sodium will add to an ethane is determined not only by the strength of the carbon–carbon bond but also by those factors which determine the strength of the corresponding methane as an acid. According to McEwen[8] the difference in acid strength for these two methanes is about 16 kcal. The difference in the free energy of addition of sodium to the free radicals is found to be greater than 12 kcal. These results give a consistent explanation of the behavior of phenylfluorene as an acid and the stability of the sodium salt.

The results of the measurements on dibiphenylene-diphenylethane may be expressed in terms of the reaction $2Na + R_2 \longrightarrow 2NaR$ without any assumptions regarding the dissociation of the ethane into a free radical. ΔF so calculated is -61.9 kcal.

Summary

1. A potentiometric method is described for determining the free energy of addition of sodium to an organic compound.
2. An e. m. f. is reported which is not accounted for by accepted ideas of the nature of the compounds studied.
3. Dibiphenylene-diphenylethane is reported to have an abnormally large electron affinity which is directly related to the strength of phenylfluorene as an acid.

CAMBRIDGE, MASS. RECEIVED APRIL 29, 1936

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[8] McEwen, THIS JOURNAL, 58, 1124 (1936).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

Mesityl Phenyl Diketone

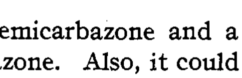
BY H. H. WEINSTOCK, JR., AND REYNOLD C. FUSON

Mesityl phenyl diketone (I) was selected for study because it appeared to afford an opportunity of determining the behavior of one of the carbonyl groups of an alpha diketone without interference from the other. It was supposed that the carbonyl group adjacent to the mesityl radical would be unaffected by most reagents, and that the diketone would, in fact, behave as a monoketone, in which, however, the carbonyl group would be unusually reactive. In general, this expectation has been supported by the experimental evidence; however, in certain reactions, both carbonyl groups seem to be directly involved.

The diketone behaves as a monoketone toward phenylmagnesium bromide, which converts it into the carbinol (II). Likewise the diketone

$(CH_3)_3C_6H_2COCOC_6H_5$

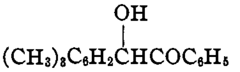
I



$(CH_3)_3C_6H_2CO\underset{\underset{OH}{|}}{C}(C_6H_5)_2$

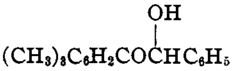
II

gave a monoxime, a monosemicarbazone and a mono-2,4-dinitrophenylhydrazone. Also, it could not be induced to react with *o*-phenylenediamine. On the other hand, toward hydrogen peroxide the diketone behaves normally. Reduction with zinc and acetic acid gave a mixture of the two isomeric benzoins (III and IV).[1]



$(CH_3)_3C_6H_2\overset{\overset{OH}{|}}{C}HCOC_6H_5$

III



$(CH_3)_3C_6H_2CO\overset{\overset{OH}{|}}{C}HC_6H_5$

IV

Vigorous reduction of the diketone yields the desoxybenzoin, V.

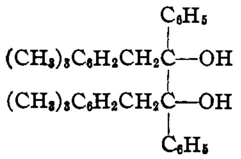
$(CH_3)_3C_6H_2CH_2COC_6H_5$

V

$(CH_3)_3C_6H_2COCH_2C_6H_5$

VI

This compound formed a phenylhydrazone and a dinitrophenylhydrazone, and with isopropylmagnesium bromide or ethylmagnesium bromide it was reduced to the pinacol (VII).



$$\begin{array}{r} C_6H_5 \\ | \\ (CH_3)_3C_6H_2CH_2C-OH \\ | \\ (CH_3)_3C_6H_2CH_2C-OH \\ | \\ C_6H_5 \end{array}$$

VII

The structure of V was proved by synthesizing it from mesitylacetyl chloride and benzene. The isomeric desoxy compound (VI) is known. Both of these desoxybenzoins yield the benzil (I) when oxidized with selenium dioxide. Here it would appear that reduction had taken place preferentially at the hindered carbonyl group. However, the explanation is evidently not so simple as this, because when either of the benzoins (III and IV) is reduced the product is invariably V, no trace of VI being produced. This is especially

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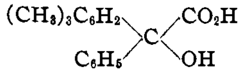
[1] Fuson, Weinstock and Ullyot, THIS JOURNAL, 57, 1803 (1935).

notable in the case of IV; here the yield of V is 78% of the theoretical amount.

The action of alkali brought about the benzilic acid rearrangement, yielding mesitylphenylglycolic acid (VIII).



$$\begin{matrix}(CH_3)_3C_6H_2\\ C_6H_5\end{matrix}\!>\!C\!<\!\begin{matrix}CO_2H\\ OH\end{matrix}$$

VIII

The structure of this acid was proved by reducing it to mesitylphenylacetic acid.

Experimental

Mesityl Phenyl Diketone (I).—This compound was first obtained by the action of phenylmagnesium bromide on mesitylglyoxal,[2] but is more conveniently made by oxidation of benzyl mesityl ketone. The following procedure gave the diketone in yields of 83%.[3] A mixture of 80 g. of benzyl mesityl ketone,[4] 42 g. of selenium dioxide, 1200 cc. of dioxane, and 5 cc. of water was heated under reflux, with stirring, for three hours. The solution was decanted from the precipitated selenium and concentrated to a volume of 200 cc. When this solution was allowed to cool, the diketone separated in the form of yellow crystals, melting at 136–137°. A mixture with a specimen prepared by the method of Gray and Fuson showed no lowering of the melting point.

The monoxime of mesityl phenyl diketone was colorless, and melted at 155°.

Anal. Calcd. for $C_{17}H_{17}NO_2$: N, 5.24. Found: N, 5.43.

The monoxime was recovered unchanged when heated for forty-eight hours with an excess of hydroxylamine.

The mono 2,4-dinitrophenylhydrazone of mesityl phenyl diketone was orange in color, and melted at 232–232.5°.

Anal. Calcd. for $C_{23}H_{20}N_4O_5$: N, 12.96. Found: N, 12.72.

This compound was also obtained when 0.5 g. of IV was boiled for two minutes with 0.4 g. of 2,4-dinitrophenylhydrazine and 2 cc. of concentrated hydrochloric acid in a solution of 50 cc. of ethyl alcohol. The melting point was 230–231°. A mixed melting point with a sample of the mono-2,4-dinitrophenylhydrazone of mesityl phenyl diketone showed no depression.

Attempted Reaction with *o*-Phenylenediamine.—The starting material was quantitatively recovered in a high state of purity after treatment of I with the calculated amount of *o*-phenylenediamine in boiling solutions of absolute alcohol or glacial acetic acid.

Reaction with Hydrogen Peroxide.—Two grams of I, 25 cc. of 30% hydrogen peroxide, and 50 cc. of dioxane were boiled under reflux for two hours. There was obtained 1.85 g. of alkali-soluble material. Treatment with boiling water gave 0.95 g. of an insoluble substance; m. p. 152°. A mixed melting point with an authentic sample of 2,4,6-trimethylbenzoic acid was 152°. On cooling of the water solution, there was obtained a white product which melted at 121° after several recrystallizations from water. A mixed melting point determination proved the substance to be benzoic acid.[5]

Reaction with Phenylmagnesium Bromide.—To a solution of phenylmagnesium bromide prepared from 0.5 g. of magnesium, 4 g. of bromobenzene and 100 cc. of dry ether was added 1 g. of mesityl phenyl diketone. The mixture was stirred for three hours, and then decomposed with dilute hydrochloric acid. The *carbinol* (II) crystallized from alcohol in the form of colorless needles melting at 169.5–170°.

Anal. Calcd. for $C_{23}H_{22}O_2$: C, 83.63; H, 6.69. Found: C, 83.67; H, 6.85.

Reduction to the Benzoins.—A solution of 2 g. of mesityl phenyl diketone in 75 cc. of glacial acetic acid was heated to boiling and 10 g. of powdered zinc was added cautiously. The mixture was heated under reflux for five minutes, partially cooled and filtered. The filtrate was diluted with water until turbidity ensued. There resulted a precipitate of 0.65 g. of crystals melting at 94–98°. Recrystallization from alcohol gave the pure *2,4,6-trimethylbenzoin* (IV). The product alone or when mixed with an authentic specimen of the compound melted at 101–102°.

To 0.2 g. of the benzoin in 30 cc. of dry, high-boiling petroleum ether was added 1 cc. of phenyl isocyanate. The solution was heated under reflux for four hours and allowed to cool. The urethan formed colorless crystals melting at 160–161°. A mixed melting point with a sample of the *urethan of 2,4,6-trimethylbenzoin* was 160–161°.

When the filtrate from which the 2,4,6-trimethylbenzoin was obtained was further diluted, there was obtained the *2′,4′,6′-trimethylbenzoin* (III); after recrystallization from alcohol, it melted at 93.5–94°.

Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.31; H, 7.14. Found: C, 80.15; H, 7.04.

The *urethan* melted at 141–142°.

Anal. Calcd. for $C_{24}H_{23}O_3N$: N, 3.76. Found: N, 3.89.

The *2,4-dinitrophenylhydrazone* melted at 211.5–212°.

Anal. Calcd. for $C_{23}H_{22}O_5N_4$: N, 12.90. Found: N, 12.72.

Oxidation converted 2′,4′,6′-trimethylbenzoin into mesityl phenyl diketone. The structure of this benzoin has been established by synthesizing it from mesitylene and phenylglyoxal.[6]

Phenyl 2,4,6-Trimethylbenzyl Ketone (V)

(a) **From I by Reduction with Zinc and Acetic Acid.**—A mixture of 7 g. of the diketone, 100 cc. of glacial acetic acid and 15 g. of zinc dust was boiled under reflux for ten hours, filtered, diluted with water and allowed to cool. The desoxybenzoin melted (from alcohol) at 163.5–164°; yield, 45%.

Anal. Calcd. for $C_{17}H_{18}O$: C, 85.7; H, 7.56; mol. wt., 238. Found: C, 85.4; H, 7.63; mol. wt., 228.

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(2) Gray and Fuson, THIS JOURNAL, **56**, 739 (1934).

(3) Hatt, Pilgrim and Hurran [*J. Chem. Soc.*, 93 (1936)] have recently prepared the diketone by a similar method.

(4) This compound was made by the method of Klages and Lickroth [*Ber.*, **32**, 1564 (1899)] who described it as a solid melting below 30°. It has been found to melt (from alcohol) at 32–32.5°.

(5) A similar result has been reported by Hatt, Pilgrim and Hurran, ref. 3.

(6) Arnold and Fuson, THIS JOURNAL, **58**, 1295 (1936).

(b) From I by Reduction with Zinc and Alkali.—A mixture of 10 g. of I, 35 g. of zinc dust, 35 g. of potassium hydroxide (in 25 cc. of water) and 250 cc. of alcohol was boiled under reflux for four hours and allowed to stand overnight. The yield of V was 33% of the theoretical amount.

(c) From I by Reduction with Tin and Hydrochloric Acid.—A mixture of 3.0 g. of I, 5 g. of granulated tin, 20 cc. of concentrated hydrochloric acid and 100 cc. of ethyl alcohol was boiled under reflux for twelve hours. The yield of V was 76%.

(d) From the Benzoins.—The ketone (V) results when either III or IV is heated with zinc and acetic acid. A typical procedure is the following: a mixture of 1 g. of 2,4,6-trimethylbenzoin, 50 cc. of glacial acetic acid and 6 g. of zinc dust was boiled under reflux for twelve hours. A yield of 0.3 g. of V was obtained; m. p. 162–163°.

(e) From IV by Reduction with Tin and Hydrochloric Acid.—A mixture of 2.0 g. of IV, 5 g. of granulated tin, 20 cc. of concentrated hydrochloric acid and 100 cc. of ethyl alcohol was boiled under reflux for twenty hours. The yield of V was 78% of the theoretical amount. The melting point of the crude material was 161–164°.

(f) From Mesitylacetic Acid.—To 7.2 g. of mesitylacetic acid was added 25 cc. of thionyl chloride; the solution was allowed to stand for two hours, then it was heated for thirty minutes at 60°. The mixture was distilled under diminished pressure, the mesitylacetyl chloride being collected at 126–130° (10 mm.). The acid chloride was dissolved in 50 cc. of dry benzene and this solution was added dropwise to a mixture of 10 g. of aluminum chloride and 50 cc. of benzene. The mixture was allowed to stand at room temperature for five hours. There was obtained 2.5 g. of product melting at 145–152°. Recrystallization from alcohol gave the pure ketone (V), melting at 163.5–164°. Mixtures with samples prepared under (a) and (b) showed no depression of the melting point.

The *phenylhydrazone* of phenyl 2,4,6-trimethylbenzyl ketone had an orange color, and melted (from alcohol) at 104–105°.

Anal. Calcd. for $C_{23}H_{24}N_2$: N, 8.54. Found: N, 8.63.

The *2,4-dinitrophenylhydrazone* of phenyl 2,4,6-trimethylbenzyl ketone was orange in color and melted at 163°.

Anal. Calcd. for $C_{23}H_{22}O_4N_4$: N, 13.39. Found: N, 13.41.

A second compound was isolated from the mixture resulting from the action of 2,4-dinitrophenylhydrazine and the ketone. It had an orange color, melted at 190° and appeared to be a second 2,4-dinitrophenylhydrazone.

Anal. Calcd. for $C_{23}H_{22}O_4N_4$: N, 13.39. Found: N, 13.21.

The pinacol (VII) was produced when phenyl 2,4,6-trimethylbenzyl ketone was treated with an excess of ethylmagnesium bromide or isopropylmagnesium bromide. The pinacol is very insoluble in alcohol, but can be recrystallized from glacial acetic acid. It melts at 241–242°.

Anal. Calcd. for $C_{34}H_{38}O_2$: C, 85.35; H, 7.95; mol. wt., 478. Found: C, 85.40; H, 7.96; mol. wt. (Rast), 437.

Oxidation of 1 g. of V with 0.5 g. of selenium dioxide in 25 cc. of dioxane and 0.5 cc. of water gave 0.6 g. of the diketone (I). The reaction was carried out by heating the mixture for ten hours at 80°.

The *p*-Chlorobenzal Derivative of Benzyl Mesityl Ketone.—A mixture of 1 g. of *p*-chlorobenzaldehyde, 10 cc. of 10% sodium hydroxide solution, 0.66 g. of benzyl mesityl ketone and 50 cc. of alcohol was allowed to stand overnight. A precipitate formed. The solution was diluted with an equal volume of water, and the product removed on a filter. There resulted 0.89 g. of product melting at 135–137°. Recrystallization from alcohol raised the melting point to 141°.

Anal. Calcd. for $C_{24}H_{21}OCl$: C, 79.85; H, 5.83. Found: C, 79.96; H, 6.08.

It was found that the foregoing procedure could be used for the detection of small amounts of benzyl mesityl ketone.

Mesitylacetic acid was prepared by reduction of mesitylglycolic acid with iodine and phosphorus, as reported by Claus.[7] A mixture of 3.0 g. of red phosphorus, 1.0 g. of iodine and 100 cc. of glacial acetic acid was allowed to stand at room temperature for fifteen minutes. There was added 5 cc. of water and 8.8 g. of mesitylglycolic acid. The mixture was boiled under reflux for four hours, and filtered while hot into 100 cc. of a saturated solution of sodium bisulfite. The yield of the acid (m. p. 166°) was 90%.

Mesitylphenylglycolic acid was not obtained as the free acid. It crystallized with one molecule of alcohol of solvation.

A mixture of 5.0 g. of mesityl phenyl diketone, 10 g. of potassium hydroxide in 20 cc. of water, and 250 cc. of methyl alcohol was boiled under reflux for ten hours. The solvent was removed at 60°, water was added and the alkali-insoluble material removed by filtration. The aqueous solution was poured into a mixture of ice and concentrated hydrochloric acid. The gum which separated was recrystallized from methyl alcohol. The yield of the colorless compound, melting at 87–89°, was 62%.

Anal. Calcd. for $C_{18}H_{22}O_4$: C, 71.52; H, 7.28; neut. equiv., 302. Found: C, 71.55; H, 7.24; neut. equiv., 300.

The *methyl ester* was obtained in good yields when the acid was treated with methyl sulfate in alkaline solution. It separated from alcohol solutions as colorless crystals, melting at 111–111.5°.

Anal. Calcd. for $C_{18}H_{20}O_3$: C, 76.06; H, 7.05. Found: C, 76.38; H, 7.04.

A second acid was obtained when the above acid was recrystallized several times from ethyl alcohol. It appeared to have one molecule of ethyl alcohol of solvation; it melted at 84–85°.

Anal. Calcd. for $C_{19}H_{24}O_4$: C, 72.15; H, 7.59; neut. equiv., 316. Found: C, 72.03, 72.36; H, 7.74, 7.80; neut. equiv., 313.

This compound was also isolated from the acidified mother liquor when I was treated with zinc and potassium hydroxide in ethyl alcohol solution in the preparation of V.

Mesitylphenylacetic acid was prepared from mesitylphenylglycolic acid by reduction with iodine and phosphorus by the procedure analogous to that utilized for the preparation of diphenylacetic acid.[8] The melting point

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[7] Claus, *J. prakt. Chem.*, **41**, 508 (1890).

[8] "Organic Syntheses," John Wiley and Sons, Inc., New York N. Y., Coll. Vol. I, p. 82.

of the colorless compound was 173–173.5°, which agrees with that given by Maxwell and Adams.[9]

Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.31; H, 7.09; neut. equiv., 254. Found: C, 80.29; H, 7.39; neut. equiv., 256.

Mesitylphenylacetic acid was also synthesized by boiling a mixture of 1 g. of mesitylphenylglycolic acid, 30 cc. of glacial acetic acid and 6 g. of zinc under reflux for eighteen hours. There was obtained 0.5 g. of product which, on recrystallization, melted at 173°. A mixed melting point with the product obtained in the iodine and phosphorus reduction of mesitylphenylglycolic acid showed no depression.

Summary

Mesityl phenyl diketone reacts as a monoketone toward the Grignard reagent, semicarbazide, 2,4-dinitrophenylhydrazine and hydroxylamine. Toward hydrogen peroxide, as well as in the benzilic acid rearrangement, the diketone behaves normally.

Reducing agents convert the diketone to a mixture of the two isomeric benzoins. Drastic reduction *affects only the hindered carbonyl group* and gives phenyl 2,4,6-trimethylbenzyl ketone.

URBANA, ILLINOIS RECEIVED APRIL 13, 1936

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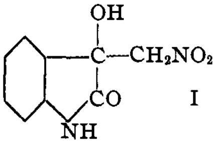
(9) Maxwell and Adams, THIS JOURNAL, **52**, 2959 (1930).

[CONTRIBUTION FROM NICHOLS LABORATORY OF NEW YORK UNIVERSITY]

Oxindole Amines from Isatin[1]

BY WILLIAM R. CONN[2] AND H. G. LINDWALL

It has been reported previously[3] that nitromethane will condense with beta-naphthisatin to yield 3-hydroxy-3-(nitromethyl)-β-naphthoxindole. It has now been found that a similar reaction with nitromethane occurs in the case of isatin, and of certain substituted isatins in the presence of diethylamine, with the formation of the corresponding aldol-like condensation products. Isatin and nitromethane yield 3-hydroxy-3-(nitromethyl)-oxindole (I); substituted derivatives of I (II, III and IV) result from the condensations employing, respectively, N-ethylisatin, 5-bromo-N-ethylisatin and N-methylisatin. Nitroethane and isatin yield an analogous product (V).



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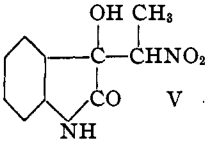
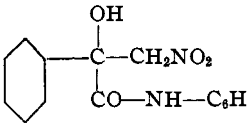


V

At room temperature or for short periods of heating, these five nitro compounds exhibit unexpected resistance toward dehydrating agents such as acetic anhydride, acetyl chloride or hydrochloric acid. When heated with neutral solvents gradual decomposition takes place with the formation of the original isatin and the nitroalkane. The extent of this decomposition can be greatly decreased by the presence of a small amount of glacial acetic acid in the solvent. Heated alone, these nitro compounds again decompose through reversal of the aldol condensation; examination of the melts shows the presence of the isatin and the nitro-alkane. Heating in water containing even small amounts of organic or inorganic base causes speedy reversal of the condensation.

For purposes of generalization, a straight-chain alpha-keto-amide, benzoylformanilide, was condensed with nitromethane. The product, VI, has properties similar to those described above for compounds I–V.



VI

Reduction of 3-hydroxy-3-(nitromethyl)-oxindole (I) catalytically with Adams platinic oxide catalyst[4] or by treatment with concentrated hydrochloric acid and mossy tin, gave the hydrochloride of 3-hydroxy-3-(aminomethyl)-oxindole (VII). Similar treatment of II and III with tin and hydrochloric acid yielded in the same manner the hydrochlorides of the aminomethyloxindoles, respectively, IX and X.

In one of several runs of the reduction of I to form VII by the tin–hydrochloric acid method, VII was obtained contaminated with a compound which was found to be the intermediate reduction

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(1) From the dissertation presented by William R. Conn to the Faculty of the Graduate School of New York University in candidacy for the degree of Doctor of Philosophy.

(2) University Fellow in Chemistry.

(3) Zrike and Lindwall, THIS JOURNAL, **57**, 207–8 (1935).

(4) "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., 1932, p. 452.