Tetrahedron Letters No.16, pp. 1139-1144, 1965 Pergamon Press Ltd.
Printed in Great Britain.

APPLICATION OF E.S.R. SPECTROSCOPY TO PROBLEMS OF STRUCTURE AND CONFORMATION. III. A NEW METHOD FOR PREPARATION OF RADICAL-ANIONS OF DIKETONES[1]

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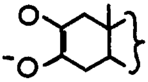
(Received 8 February 1965; in revised form 4 March 1965)

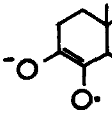
The detection and identification of acylil radical-anions formed in the oxidation of ketones or α-hydroxyketones in basic solution can serve as a proof of structure for the starting compounds.[2,3] This technique is particularly valuable in the steroid field.[3] We now report the preparation of acylils from α-bromoketones in dimethyl sulfoxide (DMSO) solutions containing potassium t-butoxide, the use of this technique to prepare acylils unavailable by other methods, and some new reactions involving the methylsulfinylcarbanion.

The formation of radical-anions from α-bromoketones may involve a reaction of the Kornblum type,[4] leading to an α-diketone or an α-ketoaldehyde, followed by electron transfer from some carbanion.[5] In support of this interpretation is the fact that α-diketones containing an acidic α-hydrogen atom, such as 1-phenylpropane-1,2-dione or cyclohexane-1,2-dione, spontaneously form the corresponding acylils under the reaction conditions.

Treatment of 2-bromo-17α-acetoxy-5α-androstan-3-one with potassium t-butoxide in DMSO produced only the Δ^2-semiquinone (I) without a trace of the Δ^3-isomer (II) observed upon base-



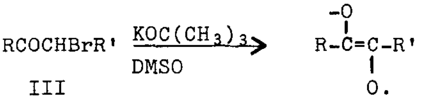
I



II

catalyzed oxidation of the ketone.[3] This technique allows the formation of aliphatic semiquinones from ketones that are not easily oxygenated in basic solution. For example, the exposure of several representative examples of 6-, 7-, 11-, or 12-keto-5α- or 5β-steroids to oxygen in basic solution has failed to yield stable radical-anions. However, acylil radical-anions are formed from 6α-bromo-5α-cholestan-7-one in DMSO containing an excess of potassium t-butoxide.

The oxidation of a ketone ($R'CH_2COR$, ArCOR) or an α-hydroxyketone (R'CHOHCOR) in basic solution usually fails to give the acylil when $R=CH_3$. However, in DMSO IIIa, b, c are converted smoothly into IVa, b, c.



$$\underset{\text{III}}{\text{RCOCHBrR}'} \xrightarrow[\text{DMSO}]{\text{KOC(CH}_3)_3} \text{R-}\overset{\overset{-}{\text{O}}}{\text{C}}\text{=}\underset{\text{O}\cdot}{\text{C}}\text{-R}' \quad \text{IV}$$

a, $R=R'=CH_3$
b, $R=C_6H_5, R'=H$
c, $R=CH_3, R'=H$

Although the oxidation in basic solution of 2-butanone or acetoin, or the reduction of biacetyl, forms 2,5-dimethylsemiquinone,[6] IVa is readily formed from the bromination product of 2-butanone. The e.s.r. spectrum is composed of 7 lines with intensities approximately 1:6:15:20:15:6:1 and with a^H = 6.06 gauss. Similarly, phenacyl bromide produces IVb,[7] Fig. 1,whose spectrum is consistent with a_{CHO}^H = 6.88, a_p^H = 1.70, a_o^H = 1.50 and a_m^H = 0.52 G.

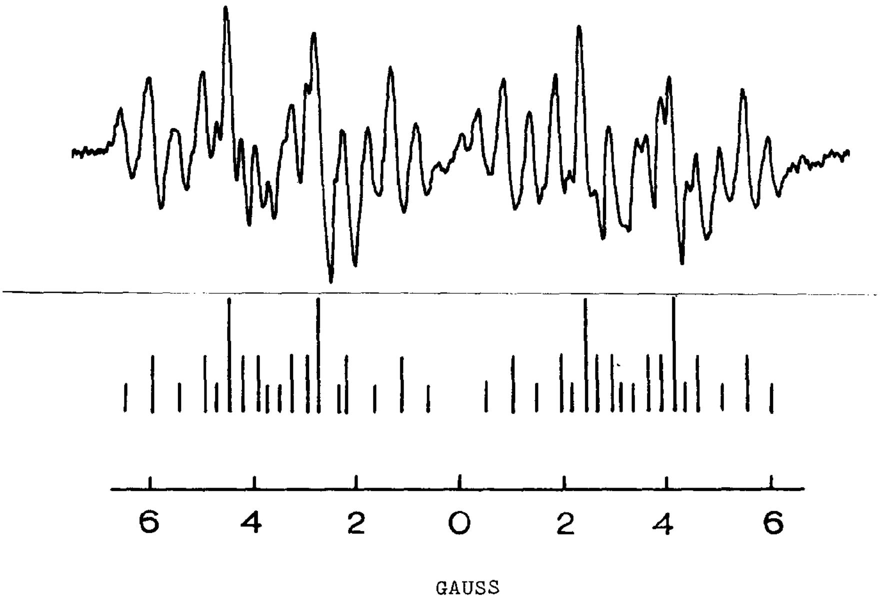


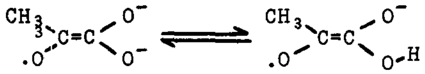
Fig. 1——First derivative e.s.r. spectrum of phenylglyoxal radical-anion prepared from 0.075 M phenacyl bromide in dimethyl sulfoxide solution containing 0.10 M potassium *t*-butoxide. Synthetic absorption spectrum composed from h.f.s.c. given in text.

The formation of IVb is surprising since the oxidation of acetophenone in basic DMSO solution does not form paramagnetic intermediates while phenylglyoxal in DMSO containing potassium *t*-butoxide in the presence or absence of a reducing carbanion (enolate anion of propiophenone) forms significant amounts of the radical-anion of 1-phenylpropane-1,2-dione, presumably *via*[8]

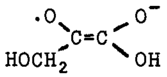
$$C_6H_5COCHO + CH_3SOCH_2^- \longrightarrow C_6H_5COCH(O^-)CH_2SOCH_3$$
$$\rightleftharpoons C_6H_5COC(OH)CH_2SOCH_3 \xrightarrow{-CH_3SO^-} C_6H_5COC(OH)=CH_2$$
$$\longrightarrow C_6H_5COCOCH_3$$

In a similar manner IVa is formed from methylglyoxal in DMSO solution.

IVc is not very stable, even in pure DMSO. However, by use of flow techniques at 28° IVc can be detected for a few (≈3) seconds after mixing one part of a solution of bromoacetone (0.15 *M*) with two parts of a solution of potassium *t*-butoxide (0.17 *M*) in DMSO. The spectrum is composed of two overlapping quartets with $a_{CHO}^{H} = 8.72$ and $a_{CH_3}^{H} = 7.46$ G. A second, more stable radical is formed (lifetime a few minutes) as IVc decomposes. This radical has an e.s.r. spectrum composed of a 1:3:3:1 quartet with $a^H = 5.7$ to 6.6 G. depending on the concentration of base. These results suggest that V is formed from IVc.

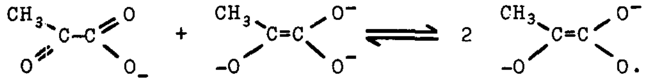


V



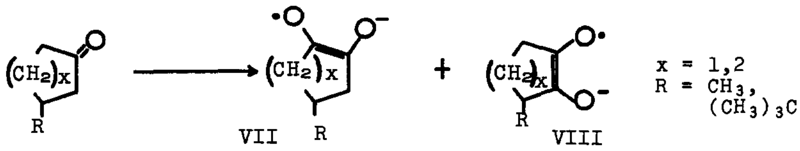
VI

This supposition was confirmed by the observation that the treatment of a mixture of 0.05 *M* pyruvic acid and 0.05 *M* lactic acid with 0.3 to 0.5 *M* potassium *t*-butoxide in DMSO also produced V.



In view of the stabilities observed for IVc and V, and the values of $a_{CH_3}^{H}$, a recent report of the synthesis of VI by treatment of 1,3-dihydroxyacetone, methylglyoxal or sugars such as glucose with aqueous potassium hydroxide in the presence of air[9] seems unreasonable. An inspection of the spectrum reported for VI (a^H = 0.81 G) reveals that the radical-anion is actually the well-known 2,5-dihydroxy-*p*-benzosemiquinone (a^H = 0.79 G).[10]

Oxygenation of 3-methylcyclohexanone or 3-methylcyclopentanone in DMSO containing potassium *t*-butoxide produces two parts of VII to one of VIII.


VII VIII

x = 1,2

R = CH_3, $(CH_3)_3C$

Bromination of these ketones in *t*-butyl alcohol in the presence of potassium *t*-butoxide followed by dilution with DMSO and base formed the same radical-anions in the same proportions. It thus appears that in unhindered systems both oxygenation and bromination in basic solution are measuring the same quantity without kinetic discrimination. The quantity being measured is apparently either the relative rates of ionization of the starting ketones or/and the relative equilibrium concentrations of enolate anions. We have observed kinetic discrimination in the reactions of 3-*t*-butylcyclopentanone in basic solution. Oxidation produces mainly VIII (> 90%) presumably because of the relief in eclipsing strain due to ionization at C-2. However, bromination of 3-*t*-butylcyclopentanone followed by treatment with DMSO produces mainly VII (>90%) probably due to the preferred bromination at C-5.[11]

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1. Reactions of Resonance Stabilized Anions. XVII. This work was supported by grants from the National Science Foundation and the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is hereby made to the donors of these funds.

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7. Phenylglyoxal radical-anion can also be formed in DMSO solutions of potassium *t*-butoxide from the pinacol ($C_6H_5COCH(OH)CH(OH)COC_6H_5$) and by reduction of the hemihydrate ($C_6H_5COCH(OH)OCH(OH)COC_6H_5$) by the enolate anion of propiophenone. The formation from the pinacol apparently involves the dissociation of dianions into radical-anions [G. A. Russell and E. T. Strom, *J. Am. Chem. Soc.*, **84**, 4155 (1962)]. The addition of bromine to 1,2-dibenzoylethylene in DMSO containing potassium *t*-butoxide and a trace of hydroxide ion also produces the phenylglyoxal radical-anion, presumably via the pinacol.

8. This represents another example of the methylation of unsaturated systems by the methylsulfinylcarbanion [C. Walling and L. Bollyky, *J. Org. Chem.*, **28**, 256 (1963); *ibid.*, **29**, 2699 (1964)]. We have also observed that in basic DMSO solutions that nitrobenzenes are oxidized to the *o*- and *p*-nitrobenzoic acids while polynuclear aromatics, such as anthracene, are converted to their methyl derivatives (*e.g.*, 9-methylanthracene, 9,10-dimethylanthracene) in the absence of oxygen (preliminary results of Mr. S. A. Weiner).

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11. 3-*t*-Butylcyclopentanone was kindly supplied by Mr. D. Rausch and Professor C. H. DePuy.