series of monomers capable of polymerization by the SFRP mechanism (see Table 6).

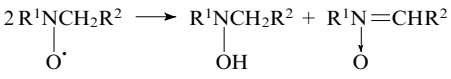


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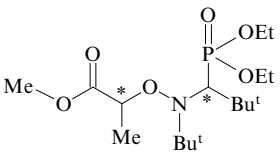
39 (SG1)

It should be noted that if a hydrogen atom is present at one of α-carbon atoms relative to the nitroxide fragment, this nitroxide radical undergoes disproportionation. Naturally, the stability of such radicals depends on the constants of disproportionation.[29] Dialkylnitroxides with primary and secondary substituents disproportionate to the corresponding hydroxylamine and nitrone according to the second-order kinetic law.

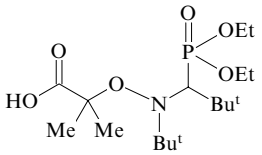


However, it was shown that nitroxide radicals containing a hydrogen atom in the α-position are stable provided the hydrogen atom is 'effectively blocked' by bulky groups in the nitroxide group plane. If the steric strains induced by these groups (their 'bulkiness') are sufficiently heavy, nitroxides undergo monomolecular dissociation.[198, 199] At the same time, the presence of a hydrogen atom adjacent to the nitroxide group makes the nitroxide unstable and leads to its decomposition at elevated temperature; these nitroxide radicals are not used in 'pseudo-living' processes.

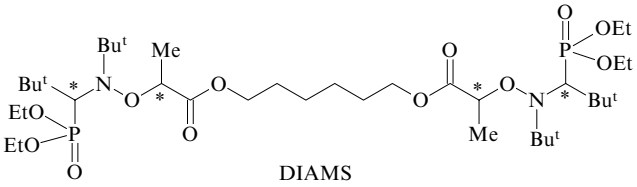
In 1995, a French–American company pioneered the commercial use of several alkoxyamines based on the stable radical SG1.[180, 200–204] They include monofunctional alkoxyamine MONAMS and bifunctional alkoxyamine DIAMS.



MONAMS



BlocBuilder®



DIAMS

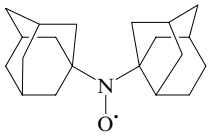
These alkoxyamines, in contrast to substituted TEMPO, dissociate to radicals at ~70–75 °C. These reagents have certain limitations as regards the molecular-weight characteristics of polymers, which is explained by the presence of chiral carbon atoms. Alkoxyamines MONAMS and DIAMS represent a mixture of diastereomers that differ in the energy of the C–ON bond dissociation, which results in non-simultaneous initiation of all chains. An alkoxyamine BlocBuilder®, which allows the CRP of different monomers to be carried out in the temperature range of 45–125 °C, proved to be the most versatile.

Indeed, in a recent study,[180] it was shown that alkoxyamines Me(Ph)CH-**39**, MONAMS and BlocBuilder® efficiently control the polymerization of not only styrene, but also BA. Alkoxyamine BlocBuilder® is the most advantageous regulator of molecular-weight characteristics and kinetic parameters of polymerization, because it does not require the introduction of additional amounts of original nitroxide and enables CRP of styrene at ~90 °C. Table 6 shows the main molecular-weight characteristics of polymers synthesized in the presence of alkoxyamines.

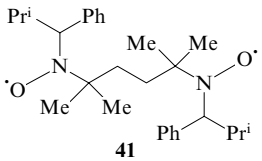
In the presence of alkoxyamines manufactured by Arkema, not only the homo-polymerization of different monomers, but also their random co-polymerization were carried out. For example, BlocBuilder® was used in the synthesis of co-polymers styrene–acrylic acid,[205, 206] MMA–St, ethyl methacrylate–styrene, BMA–St,[207] St–tBMA.[208] The co-polymerization was carried out both in bulk and in solution in the temperature range of 90–120 °C; in the majority of cases, the synthesized co-polymers were characterized by the polydispersity indices of 1.23–1.46. The isolated products of random co-polymerization could later act as the macroinitiators. Monofunctional alkoxyamine MONAMS was used in the CRP of acrylic acid,[191, 209] 2-(diethylamino)ethyl acrylate,[210] 2-hydroxyethyl acrylate,[211] in co-polymerization of St with BA.[212]

Mono- and bifunctional alkoxyamines based on the nitroxide SG1 make it possible to deliberately design and control the supramolecular architecture of macromolecules by carrying out block co-polymerization, synthesizing multiblock co-polymers, branched and star-like polymers.[213–217] Due to their unique structures, alkoxyamine BlocBuilder® and its certain derivatives were widely used for the emulsion and graft polymerization, polymerization in aqueous media and on the surface[218–228] and also in the preparation of nanostructured latexes.[229]

In their recent publication, Canadian scientists[181] studied the effect of sterically hindered di(1-adamantyl)-nitroxide (**40**) on polymerization processes. It was found that the C–O bond of the corresponding alkoxyamine dissociates at ~100 °C and control the polymerization of styrene. The PS formed had low polydispersity (~1.1). The increase in the polymerization temperature increased the PS polydispersity to 1.6 for 50% conversion. However, it should be noted that in this case, the 'pseudo-living' polymerization was rather slow, despite proceeding at relatively low temperature as compared with conditions typical of TEMPO. Different additives were introduced to accelerate the polymerization, namely, benzoic acid, pyridine, glyceraldehyde and camphorsulfonic acid.[181]

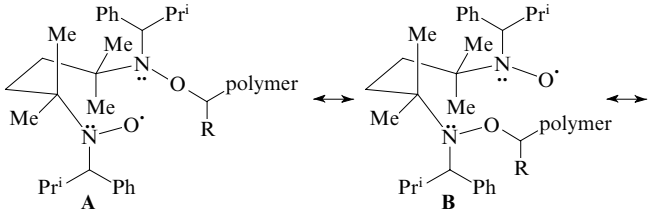


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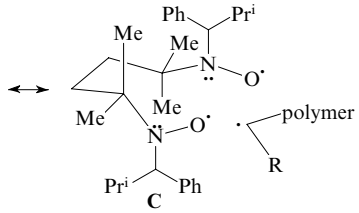


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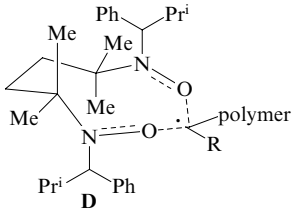
In another study,[182] bisnitroxide **41** and its analogue, bis(alkoxyamine) 2,5,5,8,8,11-hexamethyl-3,10-diphenyl-4,9-(1-phenylethoxy)-4,9-diazadodecane, were chosen as the low-temperature mediators. It was shown that these compounds efficiently control the molecular-weight characteristics of polystyrene at 70–110 °C. It was found that the homolysis constant of bis(alkoxyamine) derived from **41** in the temperature interval of 85–105 °C was approximately twice as large as that of analogous monoalkoxyamines. Presumably, the increase in the constant of the C–O bond homolysis in this bis(alkoxyamine) was due to stabilization of the mononitroxide formed (resonance structures **A**–**C**) as a result of radical delocalization over five atoms (structure **D**).



A ↔ **B**



C



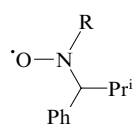
D

R = Alk, Ar.

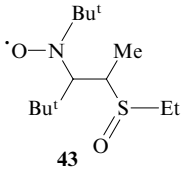
Thus, by varying the structure of the nitroxide and alkyl fragments in alkoxyamines, it is possible to optimize the conditions for the polymerization of styrene. Similar regularities were observed for the polymerization of styrene derivatives containing hydroxyl, alkyl, ester or halogen substituents in the benzene ring.[168, 183, 230, 231] It should be stressed that the nature of substituents in the benzene ring had a substantial effect on the polymerization rate. Electron-withdrawing substituents (Cl, CH_2Cl, CF_3) increased the reaction rate by an order of magnitude.[183, 230] Quite the contrary, the polymerization rate of styrene derivatives with electron-donating groups, for example, methylstyrenes, was much lower as compared with unsubstituted styrene.[168]

It was initially assumed that alkoxyamines can efficiently control only the polymerization of styrene and its analogues. Therefore, until recently, only few data pointed to the possibility of applying the approach of 'pseudo-living' radical polymerization to such monomers as vinylpyridine[184] and dienes.[186] However, with the development of new approaches to the synthesis of nitroxide radicals and various alkoxyamines,[179, 187, 195–197] wider prospects for the CRP were opened up, particularly, a possibility of its extension to different monomeric systems (acrylates, acrylamides, 1,3-dienes and AN) has appeared.

As a whole, different alkoxyamines and nitroxides were successfully used in the past decades in the polymerization of acrylic monomers so that the initial concept of impossibility of polymerizing acrylic monomers under conditions of CRP in the presence of nitroxide radicals has no longer objective grounds. In several studies, a wide spectrum of alkoxyamines capable of generating the corresponding chain propagation mediators were proposed, namely, TEMPO and its derivatives, sterically hindered five-membered cyclic and various aliphatic nitroxides,[179] DBN,[190, 232] nitroxides **35**–**37** with siloxyalkyl groups,[80, 178] diadamantylnitroxide **40**,[181] bisnitroxide **41**,[182] nitroxides **42** with different substituents,[188] β-phosphonylated nitroxide radicals such as **39**,[195–197] β-sulfonylated nitroxide radicals like **43**.[189]



42a–**c**



43

R = $Me_2NC(O)(CH_2)_2CMe_2$ (**a**), Et_3C (**b**), $Bu^tCH_2CMe_2$ (**c**).

It should be noted that in the presence of alkoxyamines, 'pseudo-living' polymerization was observed not only for acrylates, but also for 1,3-dienes,[187] acrylic acid,[191] 4-vinylpyridine,[184, 185] *N*,*N*-dimethylacrylamide[179, 185] and AN.[179]

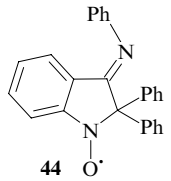
As mentioned above, until recently, the 'pseudo-living' polymerization of MMA in the presence of stable nitroxide radicals was assumed to be impossible.[192, 233, 234] Thus the MW of poly(meth)acrylates synthesized in the presence of TEMPO was always lower than the MW of polystyrene, *viz*., the polymerization stopped at conversion of 30%–40% with virtually all chains 'dead'.[192, 233, 234] The main reason for this is that TEMPO-based alkoxyamines containing an α-methyl group undergo disproportionation [reaction (13a)]. In addition, the nitroxide radicals formed in the decomposition of alkoxyamines also efficiently react with the propagating macroradicals by the hydrogen atom transfer to form hydroxylamines [reaction (13b)].[235] The significance of this reaction was later confirmed[236] by demonstrating that, in addition to the recombination of PMMA macroradicals and TEMPO, substantial contribu-

tion was made by disproportionation, which was assumed to be at least 20%. These reactions do not occur with nitroxide **39** as the regulator.[237] However, the use of compound **39** in the polymerization of MMA at 120 °C produced no positive results, namely, the control over the polymer chain propagation was absent under the mentioned conditions,[71] which was associated with the high constant of equilibrium dissociation.

French scientists have found an original solution to this problem.[193, 238] Polymerization of MMA involving alkoxyamine BlocBuilder® was carried out in the presence of small amounts of styrene (4.4% – 8.8%) at 90 °C, *i.e.*, in fact, the co-polymerization of MMA with styrene took place, all the main regularities of CRP being observed. The addition of the second co-monomer led to a substantial decrease in the equilibrium dissociation constant, which allowed the controlled polymerization to be carried out at 90 °C. The resulting polymer could further be re-initiated and effectively used in the synthesis of block co-polymers with styrene and BA.[193, 238]

At the same time, high constants of equilibrium dissociation of tertiary alkoxyamines (particularly, BlocBuilder®) allow initiation of polymerization of MMA at lower temperatures (~50 °C).[71] However, contrary to expectations, the polymerization of MMA in the presence of alkoxyamines can be partially controlled only in the initial stages of the process, mainly, due to the so-called 'penultimate unit effect'.[71] Thus for the macromolecular alkoxyamine based on nitroxide **39**, in contrast to the low-molecular-weight alkoxyamines, even at 45 °C, the equilibrium was strongly shifted from its formation to homolysis (k_d was ~35-fold larger, while k_c was ~100-fold smaller than the values obtained in model calculations). As a result, the bimolecular termination of active radicals became the prevailing process and free nitroxide did not affect the polymerization process.

Later, a group of Italian and French scientists developed new alkoxyamines based on stable nitroxide radical **44**.[55]



44

They proved to be efficient mediators of controlled polymerization of MMA. Polymerization of MMA in the presence of these compounds, in contrast to TEMPO derivatives, proceeded up to high degrees of conversion (80%), which points to the absence of disproportionation even in highly viscous media. With an alkoxyamine containing a *p*-nitrophenoxycarbonylalkyl fragment, the polymerization of MMA at 100 °C proceeded in the 'pseudo-living' mode up to conversion of 60% with linear increase in the MW of PMMA and polydispersity of 1.3 – 1.4. PMMA synthesized in the presence of alkoxyamines generated from radical **44** effected re-initiation, which was proved by the example of its block co-polymerization with BA at 120 °C. However, due to the incommensurability of the rate constants for recombination and disproportionation of these monomers, no simultaneous control over the polymerization could be achieved. The block co-polymerization process stopped after a certain period and further polymerization occurred in the uncontrolled mode.[55]

Thus, alkoxyamines are very efficient as the chain propagation regulators. The structure of the nitroxide radical that forms the alkoxyamine exerts a decisive effect on the kinetic parameters of the process and the molecular-weight characteristics of the polymers produced. Undoubtedly, from the practical viewpoint, a challenge of synthetic chemistry of polymers is associated with the development of effective methods of 'pseudo-living' polymerization under milder temperature conditions favourable for the radical polymerization of vinyl monomers under conditions of the industrial synthesis (< 100 °C). Moreover, special attention should be paid to the development of alkoxyamines that escape side reactions of reversible inhibition and also of alkoxyamines that can effectively control the polymerization of diverse monomers.

V. Conclusion

The analysis of literature data presented in this review suggests that the quest for new ways of CRP is among the topical trends in polymer chemistry. The considered versions of CRP with the *in situ* generation of the nitroxide radicals are very promising as the approaches to the synthesis of polymers with the preset molecular-weight characteristics. These methods are based on the use of commercially accessible precursors to prepare chain propagation regulators directly in the course of polymerization. In addition to their economic advantages, the chief merit of such approaches is the possibility of formation of the nitroxide radicals and alkoxyamines with the target structures by selecting the conditions of their synthesis (the choice of precursor, monomer, initiator, temperature, *etc.*). Varying the structure of chain propagation regulators enables the controlled synthesis of polymers from a wide spectrum of monomers to afford polymers with multifunctional characteristics.

A specific feature of this process is that it is not preformed nitroxides that are introduced but rather formed directly in the course of polymerization (*in situ*). The polymerization products synthesized under the action of macromolecular nitroxides differ from polymers prepared in the presence of common low-molecular-weight nitroxides in that the nitroxide group is inside the chain rather than at its end. The presence of a macromolecular substituent in a nitroxide has a substantial effect on the activity of the latter as a reversible inhibitor. The constant of 'pseudo-living' equilibrium involving macromolecular nitroxides turned out to be an order of magnitude higher as compared with polymerization involving TEMPO and other analogous low-molecular-weight nitroxides. Such a pronounced increase in this constant is associated with the decrease in the constant of reversible termination by two orders of magnitude as compared with TEMPO and ultimately ensures:

— the higher polymerization rate and the possibility of carrying out 'pseudo-living' polymerization under sufficiently mild conditions (< 90 °C), which is of extreme importance for practice;

— the possibility of the 'pseudo-living' mechanism in polymerization of a wide spectrum of monomers and, hence, the possibility of synthesizing block co-polymers, which opens up more opportunities for the macromolecular design.

At the same time, the relatively low constant of reversible termination elongates the chain and increases the

number of 'segments' from which the chain is assembled during its growth resulting in the undesired broadening of MWD, which is among the most serious drawbacks of controlled synthesis of macromolecules in the presence of nitroxides.

It is of note that despite the large number of original studies devoted to the development of *in situ* methods, several problems in this field still remain unsolved. First, it is rather difficult to find an unambiguous relationship between the structure of precursors and the efficiency of nitroxide radicals in CRP. As a whole, mention should be made of the correlation between the electronic and steric characteristics of the nitroxide fragment, on the one hand, and the polymerization conditions, on the other hand. The effect of acceleration of CRP processes involving sterically hindered nitroxides and alkoxyamines, which include high-molecular-weight species, is very important. Second, the proposed systems sometimes offer no way of synthesizing polymers with polydispersity indices attainable by the methods employing individual low-molecular-weight alkoxyamines. A certain increase in the polydispersity indices of polymers synthesized using the *in situ* approaches is a characteristic feature associated with either the polydisperse structure of high-molecular-weight nitroxides or side reactions.

Thus, the most important problems in the optimization of processes of the *in situ* controlled radical polymerization include the detailed analysis of elementary steps of macromolecular synthesis, the assessment of how the nitroxide structure, the precursor stability and other experimental parameters including the additives affect the environmental properties of polymers and also the elucidation of side processes aimed at their elimination.

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