5-Benzylidene-1,3-dioxolan-2,4-dione

By BERYL W. DOMINY and RICHARD G. LAWTON*

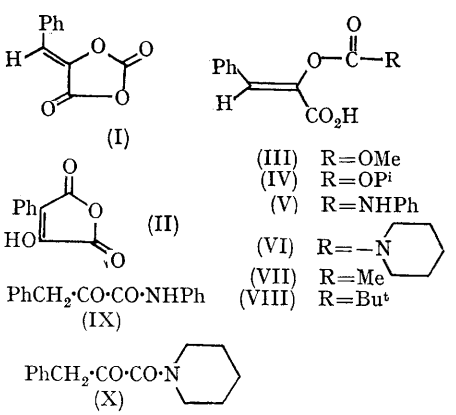
(*Department of Chemistry, University of Michigan, Ann Arbor, Michigan* 48104)

5-BENZYLIDENE-1,2-DIOXOLAN-2,4-DIONE (I) is the first example of a highly reactive class of compounds, the cyclic enol carbonic anhydrides of α-keto-acids.

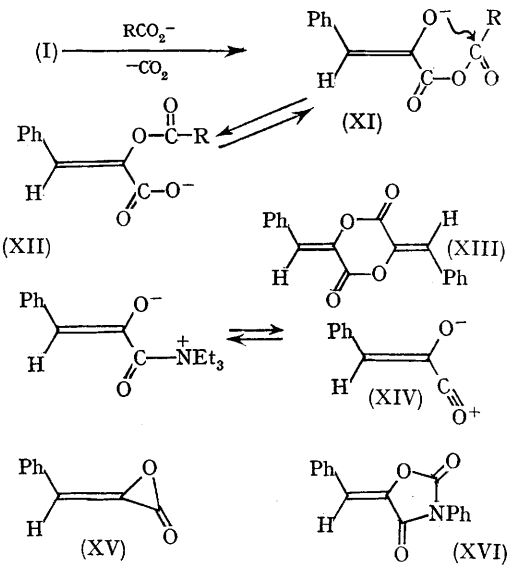
A reliable preparation of this compound has been devised: to an ice-cooled solution of phenylpyruvic acid (5·0 g.; 0·0305 mole) in 500 ml. of dry ether contained in a flask equipped with a gas inlet tube, Hershberg stirrer, and pressure-equalized Hershberg dropping funnel, was added through the gas inlet tube 3·73 g. (0·0382 mole) of redistilled phosgene. With continued cooling and slow stirring, a solution of triethylamine (6·77 g., 0·0672 mole) in 100 ml. of ether was added dropwise from the Hershberg funnel during 3 hr. Stirring was then continued as the mixture was

allowed to come to room temperature. The salt was filtered off and the filtrate evaporated. The resulting light yellow solid was crystallized from ether affording 60 to 70% yields of (I) (90% based on recovered phenylpyruvic acid). Benzylidenedioxolandione (I),† a colourless crystalline powder, has the following physical characteristics: m.p. 154—156° (decomp.), ν_{max} ($CHCl_3$) 1890m, 1850w, 1810d, s, 1670m, and 1250s cm.$^{-1}$;[1] λ_{max} (dioxan) 300 mμ (ϵ 21,000), τ (acetone) 2·2 (2H, m), 2·5 (3H, m), and 3·0 (1H, s), *M* 188 (cryoscopic, benzene), $C_{10}H_6O_4$.‡ In aqueous acetone the compound is rapidly hydrolysed with evolution of CO_2 to give phenylpyruvic acid. Further, compound (I) differs from its isomer, phenylhydroxymaleic anhydride[2] (II) [m.p. 160—162°, ν_{max} ($CHCl_3$) 1835, 1770, 1675, and 1380 cm.$^{-1}$ (all s)].

As might be expected for a compound containing two extremely reactive, nonequivalent carbonyl groups, (I) reacts with nucleophiles, by several paths, to give a variety of hitherto unavailable structures. Thus, the enol carbonic anhydride in methanol affords α-(methoxycarbonyloxy)cinnamic acid (III) [98%, $C_{11}H_{10}O_5$ m.p. 133—135°, ν_{max} ($CHCl_3$) 1770, 1700, 1645, and 1250 cm.$^{-1}$, λ_{max} (dioxan) 273 mμ (ϵ 20,900), τ ($CDCl_3$) 2·35 (2H, m) 2·6 (4H, m) and 6·1 (3H, s)]. A similar treatment with isopropanol yields the isopropyl enol carbonate (IV) [90%, $C_{13}H_{14}O_5$ m.p. 121—123°].



Primary and secondary amines similarly condense with (I) to give enol carbamates. Treatment of (I) with aniline in benzene at room temperature yields (V) [83%, $C_{16}H_{13}NO_4$, m.p. 167—169°, ν_{max} ($CHCl_3$) 1740, 1640, 1600, and 1520 cm.$^{-1}$, λ_{max} (dioxan) 275 mμ (ϵ 23,000)] while piperidine in ether precipitates the piperidine



salt of (VI) [70%, $C_{20}H_{20}N_2O_4$, m.p. 131—133°, ν_{max} ($CHCl_3$) 1720, 1635 cm.$^{-1}$]. Both enol carbamates (V) and (VI) rearrange upon long standing in chloroform–triethylamine to form the phenylpyruvic amides (IX) and (XI). Further, the enol carbonic anhydride (I) can be regenerated from the enol carbamate (V) by treatment with trifluoroacetic anhydride. The ready neighbouring-group participation implied by these latter experiments occurs throughout the chemistry of these compounds.

A second reaction pathway occurs when (I) is treated with the triethylamine salt of acetic acid in chloroform at room temperature; CO_2 is evolved and the enol acetate of phenylpyruvic acid is formed [(VII), 60%, $C_{11}H_{10}O_4$, m.p. 164—168°, (lit.[3] 168°) ν_{max} ($CHCl_3$) 1765, 1690, 1640, and 1200 cm.$^{-1}$, λ_{max} (dioxan) 273 mμ (ϵ 24,200), mixed m.p. with authentic sample 164—168°].§ The formation of enol esters from (I) and salts of carboxylic acids evidently proceeds by attack at the 4-carbonyl group followed by loss of CO_2 and intramolecular attack of the enolate on the mixed anhydride grouping (XI) → (XII). This last step

† The stereochemistry of the enol carbonic anhydride and its derived products was presumed from the physical data as well as from the assumed greater stability of the *trans*-cinnamic acid moiety.

‡ Satisfactory analytical results have been obtained for all compounds for which an empirical formula is given.

§ This same product may be obtained in 30% yield by reaction of (I) with sodium acetate in aqueous solution.

appears to be reversible since these intermediate mixed anhydrides can play a part in the reactions of certain α-acyloxycinnamic acids. For example, when α-(trimethylacetoxy)cinnamic acid (VIII) [32%, $C_{14}H_{16}O_4$, m.p. 163—165°, ν_{max} ($CHCl_3$) 1730, 1680, 1640, and 1225 cm.$^{-1}$] was heated with aniline in chloroform solution, phenylpyruvoylanilide (IX) was produced [(XII)→(XI)→(IX)]. The equilibrium [(XI) ⇌ (XII)] has frustrated our attempts to utilize the active esters derived from salts of *N*-protected amino-acids and the enol carbonic anhydride (I) as general peptide-synthesizing agents although 50—60% yields of phthalylglycylglycine ethyl ester could be obtained from phthalylglycine, the enol carbonic anhydride (I) and glycine ethyl ester.

Of interest was the formation of dibenzylidene glycolide (XIII), $C_{18}H_{12}O_4$, m.p. 233—235°, ν_{max} ($CHCl_3$) 1770, 1640, and 1275 cm.$^{-1}$, λ_{max} (dioxan) 320 mμ (ε36,000), τ (CF_3CO_2H) 2·1 (4H, m) and 2·45 (8H, m), mass spectrum: *m/e*, *P* 292, with intense peaks at 265 and 118] by either heating or treatment of (I) in benzene with a catalytic amount of triethylamine (70—80% yields). Although there are several routes to (XIII) from (I), the simplest and most direct involves the intermediacy of the enolate–acylonium zwitterion (XIV), a derivative of the α-enol-lactone (XV). Intermediates of this type were suggested by the production of the oxazolidinedione (XVI) [80%, $C_{16}H_{11}NO_3$, m.p. 237—238° (lit.[4] 238—239°), ν_{max} ($CHCl_3$) 1820, 1740, 1670, 1600, 1390, and 1200 cm.$^{-1}$ τ ($CDCl_3$) 2·13 (2H, m), 2·44 (8H, m), and 3·11 (1H, s)] on warming, or triethylamine treatment of (I) and phenylisocyanate in benzene.[5]

The cyclic enol carbonic anhydride (I) could be used for preparing, under mild conditions,[6] phenylpyruvoyl derivatives of peptides and amino-acids, which in turn could lead to synthesis of alkaloids, antibiotics, and biochemical intermediates.[7]

We thank the University of Michigan Cancer Research Institute for a research fellowship held during a portion of this work.

(*Received, July 4th*, 1968; *Com.* 894.)

[1] Note the related, unusually high carbonyl absorption of ethylene carbonate (1817 cm.$^{-1}$) and vinylene carbonate (1833 cm.$^{-1}$). J. L. Hales, J. I. Jones, and W. Kynaston, *J. Chem. Soc.*, 1957, 618.

[2] M. J. Bougault, *Compt. rend.*, 1916, 760.

[3] M. J. Bougault and R. Hemmerle, *Compt. rend.*, 1915, **160**, 102.

[4] R. Soderquist, *Svensk. kem. Tidskr.*, 1922, **34**, 189.

[5] This process is reminiscent of 1,3-dipolar additions. See *e.g.* R. Huisgen, *Angew Chem. Internat. Edn.*, 1963, **2**, 565; I. Ugi and K. Rosendahl, *Chem. Ber.*, 1961, **94**, 2233.

[6] G. E. Krejcarek, B. W. Dominy, and R. G. Lawton, following Communication.

[7] R. Brown, C. Kelley, and S. E. Wikerley, *J. Org. Chem.*, 1965, **30**, 277; M. Vondracek and Z. Vanek, *Chem. and Ind.*, 1964, 1686; Y. S. Mohammed and M. Luchner, *Tetrahedron Letters*, 1963, 1953. H. Smith, P. Wegfahrt, and H. Rapoport, *J. Amer. Chem. Soc.*, 1968, **90**, 1668.