A Simple Synthesis of Piperitenone

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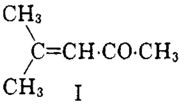
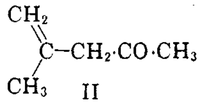
In view of its tendency to appear in an allyl-isomeric form (II), mesityl oxide (I) can act both as acceptor and as donor in Michael reactions. Thus, acrylonitrile gives with mesityl oxide a mono- and a diadduct,[1,2] the constitution of the latter having been proved unambiguously. The dimerization of mesityl oxide can be formulated as a Michael reaction, though Braude and co-workers[3] consider it to be a normal diene addition. It was our intention to elucidate whether in monoadducts of mesityl oxide with suitable acceptors the α-methylene group of II or one of the *gem.* methyl groups of I is the point of attack. That these methyl groups are activated by the carbonyl, has been known from various condensation reactions.[4,5]

When mesityl oxide was condensed with one mole of methyl vinyl ketone under the influence of sodium *t*-pentoxide in toluene solution, it could be shown that the adduct resulted from an attack at the α-methylene group. The adduct had lost one mole of water and had thus evidently undergone cyclization. If the α-methylene group had been the point of attack, V or VII would have formed *via* IV; in case of reaction at a terminal methyl group, an eight-membered ring would result from the cyclization of VI. The product is, in fact, *dl*-piperitenone (V). This can be deduced from the infrared (1661 cm.$^{-1}$) and the ultraviolet spectra (238 mμ; 295.5 mμ), as a compound such as VII should absorb at 1670 cm.$^{-1}$ [6] and 285 mμ,[6a] respectively. Furthermore, the product is decomposed by boiling formic acid into 3-methylcyclohex-2-enone and acetone, a reaction characteristic of compounds of type V,[7] and, finally, heating with palladium transformed it into thymol (VIII).[7a] The latter reaction takes place, when one attempts to hydrogenate the compound catalytically. In this case, thymol is formed together with menthone and menthols.

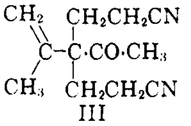
While the chemical reactions of our product are identical with those reported by Naves and co-workers[8,9] for natural piperitenone, the ultraviolet spectrum observed by these authors (243; 279; 353 mμ) is at variance with our observations. In fact, Naves works with mixtures of piperitenone, isopiperitenone, and pulegone and claims that the product used for the determination of the spectrum was almost free of these contaminations.


$(CH_3)_2C{=}CH\cdot CO\cdot CH_3$

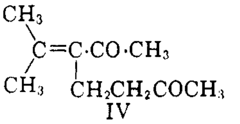
I


$CH_2{=}C(CH_3){-}CH_2\cdot CO\cdot CH_3$

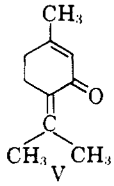
II

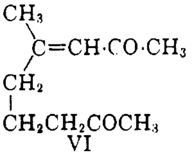

$CH_2{=}C(CH_3){-}C(CH_2CH_2CN)_2\cdot CO\cdot CH_3$

III

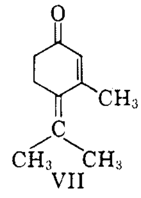

$(CH_3)_2C{=}C(CH_2CH_2COCH_3)\cdot CO\cdot CH_3$

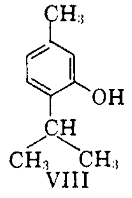
IV


V


$CH_3(CH_2CH_2CH_2COCH_3)C{=}CH\cdot CO\cdot CH_3$

VI


VII


VIII

EXPERIMENTAL

Piperitenone (V). In a nitrogen-filled flask of 1-l. capacity, mounted with stirrer, reflux condenser, and dropping funnel, a mixture of 35 g. of mesityl oxide, 25 g. of methyl vinyl ketone, and 150 ml. of toluene is cooled to 0°, and a solution of sodium *t*-pentoxide is added, prepared from 4.0 g. of sodium, 15.5 g. of *t*-amyl alcohol and 150 ml. of toluene. After 45 min., the mixture is heated at 60° for 15 min. and poured into water, containing 15 ml. of glacial acetic acid. The organic layer is washed with a 5% sodium carbonate solution and water, dried, and distilled. After recovery of 10 g. of unchanged mesityl oxide, 22 g. (41%) of piperitenone distill at 80–83° (0.05 mm.) or 130–134° (24 mm.).

Anal. Calcd. for $C_{10}H_{14}O$: C, 80.0; H, 9.4. Found: C, 79.6; H, 9.7.

2,4-Dinitrophenylhydrazone, from isobutanol dark red fine needles of m.p. 152°, $\lambda_{max}^{CHCl_3}$ 414 mμ (4.28).

Anal. Calcd. for $C_{16}H_{18}N_4O_4$: C, 58.2; H, 5.5; N, 17.0. Found: C, 58.6; H, 6.0; N, 17.3.

A higher-boiling fraction [135–138° (0.05 mm.)] was also obtained in small quantities, probably formed from 1 mole of mesityl oxide and 2 moles of methyl vinyl ketone.

Degradation with formic acid. A mixture of 12 g. of V and 30 g. of 90% formic acid was heated at 110–120° in a short column for 24 hr. so that no formic acid distilled over. Thus, 2.0 g. of acetone was obtained, which was characterized as 2,4-dinitrophenylhydrazone, from methanol m.p. 126–127°. The distillation residue was poured into a mixture of concentrated sodium chloride solution and ether and made alkaline with potassium carbonate. Distillation of the ethereal layer gave 5 g. of a distillate of b.p. 95–100° (3.5 mm.) and some unchanged V. The first fraction was identified as 3-methylcyclohex-2-en-1-one through the semi-

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(1) H. A. Bruson and T. W. Riener, *J. Am. Chem. Soc.*, **65**, 18 (1943).

(2) R. L. Frank and J. B. McPherson, *J. Am. Chem. Soc.*, **71**, 1387 (1949).

(3) E. A. Braude, B. F. Gofton, G. Lowe, and E. S. Waight, *J. Chem. Soc.*, 4054 (1956).

(4) R. Fuson, *Chem. Revs.*, **16**, 1 (1935).

(5) S. G. Powell and W. J. Wasserman, *J. Am. Chem. Soc.*, **79**, 1934 (1957).

(6) See, *e.g.*, N. H. Cromwell, F. A. Miller, A. R. Johnson, R. L. Frank, and D. J. Wallace, *J. Am. Chem. Soc.*, **71**, 3337 (1949).

(6a) J. A. Birch, *J. Roy Soc. N. S. Wales*, **83**, 245 (1949).

(7) Compare the behavior of pulegone [O. Wallach, *Ann.*, **289**, 332 (1896); **365**, 243 (1909)] and isopulegone [F. Tiemann and R. Schmidt, *Ber.*, **30**, 28 (1897)].

(7a) *Cf.* A. Jennen and F. Verdroneken, *Compt. rend.*, **245**, 183 (1957).

(8) Y. R. Naves, *Helv. Chim. Acta*, **25**, 732 (1942).

(9) Y. R. Naves and G. Papazian, *Helv. Chim. Acta*, **25**, 1032 (1942).

carbazone, from methanol m.p. 201° (lit.,[10] 201°) and the 2,4-dinitrophenylhydrazone, from methanol, m.p. 172° (lit.,[10] 170–173°).

Isomerization of V. A mixture of 8 g. of V and 0.5 g. of palladium-charcoal was heated at 180–190° for 3 hr. The product was extracted with sodium hydroxide solution (10%), from which thymol (3.3 g.; 40%) was recovered by acidification, extraction with low-boiling petroleum ether, and distillation, b.p. 130° (35 mm.). When the material, insoluble in alkali, was subjected to the same treatment, some more (1 g., 12%) thymol was isolated. The phenol was characterized by its infrared spectrum (3350 cm.$^{-1}$ (OH), 815 cm.$^{-1}$ (trisubstituted benzene)) and through thymoxy-acetic acid, from water m.p. 146° (lit.,[11] 145°).

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[10] I. Heilbron and H. M. Bunbury, *Dictionary of Organic Compounds*, Eyre and Spottis Woode, London, Vol. III, 1952, p. 350.

[11] Lambling, *Bull. soc. chim. France* [3], **17**, 360 (1897).

A Rearrangement of Diaryltrichloromethylcarbinols

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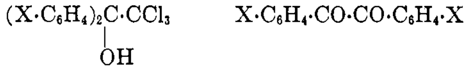
In view of the fact that diaryltrifluoromethylcarbinols rearrange in their halochromic solutions in concentrated sulfuric acid to yield fluorene derivatives,[1,2] it seemed of interest to study the behavior of the recently[3] described diaryltrichloromethylcarbinols (I) under similar conditions. When the solutions of these compounds in concentrated sulfuric acid are poured into water or alcohol, yellow crystalline compounds precipitate, which were identified as the corresponding benzils (II).



$$(X{\cdot}C_6H_4)_2\underset{OH}{\underset{|}{C}}{\cdot}CCl_3 \qquad X{\cdot}C_6H_4{\cdot}CO{\cdot}CO{\cdot}C_6H_4{\cdot}X$$

I II

X = H, F, Cl (*para*)

Rearrangement of asymmetric to symmetric diarylethanes and -ethylenes occurs in many cases; in particular one would recall the transformation of 1,1-diaryl-2,2-dichloro- or 1,2,2,2-tetrachloro-ethanes into chlorinated bibenzyls,[4–6] the preparation of α,α,β-trifluorobibenzyls from 1,1-diaryl-2,2,2-trichloroethanes under the influence of hydrogen fluoride and mercuric oxide,[7,8] and particularly the conversion of 1,1-di-(*p*-chlorophenyl) 2,2,2-trichloro- and 1,2,2,2-tetrachloroethane into 4,4′-dichlorobenzil under the influence of concentrated sulfuric acid.[9] The mechanism of the observed rearrangement can be formulated as follows in accordance with Barry and Boyer[9]:

$$Ar_2C(OH){\cdot}CCl_3 \xrightarrow{H_2SO_4} Ar_2\overset{+}{C}{\cdot}CCl_3 \qquad (1)$$

$$Ar_2\overset{+}{C}{\cdot}CCl_3 \longrightarrow (Ar)\,(Cl)\overset{+}{C}{\cdot}CCl_2Ar \qquad (2)$$

$$(Ar)(Cl)\overset{+}{C}{\cdot}CCl_2Ar \longrightarrow Ar{\cdot}\overset{+}{C}(OH)\,CCl_2Ar \qquad (3)$$

$$Ar{\cdot}\overset{+}{C}(OH){\cdot}CCl_2Ar \longrightarrow Ar{\cdot}CO{\cdot}CCl_2Ar \div H^+ \qquad (4)$$

$$ArCO{\cdot}CCl_2Ar \longrightarrow ArCO{\cdot}COAr \qquad (5)$$

This mechanism is analogous to that accepted for the transformation of, *e.g.*, diphenylglycolaldehyde into benzoin.[10]

EXPERIMENTAL

The diaryl-trichloromethyl-carbinols (I) and their acetates were obtained as described earlier.[3] In the preparation of [I (X = H)], a yield of 84% (instead of the previously reported 56%) was obtained when the preparation was carried out on a larger scale. The acetates of I may be saponified directly (without prior isolation) by refluxing the filtered reaction mixture with dilute sulfuric acid for 1.5–2 hr.

Nitration of diphenyl-trichloromethyl-carbinol (I, X = H). At −5 to −10°, a solution of 6.0 g. of diphenyl-trichloromethyl-carbinol in 15 ml. of chloroform was added dropwise, during 30 min., to a well stirred mixture of 20 ml. of nitric acid (d. 1.5) and 5 ml. of concentrated sulfuric acid. The stirring was continued for another half hour at −10° and for 4 hr. at room temperature, and the organic layer separated, washed with sodium bicarbonate solution and water and evaporated, yielding 8 g. of a yellow, very viscous product. As it could not be obtained in a crystalline state, it was acetylated by an excess of boiling acetic anhydride and 2 drops of concentrated sulfuric acid. The acetate so obtained melted at 115–130° and was a mixture of several isomers. By a number of tedious recrystallizations from acetic acid, toluene, and ethanol a small amount of colorless crystals of 154–156° was obtained. Their quantity did not suffice for the determination of the position of the two nitro groups.

Anal. Calcd. for $C_{16}H_{11}Cl_3N_2O_6$: C, 44.3; H, 2.6. Found: C, 44.3; H, 2.8.

Action of concentrated sulfuric acid on the carbinols (I). *4,4-Difluorobenzil* (II, X = F). To 2.3 g. of 1,1-di-(*p*-fluorophenyl)-1-acetoxy-2,2,2-trichloroethane, 25 ml. of concentrated sulfuric acid was added. The red color of the solution quickly turned greenish brown. The mixture was shaken for 2 hr. in a stoppered bottle and poured into cold water. The yellow 4,4′-difluorobenzil (0.6 g.; 40%), m.p. 114–120°, was recrystallized from petroleum ether (60–90°) and methanol and melted at 121.5–122.5° (lit.[6] 123–123.5°).

Anal. Calcd. for $C_{14}H_8F_2O_2$: C, 68.3; H, 3.3. Found: C, 68.1; H, 3.6.

Analogously, from the blue-violet solution of diphenyltrichloromethyl-carbinol (I, X = H) or its acetate, *benzil,*

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[1] S. Cohen and A. Kaluszyner, *Experientia*, **13**, 236 (1957).

[2] S. Cohen, *J. Am. Chem. Soc.*, **79**, 1499 (1957).

[3] E. D. Bergmann and A. Kaluszyner, *J. Org. Chem.*, **23**, 1306 (1958). *Cf.* H. F. Wilson and E. L. Wolffe, U. S. Patent **2,812,362**; *Chem. Abstr.*, **52**, 7357 (1958).

[4] E. E. Fleck, *J. Org. Chem.*, **12**, 708 (1947).

[5] W. L. Walton, *J. Am. Chem. Soc.*, **69**, 1544 (1947).

[6] W. Voegtli and P. Läuger, *Helv. Chim. Acta*, **38**, 46 (1955).

[7] S. Kirkwood and I. R. Dacey, *Can. J. Research*, **24B**, 69 (1946).

[8] S. Cohen, A. Kaluszyner, and R. Mechoulam, *J. Am. Chem. Soc.*, **79**, 5979 (1957).

[9] G. T. Barry and R. Boyer, *Can. J. Research*, **26 B**, 518 (1948).

[10] S. Danilov, *Ber.*, **60**, 2390 (1927).