

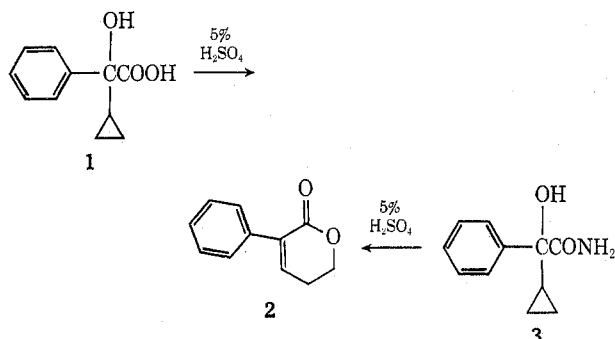
Boron Trifluoride Catalyzed Rearrangement of Cyclopropylphenylglycolamide

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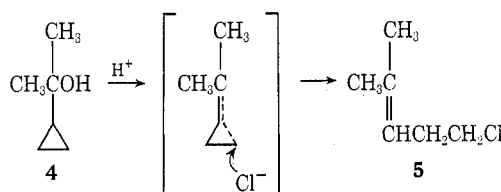
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A prior communication² described acid-catalyzed rearrangement of cyclopropylphenylglycolic acid (**1**) to form 3-phenyl-5,6-dihydro-2-pyrone (**2**). Treatment of cyclopropylphenylglycolamide (**3**) under the

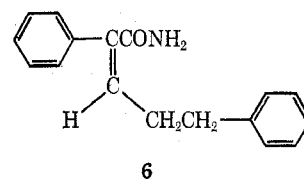


same experimental conditions utilized for **1** (5% aqueous sulfuric acid) afforded an equivalent yield of the dihydropyrone **2**. However, treatment of **3** with boron trifluoride etherate in anhydrous benzene provided, in addition to some polymeric material, a sizable amount of a nitrogen-containing solid whose infrared spectrum suggested the presence of amide carbonyl and whose mass spectrum revealed a parent ion of mass 251, corresponding to a formula of C₁₇H₁₇NO. These data suggested that the product contained an additional benzene ring, and that there was solvent participation in the BF₃-mediated rearrangement. Bruylants and Dewael³ described formation of **5** by treatment of cyclopropyldimethylcarbinol (**4**) with HCl; the validity of this work was confirmed by Favorskaya and Fridman.⁴ On the basis of a non-classical carbonium ion structure proposed for some cyclopropylmethyl cations,^{5,6} the Bruylants-Dewael reaction leading to **5** can be described as indicated.



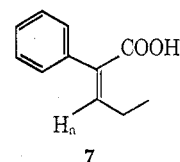
In the present work, it was speculated that a similar ion derived from **3** reacted with the benzene solvent to form **6**.

- (1) (a) National Science Foundation Undergraduate Research Participant, summer, 1971; (b) summer, 1970.
- (2) L. L. Darko and J. G. Cannon, *J. Org. Chem.*, **32**, 2352 (1967).
- (3) P. Bruylants and A. Dewael, *Bull. Sci. Acad. Roy. Belg.*, **14**, 140 (1928).
- (4) T. A. Favorskaya and S. A. Fridman, *J. Gen. Chem. USSR*, **15**, 421 (1945).
- (5) J. D. Roberts and R. H. Mazur, *J. Amer. Chem. Soc.*, **73**, 2509 (1951).
- (6) M. Vogel and J. D. Roberts, *J. Amer. Chem. Soc.*, **88**, 2262 (1966).

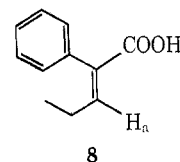


Nmr data were consistent with this structure. Ozonolysis of **6** permitted isolation of hydrocinnamic acid, which is likewise consistent with the proposed structure. Only a minute amount of the other ozonolysis product, phenylglyoxylamide, could be isolated from this reaction; a significant amount of nitrogen-containing polymeric material apparently was formed during the work-up of the reaction. Claisen^{7,8} described the ease of polymerization of phenylglyoxylamide under acidic conditions similar to those employed in the work-up of the ozonolysis reaction.

The mass spectrum of **6** showed prominent ions at *m/e* (rel intensity) 251 (100, M⁺), 160 (20, M-CH₂C₆H₅), 118 (96, phenylketene), and 91 (87, tropylium), which provide further evidence for its structure. A uv spectrum of **6** (ethanol) revealed λ 249 nm (ε 14,800), 283 sh (1260), and 291 (670). These data are consistent with those for compounds containing a styryl chromophore;⁹ moreover, they seem to indicate the configuration about the double bond in **6**. Nilsson¹⁰ reported significantly different uv spectra for **7** and **8**.



λ 249 nm (ε 11,000)
291 (370) (ethanol)
H_a = λ 6.25 (carbon tetrachloride)



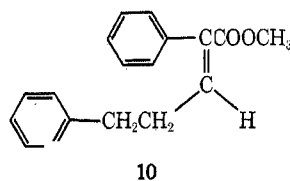
λ 235 nm sh (ε 5500) (ethanol)
H_a = 7.17 (beneath phenyl H's)
(carbon tetrachloride)

Since the primary amides of **7** and **8** would be expected to display similar uv characteristics, the parallel agreement of the uv data for **6** and **7** suggests that **6** is (Z)-2,5-diphenyl-2-pentenoamide. This assignment is corroborated by comparison of the chemical shifts of the olefinic proton of **6** (δ 6.05) with those of the olefinic protons in **7** and **8**.¹¹ The remainder of the nmr spectrum of **6** is consistent with the proposed structure, which seems firmly established.

Catalytic hydrogenation of **6** permitted isolation of the saturated amide **9**. In studies aimed at unequivocal synthesis of **6**, phenylglyoxylamide was treated with a Wittig reagent derived from triphenyl-3-

- (7) L. Claisen, *Ber.*, **10**, 1665 (1877).
- (8) L. Claisen, *Ber.*, **12**, 632 (1879).
- (9) C. G. Overberger and D. Tanner, *J. Amer. Chem. Soc.*, **77**, 369 (1955).
- (10) K. Nilsson, *Acta Chem. Scand.*, **19**, 612 (1965).
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phenylpropylphosphonium bromide; no identifiable product could be isolated. However, a reaction between this Wittig reagent and methyl phenylglyoxylate permitted isolation of methyl 2,5-diphenyl-2-pentenoate (10). Repeated attempts to effect am-



monolysis on 10 failed; either starting material was recovered or (under drastic conditions) the reaction mixture turned into an intractable tar. Attempts to effect acid- or base-catalyzed hydrolysis of 6 or 10 resulted in formation of complex mixtures. The olefinic proton of 10 appears to be buried beneath the aromatic protons. In light of the olefinic assignments in 7 and 8, 10 is concluded to be *E* isomer, possessing a configuration opposite that of 6.

A reasonable explanation for the rearrangement of 3 to the dihydropyrone 2 with aqueous sulfuric acid as contrasted with the behavior of 3 in the presence of boron trifluoride etherate and benzene is that, in aqueous environment, 3 first hydrolyzes to the acid 1, which then rearranges to the dihydropyrone 2. In boron trifluoride-benzene, no hydrolysis can occur and the amide moiety does not, under the reaction conditions, participate intramolecularly. The prior finding² that treatment of cyclopropylphenylglycolic acid (1) with boron trifluoride in benzene induces formation of the dihydropyrone 2 suggests that the differences in reaction products described herein cannot be related to the difference(s) in catalysts employed.

Experimental Section

Melting points were determined in open capillaries on a Thomas-Hoover Uni-melt apparatus and are corrected. Ir spectra were recorded in a Beckman IR-5-A instrument and nmr spectra were obtained on a Varian Associates T-60 instrument. Uv spectra were recorded on a Beckman DK-2 instrument. Elemental analyses were performed by the Microanalytical Service, College of Pharmacy, University of Iowa. Mass spectral data were supplied by Sadtler Research Laboratories, Inc., Philadelphia, Pa.

(*Z*)-2,5-Diphenyl-2-pentenoamide (6).—Cyclopropylphenylglycolamide (3)² (1.60 g, 0.0083 mol) was warmed in 150 ml of anhydrous, thiophene-free benzene until solution was achieved; then 10 ml of boron trifluoride etherate was added. The mixture was refluxed for 1 hr, allowed to stand at room temperature for 48 hr, then refluxed for 4 hr. The reaction mixture was cooled and decanted from gummy material which coated the sides of the reaction vessel. The benzene solution was washed several times with water and dried (Na₂SO₄), and volatiles were removed under reduced pressure to leave an off-white solid which was recrystallized from aqueous ethanol to afford 1.16 g (56%) of well-formed needles: mp 136–138°; ir (CHCl₃) 1670 cm⁻¹ (amide

C=O); nmr (CDCl₃) δ 2.7–3.0 (m, 4 H), 5.15 (unresolved m, 1 H), 5.9–6.2 (m, 2 H), 7.2–7.5 (m, 10 H); *m/e* 251.1323 (M⁺).

2,5-Diphenylpentanoamide (9).—Compound 6 (0.83 g, 0.0033 mol) in 50 ml of ethanol was hydrogenated in the presence of 0.1 g of 10% Pd/C in a Parr shaker apparatus at room temperature and an initial pressure of 47 psig. When 1 equiv of H₂ was absorbed, the catalyst was removed by filtration. The water-white filtrate was evaporated under reduced pressure to afford a colorless oil which crystallized on standing and was recrystallized from 50% ethanol to afford 0.43 g (51%) of platelets: mp 90–92°; ir (CHCl₃) 1670 cm⁻¹ (amide C=O); nmr (CDCl₃) δ 1.70 center (unresolved m, 4 H), 2.6 center (unresolved m, 2 H), 3.40 (t, 1 H), 7.2–7.5 (m, 10 H).

Anal. Calcd for C₁₇H₁₉NO: C, 80.75; H, 7.51; N, 5.54. Found: C, 80.60; H, 7.75; N, 5.21.

Methyl (*E*)-2,5-Diphenyl-2-pentenoate (10).—Sodium amide was prepared from 100 ml of liquid NH₃ and 1.15 g (0.05 g-atom) of Na according to a procedure of Bestmann,¹² and a Wittig procedure of Bestmann and Hartung¹³ was employed. Triphenyl-3-phenylpropylphosphonium bromide¹² (18.0 g, 0.04 mol) was added to the suspension of sodium amide in liquid NH₃ in one portion. The NH₃ was permitted to evaporate under N₂ and 200 ml of Na-dried benzene was added. The reaction mixture assumed a deep red-brown color and it was refluxed for 8 hr. The mixture was cooled and 6.56 g (0.04 mol) of methyl phenylglyoxylate (Aldrich Chemical Co.) in 30 ml of Na-dried benzene was added dropwise with stirring. The resulting tan reaction mixture was stirred for 1 hr, then it was filtered, and volatiles were removed from the filtrate under reduced pressure (steam bath) to leave a brown oil. This was distilled, collecting the fraction with bp 140–160° (1.3 mm), which was redistilled, bp 145–152° (0.7 mm), to yield 2.60 g (25%) of a straw-colored liquid: ir (CHCl₃) 1690 cm⁻¹ (ester C=O); nmr (CDCl₃) δ 2.3–2.9 (m, 4 H), 3.75 (s, 3 H), 7.0–7.4 (unresolved m, 11 H).

Anal. Calcd for C₁₈H₁₈O₂: C, 81.20; H, 6.77. Found: C, 81.56; H, 6.87.

Ozonolysis of (*Z*)-2,5-Diphenyl-2-pentenoamide (6).—Compound 6 (0.32 g, 0.00127 mol) in 200 ml of Na₂SO₄-dried methanol, maintained at –60°, was treated with excess ozone. Methanol was removed from the reaction mixture under reduced pressure from a water bath (45–50°). The residual transparent oil was treated with 35 ml of 90% formic acid and 17 ml of 30% hydrogen peroxide, and this mixture was gently warmed on a steam bath until spontaneous reflux began. When the mixture ceased to boil spontaneously, it was refluxed vigorously for 1 hr and cooled, and excess NaHCO₃ was added. The resulting mixture was extracted repeatedly with ether (extract A); then the aqueous phase was acidified with sulfuric acid and excess KI was added. Na₂SO₄ was then added until the iodine color was discharged, and the resulting mixture was extracted several times with ether. Ether was removed from the pooled extracts to afford an oil which partly solidified on standing and was recrystallized from water to afford a low-melting (30–34°) solid whose ir spectrum (CHCl₃) was superimposable upon a similar spectrum of an authentic sample (mp 40–42° from water) of hydrocinnamic acid. Tlc of the ozonolysis product in several solvent systems gave *R_f* values identical with those of the authentic sample of hydrocinnamic acid. Work-up of extract A provided a small amount of hydrocinnamaldehyde (identified by comparison of its ir spectrum with that of an authentic sample) and, in addition to polymeric material, a very small amount of off-white crystals, mp 88–91°, was isolated (lit.⁷ mp for phenylglyoxylamide 91°).

Registry No.—3, 13019-40-4; 6, 40600-00-8; 9, 40600-01-9; 10, 40600-02-0; benzene, 71-43-2; boron trifluoride etherate, 109-63-7; triphenyl-3-phenylpropylphosphonium bromide, 7484-37-9; methyl phenylglyoxylate, 15206-55-0.

(12) H.-J. Bestmann, *Angew. Chem., Int. Ed. Engl.*, **4**, 583 (1965).

(13) H.-J. Bestmann and H. Hartung, *Chem. Ber.*, **99**, 1198 (1966).