

firmation the benzylamine salt of the acid prepared by sodium and amyl alcohol reduction was made and gave no melting point depression when mixed with IX.

Isomerization of *cis*-2-Phenyl-1,2,5,6-tetrahydrobenzoic Acid (III).—The adduct of 1-phenyl-1,3-butadiene with acrylic acid, 0.2 g., m. p. 120–122°, was methylated in ether solution with diazomethane. After excess diazomethane was decomposed with glacial acetic acid, the ether and methyl acetate were distilled *in vacuo*. A solution of 0.1 g. of sodium in 10 cc. of methanol was added. After the solution was refluxed for seven and one-half hours, an equal volume of water containing 2 g. of potassium hydroxide was added. Refluxing was then continued for thirteen and one-half hours. Two volumes of water was added and the solution was treated with charcoal while hot. The solution was filtered and acidified, and the white solid, *trans*-2-phenyl-1,2,5,6-tetrahydrobenzoic acid, was separated by filtration, m. p. 101.5–102.5°. This product gave no melting point depression when mixed with the acid prepared by saponification of the adduct (VI) of 1-phenyl-1,3-butadiene and ethyl acrylate.

Isomerization of *cis*-2-Phenylhexahydrobenzoic Acid (IV).—The acid prepared by hydrogenation of the adduct of 1-phenyl-1,3-butadiene and acrylic acid was methylated and treated with sodium methoxide by the methods previously described. The crude product was treated with charcoal in hot ligroin (b. p. 90–120°) to give a white product, m. p. 105–107°. This melting point was not depressed by mixing with the product of hydrogenation of *trans*-2-phenyl-1,2,5,6-tetrahydrobenzoic acid (VI).

2-Phenyl-1,2,5,6-tetrahydroacetophenone (XI).—Methyl vinyl ketone (X), b. p. 35–40° at 120–130 mm., was prepared by cooling the du Pont azeotrope in Dry Ice-acetone, treating with potassium carbonate and anhydrous calcium chloride to remove acetic acid and water, and distilling *in vacuo* into a receiver cooled by Dry Ice-acetone. Twelve grams of ketone, 20 g. of 1-phenyl-1,3-butadiene (I), b. p. 64–72° at 4 mm., and 0.05 g. of hydroquinone were heated for seventeen hours at 100–130° in a sealed tube. The reaction mixture was dissolved in ether and the ether solution was washed with water, dried over anhydrous magnesium sulfate and distilled. Nineteen and

one-half grams (62%) of a colorless viscous oil, b. p. 118–122° at 1 mm., was obtained.

Anal. Calcd. for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 84.39, 84.26; H, 8.11, 8.38.

Hydrogenation of 2-Phenyl-1,2,5,6-tetrahydroacetophenone (XI).—Ten grams of 2-phenyl-1,2,5,6-tetrahydroacetophenone, 100 cc. of absolute alcohol and 0.1 g. of platinum oxide were shaken under hydrogen at 10 pounds pressure. The theoretical amount of hydrogen was absorbed in twenty minutes. The catalyst was removed by filtration, and 2-phenylhexahydroacetophenone (XII) was distilled as 9 g. of clear water-white oil, b. p. 115–120° at 1.5 mm., n_{25}^{25} 1.5261. The distillate solidified and was recrystallized from methanol to give a white solid, m. p. 78–78.5°.

Anal. Calcd. for $C_{14}H_{18}O$: C, 83.12, H, 8.97. Found: C, 82.97, 83.07; H, 8.78, 8.82.

This melting point corresponds to that of the 2-phenylhexahydroacetophenone produced by Kipping and Perkin¹² by acetoacetic ester synthesis from 1-phenyl-1,5-dibromopentane.

Acknowledgments.—The writers express their appreciation for grants from the Research Corporation which supported this investigation and are indebted to Rohm and Haas Company for research samples of ethyl acrylate and aqueous acrylic acid and to the du Pont Company for a sample of methyl vinyl ketone azeotrope.

Summary

Adducts of 1-phenyl-1,3-butadiene with acrylic acid, ethyl acrylate and methyl vinyl ketone are shown to be 1-substituted-2-phenylcyclohexene-3 derivatives.

(12) Kipping and Perkin, *J. Chem. Soc.*, 304–323 (1890).

KNOXVILLE, TENNESSEE RECEIVED NOVEMBER 8, 1948

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE POLYTECHNIC INSTITUTE OF BROOKLYN]

The Diene Synthesis of 1-Phenyl-1,3-butadiene with Acrylonitrile and Methyl Vinyl Ketone

BY LEO REICH¹ AND ERNEST I. BECKER

The conflicting literature concerning *cis-trans* versus *ortho-meta* isomerism in the addition of 1-phenyl-1,3-butadiene to unsymmetrical dienophiles has been reviewed by Ropp and Coyner.² In view of the proof by Ropp and Coyner that only *ortho*-substitution results, it seemed unusual to find that the addition of *trans*-piperylene to acrylonitrile gives about 10% of *meta*-substituted product in addition to the major *ortho*-substituted product,³ while in the addition of methyl acrylate,⁴ acrolein⁵ and crotonaldehyde⁵ to piperylene only

the products with the diene methyl ortho to the aldehyde or ester group were found. In view of these results, it seemed desirable to extend the diene synthesis with 1-phenyl-1,3-butadiene to acrylonitrile and methyl vinyl ketone.

The condensation of acrylonitrile with 1-phenyl-1,3-butadiene gives a colorless, viscous liquid (I-1) (see Chart I) in 60% yield. The product is unsaturated with respect to bromine in carbon tetrachloride, and its analysis is in accord with an adduct consisting of one molecule each of 1-phenyl-1,3-butadiene and acrylonitrile.

The attempted hydrolysis of this nitrile with alkali took place only very slowly, so that an alternate proof of structure was adopted. This very slow hydrolysis suggests that the compound may be the *cis*-*ortho*-derivative. The nitrile was aromatized in 32% yield with sulfur and then

(1) Taken from the thesis submitted by L. Reich in partial fulfillment of the requirements for the degree of Master of Science.

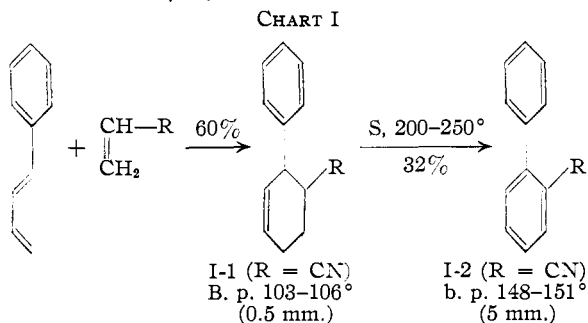
(2) G. A. Ropp and E. C. Coyner, *THIS JOURNAL*, **71**, 1832 (1949).

(3) R. L. Frank, R. D. Emmick and R. S. Johnson, *ibid.*, **69**, 2313 (1947).

(4) J. S. Meek and J. W. Ragsdale, *ibid.*, **70**, 2502 (1948).

(5) H. L. Holmes, K. Alcock, D. G. Demianiw, J. W. Robinson, C. E. S. Rooney and F. A. Sundberg, *Can. J. Research*, **26B**, 248 (1948).

hydrolyzed in two steps in 56% yield to 2-phenylbenzoic acid (I-4).



I-3: I-2, R = CONH₂ (84% from I-2), m. p. 174–175°.
 I-4: I-2, R = CO₂H (66% from I-3), m. p. 110.5–111.5°.

The condensation of 1-phenyl-1,3-butadiene with methyl vinyl ketone⁶ gives an unsaturated, colorless, oily ketone in 54% yield. On two occasions this ketone gave two semicarbazones, m. p. 148–150°, and m. p. 164–165°. A mixture of the two melted from 148–164°, but the melting point of the resolidified melt was 162–163°. Analyses of both semicarbazones agreed with the theoretical value. The explanation for the two may be due to *cis-trans* isomerism or to polymorphism.

The unsaturated product was hydrogenated to the saturated ketone. This ketone gave the expected 2,4-dinitrophenylhydrazone and alkaline permanganate converted it to the known 2-phenylcyclohexane-1-carboxylic acid. Again, no *meta*-substituted product was obtained.

Experimental

All temperatures are uncorrected.

Starting Materials.—1-Phenyl-1,3-butadiene was prepared according to Grummitt and Becker.⁷ Acrylonitrile, obtained from Eastman Kodak Co., gave a negative test for acetylenic compounds with bromine in carbon tetrachloride⁸ and was used as such. Methyl vinyl ketone was separated from its aqueous azeotrope⁹ immediately before use by cooling to 0°, saturating with anhydrous sodium carbonate, decanting the organic layer through a filter, drying over anhydrous calcium chloride for fifteen minutes, filtering and distilling, b. p. 30° (115 mm.).

1-Phenyl-1,3-butadiene and Acrylonitrile

The Adduct I-1 (see Chart I).—A mixture of 26 g. (0.20 mole) of 1-phenyl-1,3-butadiene, 14 g. (0.27 mole, 35% excess) of acrylonitrile, and 10 mg. of hydroquinone was refluxed on a steam-bath for nine hours. At this time the solution was orange. The reaction mixture was transferred to a Claisen flask and distilled under nitrogen at reduced pressure to give 26.0 g. of light yellow, viscous oil, b. p. 150–153° (5 mm.); redistillation gave 23 g. (0.13 mole, 63%) of colorless oil, b. p. 119–121° (1 mm.).

Anal. Calcd. for C₁₃H₁₃N: N, 7.65. Found: N, 7.61, 7.73.¹⁰

(6) While this work was being prepared for publication, Ropp and Coyner² also reported that 1-phenyl-1,3-butadiene adds to methylvinyl ketone. They found, as is shown here, that the adduct is *ortho*-substituted (THIS JOURNAL, **71**, 1832 (1949)).

(7) O. Grummitt and E. I. Becker, *ibid.*, **70**, 149 (1948).

(8) E. L. Carpenter, U. S. Patent 2,382,383, August 14, 1945.

(9) Kindly furnished by E. I. du Pont de Nemours and Company and purified according to directions supplied.

(10) All analyses were performed by Dr. F. Schwartzkopf, 62-12 79th Street, Elmhurst, L. I.

Aromatization of I-1: Compound I-2.—Five grams (0.027 mole) of compound I-1 was mixed with 1.65 g. (0.052 atom) of sulfur and heated at 200–250° for one-half hour and then at 250° for one and one-half hours. At this point 50 mg. of zinc dust was added and the mixture maintained at 200° for fifteen minutes. After cooling, the red residue was taken up in ether, filtered into a 10-ml. Claisen flask and distilled twice to give 1.5 g. (0.0083 mole, 32%) of light yellow 2-phenylbenzonitrile, b. p. 148–151° (5 mm.) (reported, 174° (13 mm.),¹¹ 176–177° (16 mm.)¹²).

Conversion of I-2 to I-3.—This step and the following one were carried out according to Zaheer and Faseeh.¹³ Three and six-tenths grams (20 mmoles.) of 2-phenylbenzonitrile (I-2) was refluxed with 45 ml. of 20% alcoholic potassium hydroxide for three hours. After distilling the alcohol and cooling at 0° overnight, 3.9 g. of crude yellow solid, m. p. 160–166°, was obtained. Four crystallizations from alcohol-water of 3.4 g. (19.0 mmoles.) of the crude material gave 2.85 g. (14.4 mmoles., 83.3%) of 2-phenylbenzamide, m. p. 174–175° (reported, 176°,¹⁴ 177°^{13,15}) and 0.5 g. of a red brown gum. This gum was not further investigated.

Hydrolysis of I-3 to I-4.—Three-tenths gram (1.52 mmole.) of I-3 was refluxed with 9 ml. of 20% aqueous hydrochloric acid for two hours. Upon cooling a solid precipitated which was not entirely soluble in hot 10% sodium carbonate solution. The insoluble portion was treated once more with acid. After extraction with sodium carbonate solution, 50 mg. of a green solid remained which was not hydrolyzed further with acid. The combined alkaline extracts were acidified and cooled to give 0.20 g. (1.0 mmole., 66%) of 2-phenylbenzoic acid, m. p. 108–110°. Recrystallization from aqueous alcohol gave m. p. 110.5–111.5° (reported, 111°,¹⁴ 112.5°,¹⁶ 113.5°¹³).

1-Phenyl-1,3-butadiene and Methyl Vinyl Ketone

The Addition of 1-Phenyl-1,3-butadiene to Methyl Vinyl Ketone.—A mixture of 26.7 g. (0.21 mole) of 1-phenyl-1,3-butadiene, 18 g. (0.26 mole) of methyl vinyl ketone, and 10 mg. of hydroquinone in 30 ml. of benzene was refluxed on the steam-bath for eight hours. The reaction mixture was distilled twice to give 22 g. (0.11 mole, 54%) of colorless methyl 2-phenyl-3-cyclohexenyl ketone, b. p. 98–100° (1 mm.), 136–139° (7–8 mm.); *n*_D²⁰ 1.5381.

Anal. Calcd. for C₁₄H₁₆O: C, 83.96; H, 8.05. Found: C, 83.73; H, 7.91.

The semicarbazone was prepared according to Shriner and Fuson.¹⁷ One and four-hundredths grams (5.2 mmole.) of the unsaturated ketone gave 1.20 g. (4.7 mmole., 90%) of lustrous flakes, m. p. 164–165°.

Anal. Calcd. for C₁₅H₁₅N₃O: N, 16.33. Found: N, 16.38.

On another occasion, using the same procedure, a semicarbazone, m. p. 148–150°, was obtained.

Anal. Calcd. for C₁₅H₁₅N₃O: N, 16.33. Found: N, 16.32.

A mixed melting point of the two semicarbazones gave a melting point of 148–164°. After resolidification, this mixture melted at 162–163°.

Methyl 2-Phenylcyclohexyl Ketone.—Three and sixty-three hundredths grams (0.018 mole) of the above adduct was hydrogenated (palladium on charcoal in ethanol) to

(11) S. H. Zaheer and S. A. Faseeh, *J. Indian Chem. Soc.*, **21**, 27 (1944); *C. A.*, **39**, 2913 (1945).

(12) P. Pfeiffer, I. E. Engelhardt and W. Alfuss, *Ann.*, **467**, 174 (1928).

(13) S. H. Zaheer and S. A. Faseeh, *J. Indian Chem. Soc.*, **21**, 381 (1944); *C. A.*, **39**, 4599¹ (1945).

(14) W. Schlenk and E. Bergmann, *Ann.*, **464**, 34 (1928).

(15) C. Graebe and A. F. C. Rateanu, *ibid.*, **279**, 260 (1894).

(16) E. Lehmann and W. Paasche, *Ber.*, **68**, 146 (1935).

(17) R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," 3rd edition, John Wiley and Sons, New York, N. Y., 1948, p. 170.

give 3.2 g. (0.0158 mole, 87%) of methyl 2-phenylcyclohexyl ketone, m. p. 81–82° (reported, 78–79°,¹⁸ 80–81°¹⁹).

The 2,4-dinitrophenylhydrazone was prepared according to Shriner and Fuson,²⁰ m. p. 140–141° (dec.) (reported, 140–141° (dec.)¹⁹).

2-Phenylcyclohexane-1-carboxylic Acid.—Several attempts to oxidize the methyl 2-phenylcyclohexyl ketone with sodium hypochlorite, sodium hypobromite, sodium hypoiodite, and with chromic acid in acetic acid were unsuccessful. The oxidation was successfully effected by means of alkaline permanganate according to Shriner and Fuson.²¹ From 0.50 g. (2.5 mmole.) of the ketone there

was obtained 0.15 g. (0.73 mmole., 30%) of crude 2-phenylcyclohexane-1-carboxylic acid, m. p. 98–102°. Crystallization from petroleum ether (b. p. 90–100°) gave an almost colorless product, m. p. 105–107° (reported, 104–105°,¹⁸ 105–107°,²² 105°², (*trans*) 107–108°²³).

Summary

1-Phenyl-1,3-butadiene has been shown to give *ortho*-substituted cyclohexene derivatives in the diene synthesis with acrylonitrile and methyl vinyl ketone.

(22) J. W. Cook and C. L. Hewett, *J. Chem. Soc.*, 62 (1936).

(23) C. D. Gutsche, paper presented before the Division of Organic Chemistry of the American Chemical Society in St. Louis, Mo., September, 1948.

BROOKLYN, NEW YORK RECEIVED NOVEMBER 22, 1948

(18) F. S. Kipping and W. H. Perkin, *J. Chem. Soc.*, 304 (1890).

(19) C. D. Gutsche and W. S. Johnson, *THIS JOURNAL*, **68**, 2239 (1946).

(20) Reference 17, p. 171.

(21) Reference 17, p. 198.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF LINGNAN UNIVERSITY]

Chemical Investigation of *Draba nemorosa*, L. The Isolation of Sinapine Iodide

BY H. P. KUNG AND WEI-YUAN HUANG¹

No chemical work on the Chinese drug, *Draba nemorosa*, L. (Ting Li) has been reported in the literature, although the seed of this plant has been long used in Chinese medicine,² and recently has been reported³ to be effective in the treatment of pleurisy. Chemical work in this Laboratory on this seed has resulted in the isolation of a quaternary ammonium iodide, which degradation and absorption spectra studies indicated to be sinapine iodide, previously isolated from white mustard seed (*Sinapis alba*, L.) and characterized by Gadamer.⁴ Since the melting points obtained by

Gadamer, however, are generally lower than ours, confirmation was obtained by comparison with authentic sinapine iodide isolated from white mustard seed.

The ultraviolet absorption spectra,⁵ here presented in Fig. 1, of sinapine iodide and of sinapic acid show expected similarity with that of *p*-methoxycinnamic acid.⁶ The oxidation product of the methyl ether of methyl sinapate was identified as gallic acid trimethyl ether and confirmed by comparison of the spectra.

Experimental

Isolation of Sinapine Iodide.—The 95% ethanol (hot) extract of 1 kg. of ground seeds was concentrated and defatted by repeated extraction with ether. A 95% alcoholic solution of the fat free residue after decolorization by activated alumina was concentrated to a sirupy residue, and an equal volume of aqueous (15%) hydriodic acid was added. On standing, sinapine iodide trihydrate separated in clusters of needles. Recrystallization from hot water and drying over calcium chloride yielded 2.2 g. (0.22%) of the anhydrous compound as a white powder, m. p. 186.2–187.4°⁷ (Gadamer, 178–179°). Its aqueous solution turned yellow in alkali and gave a deep red color with strong nitric acid.

Anal. Calcd. for C₁₈H₂₄O₅NI: C, 43.94; H, 5.56; N, 3.20. Found⁸: C, 43.72; H, 5.59; N, 3.00.

Sinapic Acid.—A mixture of 415 mg. of sinapine iodide, 3.6 g. of potassium hydroxide, and 10 ml. of water was refluxed for fifteen minutes, and distilled into a 1% hydrochloric acid solution in an atmosphere of nitrogen gas. An amine in the distillate was identified as trimethylamine through its picrate (m. p. 215°) and chloroplatinate (m. p. 234° dec.) in mixed melting point determinations with authentic specimens of the corresponding trimethylamine derivatives.

(5) Determined with a Beckman spectrophotometer, model DU.

(6) Landolt-Börnstein, "Physikalisch-chemische Tabellen," Erg. III, 1935, p. 1349.

(7) All melting points are corrected, using a Hershberg melting point apparatus.

(8) Microanalyses by Mr. E. F. Shelberg, through the kindness of Abbott Laboratories.

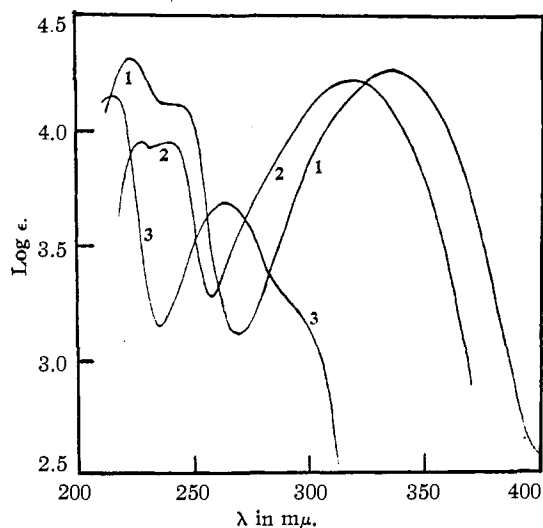


Fig. 1.—Ultraviolet absorption spectra in 95% ethanol of: 1, sinapine iodide; 2, sinapic acid; 3, gallic acid trimethyl ether.

(1) Abbott Laboratories Research Fellow.

(2) Li Shi-Chen, Pan Tsao Kang, Mu. See also Stuart, "Chinese Materia Medica," 1911, p. 155.

(3) Dr. Y. T. Tsang, private communication.

(4) Gadamer, *Arch. Pharm.*, **235**, 44 (1897).