in the entropy change ΔS, which is a component of ΔG since $\Delta G = \Delta H - T\Delta S$. Indeed, the electronic entropy factor, due to the degeneracy of the triplet state, is R ln 3 as pointed out by Holm, *et al.*,[8] but this factor will be included in the ΔS values calculated from the data if the proper equation is used. ΔG values in the literature, calculated from the incorrect equation, are too high by RT ln 3, and the ΔS values are too low by R ln 3 = 2.2 e.u. Fortunately the calculated A_i values are unaffected by this error.[14a]

(14a) NOTE ADDED IN PROOF. Holm, *et al.*, have pointed out the discrepancy, by a factor of three, between the equilibrium constants calculated from eq. 6 and those based on the actual mole fractions of the singlet and triplet molecules in solution determined from the measured susceptibilities (R. H. Holm, A. Chakravorty, and G. W. Everett, Jr., *Progr. Inorg. Chem.*, 7, in press).

William DeW. Horrocks, Jr.
Frick Chemical Laboratory, Princeton University
Princeton, New Jersey
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Nucleophilic Acylation Utilizing an Ylid Intermediate. A Simple Synthesis of Benzaldehyde-d_1[1]

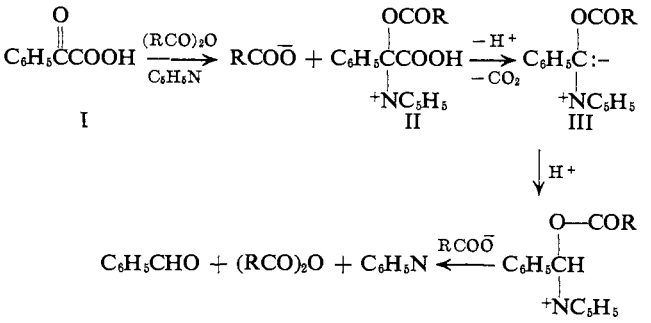
Sir:

We wish to report that α-keto acids can be decarboxylated to aldehydes under mild conditions in the presence of carboxylic acid anhydrides and pyridine,[2] and to point out some useful applications and some important general mechanistic implications of this type of reaction.

In the case of phenylglyoxylic acid (I), we have used acetic, phenylacetic, and benzoic anhydrides. The latter gives the best yield of benzaldehyde because of the avoidance of Perkin-type condensation reactions which occur with the other anhydrides.[3] In one run, a solution of 13 mmoles of phenylglyoxylic acid (I), 27 mmoles of benzoic anhydride, and 140 mmoles of pyridine in 50 ml. of benzene was heated at reflux for 13 hr. The yields of benzaldehyde and carbon dioxide were 75 and 88%, respectively. Glyoxylic and pyruvic acids were similarly decarboxylated.[4]

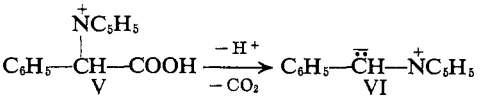
This reaction is the basis of a very simple synthesis of benzaldehyde-d_1. Phenylglyoxylic acid-d_1 is readily prepared by dissolving the commercially available[5] protium compound in heavy water and evaporating to dryness.[6] The benzaldehyde, prepared from I which had been twice subjected to exchange in this way, was shown by n.m.r. integration to contain about 92% deuterium in the aldehyde group.[7]

A reasonable path for this reaction involves nucleophilic attack of pyridine at the keto carbonyl group and subsequent or simultaneous acylation[10,11] of the carbonyl oxygen to produce the intermediate II. Loss



of a proton and carbon dioxide would produce the ylid III which, upon protonation and deacylpyridination (essentially the reverse of the first step), would yield the benzaldehyde.[12-15] Pyridine ylids of this type[17] are intermediates in many carbanionoid reactions.[18]

If this mechanism is valid, one might expect the decarboxylation of α-halo acids to be brought about by pyridine under mild conditions. That this is indeed the case is demonstrated by the reaction of pyridine with α-bromophenylacetic acid in refluxing benzene. Carbon dioxide, which is vigorously evolved, and N-benzylpyridinium bromide are quantitatively produced. Decarboxylation of the pyridinium salt V to the ylid VI is presumably a key step in this reaction.[19]



The intermediate III is mechanistically equivalent to the *conjugate base of benzaldehyde* and as such suggests a variety of conceivable synthetic and degradative uses. For example, intermediates such as III should

(1) Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

(2) Neither of the two catalysts is effective alone.

(3) T. Cohen, I. H. Song, and J. H. Fager, *Tetrahedron Letters*, 237 (1965).

(4) However, these reactions were complicated by serious side reactions, since the aldehydes were produced in much lower yield (11–15%) than carbon dioxide (43–50%).

(5) K & K Laboratories, Inc., Jamaica 33, N. Y.

(6) Another procedure for exchanging the carboxyl hydrogen involves adding heavy water to a benzene solution of the protium acid and then removing the water by azeotropic distillation.

(7) Benzaldehyde-d_1 has been prepared previously by considerably more laborious routes involving catalytic deuteration of benzoyl chloride over a poisoned palladium catalyst at 140°[8] or lead tetraacetate cleavage of a deuterated dihydrobenzoin, which was in turn prepared by reduction of benzil with lithium aluminum deuteride.[9]

(8) A. F. Thompson and N. H. Cromwell, *J. Am. Chem. Soc.*, **61**, 1374 (1939).

(9) K. B. Wiberg, *ibid.*, **76**, 5371 (1954).

(10) This step could be executed by an external acylating agent, such as the N-acylpyridinium ion, or internally by a mixed anhydride of the phenylglyoxylic acid.

(11) We should like to term this reaction "acylpyridination."

(12) Very recently, a related ylid-type mechanism has been proposed as one possibility for the decarboxylation of oxamic acid in aniline solution at 150°: J. Watson and P. Haake, *J. Org. Chem.*, **30**, 1122 (1965).

(13) An alternative mechanism, which is analogous to the thiamine-induced decarboxylation of pyruvic acid,[14] is also available. It involves removal of the α-proton of an N-acylpyridinium ion, condensation of the keto acid with the resulting zwitterion, decarboxylation, and cleavage. However, this mechanism requires dilution of the deuterium ion content of the solution by the α-hydrogen of the pyridine, and this is ruled out by the high deuterium content of the benzaldehyde produced from the deuterated acid.

(14) R. Breslow, *J. Am. Chem. Soc.*, **80**, 3719 (1958); R. Breslow and E. McNelis, *ibid.*, **81**, 3080 (1959).

(15) An entirely different type of mechanism is apparently utilized in the decarboxylation of I by amino acids and amino lactams, although that induced by simple primary amines under vigorous conditions[16] might proceed by a mechanism similar to that proposed here: A. S. Endler and E. I. Becker, *J. Phys. Chem.*, **61**, 747 (1957).

(16) W. Langenbeck, "Die Organischen Katalysatoren," 2nd Ed., Springer-Verlag, Berlin, 1949.

(17) Decarboxylations of picolinic acid and related compounds proceed through another type of ylid intermediate in which the negative charge resides on the α-carbon atom of the pyridinium ring: B. R. Brown, *Quart. Rev.* (London), **5**, 131 (1951); P. Haake and J. Mantecon, *J. Am. Chem. Soc.*, **86**, 5230 (1964).

(18) F. Kröhnke, *Angew. Chem.*, **65**, 605 (1953); F. Kröhnke, *Angew. Chem. Intern. Ed. Engl.*, **2**, 225 (1963); J. A. Berson and T. Cohen, *J. Am. Chem. Soc.*, **78**, 416 (1956).

(19) Under very much more vigorous conditions (190°), pyridine betaine hydrochloride is reported to yield methyl chloride, pyridine, and carbon dioxide: E. von Gerichten, *Ber.*, **15**, 1251 (1882).

provide routes to *nucleophilic acylations* of electrophiles other than the proton, provided the latter is not readily available. We have demonstrated the utility of this concept for the establishment of carbon–carbon bonds by performing the nucleophilic benzoylation of benzoic anhydride. The reaction of the tetramethylammonium salt of I with benzoic anhydride and pyridine in refluxing mesitylene produced a 40% yield of benzil.[2,20]

(20) No attempt was made to optimize yields.

Theodore Cohen, Il Hwan Song
Department of Chemistry, University of Pittsburgh
Pittsburgh, Pennsylvania 15213
Received June 14, 1965

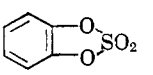
The Alkaline Hydrolysis of Catechol Cyclic Sulfate. An Extraordinary Rate Acceleration

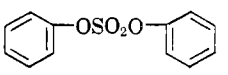
Sir:

For many years it has been known that five-membered cyclic esters of phosphoric acid are intermediates in the hydrolysis of ribonucleic acids.[1] Although most diesters of phosphoric acid are relatively resistant to alkaline hydrolysis, these cyclic phosphoric acid esters are rapidly hydrolyzed.[1,2] Studies on the simplest cyclic ester of phosphoric acid, ethylene phosphate, revealed that its salts hydrolyze in alkali at about 10^7 times the rate observed for the corresponding salts of the open chain compound, dimethyl phosphate.[3,4] The alkaline hydrolysis of ethylene phosphate has been demonstrated to occur exclusively with P–O bond cleavage, whereas dimethyl phosphate hydrolyzes in large part with C–O bond cleavage.[5,6] As a result of this difference in the modes of bond cleavage, the rate enhancement for attack at phosphorus by hydroxide ion is estimated to be greater than 10^8. Further studies have shown that this large rate enhancement is not unique for five-membered cyclic esters of phosphoric acid. The five-membered cyclic ester of phosphonic acid, lithium propylphostonate, is hydrolyzed 10^6 times as fast as the open chain compound, sodium ethyl ethylphosphonate.[7]

In an attempt to elucidate the unusual behavior of the five-membered cyclic esters of phosphoric acid, the hydrolysis of ethylene sulfate was investigated and compared to that of dimethyl sulfate. Ethylene sulfate was found to hydrolyze in alkaline solution only slightly faster than dimethyl sulfate.[8] However, whereas ethylene sulfate hydrolyzes with about 14% S–O bond cleavage in alkali, dimethyl sulfate is hydrolyzed exclusively *via* attack at carbon with concomitant C–O bond cleavage. Therefore it was not possible to measure the relative rate factor for attack at sulfur in these compounds, and the question whether the kinetic acceleration at sulfur in the five-membered ring compound is large remained unsolved.

The present communication reports a kinetic study of the alkaline hydrolysis of the five-membered cyclic sulfate, catechol cyclic sulfate (I), and its open chain analog, diphenyl sulfate (II). Nucleophilic attack of hydroxide ion at the aromatic carbon atoms in these compounds should be extremely unlikely. Thus, the difference in the rate of hydrolysis of the two esters should represent the difference in the rate of attack of


I


II

hydroxide ion at sulfur for a five-membered cyclic sulfate compared to that for its open-chain analog.

Catechol cyclic sulfate (I), m.p. 34–35°, was prepared in low yield from the reaction of catechol with sulfuryl chloride in petroleum ether in the presence of pyridine.[9] *Anal.* Calcd. for $C_6H_4O_4S$: C, 41.86; H, 2.33; S, 18.60. Found: C, 41.68; H, 2.18; S, 18.53. On alkaline hydrolysis of I the monoester, 2-hydroxyphenyl sulfate, is produced. Measurements with a Radiometer Type TTT1b titrator in conjunction with a Type SBR2C titrigraph and GK 2021 C electrode gave a second-order rate constant of 18.8 M^{-1} sec.$^{-1}$ for the alkaline hydrolysis of I at 25.0°.

Diphenyl sulfate (II), b.p. 95–97° (0.05 mm.), was obtained by allowing a mixture of phenol, pyridine, and sulfuryl chloride to react at low temperature in petroleum ether.[10] *Anal.* Calcd. for $C_{12}H_{10}O_4S$: C, 57.59; H, 4.03; S, 12.81. Found: C, 57.70; H, 4.20; S, 12.97. Alkaline hydrolysis of II led to the formation of the monoester, phenyl sulfate, and of phenol. The hydrolytic reactions were conducted in brass-enclosed Teflon reaction cells placed in a thermostated oil bath, and the rates of hydrolysis were determined by quantitative vapor phase chromatographic analysis of unreacted II as a function of time. Values of 13×10^{-6}, 30×10^{-6}, and 178×10^{-6} M^{-1} sec.$^{-1}$ were found for the second-order rate constants for the alkaline hydrolysis of II at 50.0, 60.0, and 80.0°, respectively. Extrapolation of these results to 25.0° gave a value for the second-order rate constant of 8.9×10^{-7} M^{-1} sec.$^{-1}$.

Thus, comparison of the relative rate constants observed for the alkaline hydrolysis of catechol cyclic sulfate and diphenyl sulfate, which reflects the difference in the rate of attack by hydroxide ion at sulfur in these two compounds, shows that the five-membered cyclic diester hydrolyzes 2×10^7 times faster than its open chain analog.[11] This represents the first observa-

(1) R. Markham and J. D. Smith, *Biochem. J.*, **52**, 552 (1952); D. Lipkin, P. T. Talbert, and M. Cohn, *J. Am. Chem. Soc.*, **76**, 2871 (1954); A. Fono, *Archiv. Kemi Mineral. Geol.*, **24A**, 34, 19 (1947); D. M. Brown and A. R. Todd, *J. Chem. Soc.*, 52 (1952).

(2) D. M. Brown, D. I. Magrath, and A. R. Todd, *ibid.*, 2708 (1952); T. Ukita, N. A. Bates, and H. E. Carter, *J. Biol. Chem.*, **216**, 867 (1955).

(3) J. Lecocq, *Compt. rend.*, **242**, 1902 (1956).

(4) J. Kumamoto, J. R. Cox, Jr., and F. H. Westheimer, *J. Am. Chem. Soc.*, **78**, 4858 (1956).

(5) C. A. Bunton, D. R. Llewellyn, K. G. Oldham, and C. A. Vernon, *J. Chem. Soc.*, 3574 (1958).

(6) P. Haake and F. H. Westheimer, *J. Am. Chem. Soc.*, **83**, 1102 (1961).

(7) A. Eberhard and F. H. Westheimer, *ibid.*, **87**, 253 (1965).

(8) E. T. Kaiser, M. Panar, and F. H. Westheimer, *ibid.*, **85**, 602 (1963).

(9) The preparation of I has been reported by L. Denivelle in *Compt. rend.*, **203**, 194 (1936), but we were unable to repeat his procedure nor were we able to reproduce the melting point (47°) which he obtained for this compound. The n.m.r. and infrared data which we determined were in accord with structure I.

(10) L. Denivelle, *ibid.*, **199**, 211 (1934); L. Bollinger, *Bull. soc. chim. France*, 156 (1948); H. Geis and E. Pfeil, *Ann.*, **578**, 11 (1952).

(11) The largest rate difference found previously in sulfur-containing systems was that between the alkaline hydrolysis of catechol cyclic sulfite and diphenyl sulfite, the five-membered cyclic ester hydrolyzing only 1.5×10^3 times more rapidly than its open chain analog (P. De la Mare, J. Tillett, and H. van Woerden, *J. Chem. Soc.*, 4888 (1962)). Cyclic sulfites differ considerably from cyclic sulfates in their hydrolytic behavior. For example, ethylene sulfate releases about 6 kcal./mole more heat on hydrolysis than does dimethyl sulfate, but the heats of hydrolysis of ethylene sulfite and dimethyl sulfite are nearly the same (see ref. 8 and a paper by R. E. Davis in *J. Am. Chem. Soc.*, **84**, 599 (1962)).