RADICAL CYCLISATION REACTIONS OF KETONES WITH ALKENES INITIATED BY SILVER(II) AND LEAD(IV) OXIDES*

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Acetone and 2,4-pentanedione react with α-methylstyrene in the presence of the title oxides to form 2,5-dimethyl-5-phenyl-4,5-dihydrofuran and its 3-acetyl derivative, respectively, in about 70% yields. The reaction of these ketones with styrene, which is more prone to telomerisation and polymerisation reactions, gives the corresponding 5-phenylsubstituted 4,5-dihydrofuran derivatives in lower yields (30—40%). Cyclisation reaction of acetophenone with 1-octene induced by silver(II) oxide produces 4-n-hexyl-α-tetralone and decanophenone in a 70 : 30 ratio.

The addition of aliphatic ketones and β-diketones to arylsubstituted alkenes initiated by manganese(III) acetate is known to produce 4,5-dihydrofuran derivatives. Thus, for example, the reaction of acetone with styrene leads to 2-methyl-5-phenyl-4,5-dihydrofuran, even though in a very low yield; much more fortunate reaction course was observed in the addition of 2,4-pentanedione to styrene and α-methylstyrene which gives 2-methyl-5-phenyl-3-acetyl-4,5-dihydrofuran and 2,5-dimethyl-5-phenyl-3-acetyl-4,5-dihydrofuran, respectively. The reaction product was thus always the 5-phenylsubstituted dihydrofuran derivative[1]. On the other hand, the addition of 2,4-pentanedione to styrene in the presence of thallium(III) acetate as an oxidant produces a 4-phenylsubstituted derivative[2]; a similar reaction using lead(IV) acetate as an oxidizing agent yields either one or both isomeric phenylsubstituted dihydrofurans, depending on the solvent polarity[3]. The addition of 2,4-pentanedione or ethyl acetoacetate to a nonconjugated diene induced by manganese(III) acetate proceeds analogously to give the corresponding 4,5-dihydrofuran derivative[4]. Radical cyclisation reaction was also observed in the addition of alkyl aryl ketones to alkenes[4,5]. The oxidative additions promoted by transition metal acetates are, however, little selective; in addition to the cyclic product. *i.e.* 4-alkylsubstituted α-tetralone, a straight-chain higher alkyl aryl ketone, an unsaturated ketone and a ketoacetate are also formed. Thus, for example, the addition of acetophenone to 1-butene induced by manganese(III) and cerium(III) acetates or by a mixture of manganese(III) and copper(II) acetates gives 4-ethyl-α-tetralone as the major product, along with hexanophenone, 3-hexenophenone and 4-acetoxyhexanophenone[5]. The addition of acetophenone to 1-octene initiated by di-tert-butyl peroxide seems to be more selective; as reported, it gives, however, only the higher alkyl aryl ketone, *i.e.* decanophenone (80% purity) in 10% yield[6]. In another case a mixture of a straight-chain higher alkyl aryl ketone and 4-alkylsubstituted α-tetralone was obtained[4].

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In previous communications of this series we reported on the radical additions of aliphatic and alicyclic ketones and aliphatic β-diketones to aliphatic 1-alkenes in the presence of metal oxides as initiating agents. In all cases, the reactions produced the corresponding n-alkylated ketone or 1,3-dione (1 : 1 adducts) with high selectivity and in good to excellent yields[7-10].

As an extension we have now investigated radical reactions of aliphatic ketones and β-diketones with arylsubstituted alkenes and reactions of alkyl aryl ketones with aliphatic alkenes using metal oxides as initiating agents. Comparison of selectivity in these reactions with that observed earlier in analogous addition reactions induced by metal acetates was of special interest.

EXPERIMENTAL

Silver(II) oxide was prepared by the standard procedure[11]; copper(II) oxide was obtained as reported in the previous work[9]. Lead(IV) oxide was a commercial product (British Drug Houses Ltd, London) of analytical purity grade. α-Methylstyrene, 1-octene (Fluka A.G., Buchs), styrene, acetone, 2,4-pentanedione and acetophenone (Lachema, Brno) were commercial products which were distilled immediately before use. Gas chromatographic analyses were carried out on Chrom 31 instrument (Laboratorní přístroje, Prague) equipped with a flame-ionisation detector and a steel column (1·7 m × 3 mm) packed with 7% Silicone OV-17 on Gas Chrom Q (80—100 mesh). The purification, eventually separation of the products by preparative gas chromatography was made on columns filled with 9·2% Apiezon or 10% phenyl methyl silicone on Chromaton N. ^{1}H-NMR spectra were recorded with Varian HA-100 instrument using tetramethylsilane in $CDCl_3$ as an internal reference standard. Mass spectra were measured on MCH-1303 spectrometer. The mass spectra of dihydrofurans did not yield a reliable proof of the structure owing to the McLafferty rearrangement which occurs during fragmentation.

2,5-Dimethyl-5-phenyl-4,5-dihydrofuran (*VII*)

A mixture of acetone (232 g, 4·0 mol) α-methylstyrene (2·35 g, 0·02 mol) and silver(II) oxide (4·96 g, 0·04 mol) was refluxed and stirred magnetically in a nitrogen atmosphere. After 35 h, when the α-methylstyrene conversion attained 95%, the reaction mixture was cooled to room temperature, the inorganic precipitate containing mostly metallic silver along with a small amount of silver(I) oxide was filtered off and washed with 20 ml of acetone. The filtrate was combined with the washings and freed from acetone. Distillation of the residue *in vacuo* gave 2·6 g of product *VII* (71% yield after correction on impurity) boiling at 92°C/1·6 kPa (12 Torr) which contained 4% of an unidentified substance decomposing during preparative gas chromatography. ^{1}H-NMR (δ) of compound *VII*: 1·64 s (3 H), 2·8 m (2 H), 4·45 m (1 H), 7·3 m (5 H). *VII*: $M^+ = 174$ *m/e*.

2,5-Dimethyl-5-phenyl-3-acetyl-4,5-dihydrofuran (*VIII*)

A suspension of lead(IV) oxide (4·8 g, 0·02 mol) in a mixture of 2,4-pentanedione (40 g, 0·4 mol) and α-methylstyrene (2·36 g, 0·02 mol) was stirred magnetically under nitrogen at room temperature (27°C). After 5 h, when the α-methylstyrene conversion attained 98%, the suspension was cooled to 0°C, the organometallic precipitate containing mostly lead(II) 2,4-pentanedionate was filtered off and washed with 20 ml of ether. The residual lead(II) salt in the combined filtrate and washings was decomposed by adding 10 ml of 4% nitric acid, the aqueous layer was separated and washed twice with 10 ml of ether; the organic layer combined with the extracts was made neutral with aqueous sodium hydrogen carbonate solution and dried over magnesium sulphate. The mixture was freed from ether and from the unreacted 2,4-pentanedione by distillation *in vacuo* (1·6 kPa) during which 0·04 g of 1,1,2,2-tetraacetylethane was also removed. The residue was distilled *in vacuo* to give 3·18 g of product *VIII* (70% yield after correction on impurity) boiling at 128°C/200 Pa (1·5 Torr); a small amount (5%) of an unidentified impurity could not be separated by distillation and the pure product *VIII* was obtained by preparative gas chromatography. For $C_{14}H_{16}O_2$ (216·3) calculated: 77·75% C, 7·46% H; found: 77·50% C, 7·45% H. ^{1}H-NMR (δ) of compound *VIII*: 1·67 s (3 H), 2·17 s (3 H), 2·32 t (3 H) ($J = 1·5$ Hz), 3·14 q (2 H), 7·3 m (5 H). *VIII*: $M^+ = 216$ *m/e*.

4-n-Hexyl-α-tetralone (*XI*) and Decanophenone (*XII*)

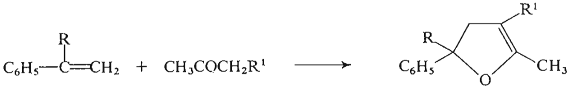
A mixture of acetophenone (18·0 g, 0·15 mol), 1-octene (1·66 g, 0·015 mol) and silver(II) oxide (5·57 g, 0·045 mol) was stirred magnetically in a nitrogen atmosphere and heated to 110°C. After 5·5 h, the 1-octene conversion attained 99% and the mixture was cooled to room temperature. The inorganic precipitate, predominantly metallic silver, was filtered off and washed twice with 20 ml of acetone. The combined filtrates were concentrated *in vacuo* and the residue was distilled to give 1·46 g of a colourless liquid boiling at 140—143°C/227 Pa (1·7 Torr) which contained, according to gas chromatographic analysis, 70·3% of 4-n-hexyl-α-tetralone (*XI*) and 29·7% of decanophenone (*XII*); separation by preparative gas chromatography gave the ketone *XI* in 29% yield and ketone *XII* in 13% yield (calculated on 1-octene charged). After recrystallization from light petroleum, decanophenone melted at 34°C (ref.[6] m.p. 35°C); for $C_{16}H_{24}O$ (232·4) calculated: 82·70% C, 10·41% H; found: 82·90% C, 10·36% H. 4-n-Hexyl--α-tetralone: for $C_{16}H_{22}O$ (230·3) calculated: 83·43% C, 9·66% H; found: 83·26% C, 9·60% H; mass spectrum (*m/e*): M^+ 230 (47%); 188 (14%); 145 (100%) ($-C_6H_{13}^+$); 117 (67%) (—CO; indanyl$^+$); 115 (52%) (—2 H; indenyl$^+$).

Addition of Acetophenone to 1-Octene Initiated by Di-tert-butylperoxide

A mixture of acetophenone (6·0 g, 0·05 mol), 1-octene (0·56 g, 0·005 mol) and the peroxide (0·146 g, 0·001 mol) (mol. ratio of the reactants = 10 : 1 : 0·2) was stirred magnetically in a nitrogen atmosphere and heated to 150°C; after 4 h, the 1-octene conversion attained 91%. The mixture was cooled to room temperature, the unreacted acetophenone and eventually 1-octene were removed by distillation *in vacuo* and the residue was distilled under reduced pressure to give 0·14 g of a product (12% yield with respect to the 1-alkene charged) which contained, according to gas chromatographic analysis, ketones *XI* and *XII* in a 1 : 1 ratio.

RESULTS AND DISCUSSION

We found that phenylsubstituted alkenes such as styrene and α-methylstyrene undergo in the presence of silver(II) and lead(IV) oxides a cyclisation reaction with acetone and 2,4-pentanedione to form 5-phenylsubstituted 4,5-dihydrofurans. Both readily and hardly enolizable ketones and diones can therefore participate in this reaction. The formation of 4,5-dihydrofurans can be described by the general equation (*A*).



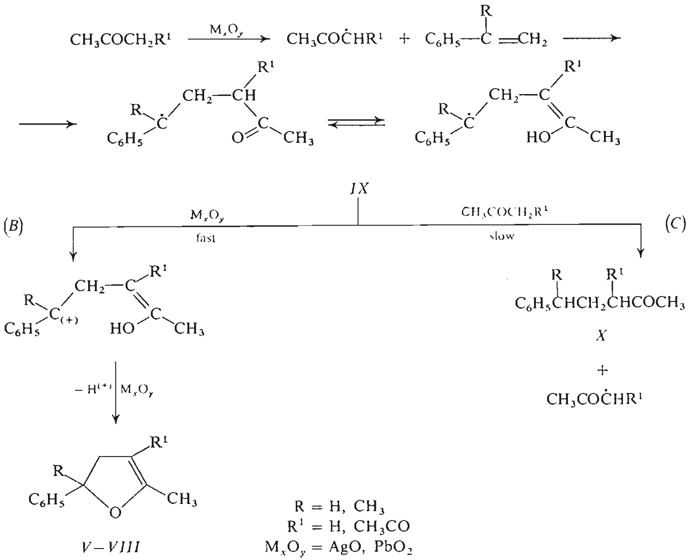
(4)

I, R = H
II, R = CH_3
III, R^1 = H
IV, R^1 = CH_3CO
V, R = R^1 = H
VI, R = H, R^1 = CH_3CO
VII, R = CH_3, R^1 = H
VIII, R = CH_3, R^1 = CH_3CO

The cyclisation reaction of α-methylstyrene with acetone and 2,4-pentanedione gave 2,5-dimethyl-5-phenyl-4,5-dihydrofuran (*VII*) and 2,5-dimethyl-5-phenyl-3-acetyl-4,5-dihydrofuran (*VIII*), respectively, in 70–71% yields. Similar reactions of styrene with the above ketones produced cyclisation products *V* and *VI* in lower yields (31–41%) which were due to the stronger tendency of styrene to undergo telomerisation and polymerisation reactions. The results of these experiments are summarised in Table I. Attempts to prepare 4,5-dihydrofurans from cyclic ketones such as cyclopentanone or cyclohexanone or to use other metal oxides (CuO and MnO_2) have not met with success; the low reaction rates and elevated temperatures favoured polymerisation of styrene and α-methylstyrene and resulted only in low yields of cyclic products.

Cyclisation reactions of 2,4-pentanedione were accompanied by the formation of a small amount of 1,1,2,2-tetraacetylethane (0·1%) as a product of dehydrodimerization, which could be, however, separated easily by distillation. Another by-product was formed in each of these reactions in an amount of 4–10%. Low stability of these compounds under the conditions of preparative gas chromatography hindered their isolation and structure determination; neither the use of column chromatography on alumina was successful. On the other hand, no formation of 4-phenylsubstituted 4,5-dihydrofurans was observed in our cyclisation reaction; these compounds are known to result as major products from reactions which are mediated by thallium(III) acetate or lead(IV) acetate[3] and proceed according to an ionic mechanism[1].

The addition of acetone[7,9] and 2,4-pentanedione[10] to aliphatic 1-alkenes initiated by silver(II) oxide has been found by us to yield exclusively noncyclic n-alkyl ketones and n-alkyl diones (1 : 1 adducts), respectively. The presence of a phenyl group in the α-position to the alkene C=C bond is thus a prerequisite for the cyclisation reactions induced by metal oxides. The formation of 5-phenylsubstituted 4,5-dihydrofurans (Scheme 1) in the presence of these initiating agents seems to be consistent with a radical mechanism and can be explained by a relatively fast rate and an ease of the oxidation and cyclisation of the intermediate radical adduct *IX* (equation (*B*)); by contrast, a substantially slower rate of hydrogen abstraction from the radical adduct *IX* by the interaction with another ketone molecule seems to suppress efficiently the formation of the noncyclic product *X* (equation (*C*)).



SCHEME 1

TABLE I

Formation of 4,5-Dihydrofurans in Cyclisation Reactions of Styrene (*I*) and α-Methylstyrene (*II*) with Acetone (*III*) and 2,4-Pentanedione (*IV*) Initiated by Metal Oxides

Reactions on a 0·02 mol alkene scale.

Alkene	Ketone	Metal oxide	MR[a]	Temp./ time, °C/h	Alkene conversion	Product (yield, %)[b]
I	*III*	AgO	200 : 1 : 2	56/20	91	*V* (41)
I	*IV*	PbO_2	20 : 1 : 1	27/3	96	*VI* (31)
II	*III*	AgO	200 : 1 : 2	56/35	95	*VII* (71)
II	*IV*	PbO_2	20 : 1 : 1	27/5	98	*VIII* (70)

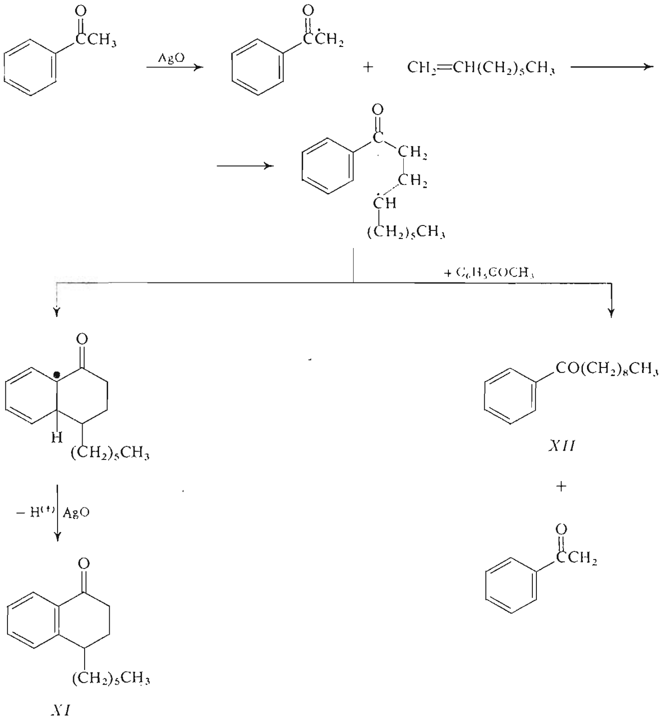
[a] Molar ratio of the ketone to the alkene and metal oxide; [b] isolated yield of the products related to the alkene charged.

These considerations are in accordance with the results reported by Heiba and Dessau[1] who obtained 5-arylsubstituted 4,5-dihydrofurans by a manganese(III) acetate induced reaction of aryl alkenes with readily enolizable carbonyl compounds; it seems probable that there exists also an analogy to the mechanism of the formation of 5-substituted 4,5-dihydrofurans by electrochemical oxidative addition of sodium 2,4-pentanedionate to alkenes[12]. In both cases a radical mechanism has been suggested to account for the course of these reactions[1,12]. The formation of dihydrofurans in the presence of silver(II) oxide or lead(IV) oxide does not appear to depend on the degree of ketone enolization; as it follows from Table I, the products of the cyclisation of acetone and of highly enolized 2,4-pentanedione[13] with styrene and α-methylstyrene were obtained in comparable yields. This contrasts with the course of similar reactions induced by manganese(III) acetate[1].

The reaction of a hardly enolizable ketone such as of acetone in the form of a transient silver enolate with styrene could be one of the possible explanations for the identical behaviour of acetone and 2,4-pentanedione in our cyclisation reactions. This suggestion is in accordance with our earlier finding that silver 2,4-pentanedionate as well as 2,4-pentanedione itself but in the presence of silver oxide, both react with an aliphatic 1-alkene in the same manner to produce exclusively C—3 n-alkyl-2,4--dione[10,14]. It is of interest that also the conversion of trimethylsilylenol ethers into 1,4-diones by the action of silver(I) oxide is assumed to proceed *via* formation of an intermediate silver enolate[15].

The course of the addition of alkyl aryl ketones to aliphatic 1-alkenes in the presence of metal oxides as initiating agents was studied using acetophenone and 1-octene as model compounds. The addition product obtained in the presence of silver(II) oxide in a total yield of 42% (with respect to the starting alkene) contained 4-n-hexyl-α-tetralone (*XI*) and decanophenone (*XII*) in a 70 : 30 ratio; this ratio did not change significantly with the concentration of silver(II) oxide in the reaction mixture. Lead(IV) and copper(II) oxides were less effective and gave the addition product only in 11—13% yields. In accordance with the preceding general considerations about the mechanism of oxidative cyclisation reactions[5,16], the formation of the cyclic ketone *XI* and noncyclic ketone *XII* in the silver(II) oxide-initiated reaction can be illustrated by Scheme 2.

In an attempt to prepare an authentic sample of pure decanophenone (*XII*) we have repeated the known procedure reporting the addition of acetophenone to 1-octene in the presence of di-tert-butyl peroxide[6]. In contrast to the literature data, the addition product (12%) was a mixture containing equal amounts (50 : 50) of the cyclic ketone *XI* and noncyclic ketone *XII*. The oxidative cyclisation reactions of phenylalkenes initiated by organic peroxides were reported to form predominantly the noncyclic products[16,17].



SCHEME 2

From the results discussed it follows that the oxidative cyclisation reaction of acetophenone with 1-octene initiated by silver(II) oxide is substantially more selective than a similar reaction initiated by manganese(III) acetate which yields four products[5]. As to the selectivity, the silver(II) oxide-initiated addition is comparable with that induced by an organic peroxide; it differs, however, from the latter by a higher total yield of the addition products *XI* and *XII* and also by the predominant formation of the cyclic product *XI*.

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