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SEMIDIONES—XVII

FORMATION OF SEMIDIONE RADICAL ANIONS FROM KETONES AND REDUCING AGENTS WITH AND WITHOUT INVOLVEMENT OF SOLVENT*

G. A. Russell, D. F. Lawson† and L. A. Ochrymowycz

Department of Chemistry, Iowa State University, Ames, Iowa 50010

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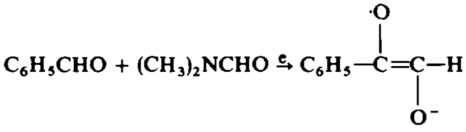
Abstract—Mechanisms for the conversion of acetophenone (or benzaldehyde) to 1-phenylpropane-1,2-semidione (or phenylglyoxal radical anions) by electrolytic reduction in dimethylformamide are considered. The intermediate $C_6H_5C(O^-)(CH_3)CH(O^-)X$ with $X = (CH_3)_2N$ is implicated. The free α-hydroxy aldehyde is apparently not a precursor of the semidione. Other examples of this rearrangement with X = alkoxy groups are suggested. 2,2,4,4-Tetramethylcyclobutanone ketyl at −50° rapidly decomposes to yield 3,3,5,5-tetramethylcyclopentane-1,2-semidione in tetrahydrofuran solution. This novel carbonylation reaction is presumed to involve carbon monoxide reacting with the ketyl, or $K^+[CO]\cdot^-$ reacting with the ketone. Decomposition of ketyls to yield semidiones in tetrahydrofuran solution apparently occurs only in the case of highly strained ketones.

Electrolytic reduction of acetophenone or benzaldehyde in dimethyl formamide (DMF) solutions at high potentials produces radical anions[1] now recognized to be 1-phenylpropane-1,2-semidione,[2] and *trans*-phenylglyoxal semidione,[3, 4] respectively. The ketyls ($C_6H_5COCH_3\cdot^-$, $C_6H_5CHO\cdot^-$) can be prepared in DMSO solution by controlled electroreduction.[5]

$$C_6H_5COCH_3 + (CH_3)_2NCHO \xrightarrow{e} C_6H_5C(O\cdot)=C(O^-)CH_3 \qquad (1)$$



$$C_6H_5CHO + (CH_3)_2NCHO \xrightarrow{e} C_6H_5-\overset{\overset{\textstyle\cdot O}{|}}{C}=\underset{\underset{\textstyle O^-}{|}}{C}-H \qquad (2)$$

We have performed several experiments designed to probe the mechanism of the carbonyl insertion process involved in reactions 1 and 2. One attractive pathway involves the formation of an intermediate α-hydroxy aldehyde which rearranges under basic conditions to the appropriate α-hydroxy ketone, reactions 3–5.

$$C_6H_5COR + 2e \rightarrow [C_6H_5COR]^{-2} \qquad (3)$$

$$[C_6H_5COR]^{-2} + (CH_3)_2NCHO \rightarrow C_6H_5C(R)(O^-)CHO + (CH_3)_2N^- \qquad (4)$$

$$C_6H_5C(R)(O^-)CHO \xrightarrow{H^+} C_6H_5COCH(OH)R \rightleftharpoons C_6H_5CH(OH)COR \qquad (5)$$

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† NDEA Predoctoral Fellow, 1967–1968.

α-Hydroxy ketones are known to spontaneously disproportionate to the semidiones in the presence of strong base.[2, 6, 7] Benzophenone dianion is a known species[8, 9] whose reactions with ketones, aldehydes, diethyl carbonate, carbon dioxide, benzonitrile, or benzaldehyde have been observed.[10, 11] We felt that DMF might also undergo carbonyl addition with this reagent. We have found the disodium salt of benzophenone reacts with DMF (ammonia–ether solvent) to yield 1,1,3,3-tetraphenylglycerol in 83% yield. This product is suggestive of the formation of the α-hydroxy aldehyde as an intermediate (Scheme 1).

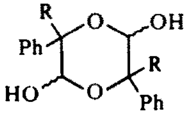
SCHEME I

$$[(Ar)_2CO]^{-2} + DMF \rightarrow (CH_3)_2N^- + Ar_2C(O^-)CHO$$

$$Ar_2C(O^-)CHO + [(Ar)_2CO]^{-2} \rightarrow Ar_2C(O^-)CH(O^-)C(Ar)_2O^-$$

$$\xrightarrow{H^+} Ar_2C(OH)CH(OH)C(Ar_2)_2OH$$

$PhC(R)(OH)CHO$
1a: R = Me
1b: R = Et



2a: R = Me
2b: R = Et
2c: R = Ph
2d: R = H

The monomeric α-hydroxy aldehydes **1a** and **1b** were prepared[12] and treated with potassium t-butoxide in DMSO or DMF. The rearranged semidiones were not observed by ESR spectroscopy even in the presence of traces of oxygen.

The cyclic dimers of α-hydroxy ketones (**2a**–**2d**) reacted with potassium t-butoxide in DMSO solution to yield the semidiones, $C_6H_5C(O\cdot){=}C(O^-)R$. Fig 1 gives the spectra of the phenylglyoxal radical anions prepared from **2d**. The spectra are of better quality and higher intensity than those prepared by the base-catalyzed disproportionation of ω-hydroxyacetophenone.[4] The spectra of Fig 1 indicate that the phenylglyoxal radical anion exists mainly in the *cis*-structure in the presence of potassium as the gegen ion ($g = 2{\cdot}00494 \pm 0{\cdot}00005$) and mainly as the *trans* isomer in the presence of cesium ion ($g = 2{\cdot}00520 \pm 0{\cdot}00005$). Methylation of the glyoxal to yield 1-phenylpropane-1,2-dione or its radical anion is a complicating side effect in DMSO solution.[4] Thus, when Triton B was employed as the base in reaction with **2d** only the 1-phenyl-propane-1,2-semidione[2] was observed.

$$C_6H_5COCHO + CH_2SOCH_3^- \rightarrow C_6H_5COCOCH_3 + CH_3SO^- \qquad (6)$$

Use of sodium methoxide as the base in DMSO caused the monomeric α-hydroxy aldehydes **2a** and **2b** to yield the semidiones. We find this surprising in view of the fact that potassium t-butoxide, a stronger base, failed to form the semidione. In other cases we have always observed a higher concentration of the semidione in the presence of the stronger base.[13]

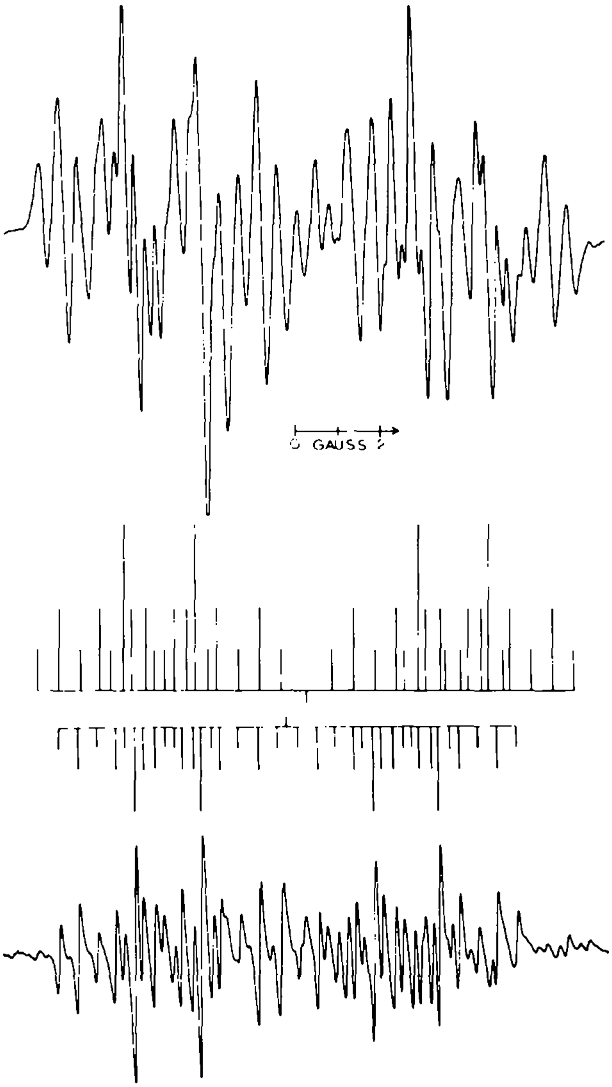
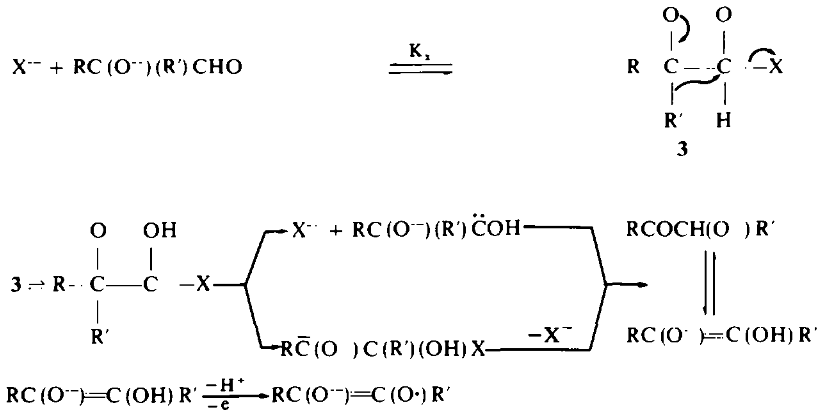


Fig 1. Phenylglyoxal semidione in DMSO solution at 25°. Top, *cis*-semidione in 0·5 *M* potassium *t*-butoxide, a^H = 6·88 (α), 1·70 (*p*), 1·50, 1·50 (*o*), 0·52, 0·52 (*m*). Bottom, *trans*-semidione in 0·5 *M* cesium *t*-butoxide, a^H = 5·59 (α), 1·52 (*p*), 1·34, 1·34 (*o*), 0·45, 0·45 (*m*).

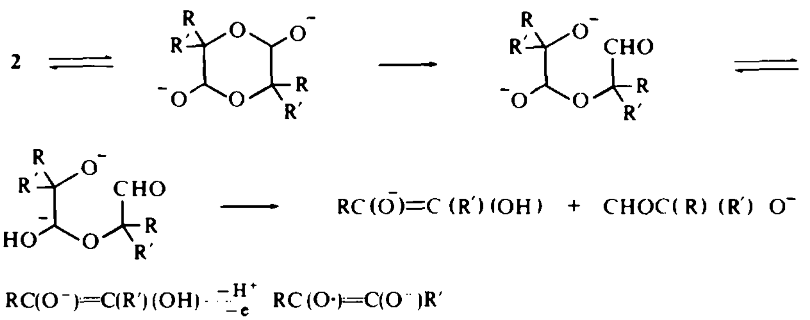
A possible explanation suggests itself for the three key observations: (a) formation of the semidione upon electrolysis of acetophenone in DMF but not from atrolactaldehyde plus potassium t-butoxide, (b) the formation of the semidione from atrolactaldehyde dimer **2a** in the presence of potassium t-butoxide, and (c) the formation of the semidione from atrolactaldehyde in the presence of methoxide ion. We suggest that intermediates of type **3** are formed and that rearrangement may involve a carbenoid pathway (Scheme 2).

Scheme II

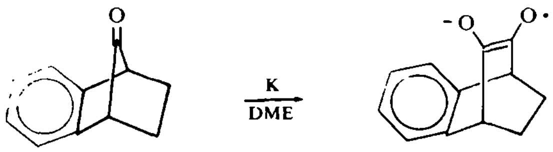


Intermediate **3** with X = NMe_2 would be formed from addition of the ketone dianion to DMF. Intermediate **3** with X = OMe would be formed more readily from **1a** than the analogous intermediate with X = $OCMe_3$. The lower nucleophilicity of t-butoxide ion relative to methoxide ion would be expected to have an appreciable effect on the value of K_x. In the case of **2**, a modification of Scheme 2 can be readily imagined (Scheme 3).

Scheme III



Treatment of acetophenone with potassium in dimethoxyethane solution fails to produce a stable radical anion. It thus seems fairly certain that in reactions 1 or 2 the additional carbonyl group is coming from the DMF. We would, however, like to indicate some other situations where the semidione is formed from a strained monoketone in the absence of DMF.*



* This phenomenon was originally called to our attention by Professor S. Winstein. Professor Winstein and his students observed that the alkali metal reduction of 7-ketobenzonorbornadiene in dimethoxyethane solution produced the benzobicyclo[2.2.2]octane-2,3-semidione, whose structure we had fully documented.[13]

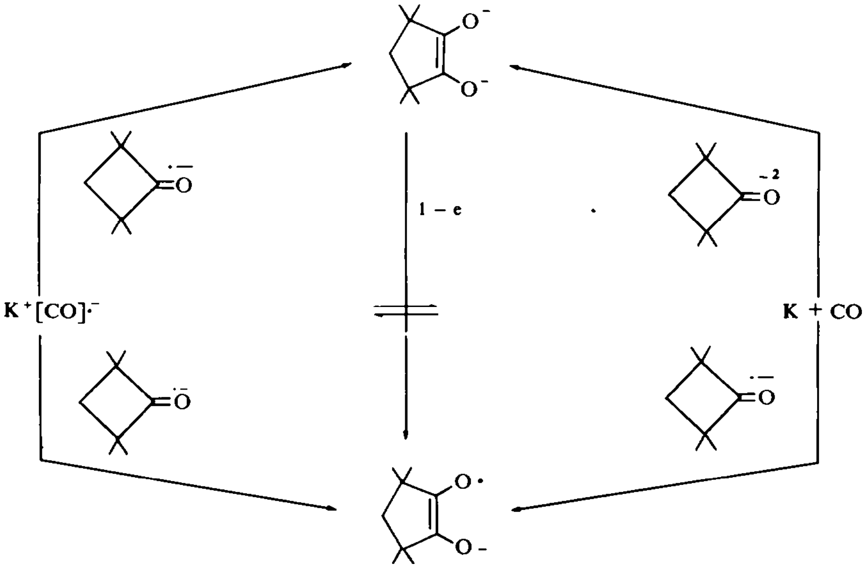
2,2,4,4-Tetramethylcyclobutanone can be reduced to the ketyl at −80° in THF by a potassium mirror. The ketyl gives a triplet splitting due to the β-methylene group, $a_{CH_2}{}^{H} = 0{\cdot}7$ gauss. A further splitting of ~0·1 gauss from the methyl hydrogen atoms is observed. ^{13}C hfs of 13·4 and 50·2 gauss were observed at −90° due to the 4 methyl groups and the carbonyl carbon atom. The g-value was 2·00374 ±0·00005 at −80°. Upon warming to −50° the ketyl decomposed (Fig 2), $t_{\frac{1}{2}} = 2$ min, and was replaced by a broad singlet ($\Delta\omega = 0{\cdot}6$ gauss), $g = 2{\cdot}00493 \pm 0{\cdot}00005$. The singlet has a natural abundance ^{13}C splitting of 5·9 gauss at +30° (Fig 3). The singlet with $g = 2{\cdot}00493 \pm 0{\cdot}00005$, $a^{C} = 5{\cdot}9$ gauss is identified as 3,3,5,5-tetramethylcyclopentane-1,2-semidione since reduction of the tetramethylcyclopentanedione in DME with Na/K alloy gave an ESR spectrum with $\Delta\omega = 0{\cdot}6$ gauss, $a^{C} = 6{\cdot}0$ gauss, $g = 2{\cdot}00493$. The tetramethylcyclopentanesemidione radical is the only ESR signal observed when 2,2,4,4-tetramethylcyclobutanone is reduced with Na/K alloy in DME at 25°. We have been unable to observe a similar behavior for 2,2,5,5-tetramethylcyclopentanone, 2,2,6,6-tetramethylcyclohexanone, or 2,2,7,7-tetramethylcycloheptanone. In these cases the ketyls are the only paramagnetic products observed.

Ward reported some time ago that the reduction of 2,2,4,4-tetramethyl-1,3-cyclobutanedione by sodium or potassium gave a product with $g = 2{\cdot}00477 \pm 0{\cdot}00002$.[14] His assignments of $a_{CO}{}^{C} = 5{\cdot}0$ gauss and $a_{CH_3}{}^{C} = 7{\cdot}57$ gauss have proven hard to rationalize with other data for ketyls and semidiones.[15] It appears that in Ward's case the actual radical anion is a semidione, perhaps 3,3,5,5-tetramethylcyclopentane-1,2,4-semitrione with $a_{CH_3}{}^{H} \cong 0{\cdot}11$ gauss, $a_{CH_3}{}^{C} = 7{\cdot}57$ gauss, $a_{C-\alpha}{}^{C} = 5{\cdot}0$ gauss, and $a_{CO}{}^{C}$ not observable as in the case of 3,3,5,5-tetramethylcyclopentane-1,2-semidione.

A possible explanation for the carbonyl insertion reaction observed for strained ketyls is that the ketyl decomposes to yield $K^{+}[CO]^{\cdot-}$ which can undergo the insertion reaction with the ketone or ketyl (Scheme 4).

$$(R)(R')CO\cdot{}^{-}K^{+} \rightarrow R{-}R' + K^{+}[CO]^{\cdot-} \qquad (6)$$

SCHEME IV



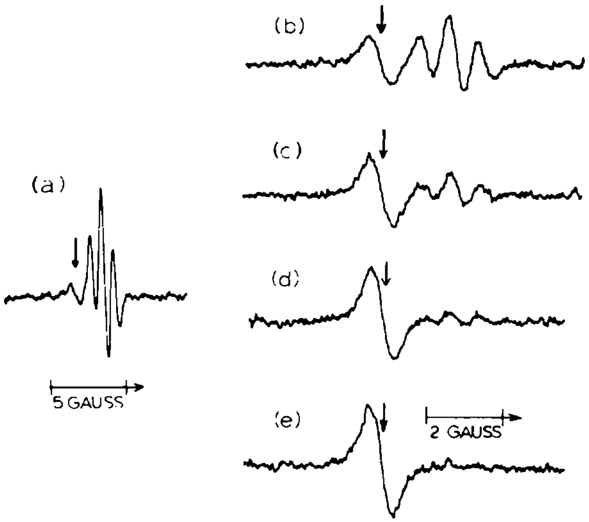


FIG 2. Spectra observed upon warming 2,2,4,4-tetramethylcyclobutanone ketyl to −50°; (a) initial spectrum, arrow indicates new signal developing; (b–e) elapsed-time spectra at 2·5, 5·0, 7·5, and 10 min., respectively.

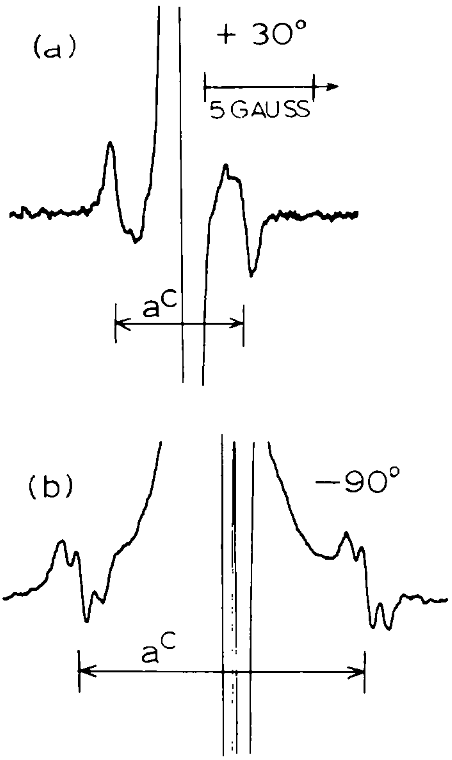


FIG 3. ^{13}C natural abundance satellites observed for (a) 3,3,5,5-tetramethylcyclopentane-1,2-semidione at +30° in THF; (b) 2,2,4,4-tetramethylcyclobutanone ketyl at −90° in THF.

A variety of implications from the observed carbonyl insertion process of strained ketones are being investigated further.

EXPERIMENTAL

1,1,3,3-*Tetraphenylglycerol.* Liquid ammonia (250 ml) was maintained under a Dry Ice condenser and a positive N_2 press. Na (2·30 g, 100 mmol) was dissolved in the ammonia and 9·11 g (50 mmol) benzophenone in 30 ml ether added. After 20 min, 20 ml DMF and 40 ml ether was added slowly. The blue-black color of disodiobenzophenone slowly faded and was discharged completely in 15 min. The mixture was stirred for an additional hr and then neutralized by the addition of 7 g NH_4Cl. After evaporation of the ammonia, the residue was treated with 200 ml water and extracted 3 times with 100 ml portions ether. The soln was dried ($MgSO_4$) and evaporated under vacuum to yield a residue that was purified by column chromatography on silica gel. Elution with hexane gave a trace of diphenylmethane, 0·83 g benzophenone and 0·37 g benzhydrol. Elution with 1:1 EtOAc–hexane yielded 8·25 g (83%) of the glycerol which could be crystallized from heptane, m.p. 195–197°; ν_{CHCl_3}, 3450, 3550 cm^{-1} (OH); mass spectrum (70 eV), m/e = 396; PMR (d_6-DMSO) δ 4·42 (d, 1, >CHOH, D_2O exchangeable, J = 9 Hz); 5·85 (d, 1, >CHOH, J = 9 Hz); 6·55 (broad s, 2, $(C_6H_5)_2COH$-, D_2O exchangeable); 6·70–6·95 (m, 6); 7·05–7·45 (m, 10); 7·53–7·80 (m, 4). (Found: C, 82·01; H, 6·24. Calc for $C_{27}H_{24}O_3$ (396·46): C, 81·79; H, 6·10%).

The above procedure was repeated using fluorenone, xanthone, thioxanthone, and acridone in place of the benzophenone. Fluorenone yielded a mixture of fluorene and fluorenol while acridone gave mainly acridan. Xanthone and thioxanthone also gave mainly products of reduction but the glycerols were also isolated in low yields.

Reagents. The mandelaldehyde (dimeric), atrolactaldehyde (monomer and dimer), 2-phenyl-2-ethylglycolaldehyde (monomer and polymer), and benzilaldehyde (dimer) have been described elsewhere.[12]

2,2,4,4-Tetramethylcyclobutanone was prepared by the method of Herzog and Buchman[16] in 20% yield; b.p. 120–128° (lit.[14] 128·5–129° at 745 Torr); IR (neat) 2980, 1785, 1465, 1370, 1025 cm^{-1}; PMR (CCl_4) δ 1·17 (s, 12), 1·75 (s, 2). The ketone gave a 2,4-dinitrophenylhydrazone with m.p. 114–115° (lit.[14] m.p. 115–116°) whose mass spectrum (70 eV) gave a molecular ion at 306.

Electron Spin Resonance Spectra. The spectra were recorded on a Varian E-3 spectrometer using deoxygenated solns in an inverted U-type mixing cell described previously.[17] The hyperfine splitting constants in DMSO soln were in excellent agreement with those reported previously for phenylglyoxal semidione,[3, 4] 1-phenylpropane-1,2-semidione,[2] 1-phenylbutane-1,2-semidione,[2] and benzil radical anion[18] reported previously in DMSO soln.

Low temp reductions were performed by use of a 14 × 100 mm tube fitted with a 4 × 100 mm Pyrex sidearm and a 7 × 75 mm open sidearm. A small pellet of K was added to the open sidearm which was then sealed. Into the 4 mm tube 50 ul of ketone was placed and cooled to −80°. The apparatus was evacuated to 10^{-6} Torr and the K distilled to form a mirror in the main reaction tube. The 75 mm sidearm was removed and solvent vacuum-transferred from Na-K alloy into the vessel to give a final ketone concentration of 10^{-3} M. The vessel was now sealed and removed from the vacuum line, cooled to −80° and inverted to mix the ketone and the solvent over the K mirror. The ketyl soln was returned to the 4 mm tube and the tube inserted in a precooled (−80°) Varian V-4502 EPR spectrometer using a V-4540 temp controller. g-Values were determined relative to aqueous solns of Fremy's salt.[19]

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