Carbonyl Ylides from Aldehydes and Carbenes

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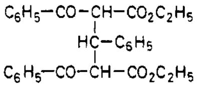
Received April 26, 1982

In 1885 Buchner and Curtius reacted ethyl diazoacetate with benzaldehyde at 160 °C and regarded the product as **1**.[1] In a revision 25 years later, Dieckmann established the 1,3-dioxolane structure **2**. The two diastereoisomers were converted to the *erythro-* and *threo*-3-phenylglyceric acids besides benzaldehyde.[2] The initial formation of the "furodiazole" **3** and replacement of N_2 by a second molecule of benzaldehyde were assumed to be the mechanism.[2]



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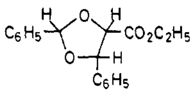

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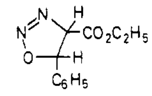

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We reinvestigated the reaction with the less nucleophilic dimethyl diazomalonate (**4**) and clarified the pathway. When **4** was heated with 12 equiv of benzaldehyde at 125 °C (11 h, 100% N_2), ^1H NMR analysis indicated 56% of the dioxolanes **6** (mp 120.5–121 °C) and **7** (oil, pure after TLC) in a 58:42 ratio as well as 10% of the oxirane **5** (oil, bp 110 °C (0.07 mmHg)).[3] Mild hydrolysis of **6** and **7** gave benzaldehyde, and the chemical shifts of the ring protons allow the structural assignment; the 5-phenyl located quasi-orthogonal to the heteroring deshields the cis-2-H in **7** stronger than the trans-2-H in **6**.

$N\equiv\overset{+}{N}-\overset{-}{C}(CO_2CH_3)_2$

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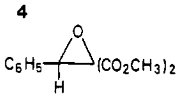

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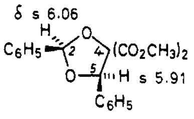

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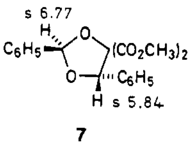

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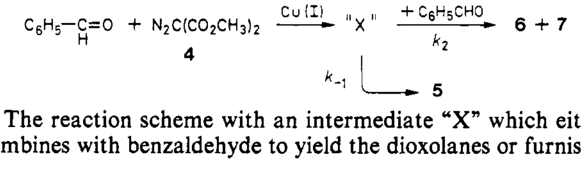
The thermolysis of diazomalonic ester is assumed to give bis(methoxycarbonyl)carbene. Kinetic measurements (disappearance of the IR absorption at 2129 cm^{-1}) provided no evidence for an "induced decomposition" of **4** in benzaldehyde. The first-order rate constant depends only slightly on the solvent; 10^5k_1 (s^{-1}) = 5.4 (decalin), 5.7 (mesitylene), 6.6 (nitrobenzene), 8.3 (benzaldehyde), 8.3 (Me_2SO), 8.4 (propylene carbonate), and 8.8 (anisaldehyde) at 130°C.

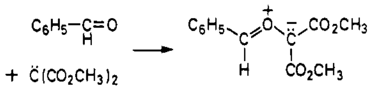
Higher yields of the dioxolanes resulted from the metal-catalyzed N_2 elimination from **4**; the slow introduction of **4** made a small stationary concentration feasible. The reaction with 1 mol % $Cu(acac)_2$ at 125 °C furnished 82% **6** and **7** (55:45) and 7% **5**. In the presence of 2 mol % Rh(II) acetate, N_2 evolution was induced at 75 °C (72% **6** and **7**, 55:45) and with Cu(I) triflate[4] even at 25 °C (87% **6** and **7**, 71:29).

When an equimolar mixture of **4** and benzaldehyde was added dropwise to 0.13 M benzaldehyde in refluxing chlorobenzene in the presence of copper powder, 72% of the oxirane **5** was obtained (eq 1). The 1:1 product **5** cannot be the intermediate on the way to the 1:2 products **6** and **7** because heating of **5** for 6 h in benzaldehyde as solvent at 125 °C produced only ~5% of the dioxolanes **6** and **7**.



The reaction scheme with an intermediate "X" which either combines with benzaldehyde to yield the dioxolanes or furnishes the oxirane in a first-order reaction is in accordance with competition experiments. The decomposition of **4** (100 °C, Cu(I) triflate catalysis) in 0.95, 1.90, 2.86, and 4.32 M benzaldehyde in chlorobenzene gave rise to dioxolanes and oxirane in ratios of 3.2, 4.5, 7.9, and 11.0. The plot of product ratios vs. benzaldehyde concentration is a straight line (r = 0.99) through the origin with k_2/k_{-1} = 2.6.

The carbonyl oxygen is the nucleophilic center of the aldehyde molecule, and the *carbonyl ylide* **8** is the logical candidate for the common intermediate "X". In the case of the metal-catalyzed decomposition of **4**, a metal carbenoid may replace the electrophilic carbene. The 1,3-dipolar cycloaddition of **8** to benzaldehyde to give **6** and **7** is of high regiospecificity and low diastereoselectivity. On heating the oxirane **5** with benzaldehyde for 8 h at 150 °C, we obtained the dioxolanes **6** and **7** in a 56:44 ratio; probably the same intermediate **8** is involved. Electrocyclic ring-opening equilibria of oxiranes with carbonyl ylides are well documented.[5]



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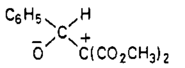

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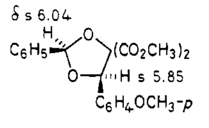
The oxatrimethylene species **9**, which can also be described as a biradical, is a less attractive alternative for "X". How can it be ruled out? The reaction of **5** with anisaldehyde (7 days, 125 °C) afforded 71% of the "mixed" dioxolanes **10** and **11** (53:47), which gave 100% benzaldehyde 2,4-dinitrophenylhydrazone on treatment with the reagent in methanolic sulfuric acid (4 days, 25 °C). The combination of **5** via **9** with anisaldehyde or by direct nucleophilic attack should have yielded **12**, and anisaldehyde would be the expected product of acetal hydrolysis. Furthermore, Robert et al. investigated the corresponding 1,3-dipolar cycloadditions of 3-aryl-2,2-dicyanooxirane via the carbonyl ylide to aromatic aldehydes.[6]



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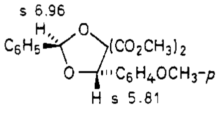

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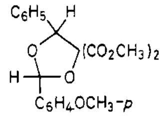

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Competing formation of dioxolanes and oxiranes was also observed for the reactions of **4** with anisaldehyde, furfural, and crotonaldehyde, respectively. Benzophenone and **4** furnished dimethyl 3,3-diphenyloxirane-2,2-dicarboxylate.

Kharasch et al. studied the Cu-catalyzed reactions of ethyl diazoacetate with cyclohexanone and acetone and obtained 1,3-dioxolanes in 4% and 9% yield, respectively;[7] an enol 2-hydroxyethyl ether was assumed as a precursor. The *intramolecular* formation of carbonyl ylides from the carbonyl group and copper carbenoids was described by Ibata[8,9] and by Bien;[10] the mesoionic 3-methyl-5-(*p*-nitrophenyl)-2-phenyl-1,3-oxazolium 4-olate ("isomünchnone") is the only *isolable* compound with carbonyl ylide activity.[9]

Registry No. 4, 6773-29-1; **5**, 82545-15-1; **6**, 82545-16-2; **7**, 82545-17-3; **10**, 82555-00-8; **11**, 82555-01-9; benzaldehyde, 100-52-7; bis(2,4-pentanedionato-*O,O'*)copper, 46369-53-3; copper(I) triflate, 42152-44-3; *p*-anisaldehyde, 123-11-5; furfural, 98-01-1; crotonaldehyde, 4170-30-3; benzophenone, 119-61-9; dimethyl 3,3-diphenyloxirane-2,2-dicarboxylate, 82555-02-0.

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[1] Buchner, E.; Curtius, Th. *Ber. Dtsch. Chem. Ges.* **1885**, *18*, 2371–2377.

[2] Dieckmann, W. *Ber. Dtsch. Chem. Ges.* **1910**, *43*, 1024–1031.

[3] Satisfactory CH analyses and spectral data were obtained for all new compounds.

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