[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY OF THE UNIVERSITY OF VIRGINIA]

Reduction of Unsaturated 1,4-Diketones by Aluminum Isopropoxide[1]

BY ROBERT E. LUTZ* AND J. S. GILLESPIE, JR.[2]

The widespread use of aluminum alkoxides for reduction of aldehydes and ketones[3] has made it desirable to ascertain the effect of this reagent on the very easily reducible conjugated system of the unsaturated 1,4-diketones. Reductions to date, including those of some α,β-unsaturated aldehydes and ketones,[3] appear to proceed specifically 1,2 to the carbonyl group. One possible exception is the reduction of quinone to hydroquinone, which, however, may be interpreted in terms of initial 1,2-reduction at one carbonyl followed by 1,5-enolization at the other. Another possible exception is the reduction of the unsaturated 1,4-diketones to saturated diketones, which was cited in a prepublication note by Campbell and Khanna[4] and interpreted as 1,6-reduction. Here also however other interpretations are possible.[4c]

In our first experiments on dibenzoylethylene[4b] (I, II) we did not isolate any of the saturated diketone (VII), nor were we able to do so in many repetitions.[4c] Our results are as follows.

Both *cis*- and *trans*-dibenzoylethylenes (I, II) when subjected to the action of a refluxing isopropyl alcohol solution of aluminum isopropoxide for two to four hours gave only oils, but under heating for one hour or less they gave the *trans*-unsaturated 1,4-glycol (IV) in yields as high as 34% (purified). It seems probable in view of the sensitive character of the glycols and the difficulties of isolation that the amounts actually formed were greater than this. No significant amount of either starting material or of saturated diketone (VII) could be isolated (these compounds are difficultly soluble and easily crystallizable and they would have been found if present).[4c]

Our results are to be compared with the similar reductions of both *cis*- and *trans*-3-heptene-2-one to the same unsaturated alcohol.[5] However, in the case of dibenzoylethylene it was shown in separate experiment that under the conditions employed, but with only a very small amount of aluminum isopropoxide present, the *cis*-isomer was isomerized readily in good yield to the *trans*-isomer. The *trans*-isomer, for reduction itself, required a much higher concentration of the reagent. The solvent alone was without effect upon the *cis*-isomer. Thus direct reduction of the carbonyl groups of the *cis*-isomer does not appear to proceed rapidly enough to compete with isomerization caused by the reagent.

The structure of the glycol (IV) was proved by catalytic reduction to the known 1,4-diphenylbutane-1,4-diol (VIa)[6a] and by chromic acid oxidation to *trans*-dibenzoylethylene. Further evidence supporting the assigned *trans*-configuration (IV) was gained by the chromic acid oxidation of the stereoisomer, *cis*-1,4-diphenyl-2-butene-1,4-diol (III), which was obtained by the rapid catalytic hydrogenation of 1,4-diphenyl-2-butyne-1,4-diol[6b] (Va) and which was presumed to have the *cis*-configuration predicted in this type of half-reduction of an acetylenic linkage[7]; this oxidation, carried out under the same conditions as were employed in the oxidation of the *trans*-glycol (IV), resulted in the formation of *cis*-dibenzoylethylene (I) and confirmed the *cis*-configuration presumed for III. Obviously there is a consistent diastereo-configurational relationship between the *cis*- and *trans*-ethylenic glycols (III and IV), the higher melting acetylenic glycol (Va) and the higher-melting saturated glycol (VIa); possibly they are *meso*, since they have consistently the higher-melting points. The lower-melting stereoisomeric acetylene glycol (Vb) was found to give on catalytic reduction exclusively the lower-melting saturated glycol (VIb) (the corresponding *cis*- and *trans*-unsaturated glycols remain unknown). Analogy to the preferential formation of the higher-melting *meso*-hydrobenzoin and of "erythro" substituted-amino alcohols in aluminum isopropoxide reduction of benzoin and desylamines,[8] seems to be inapplicable here because dibenzoylethane (V) is reduced under similar condi-

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* Harvard University Ph.D. 1925.

(1) From Doctorate Dissertation, Univ. of Virginia, May, 1949; reported at the Atlantic City Meeting of the A. C. S., Sept. 12, 1949.

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(3) *Cf.* Wilds, "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 178.

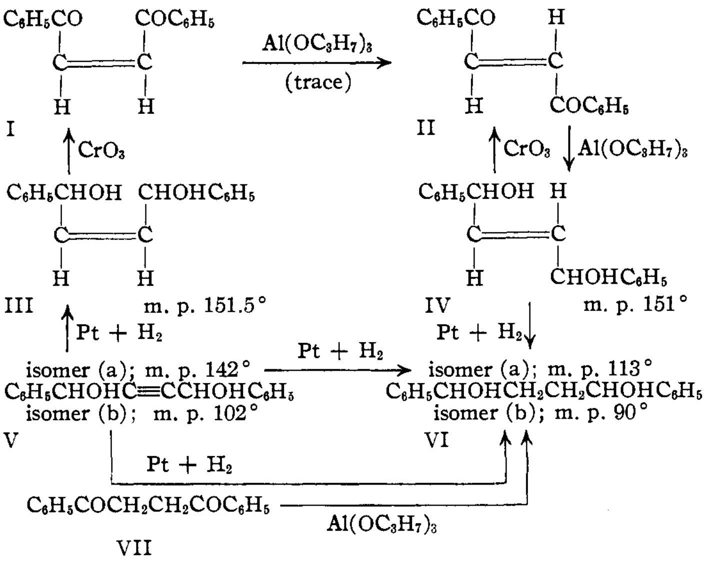
(4) (a) Campbell and Khanna, *Nature*, **161**, 54 (1949). (b) This note came to our attention after our main experiments had been completed. (c) The saturated diketones would themselves be readily reducible to the saturated glycols (*cf.* VIb) under these conditions, and if formed directly upon hydrolysis of the reaction mixture, they must have been stabilized during the reduction in some form such as the diene-diolate. On the other hand they may have arisen from secondary transformations during the chromatographing of their products. In support of the latter suggestion is an observation made by Mr. William L. Truett who repeated our principal experiment in this Laboratory after this paper had been submitted. Some of the non-crystalline product in dry benzene–petroleum ether solution upon treatment with alumina ("Alcoa," grade F-20) gave a significant amount of dibenzoylethane (VII) which was isolated (yield 10% calculated from II) and identified by mixture m. p. The unsaturated glycol (IV) was partially altered upon similar treatment but was not converted into dibenzoylethane. Apparently the non-crystalline product contained substances such as $C_6H_5COCH_2$-$CH(OR)CHOHC_6H_5$ and $C_6H_5COCH{=}CHCHOHC_6H_5$ which had been protected from further reduction in the form of complexes or enolates, and which were converted into dibenzoylethane by the catalytic action of the adsorbent.

(5) Arcus and Kenyon, *J. Chem. Soc.*, 698 (1938).

(6) (a) Zalkind and Isakovich, *C. A.*, **8**, 1419 (1914) [(*J. Russ. Phys.-Chem. Soc.*, **45**, 1902 (1913)]; (b) Zalkind and Neishtab, *J. Russ. Phys.-Chem. Soc.*, **50**, 34 (1919) [*C. A.*, **18**, 1467 (1924)]; (c) Palmer, Doctorate Dissertation, University of Virginia, 1934; Lutz and Palmer, THIS JOURNAL, **57**, 3405 (1935).

(7) *Cf.* Ott and Schroeter, *Ber.*, **60**, 624 (1927); **61**, 2119 (1928).

(8) Lutz, Freek and Murphey, THIS JOURNAL, **70**, 2015 (1948).



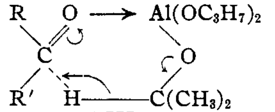
tions exclusively to the lower-melting glycol (VIb) of diastereo-configuration necessarily opposite to that of the unsaturated glycol (IV) obtained in the similar reduction of *trans*-dibenzoylethylene (II).

The one crystalline product which was obtained in the aluminum isopropoxide reduction of dibenzoylethylene is the result of the expected 1,2-reductions of the two carbonyl groups. There are many obvious ways to account for the large proportion of expectedly non-crystalline products, involving logical reactions of the sensitive unsaturated ketone and alcohol systems of starting material and of various possible primary and secondary products. 1,4-Addition of the reagent (as contrasted with 1,2-reduction by the reagent) is a complicating possibility, for example. Although 1,4- and 1,6-reductions (as distinct from addition of the reagent) could conceivably have occurred also, there is in our opinion no actual evidence for it, either here or in the work of Campbell and Khanna.[4c] At present therefore appearances still indicate that reductions may be specifically 1,2 to the carbonyl groups even when these groups are in conjugated systems.

trans-Dimesitoylethylene, $C_9H_{11}COCH{=}CH\text{-}COC_9H_{11}$, was unaffected by aluminum isopropoxide in isopropyl alcohol under two and a half hours of refluxing.

trans-Dibenzoyldimethylethylene, $C_6H_5COC(CH_3){=}C(CH_3)COC_6H_5$, was largely unaffected under similar reduction conditions, but a small yield of the lower-melting *trans*-unsaturated glycol[9] was obtained and isolated; this result corresponds in every respect except rate, to that with II.

Consideration of mechanisms of aluminum alkoxide reductions which have been put forward[10] suggests that a coördinative complex between the carbonyl group and aluminum alkoxide[10a] is involved and is in fact requisite; the electrophilic aluminum may make the carbonyl group so positive that it can abstract a hydride ion from an alcohol molecule,[10b] and at the same time it would activate the alkoxide α-hydrogen in the sense of facilitating release of hydride hydrogen,[10c] all this occurring through a resonating transition state[10d] or six-membered quasi-ring phase[10e] such as VIII. Such a mechanism would be consistent with the seeming limitation of the reagent to 1,2-reductions, and expressed in these terms it is analogous to that of 1,2-reductions of ketones by alkylmagnesium halides[11a] and 1,4-reactions between the α,β-unsaturated ketone system and the Grignard reagent[11b] and lithium aluminum hydride.[11c]



VIII

Experimental

***trans*-1,4-Diphenyl-2-butene-1,4-diol (IV).**—In one of many varied experiments 300 ml. of hot 3 *N* aluminum isopropoxide in isopropyl alcohol was added to a hot solution of 23.6 g. of II in 200 ml. of isopropyl alcohol; the mixture was refluxed for five minutes; acetone was evolved rapidly. The solvent was evaporated under reduced pressure with final heating on a bath at 80–85° for *ca.* fifteen minutes to complete the evaporation. The residue was hydrolyzed in the cold with 50% potassium hydroxide (or in some cases with acid or ice-water followed by acidification) and extracted with two 300-ml. portions of ether. Drying over sodium sulfate and evaporation gave an oil which partially crystallized on standing and which melted at 136–148° upon crystallization from ethanol; recrystallization brought the melting point to 151–152°. The yield of pure material at this point was 34% (in other runs it ranged between this and 25%). It gave mixture melting depressions with dibenzoylethane (VII) and with the unsaturated glycol (III). No evidence of the formation of VII or regeneration of II (by oxidation of the diene-diolate) was observed.

Anal. Calcd. for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 80.09; H, 6.52.

The reduction of I by the above method gave similar results; the product was identified as IV by mixture

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(9) This compound and its stereoisomer will be described in a later paper, dealing with lithium aluminum hydride reductions in this field.

(10)(a) Masdupuy and Gallais, *Compt. rend.*, **225**, 128 (1947). (b) Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, 1940, p. 352. (c) Woodward, Wendler and Brutschy, This Journal, **67**, 1425 (1945). (d) Doering and Aschner, *ibid.*, **71**, 838 (1949); a paper presented at the 112th meeting of the Am. Chem. Soc., New York, September 1947. *Cf.* also Doering, Taylor and Schoenewaldt, This Journal, **70**, 455 (1948); Neville, *ibid.*, **70**, 2499 (1948); Alexander, *ibid.*, **69**, 289 (1947); **70**, 259 (1948). (e) Baker and Linn, *ibid.*, **71**, 1399 (1949).

(11) (a) *Cf.* Whitmore and George, "The Common Basis of the Reaction of Grignard Reagents with Carbonyl Compounds; Addition, Reduction, Enolization and Condensation," 102nd Meeting, A. C. S., Atlantic City, September 9, 1941; *cf.* also Mosher, Foley and LeCombe, "Asymmetric Reduction of D-2-Methyl-1-butylmagnesium Chloride," 115th Meeting, A. C. S., San Francisco, March 27 (1949); (b) Lutz and Reveley, This Journal, **63**, 3184 (1941); (c) Lutz and Gillespie, *ibid.*, **72**, in press (1950).

melting point. In one run however a small amount of solid of m. p. 171–178° was obtained but was not studied.

Since the results of these reductions do not correspond with those reported by Campbell and Khanna,[4] we repeated our experiments on dibenzoylethylene many times, and varied the concentration of the reagent, conditions and mode of hydrolysis. In several experiments freshly prepared unclarified aluminum isopropoxide solutions were used. The results were always approximately the same and in no case was dibenzoylethane isolated. The residual oils underwent resinification under attempts at distillation or evaporation under reduced pressure, and gave only oils when oxidized by chromic acid under conditions which converted the unsaturated glycols into the unsaturated diketones.

Reduction of IV in ethanol by platinum and hydrogen at room temperature and pressure on a small scale gave an 84% yield of VIa which upon crystallization from chloroform and petroleum ether melted at 113–114° and showed no mixture melting point depression with a sample prepared by a similar catalytic reduction of the acetylene glycol[6b] of m. p. 142° (Va).

Oxidation of 1 g. of IV in 100 ml. of concd. acetic acid by 1 g. of chromic oxide in 20 ml. of 25% acetic acid, added dropwise over forty minutes at 20° and with continued stirring for a further thirty minutes, gave 0.7 g. of II of m. p. 111–112° (identified by mixture melting point). Oxidation similarly of III[6b] gave a 50% yield of I of m. p. 134–135° (identified by mixture melting point).

Inversion of I to II on a small scale was accomplished by the action of 0.09 *N* aluminum isopropoxide in isopropyl alcohol under refluxing for 2.5 hours; only II was recovered (92%). Without the added aluminum isopropoxide the cis compound (I) could be largely recovered unchanged.

***trans*-1,2-Dimesitoylethylene** was recovered practically quantitatively unchanged after treatment under the usual conditions with aluminum isopropoxide (refluxing for two and one-half hours). No acetone evolution was observed during the experiment.

Reduction of dibenzoylethane (VII) by aluminum isopropoxide as above but under reflux for four hours gave an oil which was fractionally crystallized from chloroform by additions of petroleum ether; the yield of VIb of m. p. 89–90° was 82% (identified by mixture melting point with an authentic sample[6c] prepared by catalytic reduction of Vb).

Summary

Aluminum isopropoxide in low concentration caused *cis–trans* inversion of dibenzoylethylene, and in higher concentration caused reduction to the *trans*-unsaturated glycol which could be oxidized back to *trans*-dibenzoylethylene and catalytically hydrogenated to the higher-melting saturated glycol. The *cis*-unsaturated glycol of corresponding diastereo-configuration, made by partial hydrogenation of the acetylene glycol, was reducible to the higher-melting saturated glycol, and was oxidizable to *cis*-dibenzoylethylene. Dimesitoylethylene resisted reduction; and *trans*-dibenzoyldimethylethylene was reduced like dibenzoylethylene, but slowly, to the unsaturated glycol. Dibenzoylethane was reduced readily to the lower-melting saturated glycol.

A reduction mechanism involving a coördination complex with the reagent and a transitory quasi-ring phase facilitating transfer of hydrogen, is considered.

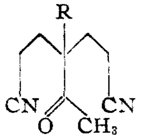
Charlottesville, Va. Received July 20, 1949

[Contribution from the School of Chemistry of the University of Minnesota]

The Action of Sulfuric Acid on γ-Acetylpimelonitriles[1]

By C. F. Koelsch[*] and H. M. Walker

γ-Acetyl-γ-phenylpimelonitrile (I, R = C_6H_5) has been converted to the corresponding acid with hot 10% sodium hydroxide, but the process is slow.[2] It was thought that a more rapid hydrolysis might be effected with sulfuric acid, but it has now been found that this reagent yields II, R = C_6H_5, rather than the expected acid. Such behavior appears to be characteristic of γ-substituted-γ-acetylpimelonitriles; the γ-methyl derivative gives II, R = CH_3, the γ-cyanoethyl derivative gives II, R = CH_2CH_2COOH, and the γ-carbethoxy derivative gives II, R = H.



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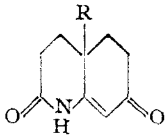
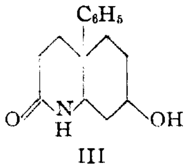
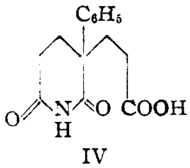


II

Structure II, R = C_6H_5, has been established for the product from γ-acetyl-γ-phenylpimelonitrile by a study of the reactions of the substance. Drastic treatment with alkali converts the compound into γ-acetyl-γ-phenylpimelic acid, showing that sulfuric acid brought about no deep-seated change in the carbon skeleton. Formation of an oxime indicates a ketone group, as does catalytic reduction to an alcohol, III. Ozonolysis, with the formation of IV, indicates the presence and position of a double bond



III



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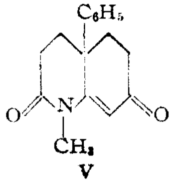

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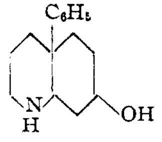

VI

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[*] Harvard University National Research Fellow 1931–1932.

(1) From the Ph.D. Thesis of Harry M. Walker, May, 1949.

(2) Bruson and Riener, This Journal, 64, 2850 (1942).