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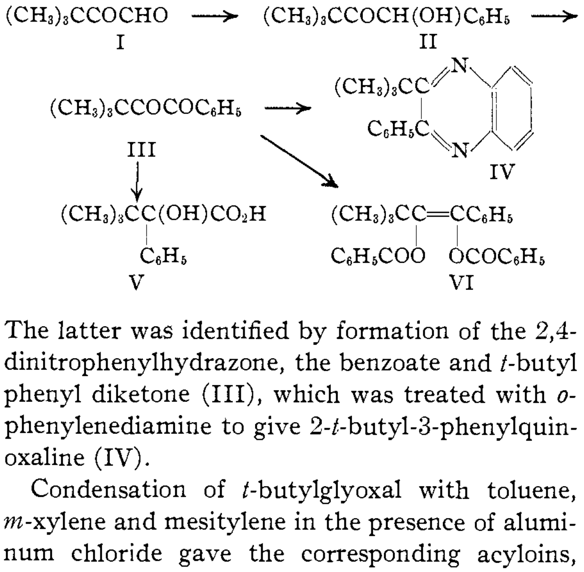
Acyloins from *t*-Butylglyoxal[1]

BY REYNOLD C. FUSON, HUGH GRAY[2] AND J. J. GOUZA

The condensation of arylglyoxals with aromatic compounds[1] provides a convenient method for making mixed benzoins. It seemed probable that the method could be used also for acyloins of the type RCOCH(OH)Ar. To test this suggestion we have prepared *t*-butylglyoxal[3] and treated it with aromatic compounds in the presence of aluminum chloride. The expected acyloins were formed in good yields.

t-Butylglyoxal (I) was synthesized from pinacolone by oxidation with selenium dioxide according to the general procedure of Riley, Morley and Friend.[4] The glyoxal was a yellow liquid boiling at 114–115°. It formed a hemihydrate, a phenylhydrazone, a 2,4-dinitrophenylhydrazone, an osazone, a semicarbazone, a dioxime and a quinoxaline derivative. Treatment with aqueous alkali transformed the glyoxal into β,β,β-trimethyllactic acid. When allowed to stand the glyoxal polymerized to a viscous liquid from which it could be regained by heating.

Condensation with benzene in the presence of aluminum chloride gave a solid product, melting at 46–47°, which proved to be the expected phenylpivalylcarbinol (II).



The latter was identified by formation of the 2,4-dinitrophenylhydrazone, the benzoate and *t*-butyl phenyl diketone (III), which was treated with *o*-phenylenediamine to give 2-*t*-butyl-3-phenylquinoxaline (IV).

Condensation of *t*-butylglyoxal with toluene, *m*-xylene and mesitylene in the presence of aluminum chloride gave the corresponding acyloins, from which the diketones were prepared by oxidation with concentrated nitric acid. The mesityl diketone was isolated as the solid mononitro derivative.

The *p*-tolyl diketone gave a quinoxaline derivative, but the *m*-xylyl and 3-nitromesityl analogs did not react with *o*-phenylenediamine under these conditions.

A rearrangement of the benzilic acid type was effected by treatment of *t*-butyl phenyl diketone with alkali, giving β,β,β-trimethylatrolactic acid (V). This is the first recorded example of such a reaction with a mixed aromatic–aliphatic 1,2-diketone.

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(1) This is the fourth paper in this series. For the preceding communication see Fuson, Emerson and Weinstock, THIS JOURNAL, **61**, 412 (1939).

(2) Röhm and Haas Research Assistant, 1938–1939.

(3) Since this work was completed the synthesis of the glyoxal and its hemihydrate was reported by Taylor, Callow and Francis [*J. Chem. Soc.*, 257 (1939)].

(4) Riley, Morley and Friend, *ibid.*, 1875 (1932).

t-Butyl phenyl diketone resembled benzil[5] in its behavior with metallic sodium; benzoyl chloride converted the sodium derivative to the dibenzoate of *t*-butylphenylacetylene glycol (VI).

Experimental

***t*-Butylglyoxal.**—A mixture of 100 cc. of methyl alcohol,[6] 5 cc. of water and 111.2 g. of selenium dioxide was refluxed, with stirring, until the selenium dioxide dissolved, and then 122 cc. of pinacolone was added rapidly. The clear solution became red and then black after a few minutes. Refluxing and vigorous stirring were continued for six hours,[7] after which the reaction mixture was cooled and the precipitated selenium was removed by filtration. The yellow filtrate was distilled at atmospheric pressure from a modified Claisen flask having a 7-in. (18-cm.) column. After rejection of a fraction distilling from 65 to 110°, a yellow distillate was collected from 110 to 120°. A high-boiling residue which contained selenium was always present. Fractionation of the yellow oil gave 60 cc. of the yellow *t*-butylglyoxal, boiling at 114–115°.[8] The yield was 52% of the theoretical amount. Analyses for carbon and hydrogen showed that the product was not entirely pure. It became viscous on standing, even in a sealed container. The refractive index of the freshly distilled glyoxal increased rapidly, a typical determination showing a rise from 1.4287 to 1.4454 during the first hour. The resulting polymer was unreactive, hence it was necessary to distill the material before use. It was also found convenient to keep the glyoxal as the hydrate. The anhydrous monomer was prepared from its hydrate by dissolving the latter in methyl alcohol and subjecting the solution to fractional distillation.

Hemihydrate.—To 5 cc. of the glyoxal was added 1 cc. of water; appreciable evolution of heat was observed. The solution was allowed to stand overnight to allow the product to crystallize. It was recrystallized from 10 cc. of benzene, m. p. 91–92°,[9] with softening at 85°.

Anal. Calcd. for $C_{12}H_{22}O_5$: C, 58.51; H, 9.01. Found: C, 58.55; H, 9.10.

The 2,4-dinitrophenylhydrazone separated from alcohol as yellow crystals, m. p. 171–172°.

Anal. Calcd. for $C_{12}H_{14}O_5N_4$: C, 48.98; H, 4.80; N, 19.04. Found: C, 49.01; H, 4.87; N, 19.19.

Treatment with phenylhydrazine gave a **phenylhydrazone** or an **osazone,** depending upon the conditions employed. An excellent yield of the phenylhydrazone was obtained by allowing an alcohol solution of equimolecular amounts of the reactants to stand at room temperature for one hour. The pale yellow phenylhydrazone was precipitated by the addition of water and crystallized from ethyl acohol, m. p. 119–120°.

Anal. Calcd. for $C_{12}H_{16}ON_2$; C, 70.55; H, 7.90; N, 13.72. Found: C, 70.11; H, 7.83; N, 13.72.

The **osazone** was prepared by dissolving the theoretical amounts of the reactants in alcohol, adding a few drops of concentrated hydrochloric acid and heating the resulting solution for six hours under reflux. The warm (50°) solution was diluted with water until turbid and allowed to cool. The bright yellow osazone was recrystallized from ethyl alcohol, m. p 119.5–120°.[10] A mixture of the osazone and the phenylhydrazone melted at about 100°.

Anal. Calcd. for $C_{18}H_{22}N_4$: C, 73.43; H, 7.54; N, 19.03. Found: C, 73.69; H, 7.60; N, 18.97.

Treatment with semicarbazide gave a **monosemicarbazone** which, after recrystallization from aqueous ethyl alcohol, melted at 134–135°.

Anal. Calcd. for $C_7H_{13}O_2N_3$: C, 49.11; H, 7.65; N, 24.55. Found: C, 49.23; H, 7.51; N, 24.35.

The dioxime was crystallized from aqueous ethyl alcohol, m. p. 100.5–101.5°.

Anal. Calcd. for $C_6H_{12}O_2N_2$: C, 49.98; H, 8.39; N, 19.43. Found: C, 50.10; H, 8.50; N, 19.11.

Wittorf,[11] who obtained this compound by the action of hydroxylamine on dibromopinacolone, reported a melting point of 101–102°.

Nitroquinoxaline.—To a refluxing solution of 1.5 g. of *p*-nitro-*o*-phenylenediamine in 25 cc. of glacial acetic acid was added 1.25 g. of *t*-butylglyoxal hydrate. The solution was refluxed for one hour, diluted with water until the appearance of turbidity, and cooled to room temperature. The nitroquinoxaline was treated with Norite and recrystallized from ethyl alcohol, m. p. 134.5–135°.

Anal. Calcd. for $C_{12}H_{13}O_2N_3$: C, 62.32; H, 5.67; N, 18.18. Found: C, 62.27; H, 5.53; N, 18.14.

β,β,β-Trimethyllactic Acid.—One gram of *t*-butylglyoxal hydrate was added to a solution of 8 g. of sodium hydroxide in 24 cc. of water. The mixture was shaken for a few minutes, and the resulting clear solution was allowed to stand at room temperature. After about one hour the sodium salt of β,β,β-trimethyllactic acid precipitated. This material was separated by filtration, dissolved in water, and the solution acidified with hydrochloric acid. The solution was extracted with three 25-cc. portions of ether, and the ether solution was dried over anhydrous magnesium sulfate. The white crystalline β,β,β-trimethyllactic acid, obtained by evaporation of the solvent, was purified by recrystallization from high-boiling petroleum ether. The yield was 93% of the theoretical amount, m. p. 86.5–87.5°. This melting point is in agreement with the findings of Favorskiĭ,[10] Wittorf[11] and Glücksmann.[12]

Phenylpivalylcarbinol.—A mixture of 54 g. (0.4 mole) of aluminum chloride and 80 cc. of dry benzene was cooled in an ice-bath and a solution of 23 g. (0.2 mole) of freshly distilled *t*-butylglyoxal in 20 cc. of dry benzene was added, with stirring, over a period of one-half hour. The reaction

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(5) Nef, *Ann.*, **308**, 264 (1899).

(6) Various other solvents (dioxane, acetic anhydride and benzene) proved to be unsatisfactory due to difficulties in fractionation of the product.

(7) In several cases formation of a solid cake of precipitated selenium during the first hour made further stirring impracticable.

(8) This boiling point is in agreement with that reported by Taylor, Callow and Francis.[3]

(9) Taylor, Callow and Francis[3] give a melting point of 85°.

(10) This compound was obtained by Favorskiĭ [*J. Russ. Phys.-Chem. Soc.*, **44**, 1339 (1912); *J. prakt. Chem.*, [2] **88**, 641 (1913)] by the action of phenylhydrazine on pivalylcarbinol.

(11) Wittorf, *ibid.*, **32**, 88 (1900); *Chem. Zentr.*, **71**, 11, 29 (1900).

(12) Glücksmann, *Monatsh.*, **10**, 770 (1889).

mixture became black during the addition. Stirring was continued for six hours (one hour in ice-bath, five hours at room temperature) and the mixture was allowed to stand overnight at room temperature. It was added, with vigorous stirring, to a mixture of 100 cc. of concentrated hydrochloric acid and 300 g. of ice. The yellow benzene layer was washed with dilute sodium bicarbonate solution and with water, and dried over anhydrous sodium sulfate. The residue, after evaporation of the solvent, distilled at 90–102° (2 mm.). The acyloin so obtained soon solidified, and was recrystallized from aqueous alcohol, m. p. 46–47°. The yield was 49% of the theoretical amount.

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.19; H, 8.49.

The **2,4-dinitrophenylhydrazone** was recrystallized from ethyl alcohol, m. p. 174–175°.

Anal. Calcd. for $C_{18}H_{20}O_5N_4$: C, 58.05; H, 5.41; N, 15.04. Found: C, 58.12; H, 5.48; N, 14.74.

Benzoate.—One-half gram of phenylpivalylcarbinol was dissolved in 1 cc. of benzoyl chloride and warmed for a few minutes. The solution was cooled and poured into 20 cc. of water, with vigorous stirring. The water was removed by decantation and the oily residue was warmed with 5 cc. of 10% sodium hydroxide solution. The mixture was cooled overnight, and the solid material was removed by filtration and washed with water. Recrystallization from ethyl alcohol gave lustrous white crystals, m. p. 96–97°.

Anal. Calcd. for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 76.94; H, 6.81.

***t*-Butyl Phenyl Diketone.**—This diketone and the others described below were made by the following method. The acyloin (0.05 mole) was added to 15 cc. of concentrated nitric acid and the mixture was warmed on the steam-cone for two hours. When cool the reaction mixture was poured into 50 cc. of water and the yellow oily layer separated. It was dissolved in ether, and the ether solution washed with aqueous sodium bicarbonate solution and with water. After the ether solution was dried over sodium sulfate, the solvent was evaporated and the residue distilled under diminished pressure, b. p. 75–76° (1 mm.); d^{20}_{20} 1.016; n^{20}_{D} 1.5086.

Anal. Calcd. for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42; M_D, 55.1.[13] Found: C, 75.71; H, 7.47; M_D, 55.8.

2-*t*-Butyl-3-phenylquinoxaline.—*t*-Butyl phenyl diketone was converted to the corresponding quinoxaline by the following procedure. The yield was nearly quantitative. To a refluxing solution of 0.6 g. of *o*-phenylenediamine and 25 cc. of glacial acetic acid was added 1 cc. of the diketone. After the refluxing had continued for two hours the solution was diluted with water to the appearance of turbidity and allowed to cool. The 2-*t*-butyl-3-phenylquinoxaline was recrystallized from aqueous ethyl alcohol, m. p. 108–109°.

Anal. Calcd. for $C_{18}H_{18}N_2$: C, 82.41; H, 6.91; N, 10.68. Found: C, 82.19; H, 6.97; N, 10.59.

p-Tolylpivalylcarbinol.—The use of toluene in the Friedel–Crafts reaction gave 21.5 g., a yield of 52% of the theoretical amount, of the acyloin, m. p. 48–49°. (The crude material boiled at 115–125° at 2 mm.)

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79. Found: C, 75.69; H, 8.67.

The diketone boiled at 97–97.5° (1 mm.); d^{20}_{20} 1.016; n^{20}_{D} 1.5125.

Anal. Calcd. for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90; M_D, 59.7. Found: C, 76.37; H, 8.01; M_D, 60.4.

2-*t*-Butyl-3-*p*-tolylquinoxaline.—By use of the procedure outlined for the phenyl analog this quinoxaline was obtained in almost the theoretical yields, m. p. 109–110°.

Anal. Calcd. for $C_{19}H_{20}N_2$: C, 82.57; H, 7.30; N, 10.14. Found: C, 82.41; H, 7.51; N, 10.18.

***m*-Xylylpivalylcarbinol.**—When *m*-xylene was used there was obtained 18.5 g. of the liquid acyloin, b. p. 133–135° (4 mm.). The yield was 42% of the theoretical amount; d^{20}_{20} 1.100; n^{20}_{D} 1.5134.

Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15; M_D, 59.6. Found: C, 76.44; H, 9.03; M_D, 60.1.

A solid material which precipitated from the crude acyloin before distillation was recrystallized from alcohol, giving 6 g. of **di-(*m*-xylyl)-pivalylmethane**, m. p. 111.5–112°.

Anal. Calcd. for $C_{22}H_{28}O$: C, 85.66; H, 9.15. Found: C, 85.84; H, 9.03.

The diketone boiled at 103–104° (1 mm.); d^{20}_{20} 1.017; n^{20}_{D} 1.5177.

Anal. Calcd. for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31; M_D, 64.3. Found: C, 76.72; H, 8.34; M_D, 65.0.

Treatment for eleven hours with a boiling solution of *o*-phenylenediamine in acetic acid failed to yield any quinoxaline. The original diketone was recovered. It was identified by conversion to 2,4-dimethyl-3,5-dinitrobenzoic acid described below.

2,4-Dimethyl-3,5-dinitrobenzoic Acid.—A mixture of 5 cc. of concentrated nitric acid and 5 cc. of concentrated sulfuric acid was cooled in an ice-bath and 0.25 cc. of *t*-butyl *m*-xylyl diketone was added dropwise, with stirring. The solution was poured on ice, with stirring, and the precipitated acid separated by filtration. It was recrystallized from glacial acetic acid, m. p. 202–203°.

Anal. Calcd. for $C_9H_8O_6N_2$: C, 45.00; H, 3.38; N, 11.66. Found: C, 45.54; H, 3.41; N, 11.35.

Claus[14] reported a melting point of 199–200° (uncorr.) for this compound.

Mesitylpivalylcarbinol.—Distillation of the excess mesitylene from the reaction product left a solid residue which was recrystallized from alcohol. There was obtained 14 g., a yield of 30% of the theoretical amount, of the acyloin, m. p. 118–118.5°.

Anal. Calcd. for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.91; H, 9.45.

***t*-Butyl 3-Nitromesityl Diketone.**—The mesitylpivalylcarbinol was heated for three hours with 15 cc. of concentrated nitric acid. The oil which was isolated by dilution of the mixture with water was dissolved in ether.

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(13) In this calculation as well as in those made for the molecular refractivity of other 1,2-diketones mentioned in this paper, an exaltation of 1.05 is ascribed to the conjugation of the two carbonyl groups and three olefinic linkages are assigned to the aromatic nucleus. See Auwers, *Ber.*, **51**, 1116 (1918).

(14) Claus, *J. prakt. Chem.*, [2] **41**, 483 (1890).

washed and dried; it distilled at 110 to 170° (*ca.* 0.5 mm.). The distillate was heated for three hours with a fresh 15-cc. portion of nitric acid. The product was isolated, dissolved in ether, washed and dried. Evaporation of the ether gave the bright yellow diketone, which was recrystallized from aqueous methyl alcohol, m. p. 58–59°.

Anal. Calcd. for $C_{15}H_{19}O_4N$: C, 64.96; H, 6.91; N, 5.05. Found: C, 64.87; H, 7.03; N, 5.15.

Like the xylyl analog this diketone failed to give a quinoxaline. Even after fifteen hours' treatment the diketone was almost entirely recovered.

β,β,β-Trimethylatrolactic Acid.—One cubic centimeter of *t*-butyl phenyl diketone was added to a solution of 2 g. of potassium hydroxide and 1 cc. of ethyl alcohol in 10 cc. of water. This mixture was refluxed until a clear solution was obtained (about six hours). Acidification with hydrochloric acid precipitated an oily material which was separated and treated with low-boiling petroleum ether. The white solid acid which separated was removed by filtration and recrystallized from high-boiling petroleum ether, m. p. 105–106°.

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.21; H, 7.75; neut. equiv., 208. Found: C, 69.33; H, 7.95; neut. equiv., 208.

Dibenzoate of *t*-Butylphenylacetylene Glycol.—A mixture of 0.26 g. of sodium, 20 cc. of dry toluene and 1 cc. of *t*-butyl phenyl diketone was refluxed in an atmosphere of nitrogen for two hours, with vigorous stirring. After addition of 1.25 cc. of benzoyl chloride, the dark brown reaction mixture was heated and stirred for a few minutes and then cooled to room temperature. The excess sodium and the precipitated sodium chloride were removed by filtration and the filtrate was concentrated to a viscous brown oil. The dibenzoate was recrystallized from high-boiling petroleum ether, m. p. 138–139°.

Anal. Calcd. for $C_{26}H_{25}O_4$: C, 77.98; H, 6.04. Found: C, 77.96; H, 6.12.

Summary

t-Butylglyoxal condenses with benzene, toluene, *m*-xylene and mesitylene to give acyloins of the type $(CH_3)_3CCOCH(OH)Ar$. Oxidation with nitric acid converts the acyloins to the corresponding diketones. In the case of the mesityl compound the diketone is isolated in the form of its mononitro derivative.

The diketones derived from benzene and toluene react normally with *o*-phenylenediamine to give quinoxalines. This reaction could not be effected with the *m*-xylyl or mesityl diketones.

t-Butyl phenyl diketone undergoes the benzilic acid rearrangement to give β,β,β-trimethylatrolactic acid. The sodium derivative of this diketone reacts with benzoyl chloride to give the dibenzoate of *t*-butylphenylacetylene glycol. The two foregoing types of reaction hitherto had been restricted to benzils and aliphatic 1,2-diketones.

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The Methylation of β-Ketonitriles

BY REYNOLD C. FUSON AND DONALD E. WOLF

The discovery that α-cyanoacetomesitylene (IV) and α-cyanopropiomesitylene gave only O-methylation products[1] suggested that the steric hindrance present in these β-ketonitriles favored O-methylation.[2] As a test of this suggestion an unhindered β-ketonitrile, *p*-bromophenacyl cyanide (I), has been methylated under similar conditions. It reacted with methyl sulfate in the presence of aqueous potassium hydroxide to give the O-methyl ether (II). When the alkylating agent was methyl iodide in the presence of sodium ethoxide, a different compound, the C-methylated product (III), was formed.

The structure of the enol methyl ether (II) was established by analysis for methoxyl and by its insolubility in alkali. Both the parent compound (I) and the C-methylated derivative (III) are soluble in 10% sodium hydroxide solution and in 10% sodium carbonate solution. Compound III was hydrolyzed easily to give *p*-bromobenzoic acid. When allowed to stand for some time it decomposed spontaneously, probably by autooxidation of its enol—a phenomenon previously noted for compounds of this type.[3]

The structure of the C-methylated product, α-(*p*-bromobenzoyl)-propionitrile (III), was established by synthesis, employing the method used by Dorsch and McElvain[4] for similar compounds. Ethyl *p*-bromobenzoate was condensed with propionitrile in the presence of sodium ethoxide. The product proved to be α-(*p*-bromobenzoyl)-propionitrile (III).

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(1) Fuson, Ullyot and Gehrt, THIS JOURNAL, **60**, 1199 (1938).

(2) This idea was developed by Kohler and his co-workers in connection with mesityl ketones. For a leading reference see Kohler and Thompson, *ibid.*, **59**, 887 (1937).

(3) Jenkins, *ibid.*, **57**, 2733 (1935).

(4) Dorsch and McElvain, *ibid.*, **54**, 2960 (1932).