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

Arylglyoxals and Steric Hindrance

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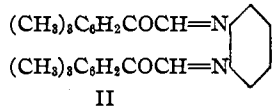
Highly hindered arylglyoxals are unique among α-keto aldehydes in the great disparity in the reactivities of the two carbonyl groups. This is presumably to be ascribed to two factors, (1) the activating effect of the keto group on the aldehyde group and (2) the influence of steric hindrance on the keto group. These two effects combine to render the aldehyde group highly reactive and to block the keto group so that it is nearly inert.

In order to examine systematically the steric effect we have made a number of arylglyoxals with varying amounts of hindrance. The two effects are extreme in mesitylglyoxal (I).[3] Perhaps the most striking evidence of this is the behavior of this glyoxal toward *o*-phenylenediamine. Even when the amine is used in excess no quinoxaline is formed. Two molecules of the glyoxal react with one of *o*-phenylenediamine to give the Schiff base (II).

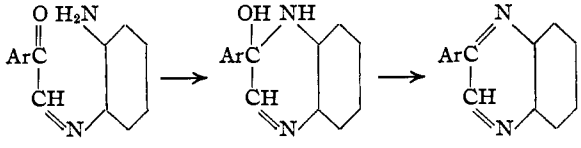
$$2(CH_3)_3C_6H_2COCHO + o\text{-}C_6H_4(NH_2)_2 \longrightarrow$$

I



II

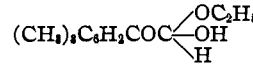
This behavior is abnormal for glyoxals. For example, phenylglyoxal[4] and 3,4-methylenedioxyphenylglyoxal[5] readily yield quinoxalines. Evidently quinoxaline formation is inhibited by the steric hindrance furnished by the mesityl radical. This is the more noteworthy because the step involving the keto carbonyl group would be intramolecular:



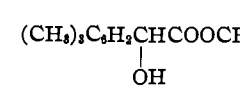
To explore the relationship between quinoxaline formation and steric hindrance we have examined a series of arylglyoxals in which the amount of hindrance gradually was increased. α-Naphthylglyoxal and 2,4-dimethylphenylglyoxal were found to give quinoxalines in the normal manner. On the other hand, 2,4,6-triethylphenylglyoxal behaved like mesitylglyoxal and gave only the dianil.

In contrast with this abnormal behavior toward *o*-phenylenediamine is the unimpaired capacity which mesitylglyoxal and 2,4,6-triethylphenylglyoxal possess for rearranging to the corresponding glycolic acids.[3]

The rearrangement was carried out also with the ethyl hemiacetal of mesitylglyoxal (III). This unusual compound formed when the hydrate was crystallized from aqueous alcohol containing a drop of hydrochloric acid. It reacted with hydroxylamine to give mesitylglyoxal monoxime. The isomeric ethyl mesitylglycolate was prepared from the acid. When rearrangement of the hemiacetal was induced by sodium methylate in methyl alcohol in the presence of a small amount of iodine, it was possible to isolate methyl mesitylglycolate (IV).



III



IV

Aluminum isopropylate brought about a similar rearrangement giving isopropyl mesitylglycolate

$$(CH_3)_3C_6H_2COCHO + (CH_3)_2CHOH \xrightarrow{Al(OCH(CH_3)_2)_3} (CH_3)_3C_6H_2CH(OH)CO_2CH(CH_3)_2$$

The behavior of 2,4,6-triethylphenylglyoxal was conspicuously different from that of mesitylglyoxal and other glyoxals in general. Under no circumstances could this glyoxal be induced to form a hydrate or a hemiacetal. However, it gave an oxime. When heated with an alcoholic sodium ethylate solution it gave a 40% yield of 2,4,6-triethylphenylglycolic acid.

Experimental

Mesitylglyoxal Ethyl Hemiacetal.—This compound was prepared by crystallizing mesitylglyoxal hydrate from aqueous ethyl alcohol containing a few drops of concentrated hydrochloric acid. After recrystallization from an ether–petroleum ether mixture the compound melted at 55.0–55.5°.

(1) Du Pont Post-Doctorate Fellow, 1937–1938.
(2) Röhm and Haas Research Assistant, 1938–1939.
(3) Gray and Fuson, THIS JOURNAL, **56**, 739 (1934).
(4) Kröhnke and Börner, *Ber.*, **69**, 2006 (1936).
(5) Kawai and Ashino, *Bull. Chem. Soc. Japan*, **13**, 480 (1938).

Anal. Calcd. for $C_{18}H_{18}O_3$: C, 70.3; H, 8.11. Found: C, 70.3; H, 8.08.

The hemiacetal was somewhat unstable, decomposing in boiling benzene. It reduced Tollens' reagent. With hydroxylamine it gave mesitylglyoxal monoxime; m. p. 138–139°. A mixed melting point determination with an authentic specimen[5] showed no depression.

Anal. Calcd. for $C_{11}H_{13}O_2N$: N, 7.33. Found: N, 7.22.

Ethyl Mesitylglycolate.—A mixture of 0.5 g. of mesitylglycolic acid, 30 cc. of ethyl alcohol and 3 drops of concentrated hydrochloric acid was refluxed for two hours, made basic with aqueous sodium carbonate and evaporated nearly to dryness. The needles so obtained were recrystallized from aqueous alcohol; yield, 0.1 g.; m. p. 53.5–54.0°; mixed m. p. with a sample of mesitylglyoxal ethyl hemiacetal (m. p. 54–55°), 39–45°.

Anal. Calcd. for $C_{13}H_{18}O_3$: C, 70.3; H, 8.11. Found: C, 70.2; H, 8.15.

This compound did not reduce Tollens' reagent.

Methyl Mesitylglycolate.—One and one-half grams of mesitylglyoxal ethyl hemiacetal was dissolved in 40 cc. of boiling methyl alcohol containing excess sodium methylate. Iodine was added to the boiling solution until the color persisted. After dilution with 200 cc. of water, the mixture was acidified with hydrochloric acid and made basic with sodium carbonate before standing overnight. It was then decolorized with sodium thiosulfate and extracted twice with ether. After the solution was dried over calcium chloride the ether was evaporated. The residue was crystallized three times from aqueous alcohol; yield, 0.2 g.; m. p. 90.0–90.5° (recorded value, 90–91°[6a]).

After refluxing for one-half hour, a mixture of 0.1 g. of methyl mesitylglycolate and 20 cc. of 25% aqueous sodium hydroxide was diluted with water, filtered and acidified with dilute phosphoric acid. It was then evaporated nearly to dryness. Two successive ether extracts of the residue were combined, dried over calcium chloride and then evaporated to dryness. The solid so obtained was crystallized from aqueous alcohol. It was dissolved in aqueous alkali, the solution boiled with Norite, filtered and then acidified with hydrochloric acid. After most of the liquid had evaporated, the desired mesitylglycolic acid crystallized; m. p. 150–151° (recorded value, 152–153°[6a,6b]).

Isopropyl Mesitylglycolate.[7]—To a solution of 4 g. of aluminum isopropylate in 150 cc. of dry isopropyl alcohol was added 12.8 g. of mesitylglyoxal. An exothermic reaction occurred and the solution turned red. The flask was heated and the isopropyl alcohol was distilled at the rate of 50 cc. an hour, the amount of solvent being kept constant by addition of fresh isopropyl alcohol. After two hours the mixture was poured into 150 cc. of a 25% solution of tartaric acid. The organic layer was removed and the aqueous layer extracted twice with 50-cc. portions of ether. The ether extracts were combined with the organic layer and the solvent removed on the water pump. The residual isopropyl mesitylglycolate distilled at 122–124° (2 mm.), and after a few hours set to a crystalline mass. After recrystallization from petroleum ether the crystals melted at 62.5–63.5°.

Anal. Calcd. for $C_{14}H_{20}O_3$: C, 71.24; H, 8.53; mol. wt., 236. Found: C, 71.37; H, 8.66; mol. wt., 236 (Rast), 239 (ebullioscopic method in benzene.)

Hydrolysis of Isopropyl Mesitylglycolate.—A solution of 5 g. of the ester in 40 cc. of a 25% solution of sodium hydroxide was refluxed for three hours. Acidification precipitated crystals of mesitylglycolic acid melting at 152°.[6a,6b]

2,4,6-Triethylphenylglyoxal.—After 25.3 g. of selenium dioxide had been dissolved by warming in 137 cc. of wet dioxane 46.5 g. of 2,4,6-triethylacetophenone was added and the mixture refluxed for three and one-half hours. It was stirred for one and one-half hours more. After most of the dioxane had been distilled, xylene was distilled from the product until the distillate was no longer cloudy. The residual xylene was removed under reduced pressure. The glyoxal distilled at 125–130° (10 mm.); d^{20}_{20} 1.011; $n^{20}D$ 1.523; M_D 66.0 (calculated 63.3). The yield was 78.5% of the theoretical amount.

Anal. Calcd. for $C_{14}H_{18}O_2$: C, 77.1; H, 8.26. Found: C, 77.6; H, 8.19.

This compound is very inert. It does not polymerize or form a hydrate when placed under water for thirty days. Likewise no solid precipitated when the glyoxal was dissolved in aqueous dioxane and the solution allowed to stand for thirty days. When 1.0 g. of the glyoxal was refluxed for two hours in 50 cc. of water containing 1 cc. of concentrated hydrochloric acid and then allowed to stand overnight, an uncrystallizable oil was obtained. A similar oil also was obtained when 1.0 g. of the glyoxal was refluxed for one hour with 50 cc. of ethyl alcohol containing 2 cc. of concentrated hydrochloric acid.

2,4,6-Triethylphenylglyoxal Monoxime.—This compound was prepared by the usual method. After one crystallization from an ether–petroleum ether mixture and another from aqueous alcohol, it melted at 107.0–107.5°.

Anal. Calcd. for $C_{14}H_{19}O_2N$: N, 5.91. Found: N, 5.98.

2,4,6-Triethylphenylglycolic Acid.—Ten grams of 2,4,6-triethylphenylglyoxal was dissolved in 100 cc. of absolute ethyl alcohol containing 6.25 g. of sodium, and the solution was refluxed for four hours. After cooling, the reaction mixture was poured into 600 cc. of water, and the resulting emulsion was extracted with several portions of ether. To the aqueous layer was added excess concentrated hydrochloric acid. This acidified solution was extracted with five 100-cc. portions of ether, the ether solution dried with sodium sulfate and evaporated to a viscous red-brown oil. Crystallization from high-boiling petroleum ether and treatment with Norite gave white crystals melting at 91–92°; yield, 4 g. or 40% of the theoretical amount.

Anal. Calcd. for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53; neut. equiv., 236. Found: C, 71.02; H, 8.43; neut. equiv., 234.

α-Naphthylglyoxal.—Using the same procedure as for 2,4,6-triethylphenylglyoxal, this glyoxal was prepared in 58% yield; b. p. 142–145° (6 mm.).

The hydrate was made by heating the glyoxal with water. It was also obtained in the form of long needles

(6) (a) Van Scherpenzeel, *Rec. trav. chim.*, **19**, 377 (1900); (b) Fuson, Matuszeski and Gray, THIS JOURNAL, **56**, 2099 (1934).

(7) This compound was made by Mr. C. H. McBurney.

by dissolving the glyoxal in a dioxane–water mixture and allowing it to cool and crystallize slowly. No attempt was made to obtain a completely pure compound, the highest melting point obtained being 89–91°.

The 2,4-dinitrophenylhydrazone crystallized from dioxane; m. p., 246.5–247.5°.

Anal. Calcd. for $C_{18}H_{12}O_5N_4$: N, 15.4. Found: N, 14.95.

2,4-Dimethylphenylglyoxal.—This glyoxal was prepared in 64% yield by the method just outlined for 2,4,6-triethylphenylglyoxal; b. p. 118–123° (13 mm.). The 2,4-dinitrophenylhydrazone after crystallization from ethyl acetate melted at 180–181°.

Anal. Calcd. for $C_{16}H_{14}O_5N_4$: N, 16.38. Found: N, 16.38.

TABLE I

	Arylglyoxal	Product	Color	M. p., °C. (corr.)
1	α-Naphthylglyoxal	α-Naphthylquinoxaline	Brown	116–116.5
2	2,4-Dimethylphenylglyoxal	2,4-Dimethylphenylquinoxaline	White	56–57
3	Mesitylglyoxal	Di-(mesitylglyoxal)-o-phenylenediamine[8]	White	183–184
4	2,4,6-Triethylphenylglyoxal	Di-(2,4,6-triethylphenylglyoxal)-o-phenylenediamine	White	136–136.5

	Formula	Analyses, % Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
1	$C_{18}H_{12}N_2$	84.35	4.72	10.93	84.44	4.91	10.84
2	$C_{16}H_{14}N_2$	82.02	6.02	11.96	82.15	5.93	12.07
3	$C_{28}H_{28}O_2N_2$	79.21	6.65	6.60	79.47	6.98	6.97
4	$C_{34}H_{40}O_2N_2$	80.27	7.93	5.51	80.30	7.88	5.60

(8) In one experiment a mixture of equimolecular amounts of the glyoxal and o-phenylenediamine was maintained for seven days at 95°. No quinoxaline was detected.

Reaction of the Glyoxals with o-Phenylenediamine.—The following general procedure was used in treating the glyoxals with o-phenylenediamine. To a boiling solution of 2.2 g. (0.02 mole) of o-phenylenediamine in 25 cc. of glacial acetic acid was added in small portions 0.01 mole of the glyoxal or its hydrate. The solution was refluxed for an hour and allowed to stand overnight at room temperature. Dilution with water gave a semi-solid precipitate. This material was recrystallized twice from aqueous alcohol. Table I shows the products obtained together with their colors, melting points and analyses.

Summary

o-Phenylenediamine reacts with α-naphthylglyoxal and 2,4-dimethylphenylglyoxal to give the corresponding quinoxalines. This reaction is inhibited, however, by introduction of extreme hindrance. Neither mesitylglyoxal nor 2,4,6-triethylphenylglyoxal forms a quinoxaline.

Mesitylglyoxal forms a stable ethyl hemiacetal which rearranges to mesitylglycolic acid when treated with sodium ethylate. Similarly mesitylglyoxal is transformed to isopropyl mesitylglycolate by aluminum isopropylate in isopropyl alcohol.

2,4,6-Triethylphenylglyoxal does not form a hydrate or hemiacetal but rearranges to 2,4,6-triethylphenylglycolic acid when heated with sodium ethylate.

URBANA, ILLINOIS RECEIVED DECEMBER 29, 1938

[CONTRIBUTION FROM THE DEPARTMENT OF BOTANY, UNIVERSITY OF MINNESOTA]

A Note on the Constitution of Linoleyl Alcohol Prepared by the Sodium Reduction of Linoleic Acid[1]

BY J. P. KASS, E. S. MILLER AND G. O. BURR

Turpeinen[2] recently prepared linoleyl alcohol by the reduction of methyl linoleate with sodium in dry butanol according to the well-known method of Bouveault and Blanc[3] as outlined by Reid and co-workers[4] for the preparation of oleyl alcohol. The abnormal behavior of his product toward halogenating reagents led Turpeinen to infer possible contamination with saturated impurities. This supposition was shown to be untenable by the hydrogenation of the alcohol to octadecanol-1 after the consumption of practically the theoretical quantities of hydrogen.

The molecular refraction of the alcohol, calculated by us on the basis of the constants reported by Turpeinen, is 87.24, while the calculated theoretical value is 85.69. This exaltation of 1.55 units is approximately one-half the difference reported by Böeseken[5] and Smit[6] between the observed and calculated molecular refractions of 9,11-linoleic acid. This, as well as the low iodine number and the peculiar behavior of the alcohol toward bromine, characteristic of the conjugated fatty acids,[6,7] led us to believe that Turpeinen's product was a mixture of the expected octadecadiene-9,12-ol-1 and a conjugated alcohol, the shift in the position of un-

(1) This work was supported by grants from the National Live Stock & Meat Board, the Rockefeller Foundation, and the Graduate School of the University of Minnesota.

(2) Turpeinen, THIS JOURNAL, **60**, 56 (1938).

(3) Bouveault and Blanc, *Compt. rend.*, **136**, 1676 (1903).

(4) Reid, *et al.*, *Org. Syntheses*, **15**, 51 (1935).

(5) Böeseken, *Chem. Zentr.*, **100**, II, 716 (1929).

(6) Smit, *Rec. trav. chim.*, **49**, 539 (1930).

(7) Böeseken and Gelber, *ibid.*, **46**, 162 (1927).