

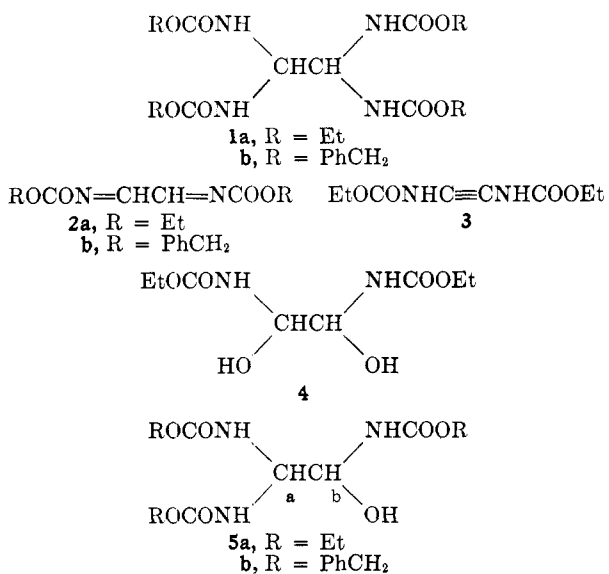
Reactions between Glyoxal and Ethyl Carbamate

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The high-melting and difficultly soluble compound obtained^{1,2} by heating glyoxal with ethyl carbamate in aqueous hydrochloric acid, which has been a source of some confusion in the literature, is undoubtedly the tetrakis(carbamate) **1a**. Originally this compound was formulated¹ as the diimide **2a**, but was erroneously indexed in *Chemical Abstracts*³ as the acetylene **3**. A choice between **2a** and **3** was made in favor of **2a** by Gaylord² who rejected formula **3** because of the absence of infrared bands attributable to the triple bond, although such absorption would not, in fact, be expected for a symmetrical acetylene. The infrared spectrum shows NH bands, and probably for this reason the Sadtler collection chooses⁴ structure **3** to describe the compound. The correct structure (**1a**) has been employed in a patent application,⁵ but without structural or analytical evidence or mention of the previous literature. We have recently synthesized compound **1a**: it proved to be identical with material obtained by following the procedure reported^{1,2} to yield **2a**, and has an infrared spectrum identical with that attributed to **3** in the Sadtler collection.⁴



Compound **1a** is readily prepared by boron trifluoride catalyzed reaction between glyoxal hydrate and ethyl carbamate in benzene solution, a general procedure for obtaining bis(carbamates) of monoaldehydes.⁶ Solubility difficulties precluded a molecular weight determination, but the highest significant peak in the mass spectrum corresponds to **1a** with loss of one -NHCOOEt

- (1) H. Pauly and H. Sauter, *Chem. Ber.*, **63**, 2068 (1930).
- (2) N. G. Gaylord, *J. Org. Chem.*, **20**, 546 (1955).
- (3) Subject and Formula Indices, *Chem. Abstr.*, **25** (1931).
- (4) "Sadtler Standard Spectra, Midget Edition," Sadtler Research Laboratories, Philadelphia, Pa., 1962, spectrum no. 13888.
- (5) Badische Anilin u Soda-Fabrik A.-G., French Patent 1,128,263 (1957) [*Chem. Zentr.*, **130**, 1605 (1959)].
- (6) R. Merten and G. Müller, *Angew. Chem.*, **74**, 866 (1962).

radical; the substance can be sublimed *in vacuo* and therefore is not polymeric. It was also obtained by repetition of the procedure previously reported^{1,2} to yield **2a**. In either case the elemental analysis agreed with the figures calculated for **1a**, which are quite distinguishable from those required by the isomers **2a** and **3**. Because good analyses for the latter were twice reported,^{1,2} we have explored the possibility that slight changes in procedure could give rise to a different product, but have isolated only **1a** or lower melting compounds which are clearly distinguishable from it. Thus an aqueous solution of glyoxal and ethyl carbamate, made mildly alkaline at room temperature, slowly precipitated the bis(carbamate) **4**, as described⁷ by Vail, *et al.* Under acidic conditions a solution of the same reactants very slowly precipitated the tris(carbamate) **5a**.⁵ This has the same appearance as compound **4** and melts in the same range, giving little depression on admixture. However, the high-resolution nmr spectrum provided excellent evidence for the structure of **5a**, in particular showing (after deuterium exchange of all protons attached to nitrogen and oxygen) two doublets corresponding to coupling of the non-equivalent protons H_a and H_b. The infrared spectrum of **5a** differs in the "fingerprint" region from that of **4** but shows very little difference from that⁴ of **1a**.

Gaylord isolated two substances from reaction of glyoxal with benzyl carbamate.² Because their infrared spectra were closely similar he assumed them to be polymorphic forms of the expected product, the diimide **2b**. The similarity between the spectra of **4** and **5a** prompted an explanation of this result; the major product should be regarded as the tetrakis(carbamate) **1b**, and the lower melting side product may well have been the tris(carbamate) **5b**.

Experimental Section

General.—Aqueous glyoxal solution was the technical grade, and "glyoxal monohydrate" was a white powder of approximate composition (CHO)₂H₂O; both were supplied by British Drug Houses Ltd. Except where otherwise stated nmr spectra were measured at 60 MHz.

1,1,2,2-Tetrakis(ethoxycarbonylamino)ethane (1a).—A solution of glyoxal monohydrate (6.4 g, 0.084 mol), ethyl carbamate (30.0 g, 0.337 mol), and boron trifluoride etherate (2.5 ml) in 200 ml of benzene was heated under gentle reflux for 12 hr. The precipitate was collected and decolorized by trituration with 500 ml of boiling methanol, leaving 21.8 g (68%) of **1a**, a microcrystalline white solid: mp 276–278° dec (the melting point varied with rate of heating; lit.² for **2a** 286–287°); nmr (CF₃COOH), δ 6.65 (broad s, 4, vanished on addition of D₂O), 5.70 (broad s, 2, sharpened on addition of D₂O), 4.25 (q, 8), and 1.26 (t, 12); mass spectrum (70 eV) *m/e* 290. Sublimation without change took place at 240° (0.2 mm).

Anal. Calcd for C₁₄H₂₆N₄O₈: C, 44.44; H, 6.93; N, 14.81; O, 33.83. Found: C, 44.50; H, 7.23; N, 14.99; O, 33.4.

This compound was also prepared by the method reported to yield **2a**:^{1,2} ethyl carbamate (17.8 g, 0.200 mol), 30% aqueous glyoxal solution (19.3 g, 0.100 mol), and 13.5 ml of hydrochloric acid (d 1.08) were heated for 12 hr on a steam bath. The precipitate was collected and washed with water and acetone (7.6 g, 40%), mp 273–275° (undepressed by admixture with the authentic sample); recrystallization from glacial acetic acid improved the color without affecting the elemental analysis. *Anal.* Found: C, 44.69; H, 7.32; N, 15.00; O, 33.7.

1,2-Bis(ethoxycarbonylamino)-1,2-dihydroxyethane (4).—Ethyl carbamate (27.6 g, 0.310 mol) and 30% aqueous glyoxal solution (30.0 g, 0.155 mol) were dissolved in 30 ml of water. The solution

- (7) S. L. Vail, C. M. Moran, and R. H. Barker, *J. Org. Chem.*, **30**, 1195 (1965).

was neutralized with solid sodium bicarbonate and maintained faintly alkaline throughout the reaction period by further additions when needed.⁷ After 4 days at room temperature 3.7 g of **4** had crystallized. Further crops of about this magnitude could be obtained by filtration every few days, but the ultimate yield was not determined: 140–155° dec, depending on the rate of heating; nmr (CD₃SOCD₃), δ 7.20 (broad s, 2, vanished on shaking with D₂O), 5.65 (d, 2, vanished on shaking with D₂O, >CHOH), 4.95 (broad s, 2, sharpened on shaking with D₂O, >CH-CH<), 4.05 (q, 4), and 1.20 (t, 6).

Anal. Calcd for C₈H₁₆N₂O₆: C, 40.70; H, 6.82; N, 11.80. Found: C, 40.43; H, 7.03; N, 11.92.

1,1,2-Tris(ethoxycarbonylamino)-2-hydroxyethane (5a).—Ethyl carbamate (15.0 g, 0.168 mol), 30% aqueous glyoxal solution (8.2 g, 0.042 mol), and 0.5 ml of hydrochloric acid were dissolved in water, and left at room temperature (warming of the solution resulted in formation of **1a**). After 5 days 1.3 g of **5a** was collected (precipitation continued in the filtrate) and recrystallized from water and then from ethyl acetate: mp 140–160° dec, depending on the rate of heating; nmr (CD₃SOCD₃), δ 7.1 (broad, 3, vanished on shaking solution with D₂O, NH), 5.91 (d, 1, vanished on shaking solution with D₂O, -OH), 5.05 (broad, 2, sharpened on shaking the solution with D₂O, >CH-CH<), 3.98 (q, 6), and 1.14 (t, 9). At 220 MHz further resolution was possible: δ 7.38 (s, 1, -CH(OH)NH-), 7.31 (s, 2, -NHCHNH-), 1.178 (t, ≈3, *J* = 7 Hz, CH₃CH₂CO₂NHCH-OH-), and 1.173 (t, ≈6, *J* = 7 Hz (CH₃CH₂CO₂NH)₂CH-): exchange of labile protons with D₂O simplified the resonances corresponding to >CH-CH<; 5.05 (d, 1, *J* = 5 Hz) and 5.01 (d, 1, *J* = 5 Hz).

Anal. Calcd for C₁₁H₂₁N₃O₇: C, 42.99; H, 6.89; N, 13.67; O, 36.45. Found: C, 42.95; H, 6.82; N, 13.70; O, 37.5.

Registry No.—**1a**, 17350-57-1; glyoxal, 107-22-2; ethyl carbamate, 51-79-6; **4**, 17350-58-2; **5a**, 17350-59-3.

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Reaction of 2,3-Dihydrobenzo[*b*]thiophen-3(2H)-one 1,1-Dioxide with Electrophiles

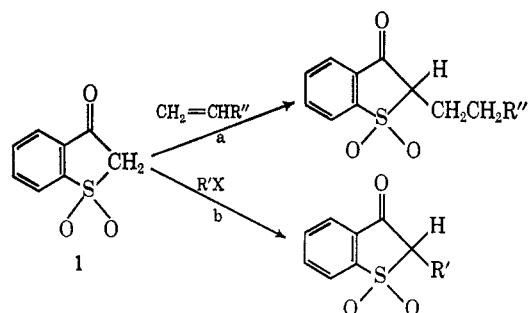
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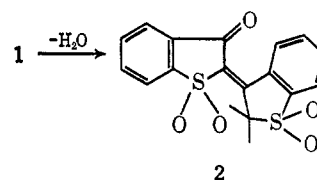
Although 2,3-dihydrobenzo[*b*]thiophen-3(2H)-one 1,1-dioxide (**1**) has been known for some time,^{1–4} no examples of alkylation or acylation of **1** have been reported. A few 2-acyl and 2-alkyl derivatives of **1** are known,^{5–7} but the synthesis of these compounds has been accomplished either by cyclization of *o*-alkyl-sulfonylbenzoate esters^{5,6} or by chlorosulfonation of propiophenones.⁷

In connection with another study, a more versatile route to certain 2-alkyl and 2-acyl derivatives of **1** was sought. Toward this end, the acylation and alkylation of **1**, as well as the Michael-type additions of **1**



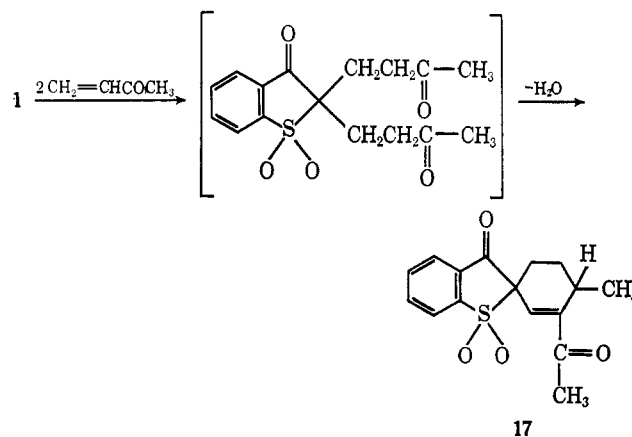
(anion) to unsaturated electrophiles, were studied. With reactive electrophiles such as acrylonitrile and methyl vinyl sulfone, sodium methoxide successfully served as a base for the Michael addition of **1** (reaction a). Table I (12–15) records products of this reaction.

In a few attempts in which alkyl halides were allowed to react with **1** in the presence of sodium methoxide, complex mixtures were obtained. This apparently slower reaction may have allowed side reactions such as ring opening of **1** by methoxide ion to occur, since hydroxide ion is known² to cleave **1** into 2-methylsulfonylbenzoic acid. An analogous example of ring cleavage of **1** by pyrrolidine is discussed below. It was ultimately found that alkylations and acylations of **1** proceeded in moderate yields in the presence of the sterically hindered diisopropylethylamine⁸ in isopropyl alcohol solution (reaction b above). Table I (3–11) lists products from this reaction. Side reactions were minimized in this system, although intermolecular dehydration of **1** to the dimer **2** was observed when relatively unreactive alkyl halides such as 1-bromopentane or chloroethyl methyl sulfide were employed.



Analogous self-condensation of 1,3-indandione to form an anhydro dimer ("Bindone") in the presence of base has previously been observed.⁹

Reaction of methyl vinyl ketone with **1** in the presence of sodium methoxide gave a low yield of the spiro compound **17**, probably proceeding through the re-



(1) N. Lanfry, *C. R. Acad. Sci., Paris*, **154**, 1517 (1912).

(2) F. Arndt, A. Kirsch, and P. Nachtwey, *Chem. Ber.*, **59**, 1074 (1926).

(3) A. W. Weston and C. N. Suter, *J. Amer. Chem. Soc.*, **61**, 389 (1939).

(4) M. Regitz, *Chem. Ber.*, **98**, 36 (1965).

(5) A. Cohen and S. Smiles, *J. Chem. Soc.*, 406 (1930).

(6) W. B. Price and S. Smiles, *ibid.*, 2858 (1928).

(7) R. F. Meyer, *J. Heterocycl. Chem.*, **3**, 174 (1966).

(8) S. Hunig and N. Kiessel, *Chem. Ber.*, **91**, 380 (1958).

(9) (a) W. Wislicenus, *ibid.*, **20**, 594 (1887); (b) W. Wislicenus and A. Kotzle, *Ann. Chem.*, **252**, 77 (1889).