furic acid for 12 hours. The solvents were removed, the product was placed in ether and the solution was washed with 10% potassium carbonate solution and with water. The ether solution was dried and the ether was removed; the residual colorless keto-ester was added to a mixture of 125 ml. of dry ethanol, 125 ml. of dry pyridine and 25 g. of hydroxylamine hydrochloride. After refluxing for 3 hours, the solvents were removed and the residue was treated with water. The crystalline, slightly discolored oxime (24 g., m.p. 85–87.5°) was recrystallized from hexane–benzene and cyclohexane; m.p. 88–88.5°. This oxime is not stable on long standing.

Anal. Calcd. for $C_{13}H_{15}O_3N$: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.97; H, 6.31; N, 6.01.

3-Carbomethoxytetralone-1 Oxime (IB).—A solution of 5.0 g. of 3-carboxytetralone-1 in 250 ml. of dry methanol was saturated with hydrogen chloride and allowed to stand overnight. The neutral product was isolated and converted to the oxime in pyridine–methanol, using 6.5 g. of hydroxylamine hydrochloride. The product (3.6 g.) was recrystallized from benzene–cyclohexane, m.p. 138–138.5°.

Anal. Calcd. for $C_{12}H_{13}O_3N$: C, 65.74; H, 5.98; N, 6.39. Found: C, 66.10; H, 6.05; N, 6.30.

2-Oxo-4-carbethoxy-2,3,4,5-tetrahydrobenzazepine (IIA).—A mixture of 5.0 g. of 3-carbethoxytetralone-1 oxime and 150 g. of polyphosphoric acid was heated to 110° and maintained at that temperature for 5 minutes. After treatment with ice and water, a solid product separated. This was removed by filtration, washed well and dried. The yield was 4.3 g. (86%), m.p. 138–140°. An analytical sample was obtained by recrystallization from ethyl acetate, m.p. 141–142°.

Anal. Calcd. for $C_{13}H_{15}O_3N$: C, 66.94; H, 6.98; N, 6.00. Found: C, 66.98; H, 6.49; N, 6.14.

2-Oxo-4-carbomethoxy-2,3,4,5-tetrahydrobenzazepine (IIB).—The rearrangement of 3-carbomethoxytetralone-1 oxime was carried out in the same way in 50% yield. The crude product (m.p. 118–119°) was recrystallized from cyclohexane–benzene; m.p. 120.5–121°.

Anal. Calcd. for $C_{12}H_{13}O_3N$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.60; H, 5.82; N, 6.37.

2-Oxo-1,2,3,4-tetrahydroquinoline-3-acetic Acid (III).—A solution of 2.0 g. of IIA in 25 ml. of concd. hydrochloric acid was heated under reflux for 2 hours. The mixture was cooled and filtered. The dried product amounted to 1.75 g. (99%); m.p. 195–203°. Recrystallization from water yielded an analytical sample, m.p. 206–208°.

Anal. Calcd. for $C_{11}H_{11}O_3N$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.59; H, 5.37; N, 6.52.

Ethyl 2-Oxo-1,2,3,4-tetrahydroquinoline-3-acetate (IVA). By Rearrangement.—A solution of 2.0 g. of lactam IIA in ethanol–benzene containing a few drops of concd. hydrochloric acid was heated under reflux for 12 hours. The product was 1.95 g. of colorless needles; the m.p. was 100–100.5° on recrystallization from hexane.

Anal. Calcd. for $C_{13}H_{15}O_3N$: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.96; H, 6.19; N, 6.16.

By Esterification.—A 2.0-g. sample of the acid III was esterified in ethanol–benzene. The yield of neutral product was 2.2 g. (97%); m.p. 88–90.5°. Recrystallization from benzene–hexane gave colorless needles of the ester, m.p. and mixed m.p. 100–101°.

Methyl 2-Oxo-1,2,3,4-tetrahydroquinoline-3-acetate (IVB).—The reaction of diazomethane in ether–methanol with 3.6 g. of the acid III provided 3.6 g. (93%) of colorless neutral product; m.p. 148–149°. Recrystallization from benzene gave an analytical sample, m.p. 150.5–151°.

Anal. Calcd. for $C_{12}H_{13}O_3N$: C, 65.74; H, 5.98; N, 6.39. Found: C, 66.07; H, 6.02; N, 6.19.

The same ester was obtained when the lactam IIB was heated under reflux (16 hours) in methanol containing a few drops of concd. hydrochloric acid.

Ethyl Carbostyril-3-acetate.—A mixture of 200 mg. of the ethyl ester IVA and 100 mg. of 5% palladium–carbon catalyst was heated to 250° and maintained at that temperature for 15 minutes. After cooling the mixture, the product was separated with hot benzene to yield 140 mg. (70%) of colorless needles, m.p. 185–187°. An analytical sample was obtained by recrystallization from benzene; m.p. 186.5–187°.

Anal. Calcd. for $C_{13}H_{13}O_3N$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.71; H, 5.81; N, 5.88.

It was found that this dehydrogenation could be effected in 74% yield by a solvent procedure with *p*-cymene. A mixture of 1.5 g. of ester IVA, 0.8 g. of 5% palladium–carbon catalyst and 15 ml. of cymene was heated under reflux for 3 hours. The catalyst was removed by filtration and washed with hot ethyl acetate. The combined solvents were reduced in volume and the product was allowed to crystallize.

BETHESDA, MARYLAND

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, WASHINGTON UNIVERSITY]

Experiments in the Colchicine Field. III.[1] A New Method for the Synthesis of Tricyclic Fused Ring Structures[2]

BY C. DAVID GUTSCHE AND HERBERT E. JOHNSON

RECEIVED MAY 19, 1955

2-(β-Phenylethyl)-benzaldehyde was converted to the hydrazone, the hydrazone was oxidized to the diazo compound, and the diazo compound was cyclized to a mixture of 2-phenylindane and 6,6a-dihydro-5*H*-cyclohepta[*a*]naphthalene (V). The proof of structure of V rests on carbon and hydrogen analysis, ultraviolet spectrum, formation of a maleic anhydride adduct, hydrogenation to a hexahydro derivative, and dehydrogenation of the latter to 8,9,10,11-tetrahydro-7*H*-cyclohepta[*a*]naphthalene (VII) which also was prepared by an unequivocal route. Compound V is of interest in that it possesses a phenylcycloheptatriene structure incorporated in a tricyclic system, a feature present in colchicine.

The ring enlargement of aromatic nuclei by means of carbomethoxydiazomethane (diazoacetic ester) was discovered and extensively studied by Buchner and his co-workers.[3] More recently diazomethane itself has been shown to undergo a similar reaction with a variety of aromatic nuclei,[4,5] and experiments in this Laboratory[6] and elsewhere[7] have shown that phenyldiazomethane also can act as a ring-enlarging agent for aromatic nuclei. The present communication concerns a derivative of phenyldiazomethane which, by virtue of an appropriate *ortho* substituent, undergoes in-

(1) The earlier articles by C. D. Gutsche and K. L. Seligman, THIS JOURNAL, **75**, 2579 (1953), and by C. D. Gutsche and F. A. Fleming, *ibid.*, **76**, 1771 (1954), are to be considered as papers I and II of this series.

(2) This work was supported, in part, by grants-in-aid from: (a) The Monsanto Chemical Co., (b) The Petrolite Corp., (c) The American Cancer Society upon recommendation of the Committee on Growth of the National Research Council.

(3) *Cf.* N. L. Drake and T. R. Sweeny, *J. Org. Chem.*, **11**, 67 (1946), for a bibliography of Buchner's contributions.

(4) W. von E. Doering and L. H. Knox, THIS JOURNAL, **72**, 2305 (1950); **73**, 828 (1951).

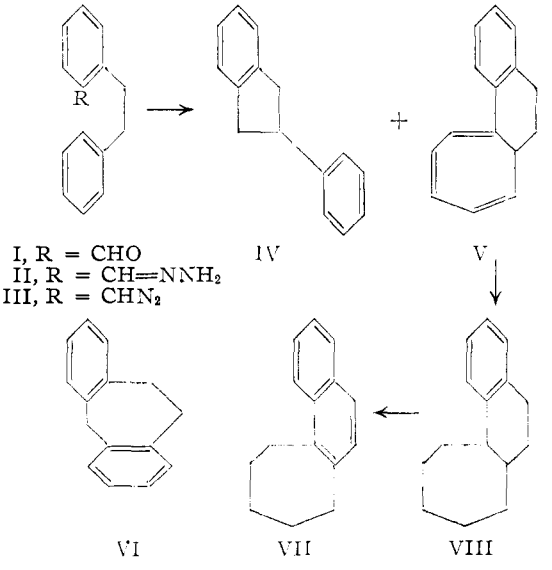
(5) W. von E. Doering and L. H. Knox, *ibid.*, **75**, 297 (1953).

(6) C. D. Gutsche and E. J. Jason, unpublished observations.

(7) W. Treibs and M. Quarg, *Angew. Chem.*, **67**, 76 (1955).

tramolecular reaction with resultant ring enlargement and simultaneous ring formation to generate a fused tricyclic structure.

Following Staudinger and Gaule's procedure for the preparation of aryldiazomethanes,[8] 2-(β-phenylethyl)-benzaldehyde (I) was synthesized by known methods, converted to the hydrazone II and oxidized with mercuric oxide to the diazo compound III. When a 0.03 *M* solution of III in petroleum ether was irradiated and refluxed, nitrogen was evolved (complete in 1–3 days) and the initial red color of the solution faded to a pale yellow. The product was comprised of a volatile oil (45%) and a non-volatile residue consisting mainly of the azine of the aldehyde I, the latter being convertible to the hydrazone II by heating with hydrazine. Careful fractionation of the volatile oil through an efficient spinning band column yielded a lower-boiling and a higher-boiling fraction which were identified as 2-phenylindane (IV) and 6,6a-dihydro-5*H*-cyclohepta[*a*]naphthalene (V),[9] respectively.



The lower-boiling fraction (30% yield from I[10]) showed no uptake of hydrogen in the presence of palladium-on-charcoal catalyst, had an analysis compatible with a $C_{15}H_{14}$ formula, an infrared spectrum in the 5–6 μ region characteristic of a 1,2-disubstituted benzene compound,[11] and an ultraviolet spectrum which indicated that there was no unsaturated grouping in conjugation with the benzene ring. By analogy to a by-product observed in other diazoalkane–aromatic ring reactions, *viz.*, toluene derivatives, it was initially thought that this material was 1,2,4,5-dibenzocycloheptadiene (VI). Compound VI, however, is a solid, and a comparison with an authentic sample ruled out this possibility. Instead, the lower-boiling fraction proved to be 2-phenylindane (IV). An authentic sample possessed a very similar ultraviolet spectrum, an identical infrared spectrum, and formed a diacetyl derivative which showed no depression in melting point when admixed with the diacetyl derivative of the lower-boiling cyclization product.

The higher-boiling fraction (9% yield from I[10]) had an analysis compatible with a $C_{15}H_{14}$ formula and an ultraviolet spectrum very similar to that of phenylcycloheptatriene.[12] It reacted with maleic anhydride to yield a high-melting adduct and absorbed almost three mole-equivalents of hydrogen to give a liquid $C_{15}H_{20}$ compound presumed to be 6,6a,7,8,9,10,11,11a-octahydro-5*H*-cyclohepta[*a*]naphthalene (VIII). Compound VIII was synthesized in an unequivocal fashion by hydrogenolysis of the known 5-keto derivative of VIII.[13] Both samples of VIII underwent dehydrogenation to 8,9,10,11-tetrahydro-7*H*-cyclohepta[*a*]-naphthalene (VII), the structure of which was established by carbon and hydrogen analysis, by its ultraviolet spectrum, and by its formation of a picrate.[14] These data indicate that structure V is an adequate formulation for the higher-boiling cyclization product.

The cyclization of the aldehyde I *via* its diazo compound III to the fused tricyclic ring structure V represents a new method for the synthesis of polycyclic compounds and an attractive one for molecules of the colchicine type. Work is continuing in an effort to extend the scope of this reaction.

Experimental[15–17]

2-(β-Phenylethyl)-benzaldehyde (I) was prepared from 2-(β-phenylethyl)-benzanilide by the procedure of Natelson and Gottfried[18] and was obtained as a pale orange oil in 67% yield.

The 2,4-dinitrophenylhydrazone of I was obtained as feathery, bright-orange needles after several recrystallizations from ethyl acetate; m.p. 178–179°.

Anal. Calcd. for $C_{21}H_{18}N_4O_4$: C, 64.60; H, 4.65. Found: C, 64.83; H, 4.56.

The azine of I was obtained as stout yellow needles after several recrystallizations from methanol; m.p. 80–81°.

Anal. Calcd. for $C_{30}H_{28}N_2$: C, 86.50; H, 6.78. Found: C, 86.02; H, 6.72.

2-(β-Phenylethyl)-phenyldiazomethane (III).—A solution of 48.0 g. (0.23 mole) of 2-(β-phenylethyl)-benzaldehyde in 200 ml. of ether was added over a period of one hour to a stirred mixture of 16.0 ml. (0.50 mole) of anhydrous hydra-

(8) F. Staudinger and A. Gaule, *Ber.*, **49**, 1897 (1916).

(9) The cycloheptatriene formulation (*cf.* structure V) is used for convenience, the possibility of valence tautomers of the norcaradiene type being realized.

(10) If recovered azine (reconvertible to II) is taken into consideration this yield figure should be doubled.

(11) C. W. Young, R. B. DuVall and N. Wright, *Anal. Chem.*, **23**, 709 (1951).

(12) The higher-boiling fraction had λ_{max}^{EtOH} (ε) 234 mμ (16,100) and 310 mμ (10,200). A. C. Cope and A. A. D'Addieco, THIS JOURNAL, **73**, 3419 (1951), have reported a phenylcycloheptatriene with λ_{max} (ε) 230 mμ (17,700) and 285 mμ (10,000). W. von E. Doering and L. H. Knox[5] have reported a phenylcycloheptatriene with λ_{max} (ε) 238 mμ (14,500) and 295 mμ (6350).

(13) C. D. Gutsche, *ibid.*, **73**, 786 (1951). Since the hydrogenation product of V was probably a mixture of *cis-trans* isomers, a direct comparison with the hydrogenolysis product of the 5-keto derivative of VIII was not attempted.

(14) The naphthalene derivative VII has been prepared recently by still a different route by Dr. R. A. Barnes (private communication). The physical constants which he reports agree very closely with those given in this paper.

(15) All m.p.'s are corrected; all b.p.'s are uncorrected.

(16) The microanalyses were performed by Miss Charlotte Peterson, Washington University.

(17) The ultraviolet spectra were obtained on a Cary recording spectrophotometer; the infrared spectra were obtained on a Perkin-Elmer model 21 recording spectrophotometer.

(18) S. Natelson and S. P. Gottfried, THIS JOURNAL, **58**, 1432 (1936).

zine and 200 ml. of ether. The reaction mixture was allowed to stand overnight at room temperature and was then washed with cold water and dried over sodium sulfate. Evaporation of the ether gave 51.0 g. (100%) of the hydrazone II as a viscous, pale yellow oil, $n^{25}D$ 1.6223.[19] This was suspended in 500 ml. of petroleum ether (b.p. 63–69°) and was treated, with stirring, with 71.0 g. (0.327 mole) of red mercuric oxide. The reaction mixture was stirred and maintained at 30–35° for 3.5 hours after which time the solids were removed by filtration, and the dark red filtrate was used without further purification; $\tilde{\nu}_{max.}$ 2070 cm.$^{-1}$ for diazo group.

Cyclization of 2-(β-Phenylethyl)-phenyldiazomethane (III).—The solution of 2-(β-phenylethyl)-phenyldiazomethane described above was diluted to 8 liters with petroleum ether (b.p. 63–69°, redistilled) and was refluxed and illuminated with a General Electric RS sun lamp until the evolution of nitrogen ceased and the red color of the solution had faded to a pale yellow. The nitrogen evolution amounted to *ca.* 60% of the theoretical, and from 1–3 days were usually required for its completion. The solvent then was removed by distillation, and the residue was distilled from a Claisen flask to give 20.0 g. (45%)[20] of a yellow liquid, b.p. 115–135° (1.0 mm.). Careful fractionation of this material through a Piros–Glover spinning band column set at a reflux ratio of 60 to 1 yielded 13.1 g. (30% over-all from I[10]) of a lower-boiling fraction with b.p. 94–96° (0.6 mm.) and 4.0 g. (9% over-all from I[10]) of a higher-boiling fraction with b.p. 101–102° (0.65 mm.).

2-Phenylindane (IV).—The lower-boiling fraction from the cyclization described above had the following physical properties: $n^{25}D$ 1.5936 (reported[21] for 2-phenylindane, $n^{25}D$ 1.5901); λ_{max}^{EtOH} in mμ (ε): 215 (17,000), 260 (1380), 267 (1750), 274 (1750); $\tilde{\nu}_{max}^{liquid}$ in cm.$^{-1}$: 649, 672, 691–702, 735–762, 839, 860, 910, 930, 982, 1002, 1025, 1032, 1078, 1100, 1153, 1181, 1222, 1243, 1268, 1290, 1303, 1322, 1358, 1460, 1485, 1497, 1595, 1612, 1673, 1751, 1812, 1872, 1910, 1953, 2870, 2920, 3040.

Anal. Calcd. for $C_{15}H_{14}$: C, 92.74; H, 7.26. Found: C, 92.66; H, 7.21.

An authentic sample of 2-phenylindane, prepared by hydrogenolysis of 2-phenylindanone-1 which was synthesized both by the method of Plattner, *et al.*,[21] and by the cyclization of 2,3-diphenylpropionic acid with polyphosphoric acid, had the following physical properties: $n^{25}D$ 1.5902; λ_{max}^{EtOH} in mμ (ε): 217 (13,200), 260 (1050), 267 (1420), 274 (1350); $\tilde{\nu}_{max}^{liquid}$ identical in every detail with the material described above from the cyclization.

Diacetyl-2-phenylindane.—The authentic 2-phenylindane and the cyclization product yielded identical diacetyl derivatives when treated with acetyl chloride and aluminum chloride in carbon disulfide. The crude product (100% yield), m.p. 79–85°, was recrystallized several times from petroleum ether (b.p. 63–69°)–ethyl acetate and was obtained as colorless, fine crystals, m.p. 98–99°.

Anal. Calcd. for $C_{19}H_{18}O_2$: C, 81.98; H, 6.52. Found: C, 82.07; H, 6.41.

6,6a-Dihydro-5*H*-cyclohepta[*a*]naphthalene (V).—The higher-boiling fraction from the cyclization had the following physical properties: $n^{25}D$ 1.6421; λ_{max}^{EtOH} in mμ (ε): 234 (16,100), 310 (10,200); λ_{min}^{EtOH} (ε) 222 (12,900), 266 (4,300); $\tilde{\nu}_{max}^{liquid}$ in cm.$^{-1}$: 660, 691–704, 733–772, 790, 826, 916, 936, 943, 972, 1022, 1042, 1075, 1110, 1158, 1168, 1187, 1200, 1222, 1248, 1263, 1300, 1332, 1356, 1378, 1400, 1434, 1456, 1490, 1528, 1611, 1628, 1720, 1810, 1830, 1913, 1950, 2840, 2890, 2940, 3020.

Anal. Calcd. for $C_{15}H_{14}$: C, 92.74; H, 7.26. Found: C, 92.38; H, 7.15.

A maleic anhydride adduct of V was obtained upon heating V with maleic anhydride at 180° for 30 minutes. Recrystallization from ethyl acetate gave fine, colorless crystals, m.p. 260–260.5°.

Anal. Calcd. for $C_{19}H_{16}O_3$: C, 78.06; H, 5.52. Found: C, 78.17; H, 5.44.

6,6a,7,8,9,10,11,11a-Octahydro-5*H*-cyclohepta[*a*]naphthalene (VIII). (A) From 6,6a-Dihydro-5*H*-cyclohepta[*a*]naphthalene (V).—A 0.74-g. sample of V was dissolved in 20 ml. of ethyl acetate, treated with 0.5 g. of 5% palladium-on-charcoal catalyst, and hydrogenated at room temperature and atmospheric pressure. After 2 hours 2.5 mole-equivalents of hydrogen had been absorbed and the uptake ceased. The product from this treatment consisted of a colorless oil, b.p. 99–100° (0.3 mm.), $n^{25}D$ 1.5571; λ_{max}^{EtOH} mμ (ε): 217 (9000), 229 (2840), 266(735), 273(784). Further hydrogenation for 40 hours at room temperature and 50 atmospheres of pressure yielded an oil which differed from the one described above only in minor details in the infrared spectrum and in lacking the 229 mμ band in the ultraviolet spectrum.

Anal. Calcd. for $C_{15}H_{20}$: C, 89.94; H, 10.06. Found for 1st hydrogenation prod.: C, 89.76; H, 9.54. Found for 2nd hydrogenation prod.: C, 90.15; H, 9.60.

(B) From 5-Keto-6,6a,7,8,9,10,11,11a-octahydro-5*H*-cyclohepta[*a*]naphthalene.—A 3.25-g. sample of the ketone[13] was dissolved in 20 ml. of ethyl acetate containing 1 ml. of 70% perchloric acid, treated with 1.0 g. of 5% palladium-on-charcoal catalyst, and hydrogenated for 14 hours at room temperature and atmospheric pressure. The product consisted of a colorless liquid, b.p. 99–100° (0.3 mm.), $n^{25}D$ 1.5529; λ_{max}^{EtOH} mμ (ε) 218 (6830), 266 (515), 273 (517).

Anal. Calcd. for $C_{15}H_{20}$: C, 89.94; H, 10.06. Found: C, 89.50; H, 9.60.

8,9,10,11-Tetrahydro-7*H*-cyclohepta[*a*]naphthalene (VII).—The two samples of VIII described above were separately subjected to the following treatment, and identical results were obtained in each case. A 0.67-g. sample of VIII was mixed with 0.20 g. of 5% palladium-on-charcoal and was heated at 345° until the evolution of hydrogen ceased (2.5 hours). The crude product, consisting of 0.68 g. of a yellow-green oil, was converted to 1.15 g. (80%) of the picrate of VII, obtained as dark orange needles, m.p. 101–102°.

Anal. Calcd. for $C_{21}H_{19}N_3O_7$: C, 59.29; H, 4.50. Found: C, 59.27; H, 4.57.

Decomposition of the picrate by passage through an alumina column[22] yielded 0.61 g. (78%) of a colorless liquid, b.p. 111° (0.3 mm.), $n^{25}D$ 1.6286, which crystallized upon standing. Two recrystallizations from methanol gave VI as colorless needles, m.p. 40–41°; λ_{max}^{EtOH} mμ (ε): 229 (93,500), 277 (5270), 287 (5850).

Anal. Calcd. for $C_{15}H_{16}$: C, 91.78; H, 8.22. Found: C, 91.73; H, 8.00.

1,2,4,5-Dibenzocycloheptadiene (VI) was prepared by cyclization of 2-(β-phenylethyl)-benzoic acid followed by hydrogenolysis and was obtained as colorless needles, m.p. 77–78° (reported[23] 78–79°); λ_{max}^{EtOH} mμ (ε): 217 (18,600), 265 (870), 271 (820), 274 (690).

ST. LOUIS, MISSOURI

(19) Upon standing at 5° the oil solidified to colorless crystals, m.p. 39–43°. Attempts to purify the hydrazone by recrystallization, however, resulted in conversion to the azine.

(20) The distillation residue consisted mainly of the azine of I which could be reconverted to the hydrazone (II) by heating overnight on the steam-bath with an excess of hydrazine. On the basis of recoverable hydrazone the yield of volatile material is *ca.* 90%.

(21) P. A. Plattner, R. Sandrin and J. Wyss, *Helv. Chim. Acta*, **29**, 1604 (1946).

(22) L. F. Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Co., Boston, Mass., 1941, p. 342.

(23) W. Triebs and H. J. Klinkhammer, *Ber.*, **83**, 367 (1949).