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The introduction of functional groups into unsaturated systems by carbonyl compounds in the presence of manganese(III) acetate

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ABSTRACT. **The review is devoted to the reactions of unsaturated systems (alkenes, alkynes, arenes, alkadienes, and alkenynes) with carbonyl compounds (aldehydes, ketones, carboxylic acids, and α-, β-, γ-, and δ-dicarbonyl compounds) initiated by manganese(III) acetate. Attention is concentrated on the regio- and stereo-chemistry of the interaction, the pathways leading to the stabilisation of the intermediate radical-adducts, and also the assessment of the synthetic possibilities of reactions of the given type.**

The bibliography includes 91 references.

I. Introduction

The development of methods for the generation of free radicals with the aid of oxidation-reduction systems, especially the salts and oxides of variable-valence transition metals (Mn^{3+}, Co^{3+}, Cu^{2+}, Fe^{3+}, Ag^{2+}, Pb^{4+}, Ce^{4+}, Mn^{4+}, Ag^{+}, Cu^{+}, Fe^{2+}, and Cr^{2+}), has been a powerful stimulus to the development of the chemistry of such radicals.[1–4] Compared with the traditional method of radical generation, oxidation-reduction methods have a greater selectivity, in particular in relation to polyfunctional organic compounds. Furthermore, radicals which cannot be generated by classical methods can be obtained with their aid.[3]

The oxidation radical generation methods, proceeding via outer- and inner-sphere mechanisms, have now been investigated most widely.[4] The fundamental difference between them consists in the fact that the oxidant not only generates the radical from the addend in the initiation stage but reacts effectively with the radical-adduct formed when the radical adds to the organic substrate; as a result of this, the synthetic result of the reaction is different from that of the reaction initiated by classical methods.[5]

In the series of oxidants listed above, manganese(III) acetate is of special interest. The one-electron oxidation by the latter of the α-C–H bonds of carbonyl compounds generates α-oxo- and αα-dioxo-alkyl radicals, which react with unsaturated substrates when the latter are present in the reaction mixture. The subject of the present review is the consideration of reactions of precisely this type where monocarbonyl compounds—aldehydes, ketones, carboxylic acids, and α-, β-, γ-, and δ-dicarbonyl compounds—serve as the addend, the initiator is manganese(III) acetate, used separately or in combination with copper(II) acetate, and the unsaturated substrates consist of alkenes, alkynes, arenes, alkadienes, alkenynes, and alkadiynes. Attention will be concentrated on the regiochemistry of the generation of the oxoalkyl radicals, the regio- and stereochemistry of the interaction of the latter with the substrates, the pathways leading to the stabilisation of the intermediate radical-adducts, and the assessment of the synthetic possibilities of the reactions of the given type, including their use for the synthesis of natural products.

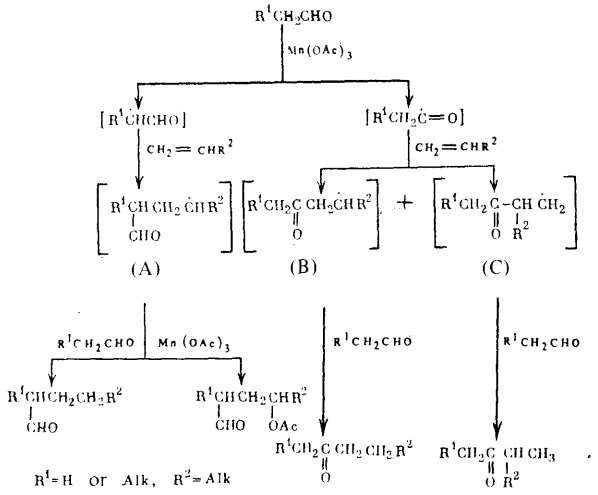
II. Reactions of alkenes with monocarbonyl compounds

1. Reactions with aldehydes

When aldehydes are oxidised by manganese(III) acetate, radicals of two types are formed—the α-formylalkyl radicals $R\dot{C}HCHO$ and the acyl radicals $RCH_2\dot{C}=O$, the type of the radical generated depending on the manganese(III) acetate concentration in the solution.[3,6] In a polar solvent (homogeneous conditions), the α-formylalkyl radicals are formed preferentially, while in the absence of solvent (heterogeneous conditions) the main product is acyl radicals, as for peroxide initiators.[7] It has been established that a primary isotope effect (k_H/k_D = 6) is observed for the reaction of CD_3CHO with $Mn(OAc)_3$, while in the reaction of CH_3CDO with $Mn(OAc)_3$ it is absent. This finding permits the conclusion that the direct interaction of the aldehyde with $Mn(OAc)_3$ yields the α-formylalkyl radicals, while the corresponding acyl radicals are apparently formed as a result of a secondary hydrogen atom transfer reaction.[3] It is also noteworthy that, in the oxidation of aldehydes without α-hydrogen atoms, for example, pivalaldehyde, acyl radicals are formed directly.[8]

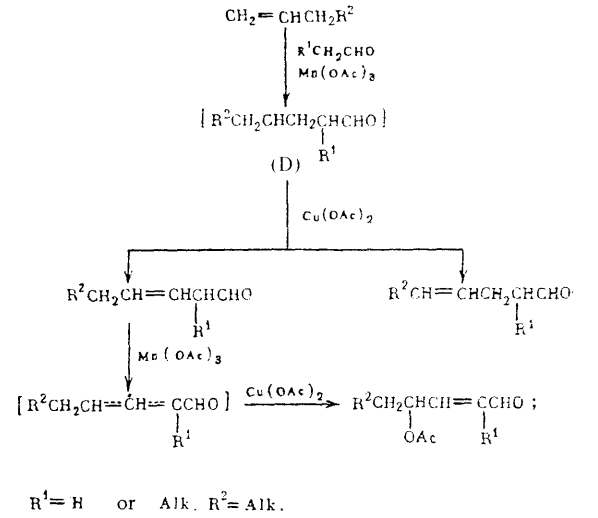
The addition of α-formylalkyl radicals to an alk-1-ene under homogeneous conditions affords radical-adducts of type (A), which are stabilised by the abstraction of a hydrogen atom or by oxidation with manganese(III) acetate via a ligand transfer mechanism.[1]

Radical-adducts of types (B) and (C) are formed under heterogeneous conditions and are stabilised by the addition of a hydrogen atom, which leads to isomeric saturated ketones:[9]



Depending on the structure of the aldehyde and the alkene, the ratio of the products listed in the above scheme is between 74:26 to 100:0 for homogeneous conditions and from 20:80 to 52:75 for heterogeneous conditions. This reaction has been proposed as a single-stage method of synthesis of higher α-alkyl-substituted aldehydes.[10]

The modification of the reaction of aldehydes with alkenes by the addition of catalytic amounts of copper(II) acetate proved to be extremely effective: the intermediate radical-adduct of type (D) was stabilised as a result of the oxidative elimination of β-protons, which led to γδ- and βγ-unsaturated aldehydes. Under the reaction conditions, the latter underwent further oxidation with formation of *trans*-4-acetoxyalk-2-enals:[11]

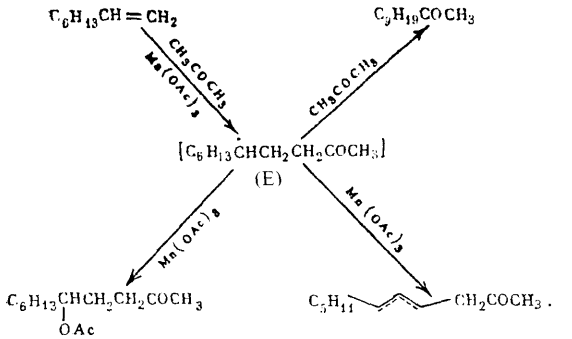


On passing from monosubstituted to 1,1-disubstituted alkenes, the chemistry of the reaction changes appreciably.[12] The main reaction products then become βγ- and γδ-unsaturated aldehydes also in the absence of copper(II) acetate. The authors explain this result by the nature of the intermediate radical-adducts, the difference between which is reflected quantitatively by the ratio of the rate constants for the oxidative elimination (k_{ox}) and abstraction of a hydrogen atom (k_{abs}). The ratio k_{ox}/k_{abs} is higher by 1–2 orders of magnitude for tertiary radical-adducts than for secondary radical-adducts. The reaction of aldehydes with β-pinene proceeds analogously, the intermediate radical-adducts undergoing skeletal isomerisation with the opening of the four-membered ring under these conditions.[13]

A mechanism, according to which the aldehyde reacts with the manganese(III) salt to form initially an oxallyl complex, has been proposed on the basis of kinetic data for the reactions of aldehydes with alkenes. The oxallyl complex decomposes reversibly with formation of α-formylalkyl free radicals, the regioselectivity of the alkylation of aldehydes by alkenes being determined by the equilibrium position.[14]

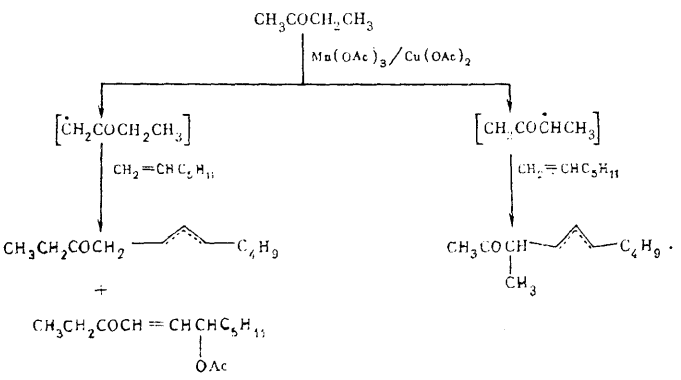
2. Reactions of ketones

The interaction of aliphatic and aromatic ketones with manganese(III) acetate leads to the formation of α-oxoalkyl radicals.[15–17] In the presence of unsaturated substrates, for example an alk-1-ene, the acetonyl radical, generated from acetone, affords the radical-adduct (E), which abstracts a hydrogen atom from the acetone or acetic acid molecule and undergoes oxidative elimination or substitution on treatment with manganese(III) acetate:[18,19]

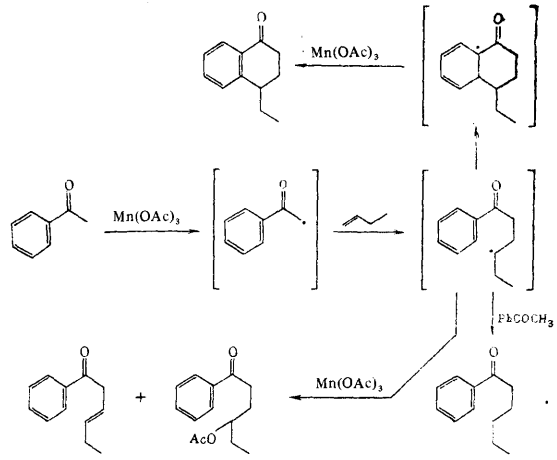


The authors established a direct proportionality between the ratio of the reaction products and the acetone concentration, and showed that, in the hydrogen atom transfer stage, acetone is four times more active than acetic acid. In addition, it was demonstrated that the addition of copper(II) acetate to the reaction mixture greatly increases the content of unsaturated ketones and γ-acetoxyketones as a result of the ability of $Cu(OAc)_2$ to oxidise alkyl radicals more effectively compared with $Mn(OAc)_3$.[5] The $Mn^{3+}/Ce^{4+}/Cu^{2+}$ relative reactivity of the ions in the oxidation of secondary radical-adducts was determined quantitatively as 1/12/350.[19]

The methylene group participates preferentially in the oxidation of ethyl methyl ketone, but the methyl group is also involved:[20]



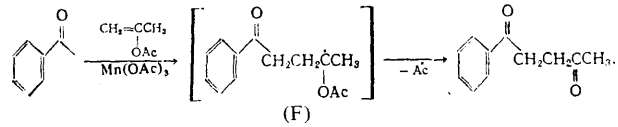
The interaction of aliphatic-aromatic ketones with alk-1-enes involves a new reaction pathway, together with those described above, namely intramolecular cyclisation leading to bicyclic compounds.[21] In particular, the reactions involving the cyclisation of acetophenone and but-1-ene yield a substituted tetralone:



The intramolecular cyclisation of δ-phenylalkyl radicals has been used to synthesise tetralin and indan derivatives.[21]

Cyclic ketones are oxidised by manganese(III) acetate, forming 2-oxocycloalkyl radicals, which interact with alkenes analogously to acyclic radicals.[20,22] It is remarkable that the ratio of the oxidative elimination products (βγ- and γδ-enones) depends on the ring size of the initial cycloalkanone.[22]

Enol ethers have also been involved in the reaction with ketones, which has made it possible to develop a single-stage method for the synthesis of 1,4-diketones—intermediates in the synthesis of jasmonoids.[23-25] For example, the addition of acetophenone to isopropenyl acetate leads initially to the radical-adduct (F), which is stabilised via the β-elimination of the acetyl radical with formation of a 1,4-diketone:[23]



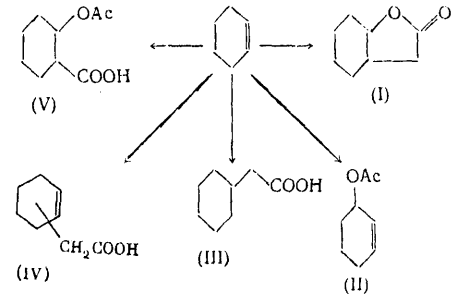
The analogous reactions of cyclohexanone, 2-octanone, and 3-methyl-2-heptanone have been investigated; the reaction involving asymmetric ketones results in the formation of a mixture of isomeric 1,4-diketones in accordance with two types of α-oxoalkyl radicals generated by the oxidation with manganese(III) acetate.[23] This reaction was subsequently extended by involving in it terpene ketones—nopinone, *cis*-verbanone, isonopinone, and isomenthone[24]—and has also been used in a key stage in the specific synthesis of 2-pentyl-2-cyclopent-1-enone—the precursor of dihydrojasmone and methyldihydrojasmonate.[25]

The telomerisation of ethylene with acetone, initiated by manganese(III) acetate, has also been investigated.[26-28] The products are 2-alkanones with a linear structure and isomeric 3-butyl-2-alkanones, formed as a result of the intermolecular rearrangement of the intermediate radical-adduct with 1,5-migration of a hydrogen atom. On catalysis by copper(II) acetate at an ethylene pressure of 100 atm, the main reaction pathway becomes the oxidative elimination of the telomeric radicals, leading to ω-unsaturated ketones.[27]

3. Reactions with carboxylic acids

The interaction of carboxylic acids with manganese(III) acetate is known to generate α-carboxyalkyl radicals.[3] The latter are capable of adding to the double bond of alkenes with formation of 3-carboxyalkyl radicals, which cyclise to alkan-4-olides in the presence of one-electron oxidants.[29-35] The formation of allyl acetates[30,32] as a result of the abstraction of the allyl hydrogen atom by the α-carboxymethyl radical and subsequent acetoxylation has been detected in a number of instances. It is notable that the selectivity of the lactonisation of the lactone:allyl acetate product ratio is 30:1 for methylstyrene and 50:1 for oct-1-ene.[32]

The lactonisation of alkenes by treatment with acetic acid and manganese(III) acetate is achieved in the presence of acetic anhydride[30] or potassium acetate.[32] The synthetic result of the application of two alternative methods is frequently the same,[30-32] but in the case of oct-1-ene the addition of potassium acetate leads to the corresponding lactone[32] whereas the main product resulting from the use of acetic anhydride is decanoic acid together with small amounts of decan-4-olide and 3- and 4-decenoic acids.[36] It is remarkable that the application of the same method involving the use of acetic anhydride by different investigators yielded different results. In the reaction involving cyclohexene, the formation of the lactone (I) and allyl acetate (II) has been detected by Bush and Finkbeiner.[30] Subsequently carboxymethylcyclohexane (III), carboxymethylcyclohexene (IV), and 1-acetoxy-2-carboxymethylcyclohexane (V) were also isolated:[37]

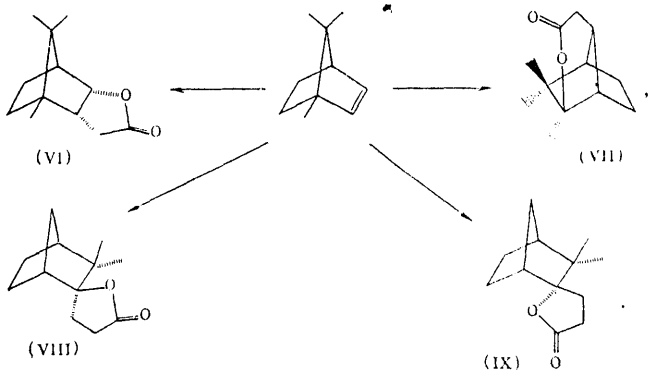


An analogous picture has been observed for cyclopentene, 1-methylcyclohexene, hex-1-ene, and 2-methylpent-2-ene.[37,38]

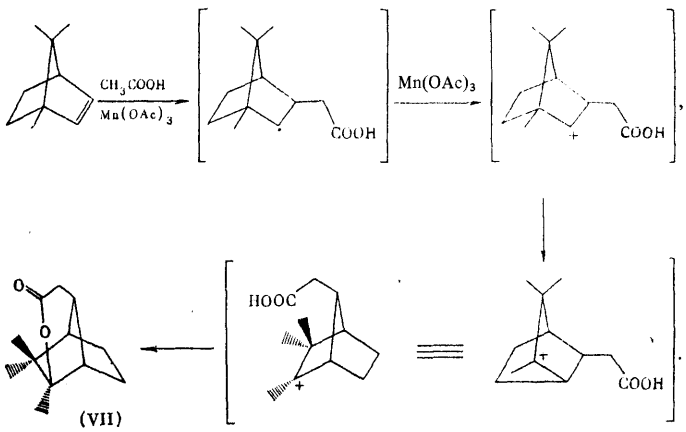
The monoterpenes *p*-menth-1-ene, 3-carene, α-pinene, bornene, and camphene have also been involved in the reaction with acetic acid initiated by manganese(III) acetate.[39-42] The products of the reactions for the first two compounds are lactones[39,40] but, on passing to α-pinene, the reaction chemistry changes appreciably.[41] The expected lactone is a minor reaction product, a mixture of the acetates of *cis*-pin-3-en-2-ol, myrtenol, and α-terpineol being mainly formed.[41] The last compound is produced as a result of the isomerisation of α-pinene via a carbonium ion mechanism under the influence of acetic acid.

The interaction of bornene with acetic acid affords a mixture of the isomeric lactones (VI)–(IX) and it has been demonstrated unambiguously that the formation of the *exo*- and *endo*-lactones (VIII) and (IX) is a result of the acid-catalysed rearrangement of

bornene to camphene and its subsequent interaction with acetic acid:[42]



The presence among the reaction products of the δ-lactone (VII), which is formed via the scheme presented below involving the Wagner–Meerwein rearrangement stage, is of separate interest:

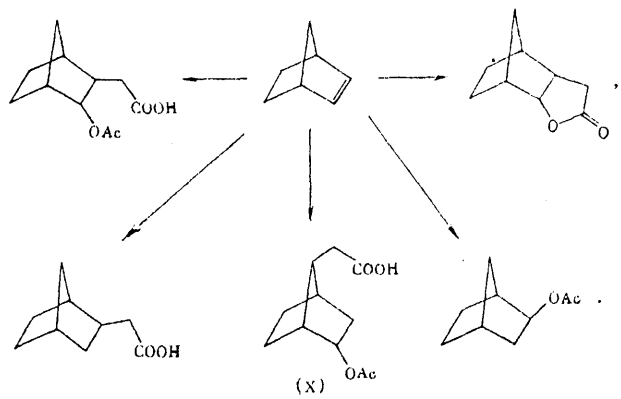


Since the Wagner–Meerwein rearrangement does not take place for radicals, the authors believe that this reaction indicates the intermediate formation of carbonium ions in the oxidation of radicals by manganese(III) acetate.[42]

Reactions of the above type have been modified by carrying them out in the presence of potassium bromide[43,44] and potassium or copper(II) acetates.[45,46] In the former case, the main reaction products are substituted allyl acetates while in the latter the main products are *trans*-alk-4-enoic acids.

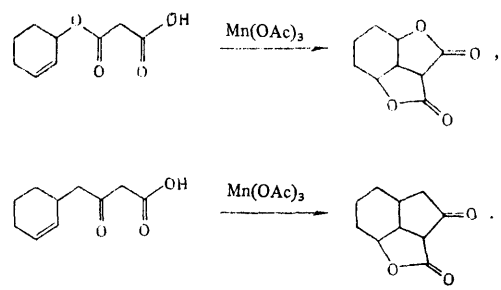
Detailed investigation of the reaction of alkenes with acetic acid has shown that (a) the use of manganese(III) acetate trihydrate is more effective in the synthesis of alkan-4-olides than the use of the anhydrous salt, that (b) acetic anhydride increases the rate of reaction as a consequence of its greater C–H acidity compared with acetic acid but the yields of alkan-4-olides are reduced as a result of the formation of unsaturated and α-acetoxy-substituted carboxylic acids, and that (c) potassium acetate increases the yield of alkan-4-olides by playing the role of a base facilitating deprotonation in the acetoxidation stage.[47] The study of the stereochemistry of the lactonisation reaction showed that the alkan-4-olides are mixtures of geometrical isomers and that their ratio varies within wide limits depending on the structure of the alkene—from 67:1 to 1:5.4.[47]

Like bornene, norbornene gives rise to a mixture of products on lactonisation, among which compound (X)—the result of the Wagner–Meerwein rearrangement of the intermediate cation—is formed in 1% yield.[47] On this basis, the authors claim that the reaction takes place almost fully via a radical mechanism and that there is no formation of intermediate carbonium ions in the oxidation of alkyl radicals by manganese(III) acetate:

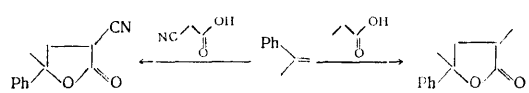


It is remarkable that this conclusion conflicts with the conclusion reached by Witkiewicz and Chabudzinski[42] that a carbonium ion is formed in an analogous reaction.

The lactonisation of alkenes by acetic acid has been used to synthesise jointed ketolactones and dilactones, which are intermediates in the synthesis of polycyclic compounds of natural origin:[48]



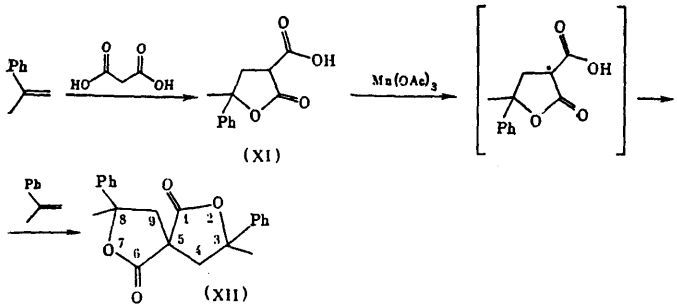
It has been reported that propionic[31,38,49] and cyanoacetic[31,50] acids also enter into the cycloalkylation reaction with alkenes and that the reaction involving α-methylstyrene results in the selective formation of 2-methyl- and 2-cyano-4-phenyl-lakan-4-olides:[31]



The interaction of camphene with cyanoaectic acid proceeds analogously.[50] On the other hand, the interaction of cyclohexene, cyclopentene, 1-methylcyclohexene, hex-1-ene, 2-methylpent-2-ene with propionic acid proceeds non-selectively.[38,49]

Malonic acid is the only dicarboxylic acid which has been introduced into the reaction with alkenes initiated by manganese(III) acetate;[51] the αα-dicarboxymethylradical adds in this reaction, in particular to α-methylstyrene with formation of the lactone (XI), which undergoes further oxidation and this leads to the

spirolactone (XII) in the form of a mixture of stereoisomers [3(*R*), 5(*R*), 8(*R*)-, 3(*S*), 5(*R*), 8(*S*)-, and 3(*R*), 5(*R*), 8(*S*)-]:



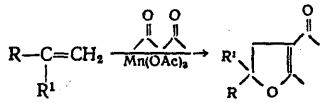
(XI)

(XII)

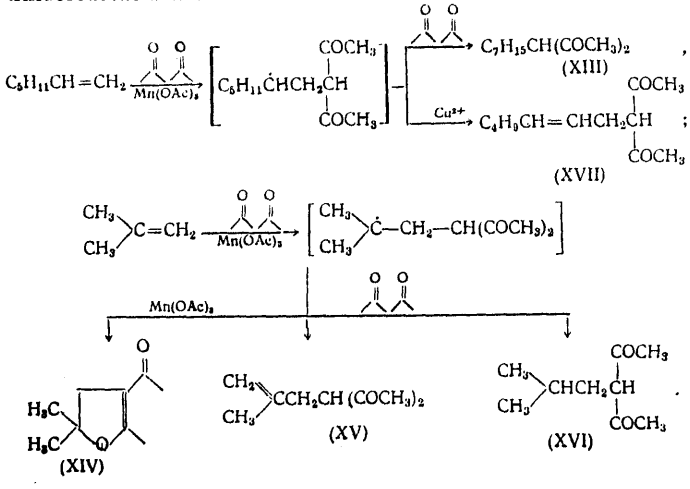
Manganese(III) acetate also initiates the interaction of carboxylic acid anhydrides with alkenes. The reaction products are saturated carboxylic acids.[52]

III. Reactions of alkenes with dicarbonyl compounds

Acetylacetone is oxidised selectively by manganese(III) acetate at the methylene group of the acetylacetonyl.[53,54] When the above reaction is carried out in the presence of α-methylstyrene,[53] styrene,[53,54] 2-methylpent-2-ene,[53] and oct-1-ene,[53] it is accompanied by oxidative cyclisation to the 4,5-dihydrofuran derivatives:



The interaction of hept-1-ene with acetylacetone results in the formation of an adduct—3-acetyl-2-decanone (XIII), while the reaction of isobutene affords, together with dihydrofuran (XIV), also the diketones (XV) and (XVI) in proportions of 35:18:3.[54] In the presence of copper(II) acetate, the unsaturated diketone (XVII) is also obtained together with compound (XIII) (in proportions of 1:2). On the other hand, in the case of isobutene the effect of the introduction of $Cu(OAc)_2$ proved to be insignificant.[54] A detailed investigation of the reaction of hex-1-ene with acetylacetone showed that, depending on the reaction conditions, there is also a possibility of the formation of a 4,5-dihydrofuran derivative of type (XIV) together with an adduct of type (XIII).[55] The content of the dihydrofuran derivative increases with increasing acetic acid/acetylacetone ratio and manganese(III) acetate concentration and when water and trifluoroacetic acid are added:

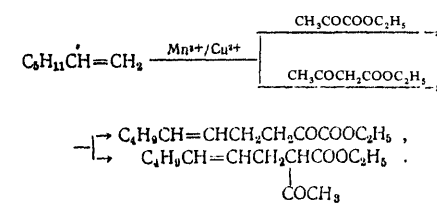


(XIII), (XVII)

(XIV) (XV) (XVI)

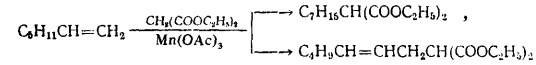
Cyclohexane-1,3-dione reacts with alkenes similarly to acetylacetone and the reaction products are substituted benzofurans.[53] Together with 1,3-diketones, the esters of carboxylic α-, β-, and γ-ketoacids and α-, β-, and γ-acetoxy-substituted aliphatic ketones have also been involved in the reaction with alkenes.[53,56,57] The selectivity in the formation of radicals on oxidation with manganese(III) acetate depends on the structure of the ketoesters. In the reaction of the acetoacetic ester, the radicals are generated from the methylene group, while in the reaction of the acetate of diacetonyl alcohol and ethyl pyruvate they are formed from the ethyl group. On the other hand, acetylpropyl acetate, methyl levulinate, and acetoxyacetone give rise to mixtures of isomeric radicals and, with decrease in the number of carbon atoms between the carbonyl and ester groups, the involvement of the methyl group in the oxidation increases appreciably.[57]

The nature of the products formed in the interaction of ketoesters with alkenes depends both on the structure of the latter and on the participation of copper(II) acetate in the reaction. In particular, styrene reacts with acetoacetic ester in the same way as with acetylacetone, forming 4,5-dihydrofuran derivatives.[53] The reaction of hept-1-ene with ethyl pyruvate and acetoacetic ester leads selectively to γδ-unsaturated ketoesters:[57]



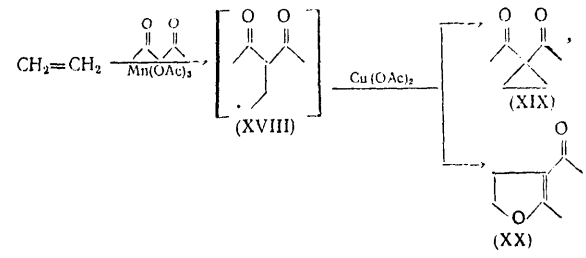
The remaining ketoesters listed above afford products with both linear and branched structures in which the double bond is in the βγ-and γδ-positions relative to the keto-group in their reactions with alkenes.[57]

Diethyl malonate has also been introduced into the reaction with alkenes initiated by manganese(III) acetate.[56,58] In the reaction with hept-1-ene, addition is observed; when the reaction is catalysed by copper(II) acetate, the main pathway becomes oxidative deprotonation:



The reaction proceeds similarly also with ethyl cyanoacetate and with diethyl butylmalonate.[56]

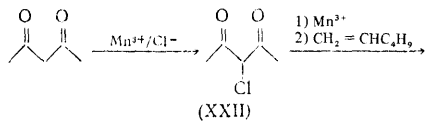
A new reaction pathway was discovered in the interaction of ethylene with β-dicarbonyl compounds.[59] The intermediate radical adduct (XVIII) undergoes oxidative 1,3-cyclisation on treatment with copper(II) acetate with formation of the *gem*-disubstituted cyclopropane (XIX) together with the dihydrofuran (XX):



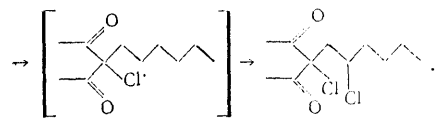
(XVIII) (XIX) (XX)

In contrast to reactions with acetylacetone and acetoacetic ester, in the interaction of ethylene with cyanoacetic and malonic esters the radical-adducts of type (XVIII) undergo oxidative elimination and prototropic isomerisation with formation of ethylidenecyanoacetic and ethylidenemalonic esters.[60]

The reactions of alkenes with dicarbonyl compounds initiated by manganese(III) acetate have been modified by carrying them out in the presence of lithium chloride.[55,61] In this case, the products are either 1,3-dichloro- or monochloro-derivatives of β-dicarbonyl compounds. In particular, 3-acetyl-3,5-dichloro-2-nonanone (XXI) was isolated in the reaction of hex-1-ene with acetylacetone. The proposed reaction mechanism involved the formation of monochloroacetylacetone (XXII), the oxidative addition of the latter to the double bond of the substrate, and the subsequent chlorination of the radical-adduct (G):[55]

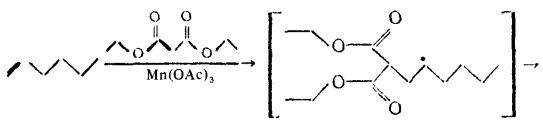


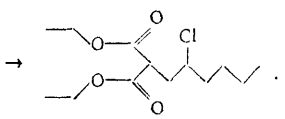
(XXII)



(G) (XXI)

The mechanism of the reaction involving diethyl malonate differs from that illustrated above by the fact that lithium chloride participates in the reaction in the stage involving the oxidation of the intermediate radical-adduct and not in the radical generation stage, which leads to the monochlorosubstituted diester (XXIII):[61]



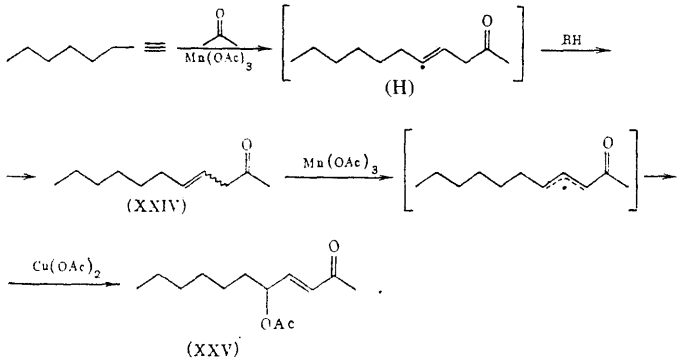


(XXIII)

Chloromalonic ester can also be used in this reaction as the dicarbonyl compound.[62]

IV. Reactions of alkynes with carbonyl compounds

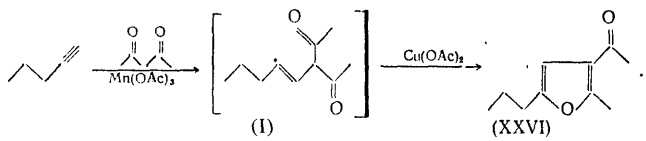
Alkynes have been investigated to an incomparably smaller extent than alkenes in reactions with carbonyl compounds initiated by manganese(III) acetate.[20,22,62,63] In particular, the interaction of oct-1-yne with acetone entails the initial formation of the vinyl radical-adduct (H), whose stabilisation as a result of the abstraction of hydrogen from the addend or the solvent leads to the βγ-unsaturated ketone (XXIV). The latter undergoes partial oxidation under the reaction conditions, being converted into *trans*-5-acetoxyundec-3-en-2-one (XXV):[20]



(H) (XXIV) (XXV)

In the reactions with cyclic ketones, the primary products are βγ-unsaturated ketones, which are converted as a result of prototropic isomerisation into 2-substituted 2-cycloalkenones, in particular the analogues of dihydrojasmone.[22]

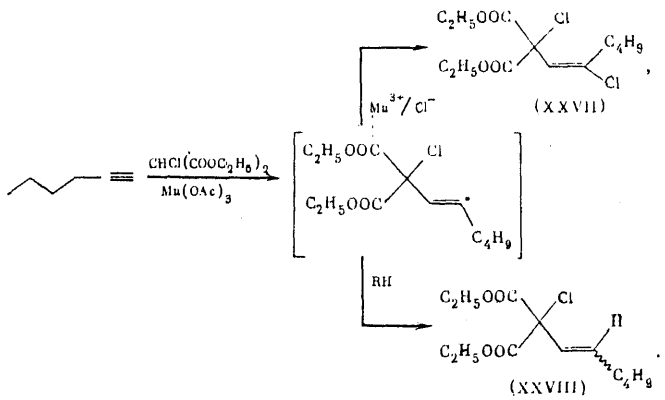
On passing from monocarbonyl to β-dicarbonyl compounds, a qualitatively new synthetic result has been achieved in reactions with alkynes. The vinyl radical-adduct (I), formed in the first stage of the reaction, undergoes oxidative cyclisation on treatment with copper(II) acetate, which leads to the furan derivative (XXVI):[63]



(I) (XXVI)

Acetylene, pent-1-yne, phenylacetylene, acetylacetone, and acetoacetic ester have been introduced into the above reaction.[63]

The reaction of chloromalonic ester with hex-1-yne has been investigated in the presence of the manganese(III) acetate–lithium chloride system[62] and it has been shown that the intermediate radical-adduct is stabilised by oxidative chlorination and addition of a hydrogen atom:

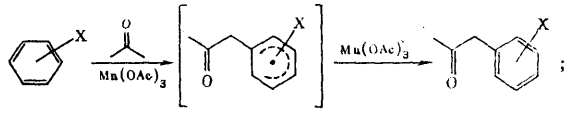


(XXVII) (XXVIII)

It has been established that the double bond in compound (XXVII) has the (*E*)-configuration, while the monochloro-derivative (XXVIII) is a mixture of geometrical isomers owing to the partial inversion of the vinyl group.[64]

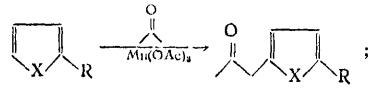
V. Reactions of arenes with carbonyl compounds

The oxoalkyl radicals generated in the oxidation of carbonyl compounds by manganese(III) acetate can interact with aromatic systems: benzene, its mono- and di-substituted derivatives, and naphthalene.[20,65–67] In the reaction with acetone, the intermediate radical-adducts are converted by oxidative elimination into *p*-, *m*-, and *o*-methylbenzyl ketones with the last predominating:[66,67]



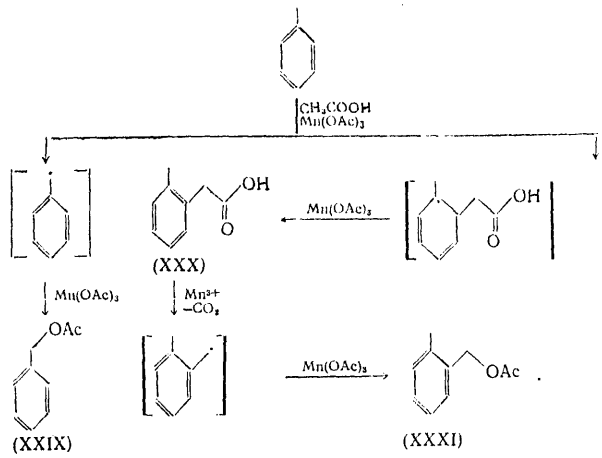
X = H, CH_3, CH_3O, Cl, CN, $COOC_2H_5$, F .

Furan, silvan, and thiophen also undergo homolytic substitution reactions with α-oxoalkyl radicals, but, in contrast to carbocyclic compounds, the reactions take place selectively via the α-carbon atom of the heteroaromatic ring:[66,68]



R = H, CH_3; X = O, S .

An analogous picture is observed in the interaction of the above heterocycles with acetylacetone.[68] The formation of benzyl acetate as a minor component has been detected in the reaction of toluene with acetone.[19] The same compound is one of the main products of the reaction of toluene with acetic acid.[69] Tolylacetic acid (XXX)—the result of the attack by the carboxymethyl radical on the aromatic nucleus—as well as methylbenzyl acetate (XXXI)—the product of the further oxidation of compound (XXX)—are formed under these conditions together with benzyl acetate (XXIX):



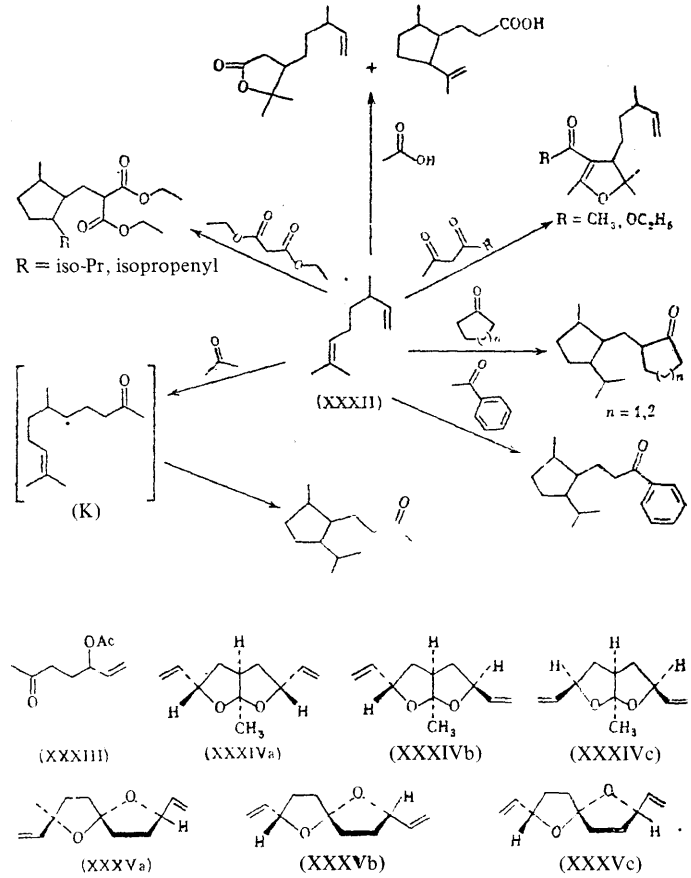
The interaction of arenes with nitromethane, leading to arylnitromethanes, is related to reactions of the type considered in this Section.[70,71]

VI. Reactions of alkadienes with carbonyl compounds

Alkadienes with isolated double bonds—octa-1,7-diene, 2,4-dimethylpenta-1,4-diene, and 2,5-dimethylhexa-1,5-diene—can interact with carbonyl compounds via both one and both double bonds,[72] which leads to 4-alkenylbutan-4-olides and bisbutan-4-olides in the reactions with acetic and cyanoacetic acids respectively. In the presence of double bonds substituted to different extents in the alkaldiene molecule, the regiochemistry depends on the nature of the carbonyl component.[73] In the reactions involving acetyl acetate and acetoacetic ester, radical attack is directed selectively to the C(6) atom of 3,7-dimethylocta-1,6-diene (XXXII), while in the reactions with cyclopentanone, cyclohexanone, acetophenone, diethyl malonate, and acetone the attack is directed to the C(1) atom. In contrast to this, the carboxymethyl radical generated from acetic acid adds to both the C(6) and the C(1) atoms.

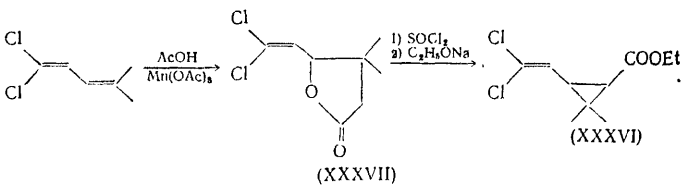
When a trisubstituted double bond is involved in the reaction, derivatives of a γ-lactone and 4,5-dihydrofuran are formed in the reactions involving acetic acid, acetylacetone, and acetoacetic ester, as in the analogous reactions of alk-1-enes.[29,31,53] The reaction involving a monosubstituted double bond leads to cyclopentane derivatives as a result of the intramolecular cyclisation of radical-adducts of type (K). The cyclopentane derivative is also the main product of the reaction of hexa-1,6-diene with acetic acid in the presence of manganese(III) acetate.[46]

An unexpected result has been obtained in the study of the reaction of acetone with butadiene.[74] It was found that the reaction products are 5-acetoxyhept-6-en-2-one (XXXIII), three isomeric 1-methyl-3,7-divinyl-2,8-dioxa-*cis*-bicyclo[3.3.0]octanes (XXXIV a–c), and three isomeric 2,7-divinyl-1,6-dioxaspiro[4,4]nonanes (XXXV a–c):



The authors proposed a mechanism involving the initial formation of compound (XXXIII), its subsequent oxidation by manganese(III) acetate, and interaction with a second butadiene molecule.[74]

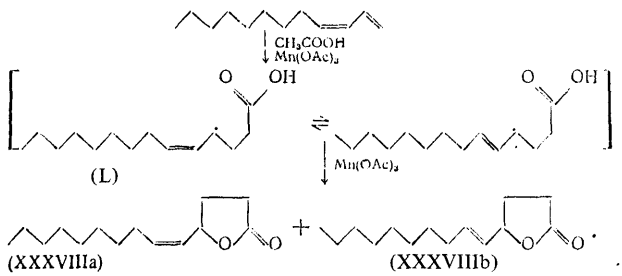
The reaction of an alkadiene with acetic acid, initiated by manganese(III) acetate, has been used as the key stage in the specific synthesis of pyrethroid (XXXVI); it involves the selective lactonisation of the tetrasubstituted alkadiene, leading to the lactone (XXXVII):[75]



(XXXVII) (XXXVI)

The analogous reaction of cyclopentadiene with acetic acid has also been described.[34]

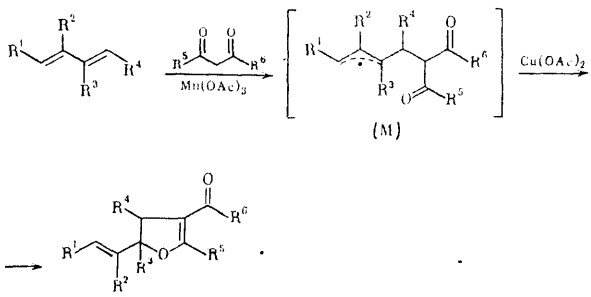
The data obtained in the stereochemical tests on the lactonisation reaction of *cis*-dodeca-1,3-diene are of individual interest.[76] It has been established that the reaction involves the inversion of the *cis*-double bond, leading to the *cis*- and *trans*-isomers of 5-tetradecen-4-olide (XXXVIIIa, b):



(L) (XXXVIIIa) (XXXVIIIb)

The change in the configuration of the double bond apparently occurs in the *cis*-allyl radical-adduct (L). We may note that the lactones (XXXVIIIa, b) have been isolated from the females of the japanese beetle, the *cis*-isomer (XXXVIIIa) being the sex pheromone of the given species.[77]

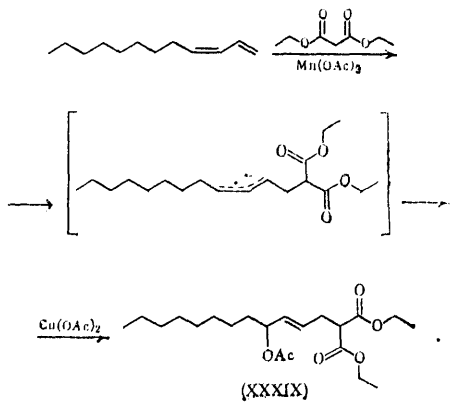
The oxidative addition of β-dicarbonyl compounds to conjugated alkadienes in the presence of manganese(III) and copper(II) acetates has also been investigated.[78–82] Butadiene, piperylene, isoprene, myrcene, methyl sorbate, crotonylideneacetone, cyclopentadiene, cyclohexadiene, bicyclopentadiene, 2,3-dimethylbutadiene, and vinylfuran were introduced as the unsaturated component, while acetylacetone, acetoacetic ester, dimedone, and diethyl acetonedicarboxylate were used as the carbonyl component. In all the cases examined, the products are derivatives of 4,5-dihydrofuran, formed as a result of the oxidative cyclisation of radical-adducts of type (M):



(M)

Reactions with isoprene and myrcene form mainly disubstituted double bonds. The activated dienes—methyl sorbate and crotonylideneacetone—react with acetylacetone preferentially via the α-carbon atom.[80]

The study of the stereochemistry of the reactions of conjugated alkadienes with β-dicarbonyl compounds has shown that *cis*-5-methylhexa-1,3-dien-5-ol and *cis*-dodeca-1,3-diene interact with acetoacetic ester and acetylacetone with partial inversion of the *cis*-double bond, while in the reaction of *trans*-5-methylhexa-1,3-dien-5-ol the configuration of the double bond is retained.[82] The degree of inversion varies depending on the structures of the unsaturated and carbonyl components: the inversion apparently occurs in the intermediate *cis*-allyl radical-adducts. The inversion of the *cis*-double bonds indicates unambiguously the formation of intermediate allyl radical-adducts, but the available experimental data did not permit a decision as to whether the inversion of the double bond of the allyl radical-adduct takes place in the coordination sphere of manganese(III) or outside it, i.e. after the decomposition of the π-allylmanganese(III) complex and the liberation of the free radical-adduct into the surrounding space,[80,82]



(XXXIX)

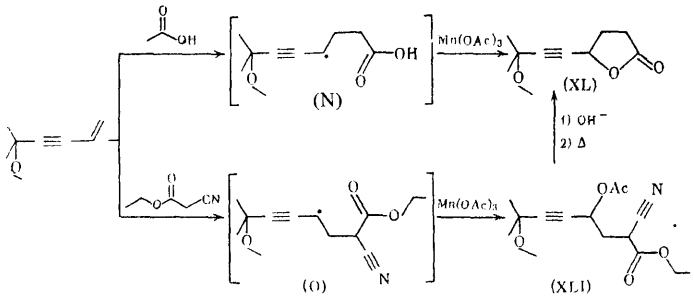
Derivatives of 4,5-dihydrofuran are obtained via the 1,2-cycloaddition of carbonyl compounds to alka-1,3-dienes. In contrast to this, the interaction of *cis*-dodeca-1,3-diene with malonic ester involves 1,4-addition with formation of the *trans*-ester (XXXIX) as a result of the stabilisation of the intermediate radical-adduct via the oxidative substitution mechanism.[82]

It has been reported that butadiene reacts with malonic ester, forming the products of both 1,2- and 1,4-addition.[81] On the other hand, in the reaction of the monoethyl ester of malonic acid cyclisation via the carboxy-group, leading to 5-vinylbutan-4-olide, takes place.[81]

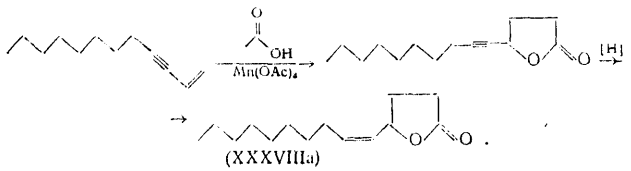
VII. Reactions of alkenynes and alkadiynes with carbonyl compounds

Conjugated alkenynes have also been involved as substrates in the interaction with carbonyl compounds initiated by manganese(III) acetate.[78,83–86] One of the motives which stimulated these investigations has been the development of the method of synthesis of 5-alkyn-4-olides—the key synthons in the synthesis of γ-butyrolactone derivatives, which are the sex pheromones of certain animals.[87–89] The lactonisation of the methyl ether of dimethylvinylethynylcarbinol was carried out by treatment with acetic acid or ethyl cyanoacetate in the presence of manganese(III) and copper(II) acetates.[85] In the former case, the reaction product was the lactone (XL), formed on cyclisation of the radical-adduct (N) via the carboxy-group. In the latter case, the radical-adduct (O) is stabilised via the 'oxidative substitution' mechanism, forming compound (XL), which is

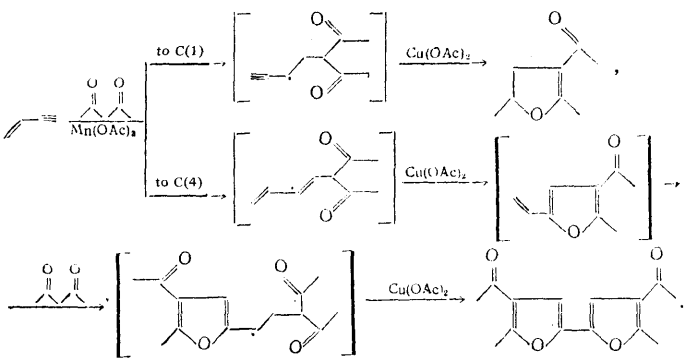
converted into the lactone (XL) as a result of alkaline hydrolysis and thermal decarboxylation-dehydration:



The method involving the direct lactonisation by treatment with acetic acid has been applied successfully in the synthesis of 5-alkyn-4-olides with different carbon skeletons, with the exception of the isoprenoid skeleton.[90] The reaction has been used as the key stage in the synthesis of (±)-*cis*-tetradec-5-en-4-olide (XXXVIIIa)—the racemate of the sex pheromone of the japanese beetle:[76]

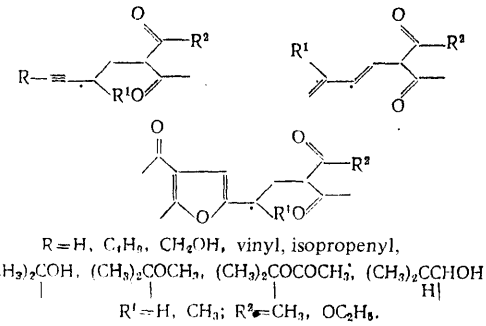


The regiochemistry of the interaction of conjugated alkenynes with β-dicarbonyl compounds in the presence of manganese(III) acetate and catalytic amounts of copper(II) acetate has been investigated[78,83,84,86] using but-1-en-3-yne (vinylacetylene) and its 2- and 4-alkyl or 2,4-dialkyl-derivatives as the substrate. In particular, it has been shown that the reaction of but-1-en-3-yne with acetylacetone is non-regioselective and leads to addition-cyclisation products with participation of the double and triple bonds:



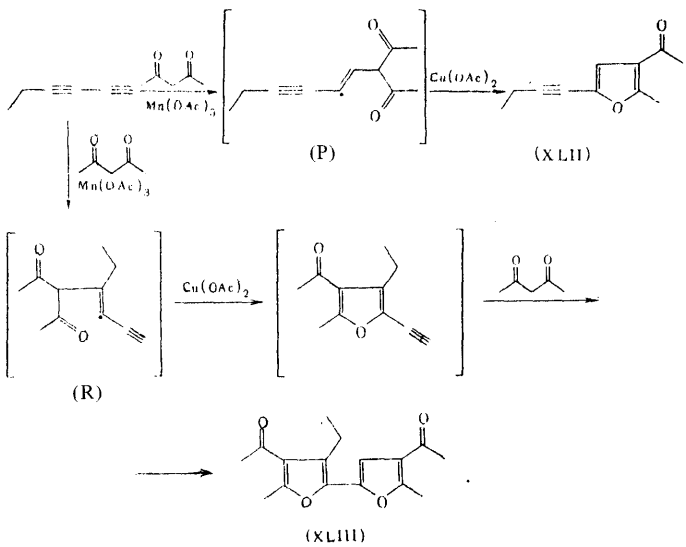
Vinylacetylene and isopropenylacetylene interact analogously with acetoacetic ester and, whereas in the former case the reactivities of both multiple bonds are comparable, in the reaction involving isopropenylacetylene an appreciable change in the regioselectivity of the process is observed with the preferential occurrence of the reaction via the double bond.[84] A similar picture has been observed for 4-substituted and 2,4-disubstituted derivatives of but-1-en-3-yne.[83,86]

The dihydrofuran and furan rings are formed in the reactions of conjugated alkenynes with β-dicarbonyl compounds as a result of the intramolecular cyclisation of secondary and tertiary propargyl, vinylpropargyl, dienyl, or α-furylalkyl radical-adducts on treatment with copper (II) acetate:



For comparison, one should note that the benzyl radical-adduct is also stabilised via cyclisation[53,54] whereas the alkyl radical-adducts, formed in the interaction of β-dicarbonyl compounds with alk-1-enes, undergo oxidative elimination on treatment with copper(II) acetate, affording γδ-unsaturated carbonyl compounds.[54,57] The set of these findings combined with data on the cyclisation of the allyl radical-adduct (Section VI) permitted the conclusion that alkyl radicals containing unsaturated groups in the α-position are stabilised, when the molecule contains at least one acetyl group, on treatment with copper acetate exclusively via the intramolecular cyclisation pathway.[84,90] It is to be expected that this postulate may have a predictive function in forecasting the structures of products of the type of reaction considered and also related processes.

The first study of the interaction of conjugated alkadiynes with β-dicarbonyl compounds initiated by manganese(III) acetate has been published recently.[91] It has been shown for the interaction of hexa-1,3-diyne with acetylacetone and acetoacetic ester that the reaction proceeds non-regioselectively with participation of both triple bonds. The intermediate radical-adducts (P) and (R) are stabilised by intramolecular cyclisation with formation of the furan derivatives (XLII) and the bifuryl derivatives (XLIII):



---o0o---

Analysis of the literature data indicates a high synthetic potential of the reactions involving the introduction of functional groups into unsaturated systems by carbonyl compounds, initiated by manganese(III) acetate. Novel methods have been developed for the synthesis of compounds of different classes, including products of natural origin. Further development of this field should occur, tentatively, in the direction involving the use of new classes of substrates as the unsaturated components, a detailed investigation of the process mechanisms, and also a wider employment of reactions of this type in specific syntheses of substances of practical importance.

References

1. J K Kochi (Editor) *Free Radicals,* Wiley, New York–London–Sydney–Toronto, 1973, Vol. 1
2. F A Minisci *Acc. Chem. Res.,* 1975, **8** 165
3. M G Vinogradov *Zh. Vses. Khim. Ova im D I Mendeleeva,* 1979, 24 175
4. D C Nonhebel, J C Walton *Free-Radical Chemistry. Structure and Mechanism* (Translated into Russian), Izd. Mir, Moscow, 1977
5. G I Nikishin, E N Troyanskii *Zh. Vses. Khim. Ova im D I Mendeleeva,* 1979, **24** 169
6. G I Nikishin *Izv. Akad. Nauk SSSR, Ser. Khim.,* 1984, 125
7. C Walling, E Heuser *Organic Reactions* (Translated into Russian), Izd. Mir, Moscow, 1966, Vol. 13, p. 130
8. G I Nikishin, M G Vinogradov, S P Verenchikov *Izv. Akad. Nauk SSSR, Ser. Khim.,* 1969, 1835
9. G I Nikishin, M G Vinogradov, S P Verenchikov, et al. *Zh. Org. Khim.,* 1972, **8** 539
10. G I Nikishin, M G Vinogradov, G P Il'ina *Zh. Org. Khim.,* 1972, **8** 1401
11. G I Nikishin, M G Vinogradov, G P Il'ina *Synthesis,* 1972, 376
12. M G Vinogradov, G P Il'ina, A V Ignatenko, G I Nikishin *Zh. Org. Khim.,* 1972, **8** 1403
13. M G Vinogradov, G P Il'ina, G I Nikishin *Zh. Org. Khim.,* 1974, **10** 1153
14. M G Vinogradov, I P Kovalev, G I Nikishin *Izv. Akad. Nauk SSSR, Ser. Khim.,* 1984, 384
15. M G Vinogradov, P A Direi, G I Nikishin *Zh. Org. Khim.,* 1976, **12** 527
16. M Okano, T Aratani *Bull. Chem. Soc. Jpn.,* 1976, **49** 2811
17. M G Vinogradov, P A Direi, G I Nikishin *Zh. Org. Khim.,* 1978, **14** 2043
18. M G Vinogradov, S P Verenchikov, G I Nikishin *Izv. Akad. Nauk SSSR, Ser. Khim.,* 1971, 200
19. E I Heiba, R M Dessau *J. Am. Chem. Soc.,* 1971, **93** 524
20. M G Vinogradov, S P Verenchikov, T M Fedorova, G I Nikishin *Zh. Org. Khim.,* 1975, **11** 947
21. E I Heiba, R M Dessau *J. Am. Chem. Soc.,* 1972, **94** 2888
22. M G Vinogradov, N A Direi, G I Nikishin *Zh. Org. Khim.,* 1977, **13** 2498
23. R M Dessau, E I Heiba *J. Org. Chem.,* 1974, **39** 3457
24. M Chatzopoulos, J Montheard *C. R. Seances Acad. Sci.,* 1977, **C284** 133
25. N Fukayima, M Okano, T Aratani *Chem. Ind.,* 1980, 86
26. O N Petrenko, M G Vinogradov, S P Verenchikov, et al., *Zh. Org. Khim.,* 1978, **14** 1386
27. M G Vinogradov, O N Petrenko, S P Verenchikov, et al. *Izv. Akad. Nauk SSSR, Ser. Khim.,* 1979, 1420
28. M G Vinogradov, O N Petrenko, S P Verenchikov, G I Nikishin, *Zh. Org. Khim.,* 1980, **16** 714
29. G I Nikishin, Yu N Ogibin, E N Troyanskii *Izv. Akad. Nauk SSSR, Ser. Khim.,* 1974, 483
30. J B Bush, H Finkbeiner *J. Am. Chem. Soc.,* 1968, **90** 5903
31. H Finkbeiner, J B Bush *Faraday Discuss. Chem. Soc.,* 1968, 150
32. E I Heiba, R M Dessau, W J Koehl *J. Am. Chem. Soc.,* 1968, **90** 5905
33. E I Heiba, R M Dessau, P G Rodewald *J. Am. Chem. Soc.,* 1974, **96** 7977
34. M Hoekman, G L Fagan, A D Webb, R E Kepner *Agr. Food Chem.,* 1982, **30** 920
35. US P. 3 758 513
36. B. P. 1 219 332
37. M Okano *J. Sci. Hiroshima Univ.,* 1976, **A40** 169; *Ref. Zh. Khim.,* 1977, 11Zh223
38. M Okano *Bull. Chem. Soc. Jpn.,* 1976, **49** 1041
39. K Witkiewicz, Z Chabudzinski *Rocz. Chem.,* 1976, **50** 1545
40. K Witkiewicz, Z Chabudzinski *Rocz. Chem.,* 1977, **51** 825
41. K Witkiewicz, Z Chabudzinski *Rocz. Chem.,* 1977, **51** 475
42. K Witkiewicz, Z Chabudzinski *Rocz. Chem.,* 1977, **51** 2155
43. J R Gilmore, J M Mellor *J. Chem. Soc.(C),* 1971, 2355
44. A Kasahara, R Saito, T Izumi *Bull. Chem. Soc. Jpn.,* 1973, **46** 2610
45. W J Klein *Rec. Trav. Chim.,* 1975, **94** 151
46. M Okano *Chem. Ind.,* 1972, 423
47. W E Fristad, J R Peterson *J. Org. Chem.,* 1985, **50** 10
48. E J Corey, M Kang, *J. Am. Chem. Soc.,* 1984, **106** 5384
49. M Okano *Chem. Lett.,* 1973, 165
50. K Witkiewicz, Z Chabudzinski *Bull. Acad. Pol. Sci. Ser. Sci. Chim.,* 1978, **26** 753
51. N Ito, H Nishino, K Kurosava *Bull. Chem. Soc. Jpn.,* 1983, **56** 3527
52. W J Klein *Rec. Trav. Chim.,* 1975, **94** 48
53. E I Heiba, R M Dessau *J. Org. Chem.,* 1974, **39** 3456
54. M G Vinogradov, T M Fedorova, G I Nikishin *Zh. Org. Khim.,* 1976, **12** 1175
55. M G Vinogradov, V N Dolinko, G I Nikishin *Izv. Akad. Nauk SSSR, Ser. Khim.,* 1982, 2313
56. M G Vinogradov, T M Fedorova, G I Nikishin *Izv. Akad. Nauk SSSR, Ser. Khim.,* 1974, 2384
57. M G Vinogradov, T M Fedorova, G I Nikishin *Zh. Org. Khim.,* 1975, **11** 1380
58. G I Nikishin, M G Vinogradov, T M Fedorova *J. Chem. Soc., Chem. Commun.,* 1973, 693
59. M G Vinogradov, O N Petrenko, S P Verenchikov, G I Nikishin *Izv. Akad. Nauk SSSR, Ser. Khim.,* 1979, 1916
60. O N Petrenko, Abstract of Candidate's Thesis in Chemical Sciences, Institute of Organic Chemistry, USSR Academy of Sciences, Moscow, 1981
61. M G Vinogradov, V N Dolinko, G I Nikishin *Izv. Akad. Nauk SSSR, Ser. Khim.,* 1984, 375
62. M G Vinogradov, V N Dolinko, G I Nikishin *Izv. Akad. Nauk SSSR, Ser. Khim.,* 1984, 2065
63. M G Vinogradov, V N Dolinko, G I Nikishin *Izv. Akad. Nauk SSSR, Ser. Khim.,* 1981, 700
64. W A Waters (Editor) *Free Radical Reactions,* Univ. Park Press, London, 1973

65. M G Vinogradov, S P Verenchikov, G I Nikishin *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1972, 1674
66. R S Min, V S Aksenov, M G Vinogradov, G I Nikishin *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1979, 2292
67. M E Kurz, V Baru, P Nguyen *J. Org. Chem.*, 1984, **49** 1603
68. R S Min, V S Aksenov, M G Vinogradov, G I Nikishin *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1981, 2315
69. E I Heiba, R M Dessau, W J Koehl *J. Am. Chem. Soc.*, 1969, **91** 138
70. M E Kurz, T R Chen *J. Chem. Soc., Chem. Commun.*, 1976, 968
71. M E Kurz, T R Chen *J. Org. Chem.*, 1978, **43** 239
72. US P. 3 758 514
73. F J McQuillin, M Wood *J. Chem. Soc., Perkin Trans. I*, 1976, 1762
74. M G Vinogradov, M S Pogosyan, A Ya Shteinshneider, G I Nikishin *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1983, 842
75. V K Promonenkov, O A Korotkova *Zh. Vses. Khim. Ova im D I Mendeleeva*, 1978, **23** 170
76. G G Melikyan, D A Mkrtchyan, K V Lebedeva, et al. *Khim. Prir. Soedin.*, 1984, 98
77. J H Tumlinson, M G Klein, R E Doolittle, et al. *Science*, 1977, **197** 789
78. G G Melikyan, D A Mkrtchyan, Sh O Badanyan *Khim. Geterotsikl. Soedin.*, 1980., 884
79. M G Vinogradov, N L Radyukina, M S Pogosyan, et al. *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1980, 1949
80. M G Vinogradov, M S Pogosyan, A Ya Shteinshneider, G I Nikishin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1981, 2077
81. M S Pogosyan, Abstract of Candidate's Thesis in Chemical Sciences, Institute of Organic Chemistry, USSR Academy of Sciences, Moscow, 1983
82. G G Melikyan, D A Mkrtchyan, V M Mkrtchyan, Sh O Badanyan *Khim. Geterotsikl. Soedin.*, 1985, 308
83. G G Melikyan, D A Mkrtchyan, Sh O Badanyan *Arm. Khim. Zh.*, 1981, **34** 1011
84. G G Melikyan, D A Mkrtchyan, Sh O Badanyan *Khim. Geterotsikl. Soedin.*, 1982, 19
85. G G Melikyan, D A Mkrtchyan, Sh O Badanyan *Arm. Khim. Zh.*, 1982, **35** 163
86. G G Melikyan, A B Sargsyan, Sh O Badanyan *Arm. Khim. Zh.*, 1986, **39** 228
87. W H Pirkle, P E Adams *J. Org. Chem.*, 1979, **44** 2169
88. U Ravid, R M Silverstein, L R Smith *Tetrahedron*, 1978, **34** 1449
89. Y Miyashita, K Mori *Agric. Biol. Chem.*, 1981, **45** 2521
90. D A Mkrtchyan, Abstract of Candidate's Thesis in Chemical Sciences, Institute of Organic Chemistry, Academy of Sciences of the Armenian SSR, Erevan, 1986
91. G G Melikyan, A B Sargsyan, Sh O Badanyan *Khim. Geterotsikl. Soedin.*, 1986, 562