

Diazoketones from Acid Chlorides of Dicarboxylic Acids

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The diazoketones, prepared from acid chlorides of dicarboxylic acids, have been characterised and the action of various reagents on them has been studied.

The method, described by Arndt *et al*¹, and also by Robinson and Bradley², has been used to prepare the following diazoketones:

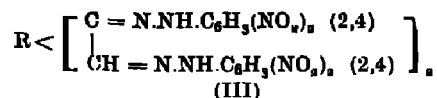
1,2-Bis-diazoacetylthane (I: $n=2$), 1,3-bis-diazoacetylpropane (I: $n=3$), 1,4-bis-diazoacetyl-*n*-butane (I: $n=4$), 1,4-bis-diazoacetyl-2-methyl-*n*-butane (I: $n=4$, 2-Me), 1,8-bis-diazoacetyl-*n*-octane (I: $n=8$), and 1,2-bis-diazoacetylbenzene (II).



The diazoketones^{3,4} (I: $n=4$ & 8) are already known, whereas (I: $n=2$, 3,4,2-Me, and II) are new.

The diazoketones (I: $n=3,4$, 2-Me) responded to the Arndt and Eistert synthesis⁵ and homologous acids and amides of dicarboxylic acids were obtained.

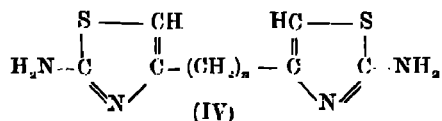
Canonica⁶ carried out the reaction of phenylhydrazine on diazoketones between temperatures 60° and 100° and obtained either the phenylosazone of the corresponding glyoxal or a phenylhydrazide of an acid by a transformation similar to that of Wolff⁷. In the present case, an ethanolic solution of 2,4-dinitrophenylhydrazine in sulphuric acid reacted, however, with each of the diazoketones at ordinary temperature and furnished exclusively the osazone of the corresponding glyoxal (III).



[where $\text{R} < = (\text{CH}_2)_n < ; \text{C}_6\text{H}_4 <]$

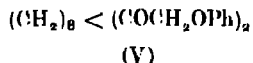
1. *Ber.*, 1927, 60, 1304.
2. *J. Chem. Soc.*, 1928, 1310.
3. Walker, *ibid.*, 1940, 1304.
4. Thomas, *ibid.*, 1940, 1319.
5. *Ber.*, 1935, 68, 204.
6. *Gazzetta*, 1950, 80, 412.
7. *Annalen*, 1912, 394, 23.

Carroll and Miller⁸ described the action of thiourea on diazoketones in absence of a catalyst. Treating this reagent with diazoketones (I: $n=4, 8$) in presence of copper powder in boiling ethanol provided $\omega\omega$ -bis-2-amino-4-thiazolylalkanes(IV) (cf. Walker³).

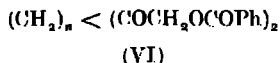


Neither the diazoketone (I: $n=3$) nor the related chloroketone yielded (IV: $n=3$).

Diazoketone (I: $n=8$) decomposed with evolution of nitrogen in presence of phenol and copper powder at ordinary temperature to afford 1,8-bis-phenoxyacetyloctane(V), m.p. 85°, characterised by formation of a 2,4-DNP.



Diazoketones (I: $n=4, 4$ -2-Me, 8) with molten benzoic acid afforded the corresponding $\omega\omega$ -bis-benzoyloxyacetylalkanes (VI).



EXPERIMENTAL

Purified acid chlorides (1 M), dissolved in dry ether, were slowly added to an ethereal solution of diazomethane (5 M) at -10° . The reaction mixture was kept at 0° overnight. Next day, on removal of the solvent under reduced pressure, diazoketones were obtained. Diazoketones (I: $n=3, 4, 4$ -2-Me) are solids, whereas (I: $n=2$ & II) are liquids which could not be purified as these decomposed on distillation.

1,2-Bis-diazoacetylthane (I: $n=2$) was prepared from succinyl chloride (5.1 g.) and diazomethane (7 g.). The liquid decomposed on distillation. Ethane-1,2-bis-glyoxal-2,4-dinitrophenylosazone, a red-brown solid, was crystallised from ethanol, m.p. 116° . (Found: C, 42.5; H, 2.9; N, 25.4. $\text{C}_{30}\text{H}_{22}\text{O}_6\text{N}_6$ requires C, 41.8; H, 2.5; N, 25.9%).

1,3-Bis-diazoacetylpropane (I: $n=3$) was prepared from glutaryl chloride (5.6 g.) and diazomethane (7 g.) as a yellow solid. The compound was crystallised from benzene, m.p. 61° . (Found: C, 45.90; H, 4.80; N, 31.8.0. $\text{C}_7\text{H}_9\text{O}_2\text{N}_4$ requires C, 46.66; H, 4.40; N, 31.10%). The diazoketone, when subjected to the Arndt and Eistert synthesis⁹, furnished pimelic acid which was crystallised from ethanol, m.p. 105° (Volhard⁹ reports m.p. 105 - 106°). (Found: Equiv., 80.8. Calc. for $\text{C}_7\text{H}_{12}\text{O}_4$: equiv., 80). With 2,4-dinitrophenylhydrazine, the diazoketone afforded propane-1,3-bis-glyoxal-2,4-dinitrophenylosazone as a red-brown solid which was crystallised from ethanol, m.p. 106° . (Found: N, 25.68. $\text{C}_{37}\text{H}_{24}\text{O}_{10}\text{N}_6$ requires

8. J. Amer. Chem. Soc., 1949, 71, 367.

9. Volhard, *Annalen*, 1895, 287, 81.

N, 25.50%). 1,3-Bis-chloroacetylpropane was obtained on interaction with HCl. This was crystallised from ethanol, m.p. 81°. (Found: Cl, 35.5. $C_7H_{10}O_2Cl_2$ requires Cl, 36.04%). It formed 2,4-DNP, m.p. 109-104°. (Found: N, 19.3. $C_{10}H_{18}O_2N_2Cl_2$ requires N, 20.1%).

1,4-Bis-diazoacetyl-n-butane (I: $n=4$) was prepared from adipyl chloride (5.5 g.) and diazomethane (6.3 g.) as a yellow solid which was crystallised from benzene-ligroin, m.p. 69° (Walker³ reports m.p. 69-71°). The derived butane-1,4-bis-glyoxal-2,4-dinitrophenylosazone was crystallised from ethanol as an orange solid, m.p. 148°. (Found: N, 24.3. $C_{32}H_{46}O_{16}N_{16}$ requires N, 25.1%). The diazoketone provided 1,4-bis-2-amino-4-thiazolyl-n-butane, crystallised from ethanol, m.p. 221° (Walker³ reports m.p. 220-22°). On heating with benzoic acid the diazoketone afforded 1,4-bis-benzoyloxyacetyl-n-butane which was crystallised from ethanol, m.p. 132°. (Found: C, 70.4; H, 5.1; -COPh, 56.3. $C_{28}H_{32}O_6$ requires C, 69.1; H, 5.7; -COPh, 54.97%).

1,4-Bis-diazoacetyl-2-methyl-n-butane (I: $n=4$, 2-Me) was prepared from 2-methyl-adipyl chloride (10 g.) and diazomethane (10.6 g.) as a yellow solid. The diazoketone was crystallised from benzene, m.p. 74°. (Found: C, 51.2; H, 6.2; N, 26.3. $C_9H_{16}O_2N_4$ requires C, 51.9; H, 5.7; N, 26.9%). When subjected to the Arndt and Eistert synthesis, the diazoketone provided 3-methylsuberic acid amide which was crystallised from hot water, m.p. 191°. (Found: N, 15.80. $C_9H_{16}O_2N_2$ requires N, 15.05%).

2-Methyl-n-butane-1,4-bis-glyoxal-2,4-dinitrophenylosazone was obtained as an orange solid which was crystallised from ethanol, m.p. 119°. (Found: N, 25.5. $C_{33}H_{48}O_{16}N_{16}$ requires N, 24.8%).

1,4-Bis-benzoyloxyacetyl-2-methyl-n-butane, prepared as before, was crystallised from ethanol, m.p. 100°. (Found: C, 70.20; H, 6.90; -COPh, 55.22. $C_{23}H_{24}O_6$ requires C, 69.70; H, 6.06; -COPh, 53.30%).

1, 8-Bis-diazoacetyl-n-octane (I: $n=8$) was obtained as a yellow solid, crystallising from benzene, m.p. 91° (Thomas⁴ records m.p. 91°). The derived octane-1,8-bis-glyoxal-2,4-dinitrophenylosazone was crystallised from ethanol as an orange solid, m.p. 142°. (Found: N, 24.1. $C_{56}H_{84}O_{16}N_{16}$ requires N, 23.6%). The diazoketone afforded with thiourea 1,8-bis-2-amino-4-thiazolyl-n-octane which was crystallised from ethanol, m.p. 180° (Walker³ reports m.p. 180-81°). (Found: S, 20.31. Calc. for $C_{14}H_{22}N_4S_4$: S, 20.64%).

1, 8-Bis-benzoyloxyacetyl-n-octane was obtained as before, crystallising from EtOH, m.p. 142°. (Found: C, 69.8; H, 6.3; -COPh, 40.8. $C_{26}H_{30}O_6$ requires C, 71.2; H, 6.8; -COPh, 47.9%).

1,8-Bis-phenoxyacetyl-n-octane (V) was isolated on heating with phenol. This was crystallised from benzene, m.p. 85°. (Found: C, 75.6; H, 7.3. $C_{24}H_{30}O_4$ requires C, 75.4; H, 7.8%). The 2,4-DNP was crystallised from EtOH, m.p. 112°. (Found: N, 15.4. $C_{26}H_{36}O_{10}N_8$ requires N, 15.2%).

1,2-Bis-diazoacetylbenzene (II) was prepared from phthalyl chloride (10.15 g.) and diazomethane (10.5 g.) as a liquid which decomposed on distillation.

Benzene-1,2-bis-glyoxal-2,4-dinitrophenylosazone was crystallised from EtOH as a brown solid, m.p. 97°. (Found: C, 45.7; H, 3.1; N, 23.9. $C_{24}H_{11}O_{16}N_6$ requires C, 44.8; H, 2.4; N, 24.6%).

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