

known components from reactions of amides other than 1f were the same ones as listed above, with slight variations in percentages. Analysis by glpc was also performed using column C (50–300°, 2°/min) and no additional components were observed.

**Hydrolysis of Diamides (Fraction D).**—The diamides (380 mg) were hydrolyzed to the corresponding diacids by exactly the same procedure used for hydrolysis of fraction C. This gave diacids (230 mg, 92%) which were esterified with  $\text{CH}_2\text{N}_2$  and analyzed by glpc (column C, 150–300°; 2°/min) and by combined glpc–mass spectrometry giving the following results in peak number (rel retention time, percentage, number of corresponding diamide in text): 1 (1.00, 0.8, 13), 2 (1.26, 6.1, 14), 3 (1.51, 21.9, 15), 4 (1.61, 6.6, 16), 5 (1.77, 25.2, 16), 6 (1.85, 8.7, 17), 7 (2.00, 12.4, 17), 8 (2.09, 7.4, 18), 9 (2.24, 4.9), 10 (2.32, 3.0), 11 (2.55, 1.2). Typical of the mass spectra obtained in this series and characteris-

tic of diesters is that observed from peak 3:  $m/e$  (rel intensity) 241 (10) ( $M - 31$ ), 199 (25); 167 (25), 126 (40), 112 (84), 98 (84), 74 (82), 55 (100). The other peaks simply gave rise to homologous spectra. Branching was firmly established by comparison of retention times to those of authentic straight-chain diesters, for example, dimethyl tridecanedioate, rel retention time 1.66, compared to 1.51 for 15.

**Acknowledgment.**—The authors express their gratitude to S. F. Osman and C. J. Dooley for combined glpc–mass spectral determinations.

**Registry No.**—1b, 24928-30-1; 1d, 41328-62-5; 1e, 41328-72-7; 1f, 41328-73-8; 1g, 4219-50-5; HF-BF<sub>3</sub>, 16872-11-0.

## Conversion of a Saturated to an Unsaturated Acid by Pyridine *N*-Oxide<sup>1a-c</sup>

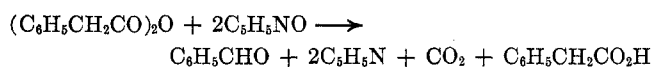
THEODORE COHEN,\* C. K. SHAW, AND JERRY A. JENKINS<sup>1d</sup>

Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260

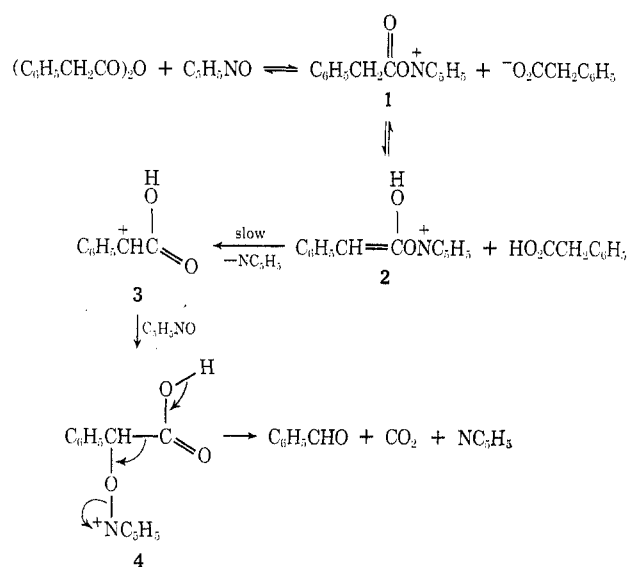
Received May 17, 1973

Oxidation of 2,3-diphenylpropanoic acid by pyridine *N*-oxide in the presence of acetic anhydride yields the normal decarboxylative oxidation product deoxybenzoin (7, 25%) in addition to the *cis* and *trans* isomers of 2,3-diphenylpropenoic acid (8, 20%) and 2-acetoxy-2,3-diphenylpropanoic acid (9, 43%). The production of 8 and 9 is taken as further evidence that a key intermediate bearing a cationic site  $\alpha$  to a carboxyl function (in this case 6) is involved in such reactions. The mass spectral fragmentation pattern of methyl 2,3-diphenylpropenoate is discussed in terms of a 1,3-methoxy migration in the parent radical cation.

Certain carboxylic acid anhydrides which possess an acidic  $\alpha$  hydrogen atom may be oxidatively decarboxylated by aromatic amine oxides.<sup>2-5</sup> For example, the oxidation of phenylacetic anhydride by pyridine *N*-oxide produces benzaldehyde and proceeds according to the following stoichiometry.



In the presence of acetic anhydride, the corresponding carboxylic acid is readily oxidized in a similar manner.<sup>2b,5</sup> The first step in the reaction is thought<sup>2-5</sup> to involve reversible acylation of the *N*-oxide to give cation 1. Deuterium isotope effect studies<sup>6</sup> and the requirement for an  $\alpha$  hydrogen atom<sup>2b,3c,5</sup> suggest the reversible formation of an enol species 2 prior to the rate-determining step in which 2 is attacked in an  $\text{S}_{\text{N}}1'$  manner<sup>7</sup> by a second *N*-oxide molecule to yield the *N*-( $\alpha$ -carboxybenzyloxy)pyridinium ion 4. In the latter step, the reactive electrophilic species 3 would be an



intermediate.<sup>8</sup> Decarboxylative fragmentation of 4 with loss of pyridine would then lead to the major observed products. The scheme is consistent with the kinetics observed by Koenig.<sup>4</sup> Some such electrophilic intermediate has been trapped by acetic acid and by pyridine, each utilized as a solvent.<sup>5</sup> In the present paper, we present additional evidence for a cationic intermediate of type 3 in the oxidation of carboxylic acids by pyridine *N*-oxide.

Although one of the most characteristic reactions of carbocations is the loss of an adjacent proton to yield

(8) The conjugate base of 3, which is the open form of an  $\alpha$ -lactone,<sup>9</sup> appeared as a reasonable intermediate at one time,<sup>8</sup> but Rüchardt<sup>10</sup> has reported experiments, which have been confirmed by Koenig,<sup>10</sup> indicating that the behavior of a related  $\alpha$ -lactone is unaffected by the presence of pyridine *N*-oxide.

(9) O. L. Chapman, P. W. Wojtkowski, W. Adam, O. Rodriguez, and R. Rucktäschel, *J. Amer. Chem. Soc.*, **94**, 1365 (1972).

(10) T. Koenig and T. Barklow, *Tetrahedron*, **25**, 4875 (1969).

(1) (a) Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. (b) Partial support was provided by Grant GU-3184 from the National Science Foundation. (c) Taken, in part, from the Ph.D. thesis of J. A. Jenkins, University of Pittsburgh, Pittsburgh, Pa., 1970. (d) NASA Predoctoral Fellow.

(2) (a) T. Cohen and J. H. Fager, Abstracts, 146th National Meeting of the American Chemical Society, Denver, Colo., Jan 1964, p 36c; (b) T. Cohen, I. H. Song, and J. H. Fager, *Tetrahedron Lett.*, 237 (1965).

(3) (a) C. Rüchardt, S. Eichler, and O. Krätz, *Tetrahedron Lett.*, 233 (1965); (b) C. Rüchardt and O. Krätz, *ibid.*, 5915 (1966); (c) C. Rüchardt, O. Krätz, and S. Eichler, *Chem. Ber.*, **102**, 3922 (1969).

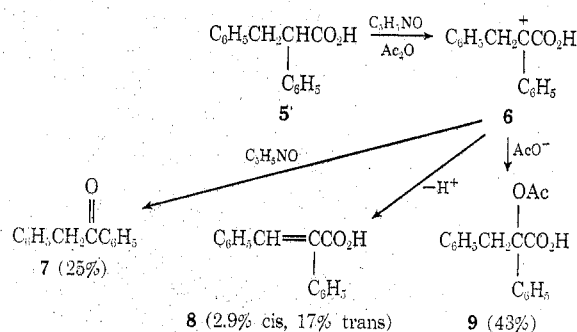
(4) (a) T. Koenig, *Tetrahedron Lett.*, 3127 (1965); (b) T. Koenig, *ibid.*, 2751 (1967).

(5) T. Cohen, I. H. Song, J. H. Fager, and G. L. Deets, *J. Amer. Chem. Soc.*, **89**, 4968 (1967).

(6) J. A. Jenkins and T. Cohen, Abstracts, 160th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1970, ORGN 172.

(7) T. Cohen, G. L. Deets, and J. A. Jenkins, *J. Org. Chem.*, **34**, 2550 (1969).

an olefin, there are no reported cases of the production of an  $\alpha,\beta$ -unsaturated carboxylic acid from the saturated acid by means of pyridine *N*-oxide. Such a process might be expected to be quite favorable for the cation **6**, which, after proton loss, would yield the extensively conjugated 2,3-diphenylpropenoic acid (**8**). The electrophilic species **6** would presumably be an intermediate in the oxidative decarboxylation of 2,3-diphenylpropanoic acid (**5**) by pyridine *N*-oxide. Alternatively, attack by the *N*-oxide on **6** would lead to deoxybenzoin (**7**), the expected redox product.



When a benzene solution of pyridine *N*-oxide was slowly added dropwise to a refluxing solution of 2,3-diphenylpropanoic acid (**5**) and excess acetic anhydride in benzene, under nitrogen, the expected products (**7**, **8**, and **9**) were formed in the indicated yields, based on 2,3-diphenylpropanoic acid consumed. A 3.2% yield of benzoin was also obtained. The *cis*- and *trans*-2,3-diphenylpropenoic acids (**8**) were identified by comparison of the glpc retention times and mass spectra of their methyl esters with those of authentic samples. The benzoin and deoxybenzoin had the same retention times as authentic samples. The ester **9** was identified by comparison of the spectral data of an isolated sample with those of an authentic specimen and by hydrolysis to the known 2,3-diphenylglycolic acid, which was identical with an authentic sample.

The benzoin may very well arise by oxidation of the deoxybenzoin by traces of air in the nitrogen that flowed through the system throughout the reaction. A control test indicated that air oxidation occurs in the presence of pyridine, but not in its absence, even when pyridine *N*-oxide is present. Benzoin is also not produced by the reaction of deoxybenzoin (**7**) with pyridine *N*-oxide in the presence of acetic anhydride.

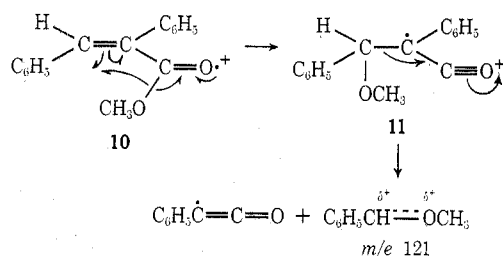
The production of acetylmandelic acid from the reaction of phenylacetic acid with pyridine *N*-oxide in the presence of acetic anhydride has been noted previously, the highest yield (10.5%) being obtained in acetic acid as solvent.<sup>5</sup> The much higher yield in the present case may be due, in part, to the deficiency of pyridine *N*-oxide as maintained by its slow addition.

It is very difficult to rationalize the production of the unsaturated acids **8** and the ester **9** without invoking an intermediate with an electrophilic site at the  $\alpha$  position. In view of the previous evidence for such an intermediate in the production of the aldehydes and ketones as well, it is satisfying to consider the same species (**6**) as the precursor of all three major products.

An interesting anomaly was observed in the mass spectral fragmentation pattern of the methyl ester (**10**) of 2,3-diphenylpropenoic acid. The base peak for the ester was *m/e* 121, corresponding to a P - 117 frag-

ment or loss of  $\text{C}_6\text{H}_5\text{CCO}$ . Such an abundant ion could arise by a 1,3-methoxyl shift and subsequent bond cleavage.

The ion also occurs, but in low abundance (2%),<sup>11</sup> in the mass spectrum of the related ester methyl 3-phenylpropenoate (methyl cinnamate). The most abundant ion (P - 31) of the latter compound is due to the loss of the methoxyl radical. It is likely that the benzene ring lowers the energy of activation for the rearrangement of **10** to **11** by stabilizing the develop-



ing radical so that this process becomes faster than loss of a methoxyl radical.

### Experimental Section<sup>12</sup>

**2,3-Diphenylpropanoic Acid (5).**—This compound was prepared<sup>13</sup> by the hydrolysis of 2,3-diphenylpropionitrile, which was itself prepared<sup>14</sup> by benzylation of the sodium salt of phenylacetone. The acid had mp 88–89°; it was long ago reported<sup>14</sup> that this material exists in three modifications with mp 82, 88–89, and 95–96°, and all three melting points have been reported in subsequent work.<sup>13,15</sup> The acid had an nmr ( $\text{CCl}_4$ ) singlet at  $\tau$  - 1.55 (1 H, acid H), multiplet at 2.70–3.15 (10 H, aryl H), and multiplet at 6.10–7.28 ppm (3 H,  $\alpha$  and  $\beta$  H).

**Reaction of 2,3-Diphenylpropanoic Acid (5) with Pyridine *N*-Oxide.**—A solution of 1.6 g (17 mmol) of pyridine *N*-oxide in 20 ml of benzene was added dropwise over a period of 2 hr to a refluxing solution of 1.9 g (8.4 mmol) of 2,3-diphenylpropanoic acid and 3.5 g (34 mmol) of acetic anhydride in 20 ml of benzene under a nitrogen atmosphere. After the solution had been heated at reflux for 18 hr, another 1.6 g of pyridine *N*-oxide in 15 ml of benzene was added in one portion. This process was repeated two additional times at 12-hr intervals and the mixture was maintained at reflux for 12 hr after the last addition of the *N*-oxide. The cooled reaction mixture was divided into two parts.

The major part (81% by weight) was thoroughly washed with saturated sodium bicarbonate (125 ml). The alkaline aqueous solution was washed once with ether and the ether wash was combined with the organic layer. The aqueous solution was made strongly acidic with dilute HCl and extracted with ether. Evaporation of the dried ( $\text{MgSO}_4$ ) ether extract gave 0.53 g of acidic material, which was treated with ethereal diazomethane to give the following four methyl esters in order of glpc retention

(11) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967, p 202.

(12) Melting points were determined on a Thomas-Kofler micro hot stage utilizing a stage-calibrated thermometer and are thus corrected. Boiling points are uncorrected. Reactions were performed under a continuous stream of nitrogen. Infrared spectra were determined on a Beckman IR-8 spectrophotometer. Proton magnetic resonance spectra were determined on a Varian A-60 instrument; chemical shifts are reported on the  $\tau$  scale, relative to internal tetramethylsilane. Analytical gas chromatography was performed on a Varian 1860-3 instrument equipped with a flame ionization detector and a Disc integrator. For determining yields, the flame responses of authentic samples were calibrated against those of various standards. Isomers were assumed to have identical flame responses. Mass spectra were determined at 70 eV on an LKB-9000 combined gas chromatograph-mass spectrometer.

(13) N. Campbell and E. Ciganek, *J. Chem. Soc.*, 3834 (1956).

(14) W. Miller and G. Rhode, *Chem. Ber.*, **25**, 2017 (1892).

(15) R. B. Meyer and C. H. Hauser, *J. Org. Chem.*, **26**, 3696 (1961); H. Normant and B. Angelo, *Bull. Soc. Chim. Fr.*, 810 (1962); D. Y. Curtin, J. A. Kampmeier, and M. L. Farmer, *J. Amer. Chem. Soc.*, **87**, 874 (1965).

time: methyl 2,3-diphenylpropanoate, methyl *cis*-2,3-diphenylpropanoate, methyl *trans*-2,3-diphenylpropanoate, and methyl 2-acetoxy-2,3-diphenylpropanoate. The first three esters were identified by comparison of retention times and mass spectra (glpc-mass spectra) with those of authentic samples prepared by similar methylation of the saturated acid **5** and the two unsaturated acids **8** (Frinton Laboratories). The mass spectra of the two unsaturated esters were nearly identical: *m/e* (rel intensity, assignment) 238 (71, P<sup>+</sup>), 207 (36, P<sup>+</sup> - OMe), 179 (79, P<sup>+</sup> - CO<sub>2</sub>Me), 178 (64, C<sub>6</sub>H<sub>5</sub>C≡CC<sub>6</sub>H<sub>5</sub><sup>+</sup>), 165 (14), 152 (21), 121 (base, P<sup>+</sup> - C<sub>6</sub>H<sub>5</sub>C=C=O, see text), 102 (14), 89 (29), 77 (29, C<sub>6</sub>H<sub>5</sub><sup>+</sup>), and 51 (29).

The last component was isolated in the following way. The above mixture of methyl esters was dissolved in 5 ml of methanol and injected by syringe into a flask containing 25 mg of pre-reduced Adams catalyst in 2 ml of methanol. The mixture was stirred under a positive pressure of hydrogen for 6 hr, and the catalyst was separated by filtration. By glpc, the methanol was shown to contain only methyl 2,3-diphenylpropanoate and methyl 2-acetoxy-2,3-diphenylpropanoate. The mixture was separated into its components by chromatography on a silica gel column (10 g, Baker) using *n*-pentane and benzene as eluents. The acetoxy ester, which eluted last, was subject to flash distillation (260° bath temperature, 2 mm) to afford 76 mg of pure material. No decomposition to the  $\alpha,\beta$ -unsaturated esters of **8** occurred upon gas chromatographic analysis of this ester. The infrared, nmr, and mass spectra of the acetoxy compound were identical with those of an authentic sample: ir (neat) 1740 (C=O), 1250 (COC), 753, 730, 705 cm<sup>-1</sup>; nmr (CDCl<sub>3</sub>)  $\tau$  2.6-3.7 (m, 10 H, aromatic), 6.3 (center of AB quartet, 2 H, benzylic protons), 6.43 (s, 3 H, OCH<sub>3</sub>), and 7.95 (s, 3 H, CH<sub>3</sub>CO); mass spectrum *m/e* 238 (P<sup>+</sup> - HOAc), 207 (P<sup>+</sup> - HOAc - OCH<sub>3</sub> or P<sup>+</sup> - C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>), 165 (P<sup>+</sup> - C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub> - CH<sub>2</sub>CO), 105, 77 (C<sub>6</sub>H<sub>5</sub><sup>+</sup>), 51, 43.

The benzene solution of the nonacidic fraction was dried and analyzed by glpc. It consisted of benzoin and deoxybenzoin, identified by coinjection with authentic samples.

The minor portion (19%) of the original reaction mixture was treated with an ethereal solution of diazomethane, a weighed quantity of benzophenone was added as an internal standard, and quantitative glpc analysis was performed on an OV-17 column, with temperature programmed at 6°/min from 170 to 190°. The yields of the five products are indicated in the text.

It was shown that *cis*-2,3-diphenylpropanoic acid did not isomerize to the *trans* isomer when its benzene solution containing acetic anhydride and pyridine *N*-oxide was maintained at reflux for 36 hr.

**Hydrolysis of Methyl 2-Acetoxy-2,3-diphenylpropanoate.**—A solution of the acetoxy ester (71 mg), isolated as above, in 1 ml of ethanol was treated with 1 ml of 1 *N* potassium hydroxide in 1 ml of 95% ethanol. The homogeneous solution was stirred at room temperature for 18 hr under nitrogen. It was acidified with dilute hydrochloric acid and extracted with ether. The ether extract was dried (MgSO<sub>4</sub>) and evaporated to give 44 mg (76% crude yield) of yellowish solid, mp 125-140°. Recrystallization

from benzene gave a colorless solid, mp 164-165° (lit.<sup>16</sup> mp 168.0-168.5°); mixture melting point with an authentic sample (mp 166.0-166.5°) of 2,3-diphenylglycolic acid was 165-167°. The ir and nmr spectra of this material were identical with those of the authentic sample.

**2,3-Diphenylglycolic Acid.**—A solution prepared by mixing 10 g of chalcone oxide<sup>17</sup> and 13 ml of 30% sodium hydroxide with 50 ml of 95% ethanol was heated at reflux for 90 min, poured into 500 ml of water, and acidified with 4 *N* hydrochloric acid (20 ml). The yellow precipitate (7.5 g, mp 161-164°) was recrystallized from benzene to give a white solid, mp 166.0-166.5° (lit.<sup>16</sup> mp 168.0-168.5°). Its nmr spectrum (acetone-*d*<sub>6</sub>) corresponded with that in the literature.<sup>16</sup>

**Methyl 2-Acetoxy-2,3-diphenylpropanoate.**—A solution of 2.0 g of 2,3-diphenylglycolic acid in 10 ml of anhydrous ether was cooled in an ice bath and treated with excess diazomethane in ether to give 2.1 g of the methyl ester, mp 88-89° (lit.<sup>18</sup> mp 88-89°); its nmr and ir spectra were consistent with the assigned structure. A mixture of 1.34 g (52.3 mmol) of this methyl ester, 10 ml of acetyl chloride, and 10 ml of *N,N*-dimethylaniline in 30 ml of chloroform was heated at reflux (62°) for 36 hr, cooled in an ice bath, and thoroughly mixed with 100 ml of ice water. The deep blue organic layer was washed extensively with water and saturated sodium bicarbonate solution. Evaporation of the dried (magnesium sulfate) organic layer yielded a deep brown oil which was chromatographed on 25 g of silicic acid gel (Baker) using benzene as the mobile phase. The resulting 1.75 g of clear, colorless liquid was distilled to give a glassy liquid (1.22 g, 78.5% yield), bp 139-140° (0.2 mm). Its spectral properties are given above.

*Anal.* Calcd for C<sub>15</sub>H<sub>18</sub>O<sub>4</sub>: C, 72.47; H, 6.08. Found: C, 72.58; H, 6.15.

**Oxidation of Deoxybenzoin (7) to Benzoin.**—A solution of 1.65 g of deoxybenzoin and 2 ml of pyridine in 20 ml of benzene was allowed to remain at room temperature under slow air ebullition for 24 hr. Analysis by glpc indicated that about 3% of benzoin was produced. None of the latter was produced in the absence of pyridine, even when pyridine *N*-oxide was present. Neither was benzoin produced when a benzene solution of deoxybenzoin containing acetic anhydride and pyridine *N*-oxide was maintained at reflux for 2.5 days.

**Acknowledgment.**—We wish to thank Mr. John Wood and Mr. Glen Herman for technical help and the former for a useful discussion.

**Registry No.**—5, 3333-15-1; *cis*-**8** methyl ester, 41366-87-41; *trans*-**8** methyl ester, 36854-27-0; **9** methyl ester, 41366-89-6; pyridine *N*-oxide, 694-59-7; 2,3-diphenylglycolic acid, 76-93-7; chalcone oxide, 5411-12-1.

(16) E. K. Raunio and W. A. Bonner, *J. Org. Chem.*, **31**, 396 (1966).

(17) E. Rohrmann, R. G. Jones, and H. A. Shonle, *J. Amer. Chem. Soc.*, **66**, 1856 (1944).

(18) M. Avramoff and Y. Sprinzak, *J. Amer. Chem. Soc.*, **85**, 1655 (1963).