U.D.C. 542.611

Hexamethylphosphoric Triamide in Organic Chemistry

H.Normant

CONTENTS

I.	Introduction	457
II.	Physical and physicochemical properties	457
III.	Chemical properties	460
IV.	Use of hexamethylphosphoric triamide as electron-donor reaction medium	461
	A. Formation of anions and metallation	461
	B. Isomerisation and polymerisation	464
	C. Use of anions	464
	D. Comparison of dipolar aprotic solvents	474
V.	Use of hexamethylphosphoric triamide as electron-acceptor reaction medium	476
	A. Formation of radical-anions	476
	B. Application of radical-anions	477
	C. Comparison of electron acceptors	481
	D. Comparison of dipolar aprotic solvents	487

I. INTRODUCTION

Chemists have recently being paying increasing attention to the effect of solvents on the occurrence of chemical reactions, especially the effect of dipolar aprotic solvents [1-5]. Among the latter the most interesting is the hexamethyltriamide of orthophosphoric acid $OP(N(CH_3)_2)_3$ (Hexametapol) or trisdimethylaminophosphine oxide. It is often denoted by the letters HMPA or HMPT†; the latter designation seems to be the better, since it reflects the triamide character of the compound. Recent publications on this solvent [6-8] refer in particular to its immense solvent power for a large number of organic and inorganic substances and macromolecular compounds, and also to its use as a copolymerisation catalyst.

The present Review presents data on the physical and chemical properties of hexamethylphosphoric triamide and its use as a reaction medium.

II. PHYSICAL AND PHYSICOCHEMICAL PROPERTIES

Triamides of orthophosphoric acid were obtained by Michaelis [9] by the reaction of phosphoryl chloride with excess of a secondary amine. When dimethylamine is used, this reaction yields the hexamethyltriamide of orthophosphoric acid:

$$O{=}PCl_3 + 6HNMe_2 \rightarrow O{=}P(NMe_2)_3 + 3Me_2\overset{+}{N}H_2Cl^-$$

When this reaction is conducted in an inert solvent, the first chlorine atom in the phosphoryl chloride molecule is easily replaced (exothermic process), but the system must be heated to effect substitution of the remaining two chlorine atoms. The hydrogen chloride liberated in the reaction is neutralised with sodium carbonate, ammonia, or other base, which diminishes the consumption of dimethylamine. After separation of the salts (dimethylamine hydrochloride, sodium carbonate, ammonium chloride) the filtrate contains HMPT, which is purified.

Hexamethylphosphoric triamide is a mobile, colourless liquid, which is miscible with water in all proportions. It forms complexes with chlorinated solvents [10], and can therefore be isolated from aqueous solutions of the latter. Table 1 gives partition coefficients for the amides—dimethylformamide (DMF), methylacetamide (MA), and HMPT—in mixtures of chloroform, methylene dichloride, and ethylene dichloride with water.

Table 1.

Compound	DMF	MA	HMPT
$CHCl_3$—H_2O	0.77	0.099	5.53
CH_2Cl_2—H_2O	0.57	0.088	2.07
ClC_2H_4Cl—H_2O	0.29	0.039	0.58

Hexamethylphosphoric triamide is miscible with polar and non-polar organic liquids, but not with saturated hydrocarbons (petroleum ether). It is an exceptional solvent for a large number of polymers [6], various gases [6], and a large number of inorganic salts [8]‡.

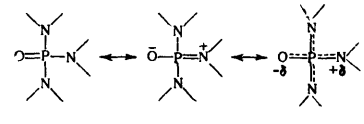
Hexamethylphosphoric triamide has a pyramidal structure [11]. The P–O bond may be more or less ionic or covalent in character in different molecules depending on the substituents [11,12]:

$$F_3P{=}O \qquad (Me_2N)_3\overset{\delta+}{P}{=}\overset{\delta-}{O} \qquad Me_3\overset{+}{P}{-}\overset{-}{O}$$

In the HMPT molecule it is usually accepted that the P–O bond is 50% ionic, whereas the NPO bond can be represented as

$$\overset{+}{N}{=}P{-}O^-$$

Thus the following limiting structures



†The abbreviation HMPTA is also used in the literature.

‡Prolonged and intimate action of HMPT on the skin must be avoided. The permissible dose for the rat is 6 g kg^{-1}.

are suggested for the HMPT molecule. The symmetrical distribution of positive charge on the grouping



and the enhanced electron density on the oxygen atom confer both electron-acceptor and electron-donor character on the HMPT molecule.

The melting point of HMPT is 7.20°C, and its cryoscopic constant 6.93 ± 0.07.[14] It boils at 235°C (760 mm)[15], 125°C (15 mm), 120°C (10 mm),[10] and 68–70°C (1 mm). The vapour pressure is very low at ordinary temperature (0.07 mmHg at 30°C),[17] and its temperature dependence has been published[18]. The density is $d_4^{20} = 1.0253$.[19] Values published for the refractive index are $n_D^{20} = 1.4582$[19] and $n_D^{25} = 1.4570$;[20] another publication[21] reports values measured by various methods at various wavelengths. The viscosity is 3.5 cS at 60°F.[15] The dielectric constant is $\epsilon_{20°} = 30$,[4] and its temperature dependence has been published[22]. The dipole moment $\mu = 4.31$ D;[13] however, values obtained for the pure liquid (5.37 D) and in benzene solution (5.54 D) differ greatly from this value[22].

Table 2.

Stretching vibration	Absorption band, μm
C—N	7.1—9.8
P—O	7.5—8.5
P—N	⩾ 13.9

The compound absorbs in the infrared[21] (Table 2). The frequency of the P–O bond is 8.7 μm.[23] The position of this band varies little[24] with the nature of the solvent: it occurs at 8.26, 8.32, 8.32, 8.30, and 8.28 μm in carbon tetrachloride, chloroform, pentachloroethane, 1,1,2,2-tetrachloroethane, and methylene dichloride respectively.

The enthalpy of formation from phosphoryl chloride and dimethylamine is $H_{f(gas)} = 114$ kcal mole^{-1}.[25]

The ^{31}P chemical shift in the nuclear magnetic resonance spectrum, relative to 85% orthophosphoric acid, is $\delta = 23.4$ ppm.[26]

1. Properties of Hexamethylphosphoric Triamide

The ability of a solvent to supply its pair of electrons to a compound AH (e.g. chloroform) can be assessed by various physicochemical methods, in particular by means of nuclear magnetic resonance[27]. For every solvent we can calculate the quantity $\delta_\infty(CHCl_3)$:

$$\Delta\delta_\infty(CHCl_3) = \delta_\infty - \delta$$

where δ_∞ and δ are obtained by extrapolating to infinite dilution solutions of chloroform in the given solvent and in an inert solvent (cyclohexane) respectively. The values in Table 3 were first determined by Martin[28], published later[29], and confirmed by another worker[4].

Infrared spectroscopy has yielded similar results. Increase in the basic strength of the solvent is accompanied by a considerable change in the C–Br frequency in aliphatic and unsaturated bromides. The same changes have been shown to occur with solvent–bromide interaction as with solvent–proton interaction[29,30].

Table 4 lists some characteristics of dipolar aprotic solvents. It is readily seen that, among the solvents included, HMPT has the lowest dielectric constant and the greatest basic strength. Because of its electric-donor power HMPT associates with organic and inorganic compounds.

Table 3.

Solvent	$\Delta\delta_\infty$	Solvent	$\Delta\delta_\infty$
Cyclohexane	0	Cyclohexanone	1.06
Dioxan	0.64	$OP(OC_4H_9)_3$	1.28
$P[N(CH_3)_2]_3$	0.68	DMF(dimethylformamide)	1.30
Ether	0.70	DMSO (dimethyl sulphoxide)	1.34
Oxolan	0.80	TMU (tetramethylurea)	1.37
Acetone	0.94	HMPT	2.03

Thus HMPT is able to form various complexes with compounds containing a labile hydrogen atom. These include, besides chloroform[31], polyhalogenated ethanes[24]. Solvation occurs at the oxygen atom of the phosphoryl group, not at a nitrogen atom. Study of the infrared spectra enables these compounds to be arranged in the sequence of diminishing electron-acceptor power:

$$CHCl_3 > CHCl_2—CCl_3 > CCl_3H—CHCl_3 > CH_2Cl_2$$

The sequence

$$(Me_2N)_3PO > (EtO)_3PO > (EtS)_3PO > (PhS)_3PO > (Et_2N)_3PO$$

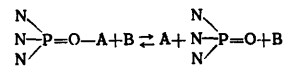
shows that the electron-donor character of HMPT exceeds that of the other phosphorus oxides, its homologue $((C_2H_5)_2N)_3PO$ coming at the end of the series[32].

Table 4.

Solvent	Dielectric constant ε	Dipole moment, D	Δν, ppm
DMF	36.7	3.90	0.78
DMSO	49	4.03	1.05
Ethylene glycol	95	4.86	0.41
Thiolan dioxide	44	4.7	0.78
HMPT	30	4.3—5.3	1.89

Acids, phenols, alcohols, aromatic amines, and glycols form stable crystalline complexes with HMPT (Table 5).[33] Among acids which form complexes with HMPT are nicotinic, isonicotinic, and *o*- and *m*-toluic acids. The toluidines (*ortho*- *meta*- and *para*) must be included with aniline; 1- and 2-naphthols and various chlorinated phenols must be included with phenol itself[34].

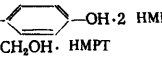
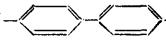
A complex formed by HMPT with a compound A containing a hydrogen atom can be broken down by a stronger acid B:



This method can be used in the separation of acids; it has been employed to separate terephthalic acid from isophthalic acid [33].

A study has been made of the infrared spectra of the complexes formed by HMPT with ketones and with hydrogen halides. The association constant of HMPT with the latter compounds increases in the sequence—HBr < HCl < HF—whereas the acidity diminishes in this sequence, from hydrogen bromide to hydrogen fluoride [35].

Table 5.

Compound		M.p., °C
$C_6H_4(COOH)_2 \cdot 2$ HMPT	*ortho-*	70
	meta-	52
	para-	128
HO——OH·2 HMPT		152
$C_6H_5CH_2OH \cdot$ HMPT		10
$C_6H_5NH_2 \cdot$ HMPT		<0
H_2N——$NH_2 \cdot 2$ HMPT		132
$C_2H_4(OH)_2 \cdot 2$HMPT		−20

It has been reported [33] that HMPT forms complexes with various unsaturated hydrocarbons—CH⋮CH, CH⋮C, CH_2:CH, CH⋮C.C_6H_5, CH_2:CH.CH:CH_2, CH_2:CH.C_6H_5—but no information is available on the structure of these complexes.

Basic solvents are known to form complexes with Lewis acids, the complex being more stable the more basic the solvent: $(C_2H_5)_2O.BF_3$ < Oxolan.BF_3 < HMPT.BF_3. Examples of crystalline complexes of HMPT with certain Lewis acids are given below.

Complex	M.p., °C	Ref.
HMPT × BF_3	175	35
HMPT × $BClPh_2$	159-160	37
HMPT × $POCl_3$	170-180	
HMPT × $POBr_3$	165-180	

Table 6.

Metal	Complex	Anion
Ag	MSX	halide
Co, Ni, Mn, Fe^{II}, Cu^{II}	MS_2X_2	halide
Pb^{II}	MS_3X_2	halide
Mg, Zn, Cd	MS_4X_2	halide
Co, Ni, Mn, Fe^{II}	MS_4X_2	ClO_4^-
Cr^{III}, Fe^{III}	MS_6X_3	halide
Ti, Sn	MS_2X_4	halide

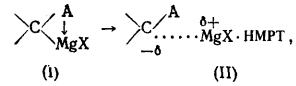
Crystalline complexes can be obtained also by the reaction of HMPT with certain metal salts. The infrared spectra and the dipole moments show that coordination with metal cations takes place at the oxygen atom in the phosphoryl group [13,38]. The number of solvent molecules involved in complex formation may vary. Neutral molecules of the type MS_2X_2 and ions of the type $[MS_4]^{2+}$ have a tetrahedral structure [13,38]. Table 6 gives the types of complexes formed with various metal salts.

Stable complexes of HMPT with thorium and uranium tetrachloride and tetrabromide have been obtained recently, and have proved to be more stable than analogous complexes with dimethyl sulphoxide [39]. Thus the more basic is a dipolar aprotic solvent, the more easily does it form complexes.

The stability of solvated organomagnesium compounds increases with increase in the basic strength of the solvent, and a more basic solvent can displace a less basic solvent from a solvate [36]:

$$2(C_2H_5)_2O.RMgX < 2\ \text{Oxolan.}RMgX < 2\text{HMPT.}RMgX.$$

Symmetrical organomagnesium compounds are soluble in HMPT. [40] Insoluble compounds RMgX.2HMPT are formed with RMgX, and very stable complexes $MgBr_2$.4HMPT with magnesium bromide [41]. Geminal organomagnesium compounds



(I) (II)

where A = OR [42] or Hal [43] are intramolecular complexes. Addition of HMPT favours stabilisation and increase in reactivity of the ionised form (II) formed from the carbenoid form (I). However, the rate of the double decomposition

$$CH_3.CH{:}CH.CH_2{-}Zn + CdCl_2 \rightleftharpoons CH_3.CH{:}CH.CH_2{-}Cd + ZnCl_2$$

decreases with increase in the basic strength of the solvent as the cadmium atom becomes more solvated [44]. Because of the immense solvating power of HMPT, organometallic compounds can be obtained by their direct reaction with metals; organocadmium compounds have been obtained in this way [45]. Among the saturated halogen compounds only the iodides have been studied. With unsaturated bromides HMPT forms complexes at 0°C. A complex of melting point 112°C, soluble in acetone, has been obtained from cadmium bromide and HMPT.

2. Use of Hexamethylphosphoric Triamide in Electrochemistry

Little use has been made of HMPT as a solvent for electrochemical purposes. The literature contains no information on its application as solvent in polarography.

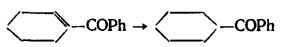
A voltametric study of HMPT has enabled a stable reference electrode of the Ag/Ag^+ type to be obtained. The electrical activity of HMPT depends considerably on the nature of the cation present and on the water content of the medium [46]; it has been studied in a medium containing sodium and lithium perchlorates with different quantities of water. The results indicate that HMPT differs greatly from other solvents [47,48]. It can also be used as a solvent for electrolysis. Metal salts which dissolve in it [49] undergo ionisation with the formation of ion-pairs, and perhaps dissociation with the formation of ions.

In some cases ionisation results in the formation of coloured anions (HMPT solvates anions weakly). Thus deeply coloured red solutions are formed on the dissolution in HMPT of certain organometallic compounds, e.g. $(C_6H_5)_3CM$, $(C_6H_5)_2CHM$, and $C_6H_5CH_2M$, where M represents an alkali metal or MgX. An ethereal solution of benzylmagnesium chloride is colourless, but a solution of

the same compound in HMPT has the characteristic red colour of the benzyl anion [47,48].

It has not proved possible to electrolyse organometallic compounds in HMPT. However, inorganic salts can be electrolysed by using a soluble anode M and a platinum cathode (where MX = $MgBr_2$, which is soluble in ether as $2(C_2H_5)_2O.MgBr_2$; and MX = CaI_2).

The electrolytic reduction of an α-unsaturated ketone to a saturated ketone takes place in HMPT with an 80% yield [49]:



3. Polarity of Solvents

The term polarity in reference to dipolar aprotic solvents must be taken as implying various physical quantities (ϵ, μ, $\Delta\delta$, ...). The nucleophilic substitution

$$n\text{-}C_4H_9Br + N_3^- \rightarrow n\text{-}C_4H_9N_3 + Br^-$$

can be used for comparing solvents. The rate constant and the activation energy of this reaction conducted in HMPT indicate the exceptional role of this solvent (a high value of k and an abnormally low value of E are observed). Satisfactory correlation is obtained between the dependence of $\lg k$ on $1/\epsilon$ and on $\Delta\delta$ (ppm). [4]

The polarity of solvents can be expressed also in terms of semi-empirical parameters, such as the constant Z [50,51] or the parameter F [52]. According to the values of Z protic and dipolar solvents can be arranged in the sequence

$$CH_3OH,\ C_2H_5OH,\ t\text{-}C_4H_9OH,\ CH_3CN,\ HCON(CH_3)_2,\ CHCl_3,\ HMPT,\ \underset{\text{Iso-octane}}{\text{Iso-octane}}$$

and according to the values of F in the sequence

$$CH_3OH,\ C_2H_5OH,\ t\text{-}C_4H_9OH,\ CH_3CN,\ HMPT,\ HCON(CH_3)_2,\ CHCl_3,\ \underset{\text{Iso-octane}}{\text{Iso-octane}}$$

The above results show the "ambivalence" of HMPT. [52]

III. CHEMICAL PROPERTIES

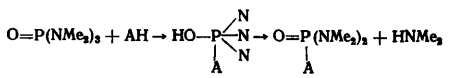
1. Action of Nucleophilic Reagents

Hexamethylphosphoric triamide exhibits considerable resistance to attack by nucleophilic reagents (unlike the amides of carboxylic acids, it does not undergo hydrolysis in alkaline media), and can itself be used as a nucleophilic and basic reagent.

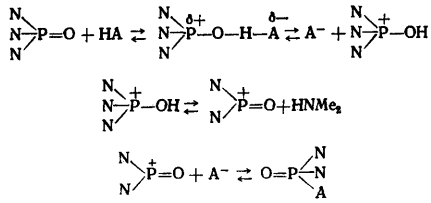
Various derivatives of the alkali metals can be obtained in HMPT. Alkali-metal hydroxides do not react with HMPT at 80°C, but do so at higher temperatures (110 to 120°C). The inertness of HMPT towards nucleophilic reagents can be explained by great steric hindrance around the positively charged phosphorus atom.

2. Action of Electrophilic Reagents

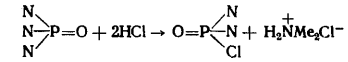
Protic acids and Lewis acids act vigorously on HMPT, with replacement of one or more dimethylamino-groups by A (from the reagent H^+A^-):



Because of the strongly developed basic character of the solvent, electrophilic reagents also form 1:1 complexes with it. These complexes, which are more or less stable, give various substitution products when heated. The mechanism of the reaction is assumed to be

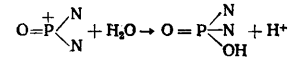


Dry gaseous hydrogen chloride reacts with HMPT according to the equation

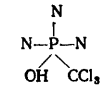


Further cleavage of P–N bonds does occur, but with great difficulty.

In aqueous media the dimethylamino-group is replaced by hydroxyl:



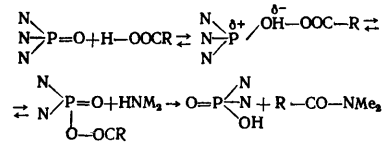
In acid media the rate of hydrolysis is of the same order as for the $CO\text{–}N(CH_3)_2$ bond [16]. The complex formed by HMPT with chloroform is unstable, and decomposes when heated. Among the reaction products $HO\text{–}P(N(CH_3)_2)_2$ has been identified [53] by nuclear magnetic resonance. According to the above scheme a pentacoordinated phosphorus derivative



should be present during the reaction, which seems improbable. Carboxylic acids yield stable complexes (1:1) with HMPT, their decomposition temperatures being 180–200°C. Transamidation [54]

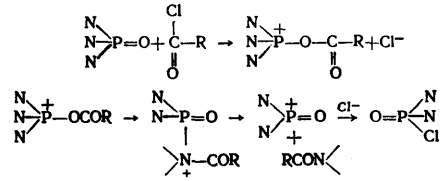
$$O{=}P(NMe_2)_3 + 3\,RCOOH \rightleftarrows O{=}P(OH)_3 + 3RCONMe_2$$

involves formation of a diamido-anhydride as an intermediate stage:



Similar reactions have been accomplished with aromatic, heterocyclic, and sulphonic acids. When the proportions of the reagents are HMPT : RCOOH = 1:3, orthophosphoric acid and the corresponding amides are formed [55].

Phenols, but not alcohols, form quite stable complexes§ in HMPT. The crystalline complexes of HMPT acid with chlorides $((CH_3)_2N)_3PO.OPCl_3$ decompose when heated, with replacement of a dimethylamino-group by chlorine:



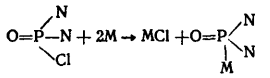
(III)

§The structure of these complexes has not been established.

The monochlorinated derivatives (III) can be obtained also (which is extraordinarily interesting) in the chlorides of inorganic acids (thionyl chloride, phosphoryl chloride)[56,57]:

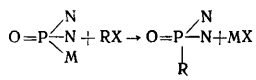
$$2O{=}P(NMe_2)_3 + O{=}PCl_3 \rightarrow 3O{=}P(Cl)(NMe_2)_2$$
$$O{=}P(NMe_2)_3 + O{=}PCl_3 \rightarrow 2O{=}P(Cl)(NMe_2)_3$$

The monochlorinated derivatives can be used to prepare derivatives of the alkali metals[5,58]:



(IV)

where M = Li, Na, K. The latter are in turn used for the preparation of various phosphoramides (V):

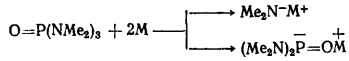


(V)

The results of several reactions will be found in Refs. 58 and 59.

3. Action of Alkali Metals

Alkali metals interact with HMPT to yield two anions (via the radical-ions)—the dimethylamide anion (VI) and the phosphorodiamidite anion (VII):



(VI)

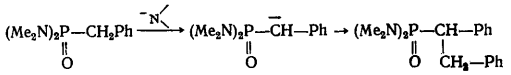
(VII)

Saturated alkyl bromides react with HMPT to form tertiary amines (VIII) and phosphoramides (IX)



(VIII) (IX)

Under these conditions benzyl chloride does not form the benzyl derivative (X), but yields the compound (XI):

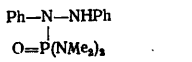


(X) (XI) (XII)

The benzyl derivative (X) can be obtained by the reaction between (IV) and benzyl chloride in a mixture of ether and benzene. Sodamide acts on the compound (X) in HMPT to give a good yield of (XII). This result indicates that, in a mixture of the two anions (VI) and (VII), the stronger base (VI) converts (X) into the carbanion (XI), which easily gives (XII).

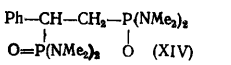
The two anions formed by the interaction of HMPT with alkali metals are able to metallate weakly acidic hydrocarbons (triphenylmethane forms blood-red solutions); this phenomenon is not observed in benzene solution[60]. The base (VI) acts as a metallating agent, and is stronger than (VII). In fact, (IV) does not react with triphenylmethane even on heating. On the other hand, the conjugate acid $OPH(N(CH_3)_2)_2$, obtained as in Ref. 61, displaces triphenylmethane from its sodium salt.

The compound (VII) gives various products with unsaturated systems. Azobenzene yields after hydrolysis the compound[62]



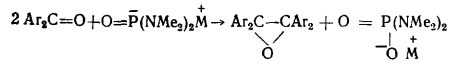
(XIII)

With phenylacetylene (or with β-bromostyrene) a twofold excess of (VII) gives the diphosphoramide[63]



(XIV)

The compound (VII) interacts with non-enolisable ketones to yield products in which the latter have condensed into epoxides[64]. In alkali-metal phosphites $MPO(OR)_2$ (sodium is the best cation) this reaction is possible also with aromatic aldehydes. No reaction occurs in non-polar solvents, but in HMPT a high yield is obtained[65]:



4. Hexamethylphosphoric Triamide as Catalyst

A few readily occurring reactions are known in which HMPT acts as a catalyst. Thus the formation of carbodiimides from isocyanates

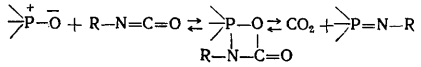
$$2R{-}N{=}C{=}O \rightarrow CO_2 + R{-}N{=}C{=}N{-}R$$

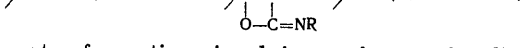
goes more rapidly, at a lower temperature, and with a better yield in the presence of small additions of HMPT[66,67] than of dimethyl sulphoxide (Table 7).

Table 7.

Solvent, mole	Phenyl isocyanate, mole	Temp., °C	Time, h	Yield, %
DMSO, 0.006	0.45	162—164	2.5	13
HMPT, 0.008	—	113—135	1.6	27

In the presence of HMPT phosphonimides are formed in similar reactions:





The rate of reactions involving exchange of radicals between trialkylborines and alk-1-enes

$$Bu_3B + CH_2{=}CH(CH_2)_7{-}CH_3 \rightarrow CH_2{=}CH{-}CH_2{-}CH_3 + Bu_2B(CH_2)_9{-}CH_3$$

is also increased by HMPT.[68] Chlorosilanes undergo disproportionation in the presence of 0.5–15% of HMPT at elevated temperature[69]:

$$2MeSiCl_2H \rightleftarrows MeSiCl_3 + MeSiClH_2$$

IV. USE OF HEXAMETHYLPHOSPHORIC TRIAMIDE AS ELECTRON-DONOR REACTION MEDIUM

A. FORMATION OF ANIONS AND METALLATION

Exchange between hydrogen and a metal yields anions or other organometallic compounds:

$$AH + MR \rightleftarrows RH + MA \quad \text{or} \quad (M^+ + A^-)$$

The equilibrium is displaced to the right if AH is a stronger acid than RH, or if R^- is a stronger base than A^-. Table 8 gives an acidity scale for various compounds AH.

The solvent plays an important part in exchanges between hydrogen and a metal. Electron-donor solvents promote ionisation of the molecules AH and MR:

$$S_1 + H\overset{\delta+}{-}\overset{\delta-}{A} \rightleftharpoons (H^+, A^-)S$$

$$S_1 + M\overset{\delta+}{-}\overset{\delta-}{R} \rightleftharpoons (M^+, R^-)S$$

and yield solvated ion-pairs. If the dielectric constant of the solvent is sufficiently high, dissociation may occur:

$$(M^+, R^-)S \rightleftarrows (M^+ + R^-), S$$

in which the cations M^+ are strongly solvated, and the anions R^- are weakly solvated. Free anions are highly reactive in dipolar aprotic solvents, especially in HMPT, in which the electron-donor character is most strongly developed.

Table 8.

AH	pK_a	Solvent	pK_a
CH_4	50	NH_3 (liq.)	34
$PhCH(CH_3)_2$	37	$PhNH_2$	27
$Ph_2C{=}CHCH_3$	36	acetone	19
$PhCH_3$	37	$t\text{-}C_4H_9OH$	19
Ph_2CH_2	35	CH_3OH	16
Ph_3CH	33	H_2O	14
$HC{\equiv}CH$	26	H_2O	—
Fluorene	25	H_2O	—
Indene	21	H_2O	—
$PhC{\equiv}CH$	21	H_2O	—
Cyclopentadiene	17	H_2O	—

1. Alkoxide and Phenoxide Anions [70]

Alcohols and phenols which are relatively strong acids can interact with alkali-metal hydrides and amides in HMPT to yield more reactive unsolvated anions RO^- or ArO^- than when hydroxylated solvents are used. Similar reactions are possible with alcohols possessing little acidity (t-butyl and allyl alcohols) and with diols, from which diglycolates are formed. With acids the reaction products are alkali-metal salts RCOOM (the silver salt is an exception), which are converted into esters.

It is also noteworthy that very many alkali-metal salts possess extraordinarily high—sometimes unlimited—solubility in HMPT.

2. Anions of Amides [70]

Aliphatic amines are too weak acids to be converted into amides by alkali-metal hydrides and amides. I am aware of only one example of such a reaction—the formation of lithium methylamide [71]

$$CH_3NH_2 + MNH_2 \rightleftarrows CH_3NH{-}M + NH_3$$

Stronger organometallic bases are required for aliphatic amines. Arylamines ArNHR (R = H, Alk, Ar), indole, carbazole, and phenothiazine form sodium derivatives with sodium hydride or sodamide in HMPT at room temperature.

Aniline may give the doubly charged anion $C_6H_5N^{2-}$; carboxyamides and amides can also react in the cold. The sodium derivatives of indole, acetanilide, and phthalimide are soluble without limit.

3. Carbanions of Hydrocarbons

The rate of exchange between hydrogen and a metal depends on the acidity of the hydrocarbon, the strength of the base, and the polarity of the solvent. The influence of these three factors will be examined in the following sections.

(*a*) Carbanions of alkynes. Organomagnesium compounds react with alkynes in HMPT in the cold [72]:

$$R{-}C{\equiv}C{-}H + i\text{-}PrMgCl \rightarrow R{-}C{\equiv}C{-}MgCl + C_3H_8$$

A similar reaction is possible with organozinc compounds [73]:

$$2\,Ph{-}C{\equiv}CH + Et_2Zn \rightarrow (Ph{-}C{\equiv}C)_2Zn + 2C_2H_6$$

The reaction takes place instantaneously in HMPT, in contrast to other polar solvents [73] (Table 9). The strength of the base plays an important part in such reactions [74]. Thus phenylacetylene (as also acetylene itself) does not react with sodium hydride in HMPT.

Table 9.

Solvent	Oxolan	DMF	DMSO	HMPT
Half reaction time at 50°C, s	129	270	200	8

In the presence of suitable bases alkynes undergo isomerisation: hept-1-yne yields a mixture of heptynes, the main component of which is the isomer hept-2-yne.

At room temperature the more basic alkali-metal amides form the alkynylides RC : CNa. It is noteworthy that acetylene and phenylacetylene, which form complexes with HMPT, do not give sodium derivatives in pure HMPT.

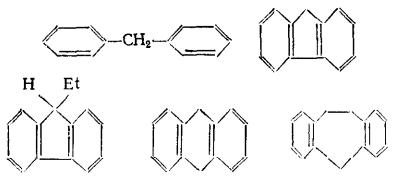
(*b*) Carbanions of triphenylmethane. In solvents of low polarity (ether, oxolan) triphenylmethane does not react with Grignard reagents to give compounds of the type $(C_6H_5)_3CM$ (where M = MgX). With isopropylmagnesium chloride in HMPT this reaction goes smoothly at 90°C. [75] Stable alkali-metal derivatives $(C_6H_5)_3CM$ (where M = Li, K, Na) can be obtained in HMPT from the corresponding hydrides and amides. In liquid ammonia metal amides form $(C_6H_5)_3CM$, but addition of ether decomposes them if M = Na, Li. In oxolan triphenylmethane cannot be metallated either by sodium hydride or by sodamide even at the boiling point of this solvent: stronger bases, e.g. $C_6H_5CH_2Na$, $CH_2 : CHCH_2Na$, are necessary for the reaction [76].

Under similar conditions triphenylgermane can be converted into $(C_6H_5)_3GeM$.

In HMPT triphenylmethane is able to react with lithium aminoalkynylides [77]:

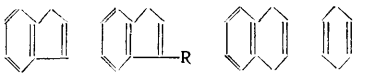
$$\rangle N{-}C{\equiv}C{-}Li + Ph_3CH \rightarrow \rangle N{-}C{\equiv}C{-}H + Ph_3CLi$$

(*c*) Hydrocarbons of the diphenylmethane type. Diphenylmethane and various hydrocarbons of related structure



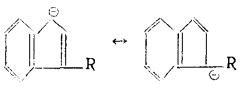
and metallated in HMPT medium [78]. Being less acidic than triphenylmethane, diphenylmethane undergoes exchange only with isopropylmagnesium chloride in HMPT. The reaction takes place at 100°C (red carbanion); on the other hand, it goes very readily at room temperature with the hydrides and still better with the amides of alkali metals. Formation of an organosodium compound is possible even in a less polar medium. Fluorene is able to give organomagnesium compounds at 135–140°C in xylene, and at 40°C in HMPT. Organozinc compounds can also be obtained in the latter solvent [73]. Dihydroanthracene can be metallated in good yield even in the cold both by isopropylmagnesium chloride and by sodium hydride. In HMPT in the cold dihydrodibenzocycloheptene is converted into a dark orange carbanion (at position 5).

(*d*) Hydrocarbons of 1,4-diene structure [72]. A study has been made of the compounds

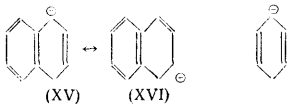


In solvents of low polarity indene reacts with ethylmagnesium bromide at 100°C to yield magnesium derivatives; with isopropylmagnesium chloride in HMPT a similar reaction takes place at only 30°C. Metallation with sodium hydride in HMPT can be accomplished at 0°C (exothermic process) with formation of a reddish-orange anion, which undergoes partial conversion into a dianion.

Alkylindenes react similarly to indene (in HMPT exchange between H and MgX begins at 35°C). The intensely coloured red anion is in a mesomeric form:



The anions formed from 1,4-dihydronaphthalene and especially from cyclohexa-1,4-diene exhibit a tendency to aromatisation:



(XV) (XVI)

The anion (XVI) can be formed when (XV) is treated with isopropylmagnesium chloride in HMPT at 90–95°C. The action of sodamide in HMPT produces considerable polymerisation.

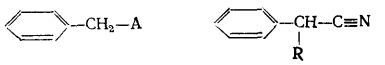
When isopropylmagnesium chloride interacts with 1,3-diphenylpropene in HMPT at room temperature, a red anion is formed:

$$Ph{-}CH{=}CH{-}CH_2Ph \rightarrow Ph{-}CH{=}CH{-}\overset{\ominus}{C}H{-}Ph$$

In this case, too, alkaline reagents cause considerable polymerisation.

4. Carbanions formed by Compounds containing Labile Hydrogen [79]

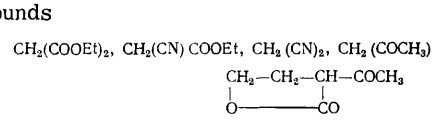
(*a*) Derivatives of phenylacetic acid. A hydrogen atom present in compounds containing phenyl and electron-acceptor groups is labile:



where A = COOH, CN. Phenylacetic acid reacts with isopropylmagnesium chloride or sodamide in HMPT in the cold to form a dianion; the disodium derivative is completely soluble in this solvent.

Benzyl cyanide on treatment with sodium hydride or sodamide in HMPT at 0°C forms a reddish-violet anion together with a certain amount of a dianion. α-Alkylbenzyl cyanides form singly charged anions at 0°C.

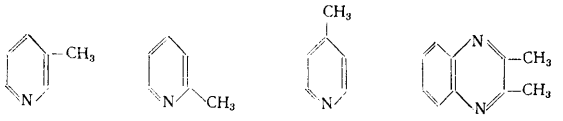
(*b*) Derivatives of malonic acid. The compounds



are metallated by sodium hydride or sodamide in HMPT at 0°C, the reaction mixture always containing a small quantity of dianions.

(*c*) Aromatic compounds containing methyl groups. Toluene and 2-methylfuran do not react with sodamide or sodium hydride in HMPT. 2-Methylthiophen reacts very slightly.

In the series of picolines

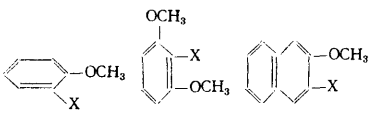


the methyl group exhibits acidic properties in positions 2 and 4, and in HMPT the 2-isomer reacts with isopropylmagnesium chloride to form a red anion. At 0°C the 2- and 4-isomers are able to react with sodamide to form sodium derivatives; with sodium hydride the reactions are very difficult. The 3-isomer is not known to react with sodamide in HMPT. 2,3-Dimethylquinoxaline is more acidic than 2-methylpyridine: it reacts with sodamide in HMPT at room temperature to form a greenish-violet dianion:

(*d*) Various compounds containing labile hydrogen. Alkaline reagents convert haloforms into CX_3^- anions, which in liquid ammonia readily add to the carbonyl group in ketones [80]. In HMPT this reaction goes with difficulty, but exchange with isopropylmagnesium chloride takes place readily. Novel organomagnesium compounds have been prepared by conducting the reaction in a 5 : 1 mixture of oxolan and HMPT at 80°C:[1,2,81,82]

$$X_3C{-}H + i\text{-}PrMgCl \rightleftarrows C_3H_8 + X_3C{-}MgCl$$
(X=Cl, Br).

Among methoxylated aromatic compounds



which are able to react to different positions, only the last forms a red carbanion on reaction with sodamide in HMPT.

In compounds containing an alkylthio-group, which is a better electron acceptor than the alkoxy-group, the anion can be stabilised by resonance:

$$-CH_2-S-R \rightarrow -\overset{\ominus}{C}H-\bar{S}-R \longleftrightarrow -CH=\overset{\ominus}{\underline{S}}-R$$

those which have been studied are [83]:

$$HC(SEt)_3,\quad H_2C(SEt)_2,\quad PhCH(SEt)_2,\quad PhCH(SPh)_2$$

These compounds react with alkali-metal amides in liquid ammonia to form carbanions. The analogous reactions in HMPT yield different results: in di- and tri-ethylthiomethane the carbon–sulphur bond is cleaved; sodamide acts on 4-phenyl-3,5-dithiaheptane at 0°C to form a dark green carbanion; and the most acidic compound $\alpha\alpha$-diphenylthiotoluene is metallated by sodium hydride at 0°C.

Acetophenone and acetonitrile react with sodium hydroxide in HMPT at 0°C with the loss of one or more protons.

Phosphonates [10] are readily converted into carbanions [84] by the action of sodium hydroxide:

$$(EtO)_2\overset{\underset{O}{\|}}{P}-CH_2-\underset{R}{\underset{|}{CH}}=C-OEt \rightarrow (EtO)_2\overset{\underset{O}{\|}}{P}-\overset{\ominus}{C}H-\underset{R}{\underset{|}{CH}}=C-OEt$$

On condensation with carbonyl compounds they give ethoxydienes

$$\begin{matrix} R_1 \\ R_2 \end{matrix}\!\!>C=CH-\underset{R}{\underset{|}{CH}}=C-OEt$$

which are difficultly accessible by other methods [85].

These few examples indicate that carbanions are formed in HMPT quite easily, with the use of weaker bases and lower temperatures than are required for reaction in other solvents.

B. ISOMERISATION AND POLYMERISATION

Various isomerisations of prototropic type can occur in alkaline media, involving mesomeric carbanions. Such reactions occur considerably more rapidly in the presence of polar solvents. In dimethyl sulphoxide the allyl rearrangement is possible at 25°C, but in t-butyl alcohol only on heating [86]:

$$C_6H_5\underset{H}{\underset{|}{C}}(CH_3)-CH=CH_2 \rightarrow C_6H_5-C(CH_3)=CH-CH_3$$

No systematic study of the various rearrangements in HMPT has yet been made, but certain results have already been obtained. The isomerisation of allylbenzene into propenylbenzene takes place in HMPT in the presence of sodium hydride in the cold [78]:

$$PhCH_2-CH=CH_2 \rightarrow Ph-CH=CH-CH_3 \quad \text{(yield 70\%)}$$

Under these conditions there is little formation of condensation products, but this becomes considerable if a stronger base (sodamide) is used, or a weak base (isopropylmagnesium chloride) at a high temperature [87]. In such cases anionic polymerisation takes place. Table 10 gives some examples of hydrocarbons which readily form anions under the influence of isopropylmagnesium chloride.

The rapid disappearance of colour on treatment with sodium hydride or sodamide is an indication of polymerisation, as in the case of allylbenzene, for example. Alkenes can be efficiently polymerised by means of organomagnesium compounds in solvents of low polarity, but under these conditions the reaction must be conducted under slight pressure in the presence of halides of metals of Groups IVb, Vb, and VIb.

The capacity for mesomerism of the allyl anion has been shown by the action of sodamide in HMPT at room temperature:

$$CH_3-\underset{CH_3}{\underset{|}{C}}=CH-S-Bu \rightarrow \overset{\ominus}{C}H_2-\underset{CH_3}{\underset{|}{C}}=CH-S-Bu \longleftrightarrow CH_2=\underset{CH_3}{\underset{|}{C}}-\overset{\ominus}{C}H-S-Bu$$

Table 10.

Hydrocarbon	Colour of anion
$PhCH_2-CH=CH-CH_3$	red
$Ph_2C=CH-CH_3$	red
$PhCH=CHCH_2CH=CH-CH_3$	pale pink
$PhCH=CHCH_2C\equiv C-C_5H_{11}$	dark blue
$PhC\equiv CCH_2CH=CH_2$	red
$PhCH_2C\equiv C-C_5H_{11}$	red

The resulting red anion is alkylated predominantly at the α-position relative to the sulphur atom [88].

The isomerisation

$$\underset{\text{(XVII)}}{PhCH=CH-CH_2OR} \rightleftarrows \underset{\text{(XVIII)}}{Ph-CH_2-CH=CH-OR}$$

(where R = C_2H_5, n-C_7H_{15}) takes place readily in HMPT under the influence of bases [89]. The ethers (XVIII) are characterised by an infrared absorption band at 1660 cm^{-1}. In acid media they form the 2,4-dinitrophenylhydrazone of the corresponding ketone, which is easily identified. The ethers (XVII) can be obtained by condensing cinnamyl bromides with sodium alkoxides in oxolan. If the same reaction is accomplished in HMPT, or the sodium derivatives of the cinnamyl alcohols (obtained in HMPT) are treated with alkyl halides RX, the ethers (XVIII) are the main products. The isomerisation of (XVII) into (XVIII) is effected by means of alkoxides in basic solvents. The ethers (XVII) dissolve in HMPT and form red anions under the action of sodamide, the colour subsequently becoming dark blue. Non-distillable products were isolated on hydrolysis. Isomerisation of (XVII) into (XVIII) is rapid in the presence of dry sodium t-butoxide in a 1 : 9 mixture of HMPT and benzene.

Thus the mesomerism of carbanions under the influence of bases in HMPT can be represented

$$Ph-CH=CH-\bar{C}H-OR \longleftrightarrow Ph-\bar{C}H-CH=CH-OR$$

However, it appears that dimethyl sulphoxide may be a better solvent for the isomerisation of alkenes. Thus in the presence of potassium t-butoxide but-1-ene isomerises into but-2-ene more readily in dimethyl sulphoxide than in HMPT and tetramethylurea [90].

C. USE OF ANIONS

Reactions involving the intermediate formation of anions occur more rapidly in dipolar aprotic solvents. Thus the rate of alkylation of derivatives of sodiomalonic ester in benzene is greatly increased by the addition of 10–20% of such a solvent [91], and the use of pure HMPT increases the reaction velocity with ethyl and butyl bromides by factors of 21 and 54 respectively. Dimethyl sulphoxide as solvent has a less marked effect on the rate of the corresponding reactions, which are accelerated by factors of 6.3 and 15 respectively.

Substitution Reactions

(*a*) Carbon–halogen bond

Halogen–halogen exchange

$$MX + RX' \rightleftarrows RX + MX'$$

involves nucleophilic substitution of X′ for X, but the result depends on the nature of the protic or aprotic solvent[3]. The specific solvation of the halogen in the alkyl halides by hydrogen bonding is significant in protic solvents. Solvation is stronger with small anions, so that the nucleophilic character of the halide anions is opposite to their basic strength:

$$I^- > Br^- > Cl^- > F^-$$

In dipolar aprotic solvents, on the other hand, nucleophilic character and basic strength of the anions coincide.

In HMPT exchange reactions often compete with those involving elimination

$$X^- + R{-}\underset{\displaystyle H}{\underset{|}{CH}}{-}CH_2{-}X' \rightleftarrows R{-}CH{=}CH_2 + HX + X'^-$$

Table 11 gives exchange results for the reaction $n\text{-}C_7H_{15}Br + MX$.[92] The conversion RBr → RCl is effected by the action of lithium chloride, although such exchange is generally accomplished by the use of halides of metals in subgroups 1b and 2b. Potassium iodide brings about a 73% yield in the reaction RBr → RI.

Table 11.

MX	Solvent	Temp., °C	Duration of reaction, h	min	Substitution, %	Elimination, %	Unchanged bromide, %
LiF	HMPT-oxolan	65	7	15	3	0	68
LiF	HMPT*	160–180	9	30	15.5	53.5	0
LiF	HMPT	100	36		1	32	46
$LiF+Li_2CO_3$	HMPT	100–110	36	30	0	51.5	5.5
LiCl	HMPT-oxolan	65	9	15	72	6.5	10
LiCl	HMPT*	160–240	5		0	25	0
LiCl	HMPT	90	48	30	34	49	17
$LiCl+Li_2CO_3$	HMPT	100	48		41.5	0	30
$LiCl+C_7H_{15}Cl$	HMPT	100	11	30		1	82
NaF	HMPT-oxolan	65	10		0.8	0	78
NaF	HMPT	90	10		0	9	87
$NaF+Na_2CO_3$	HMPT	100	10	20	0	62	6
NaCl	HMPT	90	9	20	7	0	84
KF	HMPT-oxolan	65	9		5	0	45
KF	HMPT	100	10	30	1	2	84
KI	HMPT-oxolan	65	9	45	41	0	3
KI	HMPT	110	10	20	73	0.5	8
Cu_2Cl_2	HMPT-oxolan	65	9	45	22	0	53
u_2Cl_2	HMPT	100	47	30	30	19	3

*Distilled off as produced.

In HMPT the fluoride and chloride ions are especially strong bases, and are able to eliminate hydrogen bromide from secondary bromides (Table 12).[92] The extent of elimination is increased by neutralising the hydrogen bromide evolved with lithium carbonate. This is a good method for the preparation of alkenes.

Toluene-p-sulphonates of tertiary alcohols do not form alkenes on reaction with lithium chloride in HMPT (exchange is very rapid even in the cold)[92]:

$$H_3C{-}C_6H_4{-}SO_2OC(CH_3)_3 \xrightarrow[HMPT]{LiCl} CH_3{-}C_6H_4{-}SO_2OLi + (CH_3)_3C{-}Cl$$

Which reaction occurs is greatly affected by the temperature: at ~60°C substitution is favoured; at 100–110°C elimination predominates.

Table 12.

MX	Solvent	Temp., °C	Duration, h	min	Substitution, %	Elimination, %	Unchanged, %
LiF	HMPT	90–100	8	50	0	74	11.5
LiCl	HMPT-oxolan	65	9	20	10	27	33
LiCl	HMPT	90	10	10	13	73.5	9
$LiCl+Li_2CO_3$	HMPT	90	10		7	79	4

(*b*) Carbon–oxygen bond

Table 13 gives results for alkylation with the formation of *O*-substituted products[70].

The basic character of the anions RO^- is exhibited in various elimination reactions—formation of an epoxide, formation of the alkenes, oct-1-ene and butadiene, by the action of sodium ethoxide and sodium butoxide on tetramethylene dibromide.

Table 13.

Compound	Sodium compound	Solvent	Reagent	Product	Yield, %
BuOH	NaH	HMPT	$PhCH_2Cl$	$BuOCH_2Ph$	89
BuOH	NaH	oxolan	$PhCH_2Cl$	$BuOCH_2Ph$	30
t-BuOH	NaH	oxolan-HMPT	$PhCH_2Cl$	t-$BuOCH_2Ph$	67
$CH_2{=}CH{-}CH_2OH$	NaH	ditto	$C_8H_{17}Br$	$C_8H_{17}OCH_2CH{=}CH_2$	54
$CH_2OH{-}CH_2OH$	NaH	"	$PhCH_2Cl$	$(PhCH_2OCH_2{-})_2$	71
$EtOCH_2{-}CH_2OH$	NaH	"	EtI	$EtOCH_2{-}CH_2OEt$	68
$HO(CH_2)_2OH$	NaH	"	EtBr	$EtO(CH_2)_2OEt$	61
$HO(CH_2)_3OH$	NaH	"	PhBr	$PrO(CH_2)_3OPr$	40
PhOH	NaH	"	$PhCH_2Cl$	$PhOCH_2Ph$	quant.
PhOH	NaH	"	BuCl	$PhOC_4H_9$	86
PhOH	NaH	"	$C_6H_{13}Br$	$PhOC_6H_{13}$	96
PhOH	NaH	"	$Br(CH_2)_3Br$	$PhO(CH_2)_3OPh$	quant.
PhOH	NaH	"	$Br(CH_2)_4Br$	$(PhOCH_2CH_2{-})_2$	quant.
$Me_2C(OH)CH_2Br$	$NaNH_2$	HMPT		$Me_2C{-}CH_2$ (O)	57
EtCOOH	NaH	oxolan-HMPT	C_2H_5COCl	EtCOOCOEt	40
$C_5H_{11}COOH$	NaH	–	EtI	$C_5H_{11}COOEt$	76
$O{=}C(OK)(OK)$	NaH	HMPT	$PhCH_2Cl$	$O{=}C(OCH_2Ph)(OCH_2Ph)$	67

The yield of 40% resulting from acylation should be improved in a mixture of HMPT with a non-polar solvent.

(*c*) Carbon–nitrogen bond

Table 14 gives results for alkylation with the formation of *N*-substituted products[70].

Very rapid reaction occurs in HMPT between alkali-metal azides and primary bromides with the formation of organic azides:

$$RBr + N_3^- \rightarrow RN_3 + Br^-$$

With n-butyl bromide the reaction occurs more slowly in dimethylformamide and dimethyl sulphoxide than in HMPT.

The activation energy of this reaction is 15–17 and 13.5 kcal mole^{-1} in dipolar aprotic solvents and in HMPT respectively.

Table 14.

Compound	Sodium compound	Solvent	Reagent	Product	Yield, %
$PhNH_2$	$NaNH_2$	HMPT	EtI	$PhNHEt+PhN(Et)_2$	
$PhNH_2$	$NaNH_2$	HMPT	EtBr	$PhN(Et)_2$	87
$PhNH_2$	$NaNH_2$	HMPT	PhBr	Ph_3N	21
$PhNHCH_3$	$NaNH_2$	HMPT	BuI	$PhN(CH_3)(C_4H_9)$	70
Ph_2NH	$NaNH_2$	HMPT	Et_2SO_4	Ph_2NEt	85
Indole	$NaNH_2$	HMPT	$C_6H_5CH_2Cl$	1-benzylindole	81
Carbazole	NaH	oxolan	MeI	9-methylcarbazole	quant.
Phenothiazine	NaH	oxolan	MeI	10-methylphenothiazine	quant.
Phenothiazine	NaH	HMPT	MeI	10-methylphenothiazine	84
Phenothiazine	$NaNH_2$	HMPT	MeI	10-methylphenothiazine	quant.
Phenothiazine	$NaNH_2$	HMPT	Me_2SO_4	10-methylphenothiazine	quant.
CH_3CONH_2	$NaNH_2$	HMPT	$PhCH_2Cl$	$CH_3CONHCH_2Ph$	low
$EtOCNH_2$	$NaNH_2$	HMPT	BuBr	EtOCONHBu	low
CH_3—CONHPh	$NaNH_2$	HMPT	EtI	$CH_3CONPhEt$	quant.
Phthalimide	NaH	HMPT	$Br(CH_2)_4Br$	butane-1,4-diphthalimide	quant.
Phthalimide	K_2CO_3	HMPT	—	—	quant.
Phthalimide	K_2CO_3	HMPT	$BrCH_2COCH_3$	*N*-acetonylphthalimide	80
Phthalimide	$NaNH_2$	HMPT	$BrCH_2COPh$	*N*-phenacylphthalimide	77
Saccharin	NaH	oxolan	$PhCH_2Cl$	2-benzylsaccharin	50
Saccharin	NaH	HMPT	—		50

(*d*) Carbon–carbon bond

In HMPT alkylations take place with the formation of carbanions, the study of which is of great interest. In a mixture of HMPT and a non-polar solvent high yields are obtained when alkali-metal or magnesium salts were used. Thus the reaction

$$Et_3OC(CH_2)_5—Cl + NaCN \rightarrow EtO_2C—(CH_2)_5—CN$$

can give nitriles in 90% yield [93].

Various nitriles can be obtained also by the alkylation of other nitriles [94]

$PhCH_2CN$ and CH_3CN.

Table 15. RMgBr + R′–Br.

R—	R′—	R—R′	Yield, %, in oxolan	Yield, %, in HMPT
n-C_4H_9—	*n*-C_7H_{15}—	*n*-$C_{11}H_{24}$	8	42
n-C_5H_{11}—	C_6H_5CH=CH—	C_6H_5CH=CH—C_5H_{11}	30	29
n-C_5H_{11}—	$C_6H_5C\equiv C$—	$C_6H_5C\equiv C—C_5H_{11}$	10	55
n-C_5H_{11}—	$C_5H_{11}C\equiv C$—	$C_5H_{11}C\equiv CC_5H_{11}$		58
CH_3—CH=CH—	*n*-C_7H_{15}—	CH_3CH=CH—C_7H_{15}	71	43
C_6H_5—	C_6H_5CH=CH—	C_6H_5CH=CH—C_6H_5	20	20
$C_6H_5C\equiv C$—	*n*-C_5H_{11}—	$C_6H_5C\equiv C—C_5H_{11}$	0	43
$C_6H_5C\equiv C$—	CH_2=CH—CH_2—	$C_6H_5C\equiv C—CH_2CH$=CH_2	(60) (Ref.1 & 2)	66

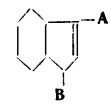
1. Condensation with Organomagnesium Compounds

In aliphatic ethers and even in oxolan aliphatic organomagnesium compounds do not react with halogenated compounds R′X in which X is not very labile, but these reactions can be conducted successfully in HMPT [95] (Table 15).

For organomagnesium derivatives of indene [96] and of fluorene [96] see Tables 16 and 17 respectively.

Reactions with organomagnesium derivatives of 2-alkylpyridines are indicated in Table 18.

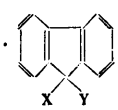
Table 16*. Organomagnesium derivatives of indene.



Organomagnesium compound	Hydrocarbon	Antagonist compound	Reaction product	Yield, %
i-PrMgCl	indene	C_2H_5I	A=C_2H_5 B=H	62
i-PrMgCl	ditto	Et_2SO_4	A=C_2H_5 B=H	92
i-PrMgCl	»	C_4H_9I	A=C_4H_9 B=H	82
i-PrMgCl	»	$CH_3C_6H_4SO_2OC_4H_9$	A=C_4H_9 B=H	64
Et_2NMgCl	»	C_4H_9I	A=C_4H_9 B=H	77
i-PrMgCl	»	$BrCH_2CH=CH_2$	B=H A=—CH_2CH=CH_2	69
i-PrMgCl	»	$CH_3CH—CH_2$ (O)	A=—CH_2—CHOH—CH_3 B=H	46
i-PrMgCl	»	$C_2H_5OCH_2Cl$	B=H A=—$CH_2OC_2H_5$	40
i-PrMgCl	»	oxolan	B=H A=—$(CH_2)_4OH$	51
i-PrMgCl	butylindene	C_4H_9I	A=B=C_4H_9	—
i-PrMgCl	ditto	CO_2 followed by esterification	A=C_4H_9 B=$COOC_2H_5$	—

*It has been shown [196] that RMgX metallises indene and fluorene derivatives in HMPT. Further reaction of the resulting organomagnesium compounds with electrophilic reagents may involve migration of the reaction centre in the case of indene (Editors).

Table 17. Fluorene derivatives.



Organomagnesium compound	Hydrocarbon	Antagonist compound	Reaction product	Yield, %
i-PrMgCl	fluorene	C_2H_5I	X=H, Y=C_2H_5	72
Et_2NMgCl	ditto	C_2H_5I	X=H, Y=C_2H_5	75
i-PrMgCl	»	$Br—CH_2—CH=CH_2$	X=H Y=CH_2—CH=CH_2	57
i-PrMgCl	»	CO_2	X=H, Y=CO_2H	81
Et_2NMgCl	9-ethylfluorene	C_2H_5I	X=Y=C_2H_5	—
i-PrMgCl	ditto	C_4H_9I	X=C_2H_5, Y=C_4H_9	20
i-PrMgCl	»	CO_2	Y=CO_2H, Y=Et	low

Under these conditions condensation can be accomplished with satisfactory yields between saturated organomagnesium compounds and alkyl halides, saturated organomagnesium compounds and alkynyl halides, and magnesium alkynyls and alkyl halides.

Organomagnesium compounds (other than aromatic Grignard reagents) react with vinyl bromide with the elimination of hydrogen bromide.

2. Condensation with Derivatives of Alkali Metals

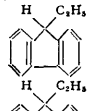
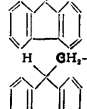
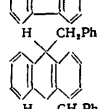
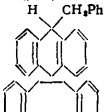
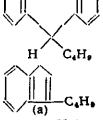
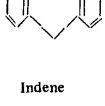
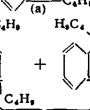
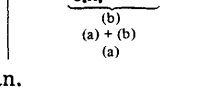
Table 19 lists some examples of condensations in which alkali-metal derivatives are used [77].

An alkyl bromide does not react with monosodium acetylide in oxolan, but such reaction is possible in dipolar aprotic solvents, in particular in dimethylformamide [97].

Table 18. Pyridine derivatives 

Solvent for Mg cpd.	Reactant	2-Substituent R	Yield, %
Oxolan	C_4H_9I	C_5H_{11}	66
Oxolan	$BrCH_2-CH=CH_2$	$CH_2CH_2CH=CH_2$	69
Ether-HMPT	$BrCH_2CH=CH_2$	$CH_2CH_2CH=CH_2$	40
Oxolan	$BrCH_2C\equiv CH$	$CH_2CH_2C\equiv CH$	30
Ether	PhCHO	$CH_2CHOH-Ph$	48
Ether-HMPT	PhCHO	$CH_2CHOH-Ph$	69
Oxolan	PhCHO	$CH_2CHOH-Ph$	71
Ether-HMPT	$CH_3COC_5H_{11}$	$CH_3-C(OH)-(CH_3)C_5H_{11}$	36
Oxolan	$CH_3COC_5H_{11}$	$CH_3C(OH)-(CH_3)C_5H_{11}$	50

Table 19.

Hydrocarbon	Metallating agent	Reagent	Reaction product	Yield, %
$PhCH_2Ph$	NaH	CO_2	$Ph_2CHCOOH$	33
$PhCH_2Ph$	$NaNH_2$	$Br(CH_2)_4Br$	$Ph_2CH(CH_2)_4CHPh_2$	87
$PhCH_2Ph$	$NaNH_2$	$ClCH_2CH_2$–N(O)	$Ph_2CHCH_2CH_2$–N(O)	70
$PhCH_2Ph$	$NaCH_2Ph$	CO_2	$Ph_2CHCOOH$	50
$PhCH_2Ph$	$NaCH_2CH=CH_2$	CO_2	$Ph_2CHCOOH$	33
Fluorene	NaH	EtI		67
Ditto	NaH	EtI*		80
«	NaH	$BrCH_2CH=CH_2^*$		55
9,10-Dihydro-anthracene	NaH	$PhCH_2Cl$		90
Ditto	$NaCH_2Ph$	$PhCH_2Cl$		50
	$NaNH_2$	BuI		68
Indene	NaH	BuI*		—
Ditto	NaH LiH	BuI	(a) + (b) (a)	61

*In oxolan.

In HMPT yields of 60–70% are obtained in such condensation (Table 20). [98]

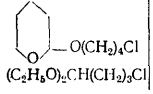
However, these reactions can be accomplished also in oxolan to which 10% of HMPT has been added, which tends to diminish the relative proportion of elimination reactions.

Table 20.

RX	Solvent	Reaction temp., °C	Further heating °C for h		Reaction product	Yield, %
n-$C_7H_{15}Br$	DMF + oxolan	40	50	4	$C_7H_{15}C\equiv CH$	52
n-$C_5H_{11}Br$	DMF + oxolan	20	100	4	$C_5H_{11}C\equiv CH$	47
n-$C_7H_{15}Br$	HMPT	5	40	1.5	$C_7H_{15}C\equiv CH$	65.6
n-$C_7H_{15}Br$	HMPT, 10 ml	20	40	3	$C_7H_{15}C\equiv CH$	72
n-$C_5H_{11}Br$	HMPT	20			$C_5H_{11}C\equiv CH$	57
$Br-(CH_2)_6-Br$	HMPT	20	40	3	$HC\equiv C(CH_2)_6C\equiv CH$	71
$C_6H_5CH=CHCH_2Cl$	HMPT	—50	0	2	$C_6H_5(CH=CH)_3C_6H_5$	8
C_4H_9OTos	HMPT	0	50	3	$C_4H_9C\equiv CH$	77
n-$C_7H_{15}Cl$	HMPT	20			$C_7H_{15}C\equiv CH$	60
n-$C_{12}H_{25}Br$	HMPT	10	70	3	$C_{12}H_{25}C\equiv CH$	72.6

The reaction goes especially well with primary halogen derivatives (bromides, chlorides) and toluene-p-sulphonates, and also when liquid ammonia is used as solvent, in which these reagents are less soluble. In HMPT the acetylide ion is a strong base, and causes considerable elimination in the cases of secondary and tertiary halides and toluene-p-sulphonates. Some of the acetylene derivatives obtained are listed in Table 21. [98]

Table 21.

RX	Solvent	Reaction temp., °C	Further heating °C for h		Reaction product	Yield, %
$C_4H_9OCH_2Cl$	HMPT	5	40	2	$C_4H_9OCH_2C\equiv CH$	32
$C_4H_9OCH_2Cl$	HMPT	—40	5	8	$C_4H_9OCH_2C\equiv CH$	12.5
$C_4H_9OCH_2Cl$	oxolan	20	75	1	$C_4H_9OCH_2C\equiv CH$	18
	HMPT	20	50	2.5		47
$(C_2H_5O)_2CH(CH_2)_3Cl$	HMPT	20	40–50	1	$(C_2H_5O)_2CH(CH_2)_3C\equiv CH$	47

Alkynes containing a trialkylgermyl group can similarly be obtained [99] in 60% yield:

$$Et_3Ge(CH_2)_4Br + NaC\equiv CH \rightarrow Et_3Ge(CH_2)_4C\equiv CH$$

The same method enables disubstituted derivatives of alkynes to be obtained under mild conditions [100] (Table 22). In procedure A sodium hydride in oxolan is used if the subsequent reaction is carboxylation or alkylation. In procedures B and C the active reagent is sodamide in HMPT in the cold:

$$CH\equiv CH \xrightarrow[\text{oxolan}]{Na} CH\equiv C-Na \xrightarrow[HMPT]{RX} R-C\equiv C-H \rightarrow$$

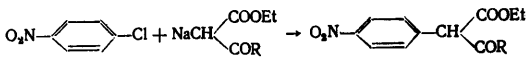
$$\xrightarrow[HMPT]{NaNH_2} R-C\equiv C-Na \xrightarrow{R'X} R-C\equiv C-R'$$

Similarly, substituted alkynylamines can be obtained [84] by the use of RX or toluene-p-sulphonates:

$$(R)(R')N-C\equiv C-Li \xrightarrow{RX} (R)(R')N-C\equiv C-R$$

Tables 23 and 24 give data on the alkylation of various compounds [101].

Nucleophilic aromatic substitution is accelerated in dipolar aprotic solvents, but this applies only to the reactions of halogenated benzenes. Thus *o*- and *p*-chloronitrobenzenes and their derivatives arylate sodiomalonic and sodioacetoacetic esters in high yield [102]:

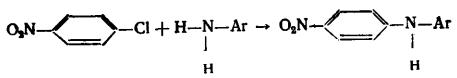


where R = OC_2H_5, CH_3. Reaction is most rapid in HMPT. The comparable solvents can be arranged in the sequence HMPT > dimethyl sulphoxide > dimethylformamide.

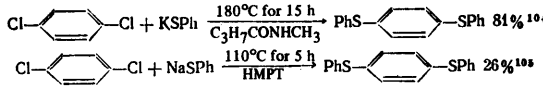
Table 22.

Alkyne	Procedure	Reagent	Product	Yield, %
Acetylene	C	BuBr	$BuC{\equiv}C{-}Bu$	50
Hexyne	B	BuBr	$BuC{\equiv}C{-}Bu$	74
Ditto	B	$C_5H_{11}Br$	$C_4H_9C{\equiv}C{-}C_5H_{11}$	77
»	B	$ClCH_2OEt$	$C_4H_9C{\equiv}C{-}CH_2OEt$	64
»	A	$Br(CH_2)_4Br$	$BuC{\equiv}C(CH_2)_4C{\equiv}CBu$	63
»	A	$Br(CH_2)_3Cl$	$BuC{\equiv}C(CH_2)_3Cl$	51
Heptyne	A(NaH)	BuI	$C_5H_{11}C{\equiv}C{-}C_4H_9$	47
Ditto	A	BuI	$C_5H_{11}C{\equiv}C{-}C_4H_9$	64
»	A	$C_7H_{15}Br$	$C_5H_{11}C{\equiv}C{-}C_7H_{15}$	79
»	A	$C_4H_9C{\equiv}C(CH_2)_3I$	$C_5H_{11}C{\equiv}C(CH_2)_3C{\equiv}CBu$	72

Partial replacement of chlorine by the dimethylamino-group does not occur in HMPT, unlike the reaction in dimethylformamide. The reaction velocity in HMPT is especially increased in the presence of copper [103]:



Reaction with *p*-dichlorobenzene occurs very slowly:



Some examples of arylation with bromobenzene and chlorobenzene under quite mild conditions have been reported in which the yields were satisfactory [70,106]. The reactions must occur by a mechanism of cleavage and addition, although the intermediate formation of dehydrobenzene has not been demonstrated.

Table 25 gives the results for several reactions [106].

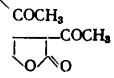
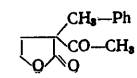
Table 23.

Metallated compound	Agent	Solvent	Reagent	Product	Yield, %
$PhCH_2COOH$	$NaNH_2$	oxolan + HMPT	$(CH_3)_2CHI$	$Ph{-}CH(CH(Me)_2){-}COOH$	60
$PhCH_2COOH$	$NaNH_2$	oxolan	$PhCH_2Cl$	$Ph{-}CH(CH_2{-}Ph){-}COOH$	70
$PhCH_2CN$	NaH	HMPT	$PhCH_2Cl$	$Ph{-}CH(CH_2Ph){-}CN + PhC(CH_2Ph)_2(CN)$	
$PhCH_2CN$	$NaNH_2$	ditto	$PhCH_2Cl$	$Ph{-}CH(CH_2Ph){-}CN + PhC(CH_2Ph)_2(CN)$	
$PhCH_2CN$	NaH	«	BuI	$Ph{-}CH(Bu){-}CN$	86
$PhCH(Bu)CN$	NaH	«	BuI	$PhC(C_4H_9)_2CN$	95

3. Alkylation of Ambident Ions

Insufficient study has hitherto been made of the relative reactivities of the different nucleophilic centres in ambident ions. Different alkylation products are obtained

Table 24.

Metallated compound	Metallating agent	Reagent	Compound obtained
$H_2C(COOEt)_2$	NaH	$BrCH_2CH{=}CH_2$	$CH_3{=}CHCH_2CH(COOEt)_2$ (A) + $(CH_2{=}CHCH_2)_2C(COOEt)_2$ (B)
$H_2C(COOEt)_2$	NaH	$Br(CH_2)_3$	$CH_2(CH_2)C(COOEt)_2$ (A) + $(COOEt)_2C(H)(CH_2)_3C(H)(COOEt)_2$ (B)
*$H_2C(COOEt)_2$	$NaNH_2$	$BrCH_2CH{=}CH_2$	A+B
$H_2C(COOEt)_2$	KOH	$BrCH_2CH{=}CH_2$	A
$H_2C(CN)(COOEt)$	NaH	$BrCH_2CH{=}CH_2$	$CH_2{=}CHCH_2CH(CN)(COOEt)$ + $(CH_2{=}CHCH_2)_2C(CN)(COOEt)$
$H_2C(CN)_2$	KOH	$PhCH_2Cl$	$PhCH_2CH(CN)_2 + (PhCH_2)_2C(CN)_2$
$H_2C(COOEt)(COCH_3)$	NaH	$BrCH_2CH{=}CH_2$	$CH_2{=}CHCH_2CH(COOEt)(COCH_3)$ + $(CH_2{=}CHCH_2)_2C(COOEt)(COCH_3)$
$H_2C(COCH_3)_2$	NaH	$BrCH_2CH{=}CH_2$	$CH_3{=}CHCH_2CH(COCH_3)_2 + (CH_3{=}CHCH_2)_2C(COCH_3)_2$
	NaH	$PhCH_2Cl$	

*In oxolan.

depending on the nature of the cation, the alkylating agent, and the solvent. Little information is yet available on the part played by HMPT ¶.

In a study of the reaction of bromoethane with sodium phenoxide and 2-naphthoxide it was shown that the percentage of *O*-alkylated products increased with the basic character of the solvent [107]† (see Table 26).

Table 25.

Ph—X	Reagent	Product	Yield, %
PhBr	EtSH	Pt—S—Et	52
PhBr	*n*-BuSH	Ph—S—Bu	66
PhBr	PhSH	Ph—S—Ph	40
PhBr	Ph—CH_2—SH	Ph—S—CH_2—Ph	12
PhBr	Et_2NH	Ph—NEt_2	65
PhBr	HN⟨⟩	PhN⟨⟩	74
PhBr	Ph—NH—CH_3	Ph_2NCH_3	55
PhBr	Ph—C≡C—H	Ph—C≡C—Ph	45
PhBr	Ph_3CH	Ph_4C	57
PhCl	Et_2NH	$PhNEt_2$	30
PhCl	HN⟨⟩	Ph—N⟨⟩	84
PhCl	Ph—NH—CH_3	Ph_2NCH_3	55
PhCl	Ph—C≡C—H	PhC≡C—Ph	40
PhCl	Ph—CH_2—CN	Ph_2CHCN	60
PhF	HN⟨⟩	PhN⟨⟩	80
PhF	$HNEt_2$	Ph—NEt_2	65

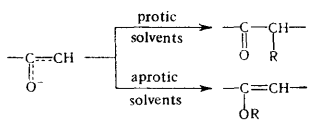
The mechanism of the reaction has been discussed [3]. Our results show that in HMPT alkylation occurs predominantly (86–100%) with the formation of *O*-substituted products [70].

When pyrrole is alkylated in a basic solvent, *N*-alkylated products are formed (at the more electronegative element) [108]. Benzyl chloride reacts with sodium indole in HMPT to give an 81% yield of *N*-benzylindole [70].

Table 26.

Solvent	Alkylation	
	C-derivative, %	*O*-derivative, %
CH_3OH	35	65
CF_3CH_2OH	93	7

In protic solvents (alcoholic alkalis) the enolates of ketones form mainly *C*-alkylated products [109]. It has recently been shown [110] that *O*-alkylated products—ethers of the enols—predominate in dipolar aprotic solvents:



¶For the influence of HMPT on the alkylation of the enolates of acetoacetic ester and pentane-2,4-dione see Refs. 196 and 197 (Editors).

†The changed ratios of *O*- and *C*-substituted products was explained [107] by selective solvation—by the formation of strong hydrogen bonds by the fluorinated alcohol (Editors).

The alkylating agent used was $(C_2H_5)_3OBF_4$ or an alkyl sulphate [110] (Table 27).

The effect of the solvent on the direction of alkylation of sodium ketones was first mentioned in a discussion of the reaction between bromoethane and the sodium derivative of diphenylacetophenone [111]:

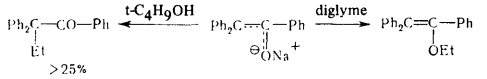
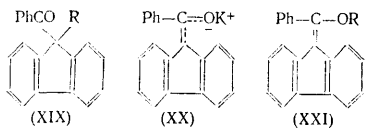


Table 27.

Ketone	Cyclohexanone		Acetophenone	Pentane-2,4-dione	Acetoacetic ester
Solvent*	DME	DMSO	DMSO	DMSO	DMSO
Unchanged material, %	32	11	16	13	0
Ether of enol, %	24	71	68.5	71	75
Other products**, %	44	18	15.5	16	25

*DME = 1,2-dimethoxyethane. HMPT was not used.
**C-Derivatives and poly-*O*- and -*C*-derivatives.

Alkylation of the potassium enolate (XX) in various solvents, including HMPT, gave *C*- and *O*-alkylated products (XIX and XXI) [112] (Table 28), isopropyl bromide being used as alkylating agent.



(XIX) (XX) (XXI)

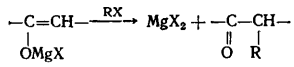
Table 28 shows that the yield of the enol ether is considerably increased in HMPT, which is capable of considerable solvation of alkali-metal cations.

Table 28.

Solvent	Dielectric constant ε	Alkylation	
		C-derivatives, %	*O*-derivatives, %
Protic			
t-C_4H_9OH	10–11	96	4
C_2H_5OH	24–55	83	17
CH_3OH	32–33	82	18
Aprotic			
Diglyme	7–7.5	61	39
Oxolan	7–7.5	90	10
HMPT	29–30	44	56
DMSO	45–49	72	28

Weaker bases, such as organomagnesium compounds, react with enolisable ketones in the presence of HMPT to give yields of magnesium derivatives of the enolic form [113]. Table 29 gives data on the reaction between various organomagnesium compounds and di-isopropyl ketone [113]. The action of n-butylmagnesium bromide at 55°C produces considerable enolisation [113] in the ketones—butanone (75%), 2,4-dimethylpentan-3-one (95%), and cyclohexanone (90%).

In HMPT magnesium enolates are alkylated at a carbon atom by alkyl sulphates, toluene-*p*-sulphonates, and methyl iodide [114]:



this being impossible in solvents of low polarity.

Table 29.

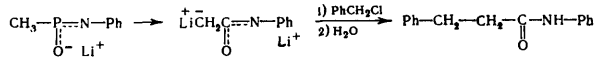
Organomagnesium compound	Enolisation	Reduction	Addition
CH_3MgBr	33	0	66
EtMgBr	100	trace	trace
Et_2Mg	40	trace	60
n-BuMgBr	100	0	trace
$(n\text{-Bu})_2Mg$	60	trace	40
i-PrMgBr	100	0	0
$(i\text{-Pr})_2Mg$	100	0	0

In the presence of strongly solvated cations (alkali-metal derivatives) *N*-alkylation takes place, with the formation of sodium iminoalkenylamines [115] (Table 30). With iodoethane high yields of *C*-alkylated derivatives are formed.

Table 30.

Solvent Base Imine	Diethylcellosolve Sodium hydride Acetophenone anil			HMPT, sodamide *N*-ethylcyclohexanimine			 *N*-ethylpentan-3-imine		
Alkylating agent	Et_3OBF_4	Et_2SO_4	EtI	Et_3OBF_4	Me_2SO_4	EtI	Et_3OBF_4	Me_2SO_4	EtI
Unchanged materials	8	9	5	29	11	15	26	17	20
Alkenylamine	88	49	5	53	75	17	29	57	0
C-Alkylated product	4	42	90	18	10	56	42	26	71
Polyalkylated product	—	—	—	—	4	12	3	0	9

Under the influence of a sufficiently strong base an ambident anion is able to form a dianion. Thus acetanilide has been quantitatively *N*-alkylated after the addition of sodamide in HMPT. [70] In liquid ammonia this reaction leads to the formation of a singly charged anion, but in excess of n-butyl-lithium in ether or oxolan a dianion is formed, with the formation of *C*-alkylated derivatives [116]:



Similar results can be obtained with methanesulphonamides [117].

4. Formation of Cyclopropane Compounds and Stereochemistry

Cyclopropane derivatives can be obtained by condensing unsaturated compounds (esters, nitriles, ketones) with carbanions formed from various α-halogen derivatives (esters, nitriles, ketones). The formation of these compounds is immensely influenced by the solvent: thus the following reaction yields the *cis*-isomer in benzene, and the *trans*-isomer in HMPT:

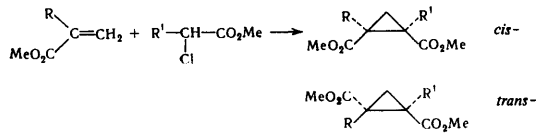


Table 31 gives some quantitative results on the formation of *cis*- and *trans*-isomers of various cyclopropane derivatives in benzene and in a mixture of benzene and HMPT [118,119].

Table 31.

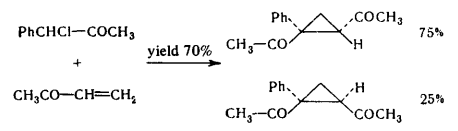
R and R′	Yield, %	Isomers, %	
		trans	*cis*
	C_6H_6		
R=R′=CH_3	71	7	93
R=H, R′=CH_3	70	17	83
R=R′=Et	55	0	100
R=H, R′=Ph	43	0	100
R=CH_3, R′=Ph	38	0	100
	C_6H_6 + HMPT (50:50)		
R=R′=CH_3	60	64	36
R=H, R′=CH_3	70	90	10
R=R′=Et	67	75	25
R=H, R′=Ph	65	56	21
R=CH_3, R′=Ph	46	43	25

A similar experiment has been made with α-chlorinated ketones. The highly reactive carbanion formed in HMPT enabled α-halogeno-ketones to be used, as the presence of a hydrogen atom in the α′-position made it possible for this reaction to compete with the Favorskii reaction; and also permitted the use of but-3-en-2-one, which under ordinary conditions polymerises before it can react. The reactions undergone by the butenone with various compounds and the yields are listed in Table 32. [120]

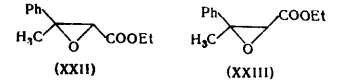
Table 32.

CH_3—CO—CH=CH_2	ROOC—CHCl—COOR	73
	Ph—CHCl—$COCH_3$	70
	Ph—CHCl—COOR	58
	CH_3—CHCl—$COCH_3$	40
	CH_3CHCl—COOR	10

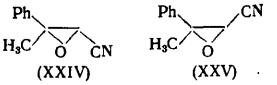
The investigations have refined the stereochemistry of the condensation



In HMPT the Darzens reaction between acetophenone and ethyl chloroacetate [121] leads to the formation predominantly of the isomer (XXII) (Table 33).



The reaction between acetophenone and chloroacetonitrile results in the epoxides (XXIV) and (XXV)



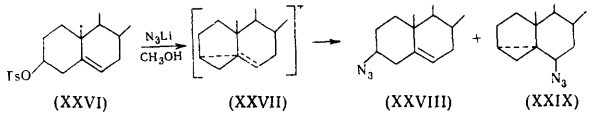
(XXIV) (XXV)

In HMPT a good yield is obtained, but approximately equal quantities of the isomers are formed [Table 34].

Table 33.

Solvent	Base	Duration of reaction, h	Yield, %	(XXII), %
Hexane	NaH	18	50	53
	NaH	8	25	50
Benzene	$NaNH_2$	8	40	50
Benzene		1.5	30	51
HMPT	$t\text{-}C_4H_9OK$	8	57	48
	NaH	1.5	70	59

Another example of the influence of the solvent on the mechanism and the stereochemistry of reactions occurs in steroid chemistry. The 5-en-3β-yl toluene-*p*-sulphonate (XXVI) [122] and the 20β-yl compound (XXX) [123] form different products, depending on the type of solvent (protic or aprotic), on reaction with alkali-metal azides. In methanol the compound (XXVI) yields, via an intermediate carbonium ion (XXVII), derivatives of an inactive steroid (XXIX) (S_N1 mechanism).

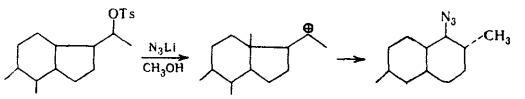


(XXVI) (XXVII) (XXVIII) (XXIX)

Table 34.

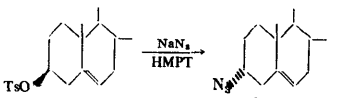
Solvent	Base	Duration of reaction, h	Yield, %	(XXIV), %
Benzene	$NaNH_2$	1.5	5	58
	$t\text{-}C_4H_9OK$	—	50	64
$t\text{-}C_4H_9OH$	$t\text{-}C_4H_9ONa$	—	60	63
HMPT-$t\text{-}C_4H_9OH$	$t\text{-}C_4H_9OK$	—	73	55
HMPT	NaH	—	62	45

The toluene-*p*-sulphonate (XXX) yields, on rearrangement of the intermediate carbonium ion (XXXI), the D-homo-derivatives (XXXII):



(XXX) (XXXI) (XXXII)

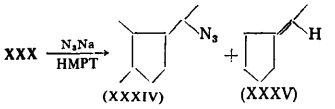
In aprotic dipolar solvents such reactions occur by an S_N2 mechanism with inversion of configuration:



(XXXIII)

The yield of the product (XXXIII) increases with the basic character of the solvent S (Table 35).

The toluene-*p*-sulphonate (XXX) forms mainly the 20α-azide (XXXIV) together with, owing to elimination, a small quantity of the derivative (XXXV):



(XXXIV) (XXXV)

Table 35.

Solvent	DMSO	*N*-Methylpyrrolidone	HMPT
(XXXIII), %	30	71	93

The yield of the product (XXXIV) also increases with the basic character of the solvent, as is evident from Table 36.

Reducing the azides with lithium tetrahydroaluminate gives good yields of the corresponding aminosteroids.

Table 36.

Solvent	DMSO	*N*-Methylpyrrolidone	HMPT
(XXXIV), %	46	53	65

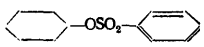
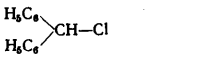
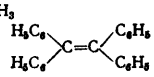
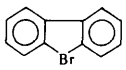
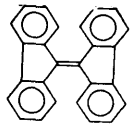
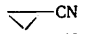
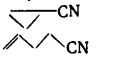
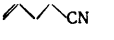
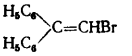
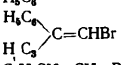
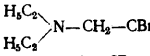
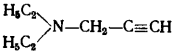
Table 37.

RMgX	Halogenated vinyl	Product	Yield, %	Ref.
$n\text{-}C_4H_9MgBr$	$n\text{-}C_3H_{11}CCl{=}CHCl$ (*cis*)	$C_5H_{11}C{\equiv}C{-}Cl$	14	124
		$+C_5H_{11}C{\equiv}C{-}C_4H_9$	10	
$n\text{-}C_7H_{15}MgBr$	$CHCl{=}CCl_2$	$C_7H_{15}C{\equiv}C{-}Cl$	48	125
$n\text{-}C_5H_{11}MgBr$	PhCH=CHBr	$PhC{\equiv}C{-}H$	27	126
PhMgBr	PhCH=CHBr	$PhC{\equiv}C{-}H$	20	126

Elimination Reactions

Reactions involving elimination may lead to the formation of carbenes, alkynes, or arynes. It has been noted earlier that the basic character of anions is most strongly developed in HMPT, so that elimination is often accompanied by nucleophilic substitution (S_N2). In HMPT elimination of hydrogen halides and of groups attached to sulphur is possible, but no systematic studies have yet been made of such processes. Halogenated vinyl compounds very readily undergo elimination under the influence of weak bases (organomagnesium compounds) in HMPT (Table 37).

Table 38.

Initial cpd.	Basic agent	Solvent	Principal product	Yield, %
	$NaNH_2$	HMPT		58 (dibrominated cpd.)
$C_6H_5CH_2Cl$	$NaNH_2$	HMPT	unchanged $C_6H_5CH_2Cl$ $(C_6H_5CH_2)_3N$ as hydrochloride	35—40 32*
$C_6H_5CH_2Cl$	$NaNH_2$	HMPT oxolan	*trans*-$C_6H_5CH{=}CHC_6H_5$ *trans*-$C_6H_5CH{=}CHC_6H_5$	— 50 (unpurified 67)
$C_6H_5CH_2Cl$	NaH	HMPT	unchanged $C_6H_5CH_2Cl$ $C_6H_5CH_3$, $C_6H_5CH_2CH_2C_6H_5$ $C_6H_5CH{=}CHC_6H_5$ + unidentifieds	65 —
$C_6H_5CH_2Br$	$NaNH_2$	HMPT benzene	$(C_6H_5CH_2)_3N$	79**
$C_6H_5CH_2Br$	NaH	HMPT	$C_6H_5CH_2{-}CH_2{-}C_6H_5$ $C_6H_5CH_3$	62 (unpurified 72) 16
	$NaNH_2$	HMPT		87
	$NaNH_2$	HMPT benzene		60
$Cl{-}(CH_2)_3{-}CN$	$NaNH_2$	HMPT		54
$Cl{-}(CH_2)_3{-}CN$	NaH	HMPT		84
$CH_3CHCl{-}(CH_2)_2{-}CN$	NaH	HMPT		31
$Cl{-}(CH_2)_4{-}CN$	NaH	HMPT		40
	$NaNH_2$	HMPT	$C_6H_5C{\equiv}C{-}C_6H_5$	80 (unpurified 89)
	see Table II in Ref.128		$C_6H_5C{\equiv}C{-}CH_3$	20—40
$C_6H_5CH{=}CH{-}Br$	NaH	HMPT	$C_6H_5C{\equiv}C{-}H$	78
	$NaNH_2$	HMPT		73
$CH_3{-}(CH_2)_5{-}CBr{=}CH_2$	$NaNH_2$	HMPT	$CH_3{-}(CH_2)_5C{\equiv}CH$	70

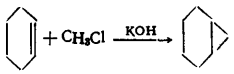
*Contains no unchanged benzyl chloride.
**Isolated as hydrochloride.

Elimination products can be obtained from various compounds by the action of H^-, NH_2^-,[127,128] and $CH{:}C^-$ [129] in HMPT. Table 38 shows that several of the reactions—the production of cyclopropyl cyanide, the production of acetylenic derivatives with and without rearrangement—give good yields. The action of such a strong nucleophile as NH_2^- on benzyl bromide in a mixture of HMPT and benzene yields tribenzylamine.

Compounds containing an α-halogen atom form stilbene or polyenes both in liquid ammonia and in HMPT. Analogous elimination is produced by the action of the acetylide ion on cinnamyl chloride, when 1,6-diphenylhexa-1,3,5-triene is obtained [129]:

$$PhCH{=}CH{-}CH_2Cl \rightarrow Ph{-}(CH{=}CH)_3Ph$$

It has been shown that these reactions do not involve the intermediate formation of carbenes, although in principle this seems possible: the reaction of chloroform and potassium hydroxide with cyclohexene in HMPT produces norcarane [130]:



Compounds containing sulphur can also undergo elimination. Thus alkenes are formed when arenesulphonates are heated in dipolar aprotic solvents [131] (Table 39):

$$-\underset{\underset{OSO_2Ar}{|}}{CH}{-}CH_2{-} \rightarrow -CH{=}CH{-} + ArSO_3H$$

Table 39.

Sulphonate	Solvent	Temp., °C	Time, h	Alkene	Yield, %
Cyclohexyl toluene-p-	DMSO	90—95	5	cyclohexene	61
	HMPT	100	6	cyclohexene	62
1-Methylheptyl benzene-	DMSO	100—107	0.75	octene	52
	HMPT	100	3	octene	61.5

When cyclohexyl benzenesulphonate is heated in the presence of sodamide in HMPT to 40°C, cyclohexene is formed (58%).[128] In HMPT the acetylide anion converts ethoxyethyl methanesulphonate into ethoxyethylene $CH_2{:}CH.OC_2H_5$.[129]

The autoxidation of thiols, disulphides, sulphones, and sulphoxides is often accompanied by undesirable β-elimination with the formation of alkenes [132]:

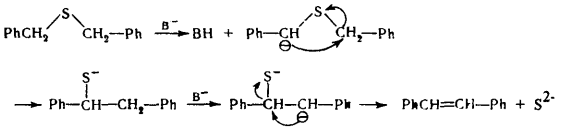
$$R-\bar{C}H-CH_2-\bar{S} \rightarrow R-CH=CH_2 + S^{2-}$$
$$R-\bar{C}H-CH_2-S-S-R \rightarrow R-CH=CH_2 + R-S-S^-$$
$$\bar{C}H_2-CH(CH_3)-SO-C_3H_7 \rightarrow CH_3-CH=CH_2 + C_3H_7SO^-$$

In protic solvents aliphatic sulphones are decomposed with difficulty to alkenes (the action of potassium hydroxide requires temperatures above 200°C), but the same compounds in HMPT undergo elimination at 80°C, although reaction is slow [133] (Table 40).

Table 40. Elimination (KOH–HMPT at 80°C).

Reactant	Product	Time, h	Yield, %
$(CH_3)_3C-S-S-C(CH_3)_3$	isobutene	20 141	36 63
$(CH_3)_3C-S-C(CH_3)_3$	isobutene	20 141	2 11
	butadiene	150	1
$i\text{-}C_3H_7-SO-C_3H_7$ $n\text{-}C_4H_9S-C_4H_9$ ‖ O	propene isomeric butenes	141 141	28 10

In the presence of a base B^- [134] HMPT promotes the conversion of dibenzyl sulphide, through an intermediate carbanion, into stilbene:



It thus becomes clear why this sulphide can be obtained in high yield in oxolan:

$$PhCH_2SH \xrightarrow[2)\ PhCH_2Cl]{1)\ NaNH_2} S(CH_2-Ph)_2 \quad (83\%)$$

whereas in HMPT a considerable amount of stilbene is formed [135].

Autoxidation of Anions

Effective autoxidation of a large number of compounds which form anions is possible at room temperature [136]. The reactions occur especially efficiently in dimethylformamide or dimethyl sulphoxide in the presence of potassium t-butoxide as base. The following mechanism is possible [137] for the oxidation of toluene—formation of carbanion

$$PhCH_2-H + B^- \rightarrow BH + BHCH_2^- \quad (1)$$

formation of benzyl radical

$$PhCH_2^- + O_2 \rightarrow Ph-CH_2^{\cdot} + O^{-\cdot} \quad (2)$$

formation of peroxy-radical

$$PhCH_2^{\cdot} + O_2 \rightarrow PhCH_2-O-O^{\cdot} \rightarrow \quad (3)$$

Autoxidation is more rapid the more rapidly is the carbanion formed.

The possibility of using HMPT as reaction medium in autoxidation was first noted by Wallace. It is to be preferred to other dipolar aprotic solvents for two main reasons.

1. It cannot give a carbanion, and therefore its oxidation is impossible. If isotopic exchange is carried out in the presence of a base between toluene, in which the methyl group is labelled with tritium, and various dipolar solvents, the times indicated in Table 41 are required for 10% exchange to occur [138].

Table 41.

Solvent	Time, min
Dimethyl sulphoxide	6
Dimethyl sulphone	12
1-Methylpyrrolid-2-one	48
Thiolan 1-monoxide	420
HMPT	14000

Table 41 shows almost complete absence of exchange with HMPT, the hydrogen atoms in which occupy the β-position with respect to the PO group. Dimethyl sulphoxide undergoes considerable autoxidation, which is possible also with diglyme and dioxan [139].

2. It is stable to the action of bases (even potassium hydroxide at 80°C), and is therefore more convenient than carboxyamides and lactams.

Table 42.

RSH (mole)	KOH/RSH	Solvent	RSH converted, %	Yield of RSO_2H, % (*a*)	Yield of R_2S_2, % (*a*)	Temp., °C	Time, h
C_6H_5SH (0.025)	4	HMPT	99	90	6.4	23.5	12
C_6H_5SH (0.025)	4	DMF	100	91	4.7	23.5	22
C_6H_5SH	4	HMPT	98	92.5	3.8	80	29
$o\text{-}CH_3C_6H_4SH$ (0.025)	4	HMPT	100	80	21	23.5	24
$o\text{-}CH_3C_6H_4SH$ (*b*) (0.025)	4	HMPT	99	95	4.5	80	24
$p\text{-}CH_3C_6H_4SH$ (0.025)	4	HMPT	100	94	6.4	80	24
$o\text{-}HOOC-C_6H_4SH$ (0.025)	4	HMPT	99	96	4.6	80	24
$(CH_3)_3CSH$ (0.024)	4	HMPT	99	71.6	25	23.5	12
$1\text{-}C_{16}H_{33}SH$ (0.025)	4	HMPT	91.6	38.4	55.6	23.5	24
$1\text{-}C_{16}H_{33}SH$ (0.025)	4	HMPT	97.5	96	0.5	80	21
$(C_5H_{11})_3CSH$	4	HMPT	100	62.5	37.4	80	42

(*a*) 100 x moles of product/theoretical moles.
(*b*) *o*-Sulphobenzoic acid is not formed.

Thiols and disulphides are oxidised to sulphonic acids in the highest yields (95–100%) in HMPT:[140]

$$RSH \rightarrow RSO_3H$$
$$R_2S_2 \rightarrow RSO_3H$$

Tables 42 and 43 [140] give data on the oxidation of thiols and disulphides by bases (only potassium hydroxide was used as base in Table 42).

The autoxidation of sulphides yields a mixture of carboxylic and sulphonic acids [141]. Tables 44 and 45 give data on the oxidation of sulphides.

The reaction of sulphoxides with potassium t-butoxide in HMPT at 80°C results in the formation of a mixture of carboxylic and sulphonic acids [142] (Table 46).

Ketones undergo autoxidation to acids, cyclic ketones forming dibasic acids (Tables 47 and 48). The reaction velocity is higher in HMPT than in the other two solvents: HMPT > t-C_4H_9OH ≫ water. Of the three bases—potassium, sodium, and lithium hydroxides—the first two are the more effective (the reactions occur with surprisingly high yields). The character of the ketones is also of significance, those of them which easily form carbanions undergoing autoxidation more rapidly [143].

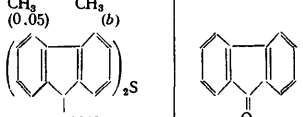
Table 43.

R_2S_2 (0.0125 M)	Solvent	Base (0.1 M)	Temp., °C	R_2S_2 converted, %	Yield of RSO_3H, %	Yield of RSH, %	Time, h
n-Bu_2S_2	HMPT	KOH	23.5	98	92.3	3	41
n-Bu_2S_2	HMPT	KOH	80	96	97	0	45
n-Bu_2S_2	DMF	KOH	23.5	87.7	88.1	0	45
n-Bu_2S_2	HMPT	NaOH	80	95	94.2	0.9	35
$(C_6H_5)_2S_2$	HMPT	KOH	23.5	97.7	88.1	—	22
$(C_6H_5)_2S_2$	HMPT	KOH	80	98	99	0	22.5
$(C_6H_5)_2S_2$	DMF	KOH	23.5	98.5	90	0.3	40
(*o*-CH_3—C_6H_4)$_2S_2$	HMPT	KOH	80	98	98	0	23

Under the influence of bases (t-butyl alcohol or potassium hydroxide) in HMPT, aromatic hydrocarbons are oxidised to the corresponding acids [138] (Table 49).

Methylthiophens are also converted into acids. The 2-isomers, which are able to form carbanions that are strongly stabilised by resonance, give high yields of the acids [144] (Table 50).

Table 44. Oxidation of benzyl sulphides [(*a*)].

Sulphide (M)	Products	Yield, %	Time, h	O_2/R_2S molar	Rate relative to toluene
$C_6H_5CH_2$—S—C_6H_5	C_6H_5COOH $C_6H_5SO_3H$ C_6H_5SH	62 44 32	23	0.145	6.30
$C_6H_5CH_2S$—CH_3 (0.05)	C_6H_5COOH CH_3SO_3H	77 73	67	0.083	3.61
C_6H_5CH(CH$_3$)—S—CH(CH$_3$)—Ph (0.05) (*b*)	C_6H_5COOH	37	26	0.063	2.74
 (0.0013)		31	68	0.225	9.79
$C_6H_5CH_2$—S—$CH_2C_6H_5$	(*c*)	(*c*)	(*c*)	0.150	6.52
$C_6H_5CH_3$ (*d*) (0.05)	C_6H_5COOH	48	24	0.023	1.00

(*a*) In 2M t-C_4H_9OK–HMPT at 80°C.
(*b*) Polymeric substances containing a carbonyl chain.
(*c*) See Table 45.
(*d*) The oxidation of toluene under these conditions has been studied by Hofmann and his coworkers.

D. COMPARISON OF DIPOLAR APROTIC SOLVENTS

The preceding discussion has shown that S_N2 and S_E2 reactions are accelerated in dipolar aprotic solvents, the reaction velocity depending on the donor power of the solvents:

dimethylformamide < dimethyl sulphoxide < tetramethylurea < HMPT.

These solvents contain various polar groups: CO in dimethylformamide and tetramethylurea, SO in dimethyl sulphoxide, and PO in HMPT, with hydrogen atoms at different distances from these groups. The differences in structure among the solvents explain their varying stability and their different behaviour, which is sometimes undesirable in certain reactions.

Table 45. Oxidation of sulphides (*a*).

Sulphide (M)	Products (yield, %)	Time, h	O_2/R_2S molar	Rate relative to toluene
C_6H_5S—CH_3 (0.05)	$C_6H_5SO_3H$ (36.8) CO_2 (36.0)	46	0.0104	0.45
(*n*-C_4H_9)$_2$S (0.05)	*n*-$C_4H_9SO_3H$ (8.5) *n*-C_3H_7COOH (10.9)	45.5	0.0033	0.15
(t-C_4H_9)$_2$S (0.05)	none	21	0	0
 (0.05)	CH_2—COOH CH_2—COOH (5—10) (*b*)	70	0.0056	0.21
$(C_6H_5CH_2)_2S$ (0.05)	(*c*)	(*c*)	0.150	6.52
$(C_6H_5CH_2)_2S$ (0.05)	(*d*)	(*d*)	0.023	1.00

(*a*) In 2M t-C_4H_9OK at 80 ± 0.5°C.
(*b*) Approximate representation of product of reaction.
(*c*) See Table I in Ref. 141.
(*d*) See Table 44.

Table 46.

Sulphoxide (mole)	Base (mole)	HMPT, ml	Duration of reaction, h	Products (mole, yield, %) (*a*)
$CH_3S(=O)CH_3$ (75 ml)	KOH (0.15)	—	68	CH_3SO_3H (*c*) (0.001) CO_2 (0.0028)
$CH_3S(=O)CH_3$ (*b*, *c*) (0.5)	t-C_4H_9OK (0.15)	75	23	CH_3SO_3H (*d*, *f*) (0.011, 23) CO_2 (0.12, 24)
$C_6H_5S(=O)CH_3$ (*b*)	t-C_4H_9OK (0.038)	25	69	$C_6H_5SO_3H$ (0.103, 86.4) CO_2 (0.00882, 67)
$C_6H_5CH_2S(=O)CH_2$—Ph (*b*) (0.025)	t-C_4H_9OK (0.15)	75	20	C_6H_5COOH (*e*) (0.22, 88) C_6H_5CH=CHC_6H_5 (*e*) (0.0061, 24)

(*a*) 100 x moles of product/mole of reactant.
(*b*) No reliable data from infrared spectra on formation of sulphone.
(*c*) Acetic acid (infrared and mass spectra) and formaldehyde (2,4-dinitrophenylhydrazone, m.p. 166°C) were isolated quantitatively.
(*d*) Verified by gas–liquid chromatography.
(*e*) Verified by gas–liquid chromatography.
(*f*) Russell and his coworkers found methanesulphonic acid and dimethyl sulphone on oxidation with a mixture of potassium t-butoxide and dimethyl sulphoxide [137].

1. Reactivity of Polar Group

A negative charge on oxygen gives the solvent a basic character. The atom adjacent to the oxygen (carbon, sulphur, or phosphorus) acquires a positive charge, which favours attack by nucleophilic agents B^-, either present initially or formed during the reaction. As a result, dimethylformamide and tetramethylurea may form amide ions able to compete with B^-:

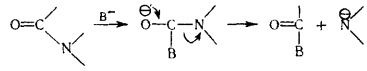


Table 47. Influence of solvent and base on the oxidation of acetophenone (*a*).

Base	Solvent	Temp., °C	Yield of benzoic acid, %	$10^2 O_2$(c)/ketone molar	Time, h
t-C_4H_9OK	t-C_4H_9OH	23.5	66	1.60	45
t-C_4H_9OK	HMPT	23.5	88	4.88	44
KOH	HMPT	80	62	2.14	44
KOH	HMPT	23.5	35	0.42	44
NaOH	HMPT	80	60	2.00	21
NaOH	HMPT	23.5	46	0.43	21
LiOH	HMPT	80	14	0.009	24.5
LiOH	HMPT	25.0	—		24.5
LiOH	H_2O	80	—		42

(*a*) The concentrations used were 0.05 M acetophenone and 0.15 M base with an oxygen pressure of 1 atm.
(*b*) 100 x theoretically calculated moles of acid per mole of ketone. Except for the use of lithium hydroxide, the whole of the ketone is converted with a yield of 90–100%.
(*c*) Calculated from rate of consumption of oxygen.

Table 48. Oxidation of cyclic ketones (*a*).

Ketone	Temp., °C	Time, h	Base	Acid (yield, %)
Cyclohexanone	23.5	20	CH_3ONa	adipic (100)
Cyclohexanone	80	24	CH_3ONa	adipic (>90)
Cyclohexanone (*b*)	23.5	78	NaOH	adipic (94)
Cyclohexanone (*b*)	80	68	NaOH	adipic (82)
Cyclohexanone (*b*)	23.5	24	NaOH	adipic (81)
Cyclohexanone (*b*)	80	19	NaOH	adipic (88)
Cyclopentanone	23.5	23	CH_3ONa	glutaric (95)
Cyclopentanone	80	23	CH_3ONa	glutaric (100)
Cyclopentanone (*b*)	23.5	26	NaOH	glutaric (49)
Cyclopentanone (*b*)	80	24	NaOH	glutaric (76)
Cyclopentanone	23.5	19	CH_3ONa	pimelic (44)
Cyclopentanone	80	21	CH_3ONa	pimelic (41)
Cyclopentanone	80	21	CH_3ONa	dodecanoic (40)

(*a*) The concentrations used were 0.025 M ketone and 0.15 M base with 75 ml of HMPT.
(*b*) Results obtained mainly by the use of potassium hydroxide.

Such decomposition is improbable with HMPT, in which the phosphorus atom is sterically blocked, so that it is considerably more difficult for HMPT to form ions like the amide ions formed by dimethylformamide and tetramethylurea.

Strong bases (organic compounds of alkali metals) act effectively on dimethylformamide, dimethyl sulphoxide, and tetramethylurea, but do not act on HMPT under the conditions normally employed. Nor do organomagnesium compounds react with tetramethylurea and HMPT.[145,146]

Table 49.

ArH	ArCOOH	Yield, %
Toluene	benzoic acid	25—30
o-Xylene	phthalic acid	35—40
m-Xylene	isophthalic acid	50
p-Xylene	terephthalic acid	15
Tetralin	phthalic acid	46

Thus organometallic compounds (of the alkali metals and magnesium) can be obtained in HMPT. On the other hand, it is desirable to prepare them in a mixture of HMPT and a non-polar solvent (benzene, toluene). This precaution is unnecessary with unreactive organometallic compounds. Thus organocadmium, organozinc, organotin, etc. compounds can be obtained by direct reaction between the metal and the halogen derivatives in pure HMPT.

Table 50. Oxidation of alkylthiophens in HMPT.

Reactant (0.5 mole)	Base (0.15 M)	Temp., °C	Product	Yield, % (*a*)	Duration, h	Rate of consumption of oxygen	Rate of relative to toluene
2-Methylthiophen	t-C_4H_9OK	80	thiophen-2-carboxylic acid	75.8	70	0.0380 0.0320	1.50 (*b*)
2,5-Dimethylthiophen	t-C_4H_9OK KOH	23.5 80	thiophen-2-carboxilic acid	19.9 2.2	48 25	0.0075 0.0013	0.32 0.06
3-Methylthiophen	t-C_4H_9OK	80	thiophen-3-carboxylic acid	13.4 19.2	23 70	0.0334 0.0008 0.0007	1.40 0.03 (*c*)
Toluene	t-C_4H_9OK	80	benzoic acid	47.8	24	0.0230	1.00

(*a*) All yields based on theoretical.
(*b*) Rate of oxidation = moles of oxygen per mole of reactant per minute.
(*c*) Mean of two separate reactions.

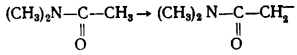
Sodium hydride can be used in various reactions with dimethylformamide, but it partly reacts with the latter even at room temperature[147]. Its use in reactions with dimethyl sulphoxide as solvent is not without danger, as the latter contains oxygen, and explosions are possible even at low temperatures[148].

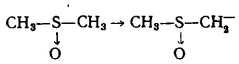
Alkali-metal hydrides and amides do not interact with tetramethylurea or HMPT.

Alkali-metal hydroxides react readily with dimethylformamide, dimethyl sulphoxide, and tetramethylurea, but do not react with HMPT even at 80°C.

2. Electron-acceptor Effect of Polar Group

The electron-acceptor effect of the polar group makes an α-hydrogen atom labile; on loss of a proton the solvent is converted into a carbanion. Thus dimethylacetamide and dimethyl sulphoxide yield the corresponding carbanions:





Tetramethylurea and HMPT, in which the hydrogen atoms are in the β-position, are able to lose these atoms only in exceptional circumstances. The resulting carbanions are able to undergo the same reactions as those produced during substitution, addition, autoxidation, etc.

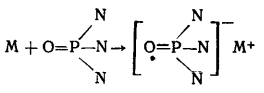
The ease with which the "dimsyl" anion is formed and its reactivity make it an excellent agent in syntheses [149]. On the other hand, dimethyl sulphoxide is not recommended as a solvent for reactions involving carbanions.

From the points of view of basic character and stability HMPT is regarded as the most suitable among dipolar aprotic solvents for the production and application of anions. At present most of these reactions are accomplished in liquid ammonia, but a great future belongs to HMPT, in view of the convenience of operation, absence of protolysis (e.g. preparation of $(C_6H_5)_3CM$), better solubility of various agents (e.g. higher aliphatic bromides).

V. USE OF HEXAMETHYLPHOSPHORIC TRIAMIDE AS ELECTRON-ACCEPTOR REACTION MEDIUM

A. FORMATION OF RADICAL-ANIONS

Normant and his coworkers were the first to observe that HMPT is able to dissolve alkali metals (lithium, sodium, potassium) with the formation of light blue solutions [150]. It was shown simultaneously that the solutions contained radical-anions and were paramagnetic [151-153]:



Electron spin resonance spectra were recorded for various concentrations

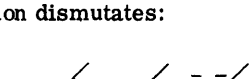
$$M + n\ \text{HMPT} \leftrightarrows (M^+ \ldots e^-)_n\ \text{HMPT}$$

The stability of the radical-ions depends on the concentration and the nature of the cation. At concentrations near molar the blue colour disappears after 10–15 min with potassium, and after 5–6 h with sodium and lithium.

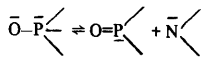
Other metals—magnesium [154] and the alkaline-earth metals (calcium, strontium, barium) [155]—also dissolve in HMPT. Freshly prepared solutions of these metals are light blue, having an absorption maximum at 770 nm. At the same concentration solutions of magnesium are more stable than those of sodium; solutions of the alkaline-earth metals have little stability, especially those of barium. In time the blue colour of the radical-anions passes into pale yellow (λ_{max} = 390 nm).

We have previously reported that this decomposition yields two anions and have suggested a mechanism [156].

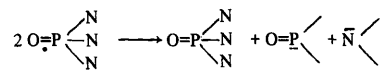
The most probable scheme seems to be that the mesomeric radical-anion dismutates:



The resulting dianion is in turn converted into two anions:



The overall equation is



Polycyclic hydrocarbons are able to act as electron acceptors towards metals, and several radical-ions have recently been obtained in HMPT. The ease of formation of radical-ions depends on three main factors [157]—(*a*) the electron affinity of the hydrocarbon, which is always lower than that of a non-enolised ketone [158] (benzene < < phenanthrene < biphenyl < anthracene < *o*- and *p*-terphenyls < benzophenone < fluorene), (*b*) the reducing power of the metal (alkali metals > magnesium > alkaline-earth metals), and (*c*) the solvating power of the solvent (highest with HMPT, then dimethoxyethane and oxolan).

Biphenyl and naphthalene in oxolan form with lithium and sodium radical-ions which are used in various syntheses [159-161].

Radical-ions of naphthalene (1) and anthracene (2) are obtained also with sodium in HMPT. [162] Solutions of (2) are stable, but those of (1) decompose with time. This latter process has not yet been investigated; either the solvent may be decomposed by the radical-ion, or electron transfer may occur from naphthalene to HMPT. The acceptor powers of naphthalene and of HMPT cannot be compared by spectrophotometric methods, since unstable solutions of radicals are formed. Insufficient work has been done on determining the reduction potential of HMPT. Biphenyl and naphthalene do not form radical-ions with magnesium in oxolan, but their formation is possible in liquid ammonia [163]. The appearance of radical-ions in HMPT has also been observed by means of electron spin resonance [155].

Products of the interaction of naphthalene with magnesium in liquid ammonia are green after removal of most of the solvent; the magnesium–naphthalene–ammonia compound is decomposed by dimethyl sulphoxide and is insoluble in oxolan, but is dissolved by HMPT to form stable green solutions. Other radical ions of the type $ArH{\cdot}Mg^+$ can be obtained from these solutions [164]. In HMPT magnesium forms radical-ions with anthracene, pyrene, and 1,1-diphenylethylene [154]. Radical-ions of biphenyl can also be obtained in HMPT by the action of such metals as calcium, strontium, and barium.

Naphthalene, being a better electron acceptor than biphenyl, is able to accept an electron from the radical-ion of the latter to form the corresponding green radical-ions [155]:

$$\text{Ph—Ph}^{\cdot} + \text{Naph} \rightleftarrows \text{Naph}^{\cdot} + \text{Ph—Ph}$$

The electronic spectra of the various radical-ions obtained in HMPT do not depend significantly on the nature of the cation (Na^+ or Mg^{2+}), but their absorption maxima are slightly displaced to longer wavelengths in oxolan. HMPT is a good solvent for the preparation of ketyls [165].

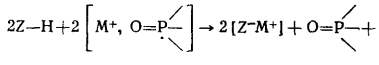
Radical-anions may be produced not only on the dissolution of metals but also during the electrolysis of alkali-metal salts in certain solvents (ammonia and the lower amines). Two laboratories have recently shown—simultaneously and independently—that HMPT may also be such a solvent [49,166]. When magnesium bromide is electrolysed with a calomel electrode in HMPT, an unstable light blue coloration appears around the cathode [49], and this is stabilised by the addition of lithium chloride [166]. In alcoholic medium (HMPT absent) evolution of hydrogen is observed. In HMPT containing a minute amount of alcohol a weak light blue coloration is evident in the catholyte, and electrolysis is not accompanied by hydrogen evolution. These facts indicate that HMPT accepts an electron with formation of a radical-ion.

B. APPLICATION OF RADICAL-ANIONS

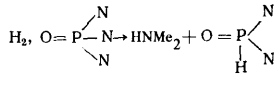
The solutions of radical-ions formed when alkali metals are dissolved in HMPT can be used for those reactions—metallation, reduction, isomerisation, polymerisation, etc.—which occur in solutions of these metals in liquid ammonia [151].

1. Formation of Anions and Metallation

Solutions of radical-anions are nucleophilic reagents, able to replace labile hydrogen in compounds containing it:



the anion Z^- or a metallated product being obtained. Hydrogen is not evolved in these reactions, but is bound by the HMPT into a complex, which decomposes according to the equation



The reactions occur more effectively with potassium and lithium than with sodium. For these reactions the HMPT can be mixed with other solvents (ether, oxolan, benzene). The radical-ions tend to decompose, and the stoichiometric quantity of ZH is introduced into the reaction mixture at the very start in order to avoid such decomposition.

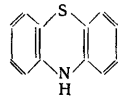
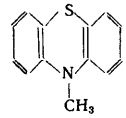
Table 51 gives results for the production of several heteroanions [167]. Information on the metallation of certain "acidic" hydrocarbons is given in Table 52. [168]

The aprotic solvent HMPT enables very weak acids (e.g. toluene) to be metallated by alkali metals. The action of lithium or potassium produces the deep red colour characteristic of the benzyl radical. Carboxylation yields phenylacetic acid, but always in low yield (the red solutions are decolorised). 1,3-Diphenylpropane and ethylbenzene have also been detected among the decomposition products.

Metallation by alkali metals in HMPT should be applicable to macromolecules containing labile hydrogen atoms—polyvinyldiphenylmethane, polyvinylfluorenone.

Alkynes, which are stronger acids than the above hydrocarbons, are not metallated by alkali metals when the solvent is HMPT alone. When a mixture of hexyne and HMPT is shaken with potassium and heated at 55°C, 37% of hexyne is recovered: the radical-ion decomposes. Even phenylacetylene, a relatively acidic compound, is not metallated. The phosphorodiamidite anion, which appears on decomposition of the radical-ion, is bound to both ends of the triple bond.

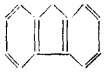
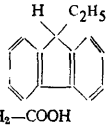
Table 51.

Metallated compound	Metal	Reactant	Product	Yield, %
n-C_4H_9OH	Na	$PhCH_2Cl$	$C_4H_9OCH_2Ph$	77
$Ph-NH-C_2H_5$	K	C_2H_5I	$Ph-N(C_2H_5)_2$	77
	Na	CH_3I		85
CH_3CONH_2	K	$PhCH_2Cl$	$CH_3CO-NH-CH_2Ph$	negligible*

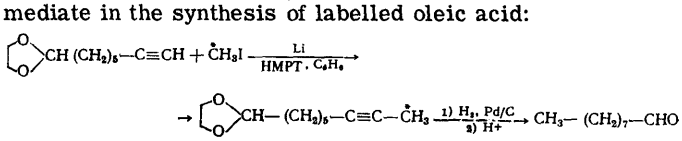
*Negligible yield also when sodamide employed.

This great difference in the behaviour of alkali metals is HMPT and in liquid ammonia can be explained by the formation of complexes between alkynes and HMPT. However, metallation is possible in a mixture of HMPT and a non-polar solvent (benzene, toluene, etc.), where the complexes will be decomposed. Table 53 gives results obtained by the use of a mixed solvent [169].

Table 52.

Hydrocarbon	Metal	Reactant	Product	Yield, %
Ph_3CH	Na	CO_2	$Ph_3C-COOH$	50
—	K	$PhCH_2Cl$	Ph_3C-CH_2-Ph	90
—	K	$PhCOCl$	$Ph_3C-CO-Ph$	70
—	K	$Br(CH_2)_4Br$	$Ph_3C(CH_2)_4CPh_3$	60
Ph_2CH_2	Na	CO_2	$Ph_2CH-COOH$	30
—	K	n-C_4H_9I	$Ph_2CH-C_4H_9$	64
—	K	$PhCH_2Cl$	Ph_2CH-CH_2-Ph	66
—	K	$Br(CH_2)_4Br$	$Ph_2CH(CH_2)_4CHPh_2$	87
—	Li	—	—	90
—	Li	—	—	65
	Na	C_2H_5I		73
$PhCH_3$	Li	CO_2	$PhCH_2-COOH$	negligible
Ph_3GeH	K	n-C_4H_9Br	$Ph_3Ge-C_4H_9$	62

The same conditions have been effectively applied to the preparation of nonanal [170], which is formed as an intermediate in the synthesis of labelled oleic acid:

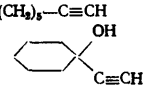


The yield of the labelled compound is 95% based on the iodomethane.

Formation of carbanions is successful if the functional group of the compound is attached to an active CH_2 or CH_3 group [154] (Table 54). In some cases (acetophenone,

acetonitrile) it is necessary to use a mixture of HMPT with an inert solvent to avoid the formation of condensation products. A mixture of solvents is also in carbonylation and acylation.

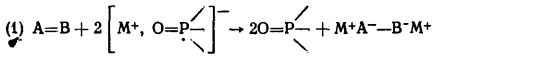
Table 53.

Alkyne	Reactant	Product	Yield, %
$Et_2NCH—C\equiv CH$	$Br(CH_2)_4Br$	$C\equiv C—CH_2NEt_2$ $(CH_2)_4$ $C\equiv C—CH_2NEt_2$	50
$PhC\equiv CH$	CO_2	$PhC\equiv C—COOH$	70
$HC\equiv CH$	$n\text{-}C_6H_{13}Br$*	$CH_3(CH_2)_5—C\equiv CH$	14
$HC\equiv CH$			50

*HC : C, a stronger base in HMPT, causes the elimination of hydrogen bromide.

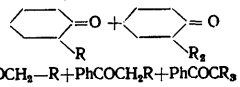
2. Reduction of Unsaturated Compounds

The transfer of electrons from a radical-ion to an unsaturated system A=B results in the formation of a dianion:



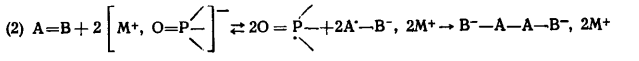
HMPT is again regenerated, and may in principle act in catalytic quantities.

Table 54.

Metallated compound	Metal	Reactant	Products
$PhCH_2COOH$	Na	CO_2	$PhCH(COOH)_2$
$Ph—CH_2—CN$	K	$PhCH_2Cl$	$PhCH(CN)—CH_2—Ph + PhC(CN)—(CH_2Ph)_2$
$CH_2(COOEt)_2$	K	$CH_2=CHCH_2Br$	$RCH(COOEt)_2$*
$CH_2(CN)(COOEt)$	K	$CH_2=CHCH_2Br$	$R—CH(COOEt)(CN) + R_2C(COOEt)(CN)$
	K	$CH_2=CHCH_2Br$	
$PhCOCH_3$	K	$CH_2=CHCH_2Br$	$PhCOCH_2—R + PhCOCH_2R + PhCOCR_2$
CH_3CN	K	$C_7H_{15}Br$	$C_7H_{15}CH_2CN + C_7H_{15}(C_7H_{15})CH—CN$

*$R = CH_2 : CHCH_3$.

Another possible path for this reaction is the formation of a dimeric dianion alone:



Let us examine reaction (1) in greater detail. In HMPT—an aprotic solvent—the monomeric dianion is produced in the free form, and can then be used in various reactions (reduction, alkylation, etc.), in contrast to liquid ammonia and primary amines, in which the monomeric dianion is present in protonated form. On treating a solution of azobenzene in HMPT with an alkali metal, we obtain the compound (XXXVI), which is hydrolysed to 1,2-diphenylhydrazine (XXXVII) and alkylated by iodomethane to (XXXVIII):[171]

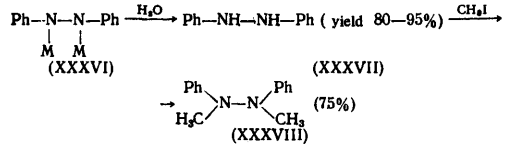
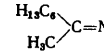
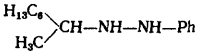
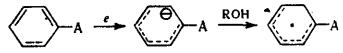


Table 55.

Unsaturated compound (0.1 M)	Metal (0.2 g-atom)	Product	Yield, %
$PhCH=N—Bu$	K	$Ph—CH_2—NH—Bu$	70
$PhCH=N—Bu$	Li	$Ph—CH_2—NH—Bu$	65
$C_6H_{11}N=CH—CH(CH_3)_2$	Li	$C_6H_{11}NH—CH_2—CH(CH_3)_2$	50
$Ph_2C=N—NH—Ph$	Li	$Ph_2C=NH + Ph—NH_2$	33 33
	Li		60
$Ph_2C=N—OH$	Li	$+PhNH_2$ $Ph_2C=NH+$ $PhCH=N—Ph$	8 50 10
$(C_5H_{10})C=NOH$	Li	$(C_5H_{10})CH—NH_2$	25

Compounds containing the grouping CH : N (imines, oximes, hydrazones) may undergo reduction. Thus benzophenone phenylhydrazone (Table 55) is reduced in a protic medium (oxolan and t-butyl alcohol); the yield of benzophenone oxime is determined using thin-layer chromatography by hydrolysis and conversion to the 2,4-dinitrophenylhydrazone. Rearrangements of this type have been found only with aldoximes [172,173].

In the case of ethers of phenols and arylamines subject to the action of alkali metals the benzene ring may undergo either reduction or cleavage. In protic medium elimination is insignificant, since the resulting radical-ion adds a proton and is converted into a radical:



where A = OR, NR_2. The latter, in its turn, is reduced, and then protonated. Hydrolysis of the final product yields cyclohexenone (data on the Birch reduction):

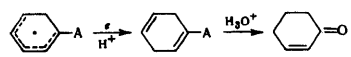
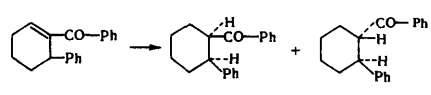


Table 56 gives results for the reduction of certain aromatic compounds in a mixture of HMPT and t-butyl alcohol [171,174].

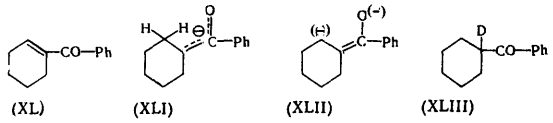
The chemical reduction of α-ethylenic ketones by alkali metals in liquid ammonia and primary amines results in the formation of saturated ketones. This reaction can be effected also in HMPT using lithium and potassium (yield 80%) and the same ratio of isomers for the ketone (XXXIX):[175]



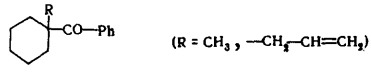
(XXXIX) *cis* (80%) *trans* (20%)

Data on the reduction of several ketones are given in Table 57. [174]

Electrolytic reduction involves electron transfer from the radical-ion to the substance which is reduced. The ketone (XL) is converted into a high yield (around 80%) of the saturated ketone when an ethereal solution of magnesium bromide or calcium iodide is used as electrolyte.



(XL) (XLI) (XLII) (XLIII)



(XLIV)

Table 56.

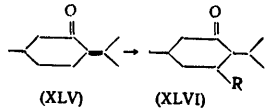
Aromatic compound	Product	Yield, %
Anisole	cyclohex-2-enone	50
Phenetole	cyclohex-2-enone	25
NN-Dialkylanilines (CH_3, C_2H_5)	cyclohex-2-enone	20
2-Ethoxynaphthalene	tetralone	60
1-Methoxynaphthalene	1-methoxynaphthalene	15
	1,2-dihydronaphthalene	15
	1,4-dihydronaphthalene	30

The mechanism of this reduction in an aprotic solvent has not yet been finally established. Some results indicate that the enolate ion (XLI) is formed more rapidly than the dianion (XLII). In fact treatment of the ketone (XLI) with a solution of lithium in HMPT followed by the action of deuterium oxide yields the α-deuterated ketone (XLIII). The same lithium derivative yields α-alkylated ketones (XLIV). [176]

Table 57.

Unsaturated ketone	Yield of saturated ketone, %	Unsaturated ketone	Yield of saturated ketone, %
CH_3—CO—CH=C$(CH_3)_2$	60	$CH_3COC(CH_3)$=CH—CH$(CH_3)_2$	55
CH_3COCH=CH—Ph	30	Isophorone	60
CH_3COCH=CH—Et	30	Carvone	40
CH_3COCH=CH—CH$(CH_3)_2$	40	Pulegone	65
CH_3COCH=CH-*n*-C_5H_{11}	45		

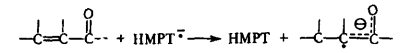
Formation of an α-substituted ketone (XLVI) is possible from pulegone (XLV):



(XLV) (XLVI)

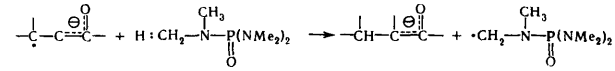
where R = CH_3 (60%), allyl (63%).

Formation of the enolate ion (XLI) has been clearly established when liquid ammonia is used as solvent. With HMPT as solvent a radical mechanism also seems possible, in which (*a*) the ketone is reduced to a radical-ion:



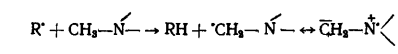
(XLVII)

(*b*) The radical-ion (XLVII) forms the enolate ion (XLVIII) with a methyl hydrogen of the HMPT, which gives the radical (XLIX):



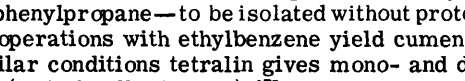
(XLVIII) (XLIX)

It is known that tertiary amines can act as hydrogen donors towards radicals [177,178]:

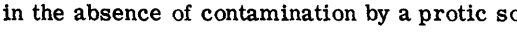


The radical (XLIX) may be formed by the action of alkali metals on HMPT in the presence of various aliphatic–aromatic hydrocarbons. The action of potassium on toluene enables various derivatives—in particular ethylbenzene and 1,3-diphenylpropane—to be isolated without protonation. The same operations with ethylbenzene yield cumene [179]. Under similar conditions tetralin gives mono- and di-methyltetralins (undoubtedly dimers). [179] The same results have been achieved by the electrolytic reduction of tetralin in HMPT in the absence of contamination by a protic solvent [166].

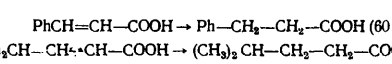
Under the same reduction conditions α-ethylenic acids are converted into saturated acids [174]:



In a mixture of HMPT with ether or oxolan lithium does not reduce oct-3-yne or hex-3-yne, but causes them to isomerise into alk-1-ynes [174]:

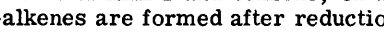


In a 1:5 mixture of HMPT and benzene, on the other hand, only *trans*-alkenes are formed after reduction:

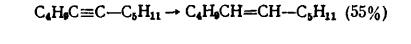


3. Reduction with Elimination

The transfer of electrons from a radical-ion to a molecule A–B may result in the formation of (*a*) an anion and another radical:



or (*b*) two anions:



Rupture of the bond in the molecule AB is facilitated when the anions A^- and B^- are stabilised by conjugation. Table 58 gives several examples [180].

‡Since these results are unpublished [174], it is not possible to amend the formulae and the text (Ed. of Translation).

Hexa-alkyldigermanium compounds have recently been cleaved by means of potassium in HMPT to give a quantitative yield of the potassium derivatives, which are stable in HMPT and condense with halides of metals in the same group to give mixed compounds[181] $R_3Ge-MR'_3$, where M = Ge, Si, Sn.

Table 58.

Initial cpd.	Metal	Reagent	Product	Yield, %
$PhCH_2Cl$	K	H_2O	$PhCH_3-CH_2-Ph$	75
$PhOCH_3$	K	H_2O	Ph—OH	80
PhO—$CHPh_2$	K	H_2O	Ph—OH+Ph_2CH_2+Ph_3COH	*
Ph_3P	K	C_2H_5I	$Ph_2P-C_2H_5$	58
$CH_3S-S-CH_3$	K	$PhCH_2Cl$	CH_3S-CH_2-Ph	81
$CH_3S-S-CH_3$	K	$ClCH_2CH_2OH$	$CH_3S-CH_2-CH_2OH$	56
$CH_3-NH-NH-Ph$	Li	H_2O	$PhNH_2$	14
Ph_3C-CH_2Ph	K	CH_3I	Ph_3C-CH_3	72
$Ph_3Ge-GePh_3$	K	$PhCH_2Cl$	Ph_3Ge-CH_2-Ph	56

* PhOH 47%; CH_3Ph_3 52%; Ph_3COH 46%.

The cleavage of ethers by alkali metals in HMPT has been studied in part in Ref. 89. Reduction is possible when the ether contains a weakly acceptor group. Aliphatic ethers cannot be cleaved. Diaryl ethers give phenols. Data on the cleavage of alkyl aryl ethers are given in Table 59, and data on aryl benzyl ethers in Table 60.

Table 59.

Ether	Products (yield, %)
$C_6H_5O-CH_3$	C_6H_5OH (76-80)
$C_6H_5O-C_2H_5$	C_6H_5OH (20) + C_6H_5OH.HMPT complex (65)
2-$C_{10}H_7-OCH_3$	$C_{10}H_8$ (48) + 2-naphthol.HMPT complex (38)
2-$C_{10}H_7OC_2H_5$	2-naphthol.HMPT complex (51)

Reduction does not always proceed smoothly: the carbanion may cause elimination with the formation of 1,2-diphenylethane, as has already been observed in liquid ammonia[182]:

$$PhCH_2^- + Ph-CH_2-OCH_2-Ph \rightarrow Ph-CH_2-CH_2-Ph + PhCH_2O^-$$

Ethers may undergo the Wittig rearrangement[183], which results in the formation of alcohols:

$$Ar-O-\bar{C}< \rightarrow Ar-\underset{|}{\overset{|}{C}}-O^-$$

Table 61 shows the reduction of some β-unsaturated ethers.

The reduction of aryl toluene-*p*-sulphonates by potassium in HMPT yields mainly phenols, but when aryl phosphates are reduced, hydrocarbons are formed[89]:

$$ArO-\underset{\underset{O}{\|}}{P}-(OEt)_2 \xrightarrow[2)\ H_2O]{1)\ K,\ HMPT} Ar-H$$

Table 60.

Ether	Cleavage product (yield, %)
$C_6H_5CH_2OC_6H_5$	$C_6H_5CH_3$ (21) + C_6H_5OH (55) + C_6H_5OH.HMPT complex (16)
$C_6H_5CH_2OC_6H_5$	C_6H_5OH (29) + C_6H_5OH·HMPT complex (31)
$C_6H_5CH_2OC_7H_{15}$	$C_6H_5CH_3$ (60) + $C_7H_{15}OH$ (70)
$(C_6H_5CH_2)_2O(K)$	$C_6H_5CH_3$ (60) + $C_6H_5CH_2OH$ (44) + $C_6H_5CHOHCH_2Ph$ (15)
$(C_6H_5CH_2)_2O(Li)$	$C_6H_5CH_3$ (20) + $C_6H_5CH_2OH$ (33) + $C_6H_5CHOHCH_2Ph$ (27)+ + $C_6H_5CH_2CH_2Ph$ (2)
$(C_6H_5)_2CHOC_6H_5$	$(C_6H_5)_2CH_2$ (50) + C_6H_5OH (44) + C_6H_5OH.HMPT complex (12) + $(C_6H_5)_3COH$ (44)
$(C_6H_5)_2CHOC_7H_{15}(K)$	$(C_6H_5)_2CH_2$ (53) + $C_7H_{15}OH$ (64) + $Ph_2CHC_7H_{15}$
$(C_6H_5)_2CHOC_7H_{15}(Li)$	$(C_6H_5)_2CH_2$ (42) + $C_6H_5CHOHC_6H_5$ (4) + $C_7H_{15}OH$ (64) + + $(C_6H_5)_2CHC_7H_{15}$
$(C_6H_5)_3COC_7H_{15}$	$(C_6H_5)_3CH$ (73) + $C_7H_{15}OH$ (66)

Such reduction can be effected also in liquid ammonia[184]. Non-aliphatic mixed ethers containing a heteroatom Z can be converted under the same conditions into two anions:

$$Ar-O-Z \rightarrow Ar-O^- + Z^-$$

where Z = B, Si, Ge, Sn. On protonation ZH is obtained (indirect reduction of ZX to ZH), and on alkylation the derivatives Z–R[185] (see Table 62).

Table 61.

Ether	Products (yield, %)
$CH_2=CHCH_2OC_6H_5$	C_6H_5OH (26) + C_6H_5OH.HMPT complex (33)
$CH_2=CHCH_2OC_7H_{15}$	$C_7H_{15}OH$ (73)
$C_6H_5CH=CHCH_2OC_6H_5$	C_6H_5OH (44) + C_6H_5OH.HMPT complex (46)
$C_6H_5CH=CHCH_2OC_7H_{15}$	$C_7H_{15}OH$ (67)
$CH_2-CH=CH-CH_2$ | ——O—— |	$CH_3-CH=CH-CH_2OH$ (29)
$CH_2-CH=CH-CH_2$ | ——O—— |	$CH_3-CH=CH-CH_2OC_4H_9$ (43)

4. Condensation and Polymerisation

Since HMPT is widely used as a Lewis base in many processes, including those involving organometallic compounds, it may find application also in anionic polymerisation[186]. This type of polymerisation is observed in radical-ionic solutions of alkali metals with various activated vinyl compounds[157,158,187]. The species M^+, HMPT$^\cdot$ and M^+, $ArH^\cdot$, which are formed in HMPT, may serve as radical-ions.

In the presence of sodium in HMPT *trans*-stilbene gives a dianion, protonation of which yields *"meso"*-1,2,3,4-tetraphenylbutane [150]:

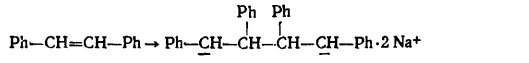
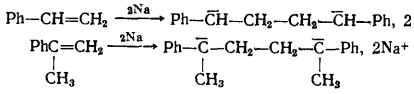


Table 62.

Compound A.OR	Reagent	Products (yield, %)
$B(OC_6H_5)_3$	n-C_4H_9Br	C_6H_5O—n-C_4H_9 (93)
$(CH_3)_3SiOC_6H_5$	H_2O	C_6H_5OH (17) + C_6H_5OH.HMPT complex (53)
$(CH_3)_3SiOC_6H_5$	n-C_4H_9Br	C_6H_5O—n-C_4H_9 (83)
$(C_6H_5)_3SiOC_6H_5$	C_3H_5Br	$C_6H_5OC_2H_5$ (67) + $(C_6H_5)_3SiOSiPh_3$ (12)
H_3C, H_5C_6 $Si(OC_6H_5)_2$	C_2H_5Br	$C_6H_5OC_2H_5$ (65) + C_6H_5OH.HMPT (22)
$HSi(OC_6H_5)_3$	$ClSi(C_6H_5)_3$	$C_6H_5OSi(C_6H_5)_3$ (34)
$(C_3H_5)_3GeOC_6H_5$	$ClCH_2C_6H_5$	$C_6H_5OCH_2C_6H_5$ (92)
$(C_4H_9)_3SnOC_6H_5$	C_4H_9Br	$C_6H_5OC_4H_9$ (79), $Sn(C_3H_9)_4$ (77)

Styrene and α-methylstyrene have been dimerised in oxolan solution in the presence of sodium, which is used as electron donor with respect to the carbon atom adjacent to the phenyl group [188]:

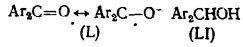


This condensation goes still further with potassium in oxolan at between −40° and −30°C and in the presence of small quantities of HMPT as electron donor. After hydrolysis the reaction mixture contains a certain amount of dimers; all the polymers obtained are of low molecular weight. Solutions of diphenylmagnesium in HMPT are used as initiator for the anionic polymerisation of styrene, α-methylstyrene, and 2-vinylpyridine. The stability of the active centres has been determined spectrophotometrically. Polymerisation is quantitative [189]. Naphthalene–magnesium–HMPT solutions also bring about the polymerisation of styrene [164].

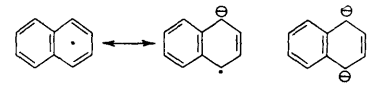
From the results obtained and some unpublished data [190] it can be concluded that HMPT–alkali-metal systems, even when present in small quantities, considerably increase the rate of polymerisation. They enable lower temperatures to be used and various difficult copolymerisations to be brought about more completely. The polymerisation promoters used are active in the presence of HMPT.

C. COMPARISON OF ELECTRON ACCEPTORS

When electron acceptors are used, they are generally completely regenerated (in the case of reduction) or 50% reduced (in the production of anions and metallation). Compounds containing one or more multiple bonds—aromatic ketones and polycyclic hydrocarbons—are acceptors. In the presence of metals aromatic ketones form radical-ions (ketyls) (L), which are converted into alcohols (LI) on protonation followed by reduction:



Polycyclic hydrocarbons react with active metals to yield radical-ions and dianions. Thus naphthalene is able to form the radical-ion (LII) or the dianion (LIII):



(LII) (LIII)

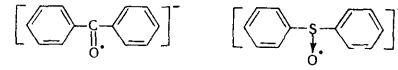
The latter (LIII) is protonated and converted into dihydronaphthalene by a compound Z–H capable of forming Z^- or a metal derivative Z–M.

The system (L) acceptor–alkali metal is most effective in oxolan in various reactions involving metallation followed by carbonylation, especially when the products are to undergo chemical separation [159–171]. But the presence of the acceptor and its reduction product in the reaction medium is very often an undesirable condition for studying the reaction and isolating the products. This difficulty disappears when the system HMPT—alkali metal is used, since the acceptor and its reduction product are then soluble in water, and can easily be separated.

D. COMPARISON OF DIPOLAR APROTIC SOLVENTS

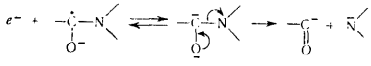
The solvents—dimethylformamide, tetramethylurea, and dimethyl sulphoxide—have been compared above from the viewpoint of their donor power. These same solvents can be acceptors of electrons, because of the presence of a polar group, and are able to form radical-ions, though these are unstable.

Aromatic ketones, in virtue of their carbonyl group, also form radical-ions (LIV), in which delocalisation of the negative charge promotes stabilisation:



(LIV) (LV)

Amides, which are not stabilised, decompose rapidly into two anions [191–193]:

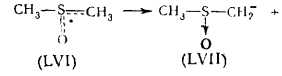


In tetramethylurea alkali metals form fairly unstable light blue solutions, the colour of which is preserved for several seconds at ordinary temperatures and for 1 min at −40°C. [191,192] Only triphenylmethane is metallised in this solution by a potassium–sodium alloy.

Similar phenomena are observed when HMPT is used as solvent, but the radical-ions formed are more stable. At ordinary temperatures the mean lifetime of such a radical-ion varies from 10–15 min with potassium to several hours with lithium and sodium.

Aromatic sulphoxides approach diaryl ketones, since their polar group SO is conjugated with phenyl groups. The radical-ion (LV), however, is less stable.

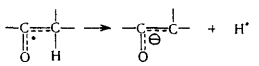
In the presence of potassium, solutions of diphenyl sulphone in 1,2-dimethoxyethane yield a light blue coloration, which is unstable even at −70°C and gives an electron spin resonance signal [194]. With dimethyl sulphoxide under the same conditions, alkali metals form the "dimsyl" anion (LVII):[195]



(LVI) (LVII)

The radical-ion (LVI) would be unstable, but would play the same part as amides containing hydrogen in the α-position

relative to the carbonyl group (dimethylacetamide, *N*-methylpyrrolidone) and enolisable ketones, which yield enolate anions with alkali metals:



The stability of the radical-ions formed by different solvents can be placed in the sequence—HMPT$^{\cdot}$ < < $((CH_3)_2N)_2CO^{\cdot}$ > $(CH_3)_2CO^{\cdot}$—in which HMPT is the only dipolar aprotic solvent that enables active solutions of metals to be used in syntheses.

REFERENCES

1. A. J. Parker, Quart. Rev., **16**, 163 (1962).
2. A. J. Parker, Adv. Org. Chem., 51 (1965).
3. B. Tchoubar, Bull. Soc. chim. France, 2069 (1964).
4. J. J. Delpuech, Tetrahedron Letters, 2111 (1965).
5. F. Madaule-Maury, Bull. Soc. chim. France, 1457 (1966).
6. C. Rivat, 2^{e} Thèse Faculté des Sciences de Rouen (1965).
7. T. Takaoka, Yuki Gosei Kagaku Kyokaishi (J. Org. Synthetic Chem.), **24**, 412 (1966).
8. L. Robert, Chemie et Industrie, **97**, 337 (1967).
9. A. Michaelis, Annalen, **326**, 129 (1903).
10. Hoechst AG., BRD P. 1 121 247.
11. J. W. Bell, J. Heisler, H. Tannenbaum, and J. Goldenson, J. Amer. Chem. Soc., **76**, 5185 (1954).
12. L. Larson, Svensk. kem. Tidskr., **71**, 336 (1959).
13. M. Schafer and C. Curran, Inorg. Chem., **4**, 623 (1965).
14. J. Ducom, Compt. rend., **264C**, 722 (1967).
15. M. Levine, US P. 2 619 427; Chem. Abs., **47**, 2510a (1953).
16. D. F. Heath and P. Casapieri, Trans. Faraday Soc., 47, 1093 (1951).
17. G. A. Trementozi and G. M. Kosolapoff, BP 675 294.
18. S. T. Preston, J. Gas. Chromatogr., **1**, (3), 8–10 (1963).
19. H. Tolkmith, J. Amer. Chem. Soc., **75**, 5275 (1953).
20. R. L. Heider, US P. 2 603 660; Chem. Abs., **47**, 4900f (1953).
21. A. M. Chauseau, Dipl. Etudes Sup. Sci. Phys., Paris, 1966.
22. J. E. Dubois and H. Viellard, J. Chim. phys., **62**, 699 (1965).
23. J. T. Donoghuc and R. S. Drago, Inorg. Chem., **1**, 866 (1962).
24. M. W. Hanson and J. B. Bouck, J. Amer. Chem. Soc., 79, 5631 (1957).
25. S. B. Hartley et al, Quart. Rev., **17**, 204 (1963).
26. N. Miller et al., J. Amer. Chem. Soc., **78**, 3557 (1956).
27. M. L. Martin, Ann. Physique, **7**, 35 (1962).
28. T. Cuvigny and H. Normant, Bull. Soc. chim. France, 2001 (1964).
29. G. J. Martin and M. L. Martin, J. Chim. phys., 1223 (1964).
30. G. J. Martin and M. L. Martin, Compt. rend., **257**, 1048 (1963).
31. L. F. Audrieth and R. Steinman, J. Amer. Chem. Soc., 63, 2115 (1941).
32. M. W. Hanson and J. B. Bouck, J. Amer. Chem. Soc., 79, 5631 (1957).
33. A. C. MacKinnis, US P. 2 756 252; Chem. Abs., **51**, 1275g (1957).
34. Bouillenne-Walrand, J. Khaladji, and G. Wetroff, Bull. Soc. roy. Sci. Liège, **31**, 818 (1962).
35. D. N. Shchepkin, Teor. Eksper. Khim., **2**, 276 (1966); Chem. Abs., **65**, 13515 (1966).
36. J. F. Normant, Thèse, Paris, 1963; Bull. Soc. chim. France, 1888 (1963).
37. H. J. Vetter, Z. Naturforsch., **196**, 73 (1964).
38. J. T. Donoghue, Diss. Abs., **24**, 3535 (1964).
39. K. W. Bagnall, J. Chem. Soc. (A), 737 (1966).
40. J. Fauvarque and J. F. Fauvarque, Compt. rend., **263C**, 488 (1966).
41. F. Fauvarque, D. E. S. Sci. Phys., Paris, 1964.
42. B. Castro, Bull. Soc. chim. France, in the press.
43. L. Villiéras, Bull. Soc. chim. France, in the press.
44. C. Agami and C. Prévost, Compt. rend., **263C**, 304 (1966).
45. J. Chenault and F. Tatibouet, Compt. rend., **262C**, 499 (1966).
46. J. E. Dubois, P. C. Lacaze, and A. Marie de Fiquelmont, Compt. rend., **262C**, 181 (1966).
47. J. E. Dubois, P. C. Lacaze, and A. Marie de Fiquelmont, Compt. rend., **262C**, 249 (1966).
48. H. F. Ebel and R. Schneider, Angew. Chem. Internat. Edn., **4**, 878 (1965).
49. P. Angibaud, H. Rivière, and B. Tchoubar, unpublished results.
50. E. M. Kosower, J. Amer. Chem. Soc., **80**, 3253 (1958).
51. E. M. Kosower, J. Chem. Phys., **61**, 230 (1964).
52. J. E. Dubois and A. Bienvenue, Tetrahedron Letters, 1809 (1966).
53. G. Martin, personal communication.
54. R. L. Heider, US P. 2 603 660; Chem. Abs., **47**, 4900 (1953).
55. J. Kopecky and J. Smejkal, Chem. and Ind., No. 36, 1529 (1966).
56. P. Lester, US P. 2 678 335; Chem. Abs., **49**, 6300 (1954).
57. B. Pianka and B. D. Owen, J. Appl. Chem., **5**, 525 (1955).
58. H. Normant and J. F. Brault, Compt. rend., **264C**, 707 (1967).
59. H. Normant and J. F. Brault, unpublished results.
60. H. Normant, T. Cuvigny, J. Normant, and B. Angelo, Bull. Soc. chim. France, 3442 (1966).
61. A. Szwiedsak, Bull. Acad. polon. Sci., Ser. Sci. chim., **13**, 609 (1965).
62. H. Normant and M. Larchevêque, Compt. rend., **260C**, 5063 (1965).
63. H. Normant, T. Cuvigny, J. Normant, and B. Angelo, Bull. Soc. chim. France, 3449 (1966) (structure established later by n.m.r. method).
64. H. Normant, T. Cuvigny, J. Normant, and B. Angelo, Bull. Soc. chim. France, 3443 (1966).
65. J. F. Normant, Bull. Soc. chim. France, 3601 (1966).
66. J. J. Monagle and H. R. Nace, US P. 3 056 835; Chem. Abs., **58**, 3362 (1963).
67. J. J. Monagle, J. Org. Chem., **27**, 3851 (1962).
68. A. J. Rutkowski, E. J. Inchalik, and A. Schriesheim, US P. 3 313 225; Chem. Abs., **61**, 4393e (1964).
69. Rhône Poulenc, French P. 1 444 735; Chem. Abs., **66**, 39477 (1967).
70. H. Normant and T. Cuvigny, Bull. Soc. chim. France, 1867 (1965).
71. E. Rengade, Ann. Chim. Phys., **11**, 348 (1907).
72. H. Normant and T. Cuvigny, Bull. Soc. chim. France, 2004 (1964).
73. O. Yu. Okhlobystin and L. I. Zakharkin, Zhur. Org. Khim., **3**, 257 (1965).

74. T. Cuvigny and H. Normant, Bull. Soc. chim. France, 1876 (1965).
75. T. Cuvigny and H. Normant, Bull. Soc. chim. France, 2022 (1965).
76. T. Cuvigny and H. Normant, Bull. Soc. chim. France, 1873 (1965).
77. J. Ficini and G. Barbara, Bull. Soc. chim. France, 2787 (1965).
78. T. Cuvigny and H. Normant, Bull. Soc. chim. France, 1874 (1965).
79. H. Normant and T. Cuvigny, Bull. Soc. chim. France, 1881 (1965).
80. H. G. Viche and P. Valange, Chem. Ber., 96, 420 (1963).
81. H. Normant and J. Villiéras, Compt. rend., 260, 4525 (1965); J. Villiéras, Compt. rend., 261, 4137 (1965).
82. J. Villiéras, Bull. Soc. chim. France, 1511, 1520 (1967).
83. H. Normant and T. Cuvigny, Bull. Soc. chim. France, 1883 (1965).
84. J. Ficini and G. Barbara, Bull. Soc. chim. France, 2787 (1965).
85. G. Strutz and G. Lavielle, Compt. rend., 261, 2679 (1965).
86. D. J. Cram, et al., J. Amer. Chem. Soc., 84, 4358 (1962).
87. T. Cuvigny and H. Normant, Bull. Soc. chim. France, 2003 (1964).
88. H. Normant and T. Cuvigny, Bull. Soc. chim. France, 1884 (1965).
89. H. Normant and T. Cuvigny, Bull. Soc. chim. France, 3344 (1966).
90. J. Luchesi, Chimie et Industrie, 47, 1313 (1965).
91. H. E. Zaug, et al., J. Amer. Chem. Soc., 82, 2895 (1960).
92. J. F. Normant and H. Deshayes, Bull. Soc. chim. France, 2455 (1967).
93. B. T. Freure and H. J. Decker, Chem. Abs., 57, 11032e (1962).
94. H. Normant and T. Cuvigny, Bull. Soc. chim. France, 1882, 1887 (1965).
95. J. F. Normant, Bull. Soc. chim. France, 1888 (1963).
96. T. Cuvigny and H. Normant, Bull. Soc. chim. France, 2003 (1964).
97. T. F. Rutledge, J. Org. Chem., 22, 649 (1957).
98. J. F. Normant, Bull. Soc. chim. France, 859 (1965).
99. P. Mazerolles, M. Lesbre, and S. Marre, Compt. rend., 261, 4134 (1965).
100. T. Cuvigny and H. Normant, Bull. Soc. chim. France, 1877 (1965).
101. H. Normant and T. Cuvigny, Bull. Soc. chim. France, 1882 (1965).
102. J. Bourdais and C. B. Mahieu, Compt. rend., 263C, 84 (1966).
103. B. P. 839420; Chem. Abs., 54, 24549g (1960).
104. J. R. Campbell, J. Org. Chem., 29, 1830 (1964).
105. H. Normant and T. Cuvigny, Bull. Soc. chim. France, 1870 (1965).
106. P. Caubère, Bull. Soc. chim. France, in the press.
107. N. Kornblum, et al., J. Amer. Chem. Soc., 85, 1141 1148 (1963).
108. C. F. Hobbs, et al., J. Amer. Chem. Soc., 84, 43 (1962).
109. J. M. Conia, Rec. Chem. Progr., 24, 43 (1963).
110. G. J. Heiszwolf and H. Kloosterziel, Chem. Comm., 51 (1966).
111. H. D. Zook and W. L. Cumby, J. Amer. Chem. Soc., 82, 1258, 1387 (1960).
112. J. P. Boisset, J. Boyer, and J. Rouzaud, Compt. rend., 263C, 1253 (1966).
113. J. Fauvarque and J. F. Fauvarque, Compt. rend., 263C, 488 (1966).
114. G. Stork and S. R. Dowd, J. Amer. Chem. Soc., 85, 2178 (1966).
115. G. J. Heiszwolf and H. Kloosterziel, Chem. Comm., 767 (1966).
116. R. L. Gay, S. Boatman, and C. R. Hauser, Chem. and Ind., 1789 (1965).
117. E. J. Corey and G. T. Kwiatkowski, J. Amer. Chem. Soc., 88, 5652 (1966).
118. L. L. McCoy, J. Amer. Chem. Soc., 82, 6416 (1960); 84, 2246 (1962).
119. L. L. McCoy and C. W. Nachtigall, J. Org. Chem., 27, 4312 (1962).
120. M. Causse-Toller and R. Fraisse-Jullien, Bull. Soc. chim. France, 430 (1966).
121. J. Seyden-Penne, C. Gibert, and B. Daurée, Compt. rend., 263C, 895 (1966).
122. A. Cavé, F. X. Jarreau, Qui Khuong Huu, M. Leboeuf, N. Serban, and R. Goutarel, Bull. Soc. chim. France, 701 (1967).
123. M. Leboeuf, A. Cavê, and R. Goutarel, Compt. rend., 264C, 1090 (1967).
124. J. F. Normant, Bull. Soc. chim. France, 1868 (1963).
125. J. F. Normant, Bull. Soc. chim. France, 1876 (1963).
126. J. F. Normant, Bull. Soc. chim. France, 1888 (1963).
127. T. Cuvigny, H. Normant, and J. F. Normant, Compt. rend., 258, 3502 (1964).
128. P. Caubère, Bull. Soc. chim. France, 1293 (1966).
129. J. F. Normant, Bull. Soc. chim. France, 859 (1965).
130. A. Schriensheim, C. A. Rowe, and W. Bartok, Compt. rend., 59, 3772g (1963).
131. H. R. Nace, J. Amer. Chem. Soc., 81, 5428 (1959).
132. T. J. Wallace, et al., J. Amer. Chem. Soc., 85, 2739 (1963).
133. T. J. Wallace, et al., Chem. and Ind., 1268 (1965).
134. T. J. Wallace, et al., Proc. Chem. Soc., 173 (1963); J. Chem. Soc., 1271 (1965).
135. H. Normant and T. Cuvigny, Bull. Soc. chim. France, 1867 (1965).
136. G. A. Russell, Preprints, 17th Nat. Org. Symp. Bloomington, June 25–29th 1961.
137. G. A. Russell, et al., J. Amer. Chem. Soc., 84, 2652 (1962).
138. J. E. Normant, et al., J. Amer. Chem. Soc., 20, 2523 (1965).
139. T. J. Wallace, J. Org. Chem., 20, 3770 (1965).
140. T. J. Wallace, A. Schriesheim, Tetrahedron, 21, 2271 (1965).
141. T. J. Wallace, et al., J. Org. Chem., 30, 3147 (1965).
142. T. J. Wallace, J. Org. Chem., 30, 4017 (1965).
143. T. J. Wallace, et al., J. Org. Chem., 30, 3768 (1965).
144. T. J. Wallace and F. A. Baron, J. Org. Chem., 30, 3520 (1965).
145. H. Normant, Bull. Soc. chim. France, 1436 (1963).
146. A. Lüttringhaus and H. W. Dirksen, Angew. Chem. Internat. Edn., 3, 266 (1964).
147. W. E. Truce and F. E. Roberts, J. Org. Chem., 28, 961 (1963).
148. D. B. Denney and L. Saferstein, J. Amer. Chem. Soc., 88, 1839 (1966).
149. E. J. Corey and M. Chaykowsky, J. Amer. Chem. Soc., 84, 866 (1962).
150. T. Cuvigny, J. Normant, and H. Normant, Compt. rend., 258, 3503 (1964).

151. H. Normant, T. Cuvigny, J. Normant, and B. Angelo, Bull. Soc. chim. France, 1561 (1965).
152. G. Fraenkel, S. H. Ellis, and D. T. Dix, J. Amer. Chem. Soc., 87, 1406 (1965).
153. H. Normant, T. Cuvigny, J. Normant, and B. Angelo, Bull. Soc. chim. France, 3441 (1965).
154. M. Fontanille and P. Sigwalt, Compt. rend., 262C, 1208 (1966).
155. M. Fontanille and P. Sigwalt, Compt. rend., 263C, 316 (1966).
156. H. Normant, T. Cuvigny, J. Normant, and B. Angelo, Bull. Soc. chim. France, 3442 (1965).
157. J. Vidal and Y. Chauvin, Rev. Inst. franc, Pétrole, 19, 1222 (1964).
158. B. J. McClelland, Chem. Rev., 64, 301 (1964).
159. H. Normant and B. Angelo, Bull. Soc. chim. France, 354 (1960).
160. H. Normant and B. Angelo, Bull. Soc. chim. France, 1988 (1961).
161. H. Normant and B. Angelo, Bull. Soc. chim. France, 810 (1962).
162. S. Boileau and P. Sigwalt, Compt. rend., 262C, 1135 (1966).
163. C. Ivanoff and P. Markov, Naturwiss., 50, 688 (1963).
164. J. P. Pascault and J. Golé, Compt. rend., 264C, 115 (1967).
165. H. Normant, unpublished results.
166. H. W. Sternberg, R. E. Markby, I. Wender, and D. M. Mohilner, J. Amer. Chem. Soc., 89, 186 (1967).
167. H. Normant, T. Cuvigny, J. Normant, and B. Angelo, Bull. Soc. chim. France, 3447 (1965).
168. H. Normant, T. Cuvigny, J. Normant, and B. Angelo, Bull. Soc. chim. France, 3448 (1965).
169. H. Normant, T. Cuvigny, J. Normant, and B. Angelo, Bull. Soc. chim. France, 3449 (1965).
170. L. Pichat and J. P. Guermont, personal communication.
171. H. Normant and M. Larchevêque, Compt. rend., 260, 5062 (1965).
172. P. Grammaticakis, Compt. rend., 210, 716 (1940).
173. E, Pfeit and H. Barthe, Annalen, 593, 81 (1965).
174. M. Larchevêque, unpublished results.
175. P. Angibeaud and H. Rivière, Compt. rend., 263C, 1076 (1966).
176. P. Angibeaud, M. Larchevêque, H. Normant, and B. Tchoubar, Bull. Soc. chim. France, in the press.
177. D. A. Edwards, J. A. Kerr, A. C. Lloyd, and A. F. Trotman-Dickenson, J. Chem. Soc., (A), 1500 (1966).
178. R. F. Bridger and G. A. Russell, J. Amer. Chem. Soc., 85, 3761 (1963).
179. H. Normant, T. Cuvigny, and G. Martin, unpublished results.
180. H. Normant, T. Cuvigny, J. Normant, and B. Angelo, Bull. Soc. chim. France, 3450 (1965).
181. E. J. Bulten and J. G. Noltes, Tetrahedron Letters, 4389 (1966).
182. P. O. Shorygin and S. A. Skoblinskaja, Compt. rend., Acad. Sci. U. R. S. S., 14, 505 (1937).
183. G. Wittig and L. Löhmann, Annalen, 550, 260 (1943).
184. G. W. Kenner and N. R. Williams, J. Chem. Soc., 522 (1955).
185. H. Normant and T. Cuvigny, Bull. Soc. chim. France, 3347 (1966).
186. C. Rivat, 2e Thèse, Faculté des Sciences de Rouen, 1965, p. 11.
187. P. Sigwalt, Bull. Soc. chim. France, 423 (1964).
188. C. E. Frank, et al., J. Org. Chem., 26, 307 (1961).
189. M. Fontanilie and P. Sigwalt, Compt. rend., 263C, 624 (1966).
190. P. Sigwalt and P. Rempp, personal communication.
191. A. Lüttringhaus and H. W. Dirksen, Angew. Chem. Internat. Edn., 3, 260 (1964).
192. H. W. Dirksen, Ph. D. Thesis, Universität Freiburg, 1961.
193. H. Bredereck, F. Effenberger, and R. Gleiter, Angew. Chem. Internat. Edn., 4, 951 (1965).
194. E. T. Kaiser, et al., J. Amer. Chem. Soc., 88, 1037 (1966).
195. A. Lewith and N. McFarlane, Proc. Chem. Soc., 108 (1964).
196.§ A. L. Kurts, I. P. Beletskaya, A. Macias, and O. A. Reutov, Tetrahedron Letters, 3679 (1968).
197.§ A. L. Kurts, I. P. Beletskaya, N. K. Genkina, and O. A. Reutov, Dokl. Akad. Nauk SSSR, 186, 817 (1969).

Laboratoire de Synthèse organique,
La Sorbonne,
Paris

§Added by Editors.