[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Syntheses of Some 4-Substituted Bicyclo[2.2.2]octane-1-carboxylic Acids[1]

BY JOHN D. ROBERTS, WALTER T. MORELAND, JR.,[2] AND WINIFRED FRAZER

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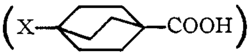
A series of 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids () and ethyl esters with X = H, Br, -OH, $-CO_2C_2H_5$, $-NH_2$ and $-C{\equiv}N$ has been synthesized from diethyl 2,5-dioxobicyclo[2.2.2]octane-1,4-dicarboxylate.

For use in an investigation[3] of electrical effects of substituent groups in saturated systems, we have prepared a series of 4-substituted bicyclo[2.2.2]-octane-1-carboxylic acids from diethyl 2,5-dioxobicyclo[2.2.2]-1,4-dicarboxylate (I). I was prepared by a modification of the procedure of Guha[4] in which diethyl succinate was condensed with sodium ethoxide and the product treated directly with ethylene dibromide without isolation of the intermediate diethyl succinoylsuccinate. Reduction of I to diethyl bicyclo[2.2.2]octane-1,4-dicarboxylate (III) was accomplished in 50–70% yield by Raney nickel desulfurization[5] of the bis-(trimethylene)-mercaptol (II) obtained from the condensation of I with propane-1,3-dithiol. Several attempts to reduce I by the Wolff–Kishner and Clemmensen procedures gave less than 15% yields of bicyclo[2.2.2]octane-1,4-dicarboxylic acid. The key intermediate for the synthesis of the various unsymmetrically substituted acids and esters, ethyl hydrogen bicyclo[2.2.2]octane-1,4-dicarboxylate (IV), was obtained by hydrolysis of the diester III with one equivalent of alkali.

Ethyl 4-carboxamidobicyclo[2.2.2]octane-1-carboxylate (V) was best prepared by successive treatments of IV with triethylamine, ethyl chlorocarbonate (−10°) and anhydrous ammonia. This procedure[6] gave an 88% yield of V as compared to 50–55% yields obtained in the reaction of the acid chloride of IV with aqueous or anhydrous ammonia. Treatment of V with bromine and sodium ethoxide in ethanol gave a low yield of the urethan VI which on acid hydrolysis yielded 4-aminobicyclo[2.2.2]octane-1-carboxylic acid (VII). Ethyl 4-cyanobicyclo[2.2.2]octane-1-carboxylate (VIII) was obtained by dehydration of V with phosphorus oxychloride in ethylene dichloride. The corresponding cyano acid IX was prepared by alkaline hydrolysis of VIII.

The reaction of the silver salt of the monoester (IV) with bromine in dichlorodifluoromethane (Freon 12)[7] gave ethyl 4-bromobicyclo[2.2.2]-octane-1-carboxylate (X) which was hydrolyzed to the corresponding bromo acid XI with 48% hydrobromic acid. Under alkaline conditions, hydrolysis of X appeared to give XI mixed with more or less of 4-hydroxybicyclo[2.2.2]octane-1-carboxylic acid (XIV). Indeed, an 81% yield of XIV could be obtained by refluxing X with 1% aqueous alkali for 24 hours. Although replacement of halogen by hydroxyl at the bridgehead of a bicyclic ring system has not been observed to occur at an appreciable rate with bicyclo[2.2.1]heptane derivatives,[8] the reaction appears to proceed without rearrangement, albeit slowly as compared to an aliphatic tertiary bromide, with 1-bromobicyclo-[2.2.2]octane[9] where the bridgehead cation may be presumed to be substantially less strained. Attempts to hydrolyze X to the corresponding hydroxy ester (XV) with silver oxide or silver nitrate in acetone–water mixtures were unsuccessful and it is probable that, in the basic hydrolysis of X, the expulsion of the bromide ion is markedly facilitated by the electrostatic effect of the anionic carboxylate group formed by the hydrolysis of the ester group. Strong alkaline hydrolysis of X gave a mixture of products containing only about 20% of XIV. The hydroxy ester XV was prepared by treatment of the silver salt of XIV with ethyl iodide in ether.

Ethyl bicyclo[2.2.2]octane-1-carboxylate (XII) and the corresponding acid XIII were both obtained from hydrogenolysis of the bromo ester X in absolute ethanol containing sodium ethoxide over a Raney nickel catalyst.

A flow sheet for the various reactions described above is given in Fig. 1.

Experimental

Diethyl 2,5-Dioxobicyclo[2.2.2]octane-1,4-dicarboxylate (I).—In a thoroughly-dried three-necked 5-l. flask fitted with a reflux condenser, dropping funnel and mechanical stirrer and containing a nitrogen atmosphere was placed 92 g. (4.0 g.-atoms) of freshly-cut sodium slices. Absolute ethanol (about 1.5 l., dried by the ethyl formate method)[10] was distilled into the flask through the dropping funnel. When the dissolution of the sodium was complete, 348 g. (2.0 moles) of diethyl succinate was added and the mixture refluxed for 14 hours. Most of the ethanol was distilled in a stream of dry nitrogen and finally the flask was heated for 4 hours at 140–160° in an oil-bath at 5–10 mm. Dry nitrogen was admitted and the yellow-to-dark brown solid allowed to cool.

Freshly-distilled ethylene dibromide (2600 g., 13.6 moles) was added rapidly and a vigorous reaction usually ensued which was controlled by an ice-bath when necessary. The cake was carefully broken up and the mixture heated with

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[1] Presented before the Division of Organic Chemistry at the Atlantic City Meeting of the American Chemical Society, September, 1952.

[2] U. S. Atomic Energy Commission Predoctoral Fellow, 1951–1952.

[3] J. D. Roberts and W. T. Moreland, Jr., THIS JOURNAL, in press.

[4] P. C. Guha, *Ber.*, **72**, 1359 (1939); P. C. Guha and C. Krishnamurthy, *ibid.*, **72**, 1374 (1939).

[5] J. Bougault, E. Cattelain and P. Chabrier, *Bull. soc. chim.*, [5] **5**, 1699 (1938); **7**, 780, 781 (1940); R. Mozingo, D. E. Wolf, S. A. Harris and K. Folkers, THIS JOURNAL, **65**, 1013 (1943).

[6] T. Wieland, W. Schäfer and E. Bokelmann, *Ann.*, **573**, 99 (1951); R. A. Boissonnas, *Helv. Chim. Acta*, **34**, 874 (1951).

[7] J. D. Roberts and V. C. Chambers, THIS JOURNAL, **73**, 3176 (1951).

[8] P. D. Bartlett and L. H. Knox, *ibid.*, **61**, 3184 (1939); W. v. E. Doering and E. F. Schoenewaldt, *ibid.*, **73**, 2333 (1951).

[9] Private communication from Professor W. v. E. Doering, Yale University.

[10] A. I. Vogel, "Practical Organic Chemistry," Longmans, Green and Company, London, 1948, p. 167.

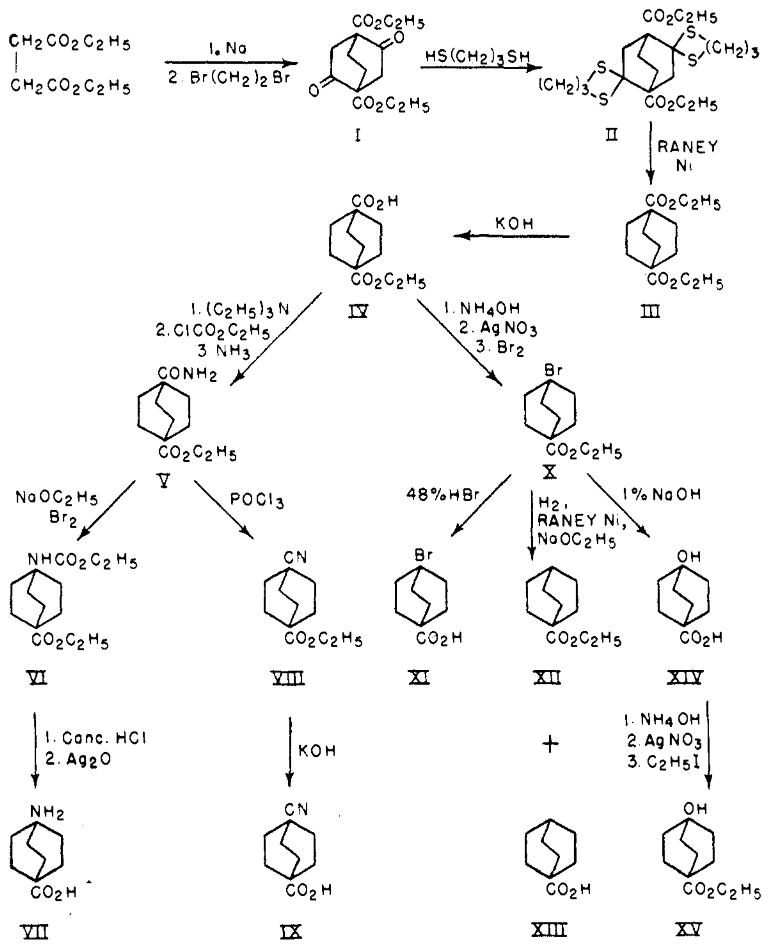

Fig. 1.—Flow sheet of reactions.

stirring under reflux until neutral to litmus (18–36 hours). The mixture was then steam distilled until a yellow solid began to collect in the condenser. About 2300 g. of ethylene dibromide was recovered from the steam distillate.

The residue from the steam distillation was allowed to cool with occasional agitation to prevent formation of a solid cake and then filtered. The gummy solid was washed several times with water and dissolved in hot acetone. The acetone solution when cooled and diluted with water deposited a straw-colored crystalline solid which was washed with 1% sodium hydroxide solution until nearly white and the basic washings no longer gave a color with ferric chloride solution.[4] Recrystallization of the base-insoluble material from 95% ethanol gave 90 g. (32%) of crude I, m.p. 108–110.5° (m.p. of pure I is 112°).[4] Prompt acidification of the 1% sodium hydroxide washings gave, after crystallization from 95% ethanol, 31 g. (12%) of diethyl succinoylsuccinate, m.p. 124–128°.

Bis-(trimethylene)-mercaptol of Diethyl 2,5-Dioxobicyclo-[2.2.2]octane-2,4-dicarboxylate (II).—The procedure was modified after that of Hauptmann.[11] The ketoester I (14 g., 0.050 mole) was dissolved in the minimum amount of chloroform in a separatory funnel, 21.6 g. (0.20 mole) of propane-1,3-dithiol was added and hydrogen chloride bubbled through the mixture for 6–8 hours at 0°. The chloroform solution was washed with 25-ml. portions of 2 *N* sodium hydroxide solution until no further reaction occurred and then washed with water, dried over sodium sulfate, concentrated on a steam-cone and, finally, heated at 100° for 1 hour at 35 mm. The resulting viscous oil was boiled with *n*-hexane until a powdery white solid formed. The mixture was filtered hot and the resulting crude II (18.7 g., 81%), m.p. 115–118°, was used directly in the desulfurization reaction. Evaporation of the hexane extract yielded 1.3 g. (6%) of less pure II, m.p. 108–115°. An analytical sample of II crystallized from an *n*-hexane–acetone mixture as rectangular white prisms, m.p. 119.0–120.0°.

Anal. Calcd. for $C_{20}H_{30}O_4S_4$: C, 51.91; H, 6.54; S, 27.71. Found: C, 52.14; H, 6.61; S, 27.82.

The corresponding bis-(dimethylene)-mercaptol of I, prepared in a similar manner, recrystallized from *n*-hexane–acetone as white prisms of m.p. 91.8–92.7°.

Anal. Calcd. for $C_{18}H_{26}O_4S_4$: C, 49.75; H, 6.01; S, 29.50. Found: C, 49.68; H, 6.18; S, 29.85.

Diethyl Bicyclo[2.2.2]octane-1,4-dicarboxylate (III).—In a typical experiment, 40 g. (0.0865 mole) of II was refluxed for 48 hours with 600 g. of Raney nickel hydrogenation catalyst[12] in 500 ml. of 95% ethanol. The nickel was filtered, the solvent removed through a 20-cm. Vigreux column and the residue distilled under reduced pressure. The yield of III was 11.4 g. (52%), b.p. 145–155° (5 mm.), n^{25}_{D} 1.4660. An additional 4 g. (18%) of III was obtained by extraction of the filtered nickel for 24 hours with ether in a soxhlet extractor. On redistillation, a small sample of III showed b.p. 113–115° (0.3 mm.), n^{25}_{D} 1.4667 [lit.[4] b.p. 140–145° (3 mm.), n^{30}_{D} 1.4723]. Since the refractive index was substantially different from the literature value the material was subjected to combustion analysis.

Anal. Calcd. for $C_{14}H_{22}O_4$: C, 66.11; H, 8.72. Found: C, 66.09; H, 8.88.

Ethyl Hydrogen Bicyclo[2.2.2]octane-1,4-dicarboxylate (IV).—The diethyl ester III (9.50 g., 0.0374 mole) and 2.10 g. (0.0374 mole) of solid potassium hydroxide were dissolved in 50 ml. of 95% ethanol and heated under reflux for 13 hours. The cooled reaction mixture was diluted with 100 ml. of water and extracted with 40 ml. of ether. The ether layer was washed with water, dried over magnesium sulfate and the ether removed. The residue was distilled through a semi-micro fractionating column[13] and yielded 1.63 g. (17%) of III, b.p. 145–146° (4 mm.), n^{25}_{D} 1.4669.

The alkaline extraction residue was acidified with 6 *N* hydrochloric acid and extracted three times with 20-ml. portions of chloroform. The aqueous layer was discarded, the chloroform solution chilled and filtered to remove some insoluble bicyclo[2.2.2]octane-1,4-dicarboxylic acid. The chloroform filtrate was dried over magnesium sulfate and concentrated on a steam-cone. The residue was boiled with 10 ml. of benzene, filtered hot and the filtrate diluted with 50 ml. of hot *n*-hexane. The mixture was heated to boiling, filtered hot and on cooling, 4.0 g. (58%) of IV, m.p. 145.2–148.0°, was obtained. The various insoluble fractions yielded a total of 0.58 g. (8%) of the dicarboxylic acid, m.p. > 360° (lit.[4] m.p. 386°). The yields of the acids were based on unrecovered III.

An analytical sample of IV was obtained as shiny white platelets from benzene-*n*-hexane, m.p. 149.0–150.5°.

Anal. Calcd. for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.56; H, 7.95.

Ethyl 4-Carboxamidobicyclo[2.2.2]octane-1-carboxylate (V).—The best procedure for conversion of IV to V was based on those of Wieland[6] and Boissonnas.[6] A solution of 3.39 g. (0.015 mole) of monoacid ester IV and 1.5 g. (0.015 mole) of triethylamine in 70 ml. of chloroform was cooled in an ice-salt-bath and 1.6 g. (0.015 mole) of ethyl chlorocarbonate added rapidly with continuous agitation. After 15 minutes, anhydrous ammonia was passed through for 5

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[11] H. Hauptmann and M. M. Campos, THIS JOURNAL, **72**, 1405 (1950); H. Hauptmann, *ibid.*, **69**, 562 (1947).

[12] Obtained from the Raney Catalyst Co. as an aqueous suspension. Before use the nickel was washed with water until neutral to litmus and then stored under absolute ethanol.

[13] C. Gould, G. Holzman and C. Niemann, *Anal. Chem.*, **20**, 361 (1948).

minutes. The mixture was removed from the cooling bath, stirred at room temperature for 1 hour and allowed to stand overnight. The suspension was filtered and the chloroform in the filtrate removed through a 15-cm. Vigreux column. The residue was boiled with 15 ml. of benzene and filtered hot. The benzene solution was diluted with 45 ml. of boiling *n*-hexane and on cooling deposited 2.93 g. (87%) of the crude amide V, m.p. 132–139°.

A small sample recrystallized twice from benzene–*n*-hexane mixtures was obtained as long white needles, m.p. 143.6–145.0°.

Anal. Calcd. for $C_{12}H_{19}O_3N$: C, 63.97; H, 8.50; N, 6.22. Found: C, 63.72; H, 8.68; N, 6.23.

Ethyl 4-(N-Carboethoxy)-aminobicyclo[2.2.2]octane-1-carboxylate (VI).—The amide V (2.13 g., 0.00095 mole) was dissolved in a solution of 0.46 g. (0.020 g.-atom) of sodium in 35 ml. of absolute ethanol. The mixture was cooled in an ice-bath and 1.6 g. (0.010 mole) of bromine added dropwise. The whole was refluxed for 15 minutes on a steam-cone, cooled, diluted with 300 ml. of water and resulting crystalline precipitate of 0.80 g. (31%) of urethan VI collected. The crude material had m.p. 96.4–99.4°. An analytical sample recrystallized from *n*-hexane had m.p. 99.0–100.0°.

Anal. Calcd. for $C_{14}H_{23}O_4N$: C, 62.43; H, 8.61; N, 5.20. Found: C, 62.34; H, 8.65; N, 5.19.

Ether extraction of the aqueous filtrate gave 0.07 g. (3%) of the starting amide V, m.p. 139–143°. Acidification of the residue from the extraction yielded a mixture of acids from which no 4-N-carbethoxamidobicyclo[2.2.2]octane-1-carboxylic acid could be isolated.

4-Aminobicyclo[2.2.2]octane-1-carboxylic Acid (VII).—VI (0.40 g., 0.0015 mole) was refluxed with 20 ml. of concentrated hydrochloric acid for several hours. The mixture was filtered and on evaporation to dryness yielded the hydrochloride of VII. This substance was purified by precipitation from absolute ethanol by addition of anhydrous ether. The yield of purified salt as white platelets was 0.22 g. (71%). The material darkened at 322° but did not melt below 376°.

The hydrochloride (0.155 g., 0.00076 mole) was dissolved in water and shaken with freshly-prepared silver oxide (0.00076 mole). The silver chloride was removed by centrifugation and the amino acid VI precipitated by addition of absolute ethanol and ether. Pure VI was obtained as white needles which decomposed without melting at 365°. The crystals disintegrated to a fine powder on drying at 25° and 35 mm. over phosphorus pentoxide for 18 hours.

Anal. Calcd. for $C_9H_{15}O_2N$: C, 63.88; H, 8.94; N, 8.28. Found: C, 63.80; H, 9.06; N, 8.12.

Ethyl 4-Cyanobicyclo[2.2.2]octane-1-carboxylate (VIII).—A solution of 3.24 g. (0.0144 mole) of the amide ester V in 50 ml. of ethylene dichloride and 5 ml. of phosphorus oxychloride was refluxed on the steam-cone for 20 minutes.[14] The solvent and excess phosphorus oxychloride were removed under reduced pressure, the residue was treated with excess 2 *N* sodium hydroxide solution and extracted with *n*-pentane. The extract was washed with water, dried over magnesium sulfate and the pentane removed. Reduced pressure distillation gave 1.80 g. (60%) of slightly colored VIII, b.p. 146° (5 mm.), $n^{25}D$ 1.4764.

The analytical sample was distilled twice through a semi-micro column[13] and was a colorless, almost-odorless liquid of b.p. 115° (0.7 mm.), $n^{25}D$ 1.4768.

Anal. Calcd. for $C_{12}H_{17}O_3N$: C, 69.53; H, 8.27; N, 6.76. Found: C, 69.51; H, 8.26; N, 6.78.

4-Cyanobicyclo[2.2.2]octane-1-carboxylic Acid (IX).—A solution of 0.15 g. (0.00072 mole) of the cyanoester VIII and 0.041 g. (0.00072 mole) of potassium hydroxide in 5 ml. of 95% ethanol was refluxed for 2 hours. The cooled solution was diluted with 15 ml. of water, washed with ether, acidified with 6 *N* hydrochloric acid and extracted twice with ether. The extract was dried over magnesium sulfate, the ether removed and the residue recrystallized from an ether–*n*-hexane mixture. The yield of thick white needles of IX was 0.040 g. (32%), m.p. 298–300° (dec.).

Anal. Calcd. for $C_{10}H_{13}O_2N$: C, 67.02; H, 7.31; N, 7.82. Found: C, 67.10; H, 7.45; N, 7.89.

Ethyl 4-Bromobicyclo[2.2.2]octane-1-carboxylate (X).—The silver salt of the ester acid IV was prepared in 84% yield by the procedure described for cyclopropanecarboxylic acid.[7] The well-dried silver salt, 8.0 g. (0.0240 mole), was treated with 3.84 g. (0.0240 mole) of bromine in 100 ml. of dried commercial dichlorodifluoromethane.[7] The solvent was removed and the residue taken up in *n*-pentane. The extract was washed with dilute sodium bisulfite, dilute sodium bicarbonate and water then dried and the pentane removed through a 30-cm. Vigreux column. The residue was distilled through a semi-micro column and yielded 4.10 g. (55%) of the bromoester X, b.p. 113–115° (1 mm.), $n^{25}D$ 1.5023.

A small sample redistilled for analysis had b.p. 133–134° (10 mm.), $n^{25}D$ 1.5020.

Anal. Calcd. for $C_{11}H_{17}O_2Br$: C, 50.58; H, 6.56; Br, 30.60. Found: C, 50.78; H, 6.63; Br, 30.33.

4-Bromobicyclo[2.2.2]octane-1-carboxylic Acid (XI).—The bromoester X (0.17 g., 0.00064 mole) was refluxed for 1.5 hours with 3 ml. of 48% hydrobromic acid. The mixture was diluted with water and extracted with ether. The extract was washed with water and dried over magnesium sulfate. Evaporation of the ether left the crude bromoacid which was recrystallized from a *n*-hexane–benzene mixture and yielded 0.070 g. (47%) of white needles, m.p. 268–270° (sealed tube).

Anal. Calcd. for $C_9H_{13}O_2Br$: C, 46.37; H, 5.62; Br, 34.28. Found: C, 46.34; H, 5.63; Br, 34.11.

Ethyl Bicyclo[2.2.2]octane-1-carboxylate (XII) and Bicyclo[2.2.2]octane-1-carboxylic Acid (XIII).—The bromoester X (2.07 g., 0.0079 mole) was mixed with a suspension of 1.5 g. of Raney nickel catalyst[12] in a solution of 1 g. (0.045 g.-atom) of sodium in 30 ml. of absolute ethanol. The mixture was stirred in an atmosphere of hydrogen at room temperature for 4 hours at the end of which time 75% of the theoretical amount of hydrogen had been absorbed. The reaction mixture was very thick because of precipitation of sodium bromide, so 10 ml. more of ethanol was added and the reduction continued until the absorption of hydrogen ceased. The total reaction time was 8 hours and the hydrogen uptake was 101% of the calculated amount.

The catalyst was filtered and washed with water and alcohol. The combined filtrate and washings were diluted with water and extracted with ether. The ethereal extract was washed with water, dried over sodium sulfate and the ether removed. The residue on distillation through a semi-micro column[13] gave 0.21 g. (17%) of XII, b.p. 75–76° (3 mm.), $n^{25}D$ 1.4668.

Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.54; H, 9.99.

The alkaline aqueous residue was acidified with 6 *N* hydrochloric acid and extracted with ether. The extract was dried over magnesium sulfate and evaporated to dryness. The residue was recrystallized from water to give 0.54 g. (45%) of bicyclo[2.2.2]octane-1-carboxylic acid as shiny white platelets, m.p. 140.8–141.3°. The product was very soluble in ethanol, benzene, ether and *n*-hexane.

Anal. Calcd. for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.85; H, 9.33.

In a subsequent preparation where particular care was taken to exclude moisture the yield of the ester XII was 58% and that of the acid XIII was 4%.

4-Hydroxybicyclo[2.2.2]octane-1-carboxylic Acid (XIV).—The bromoester X (0.511 g., 0.00195 mole) was refluxed with 50 ml. of 1% sodium hydroxide solution for 24 hours, cooled, acidified with 6 *N* hydrochloric acid and extracted continuously with ether for 24 hours. The extract was dried over magnesium sulfate and concentrated to small volume. *n*-Hexane was added to the boiling ether solution until a permanent cloudiness appeared and then the mixture was allowed to cool in a refrigerator. The first crop of white needles of XIV, 0.219 g. (66%), had m.p. 221–224°. A second crop obtained by addition of more *n*-hexane to the mother liquor amounted to 0.050 g. (15%) and had m.p. 213–222°. The material was purified by dissolving it in benzene containing just enough ether for complete dissolution and then adding *n*-hexane in volume equal to that of the benzene. The resulting white needles had m.p. 222.9–225.0°.

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[14] The procedure was modeled after those of J. P. English, J. H. Clark, R. G. Shepherd, H. W. Marson, J. Krapcho and R. O. Roblin, Jr., THIS JOURNAL, **68**, 1046 (1946).

Anal. Calcd. for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.76; H, 8.50.

Ethyl 4-Hydroxybicyclo[2.2.2]octane-1-carboxylate (XV).—The silver salt of the hydroxyacid XIV was prepared in 88% yield by addition of silver nitrate to a solution of XIV in the minimum of dilute aqueous ammonia. The silver salt (0.66 g., 0.0025 mole) was heated under reflux for 14 hours with 0.5 ml. of ethyl iodide in 20 ml. of ether. The mixture was filtered, the ether evaporated and the residue distilled through a semi-micro column.[1] The yield of hydroxyester, b.p. 155° (17 mm.), m.p. 48.5–50.0°, was 0.20 g. (40%).

Anal. Calcd. for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.40; H, 9.11.

CAMBRIDGE 39, MASSACHUSETTS

[CONTRIBUTION FROM THE WM. H. CHANDLER CHEMISTRY LABORATORY, LEHIGH UNIVERSITY]

The Synthesis of 2,2-Diphenylcyclopentanone and Some of its Derivatives

BY NELSON R. EASTON AND SAMUEL J. NELSON[1]

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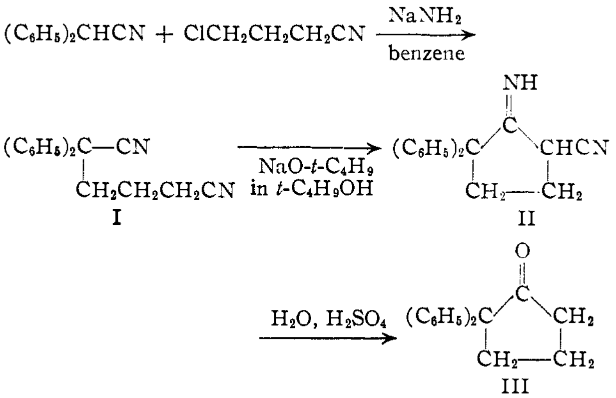
The synthesis of 2,2-diphenylcyclopentanone through the cyclization of the dinitrile is reported. Various reactions of the diphenylcyclopentanone are discussed.

The synthesis of 5,5-diphenyl-2-cyclopentenone by the cyclization of 2,2-diphenyl-4-pentenoic acid has been described[2] and from this 2,2-diphenylcyclopentanone has been prepared[3] by hydrogenation over platinum oxide.

We have also been interested in the preparation of 2,2-diphenylcyclopentanone and have developed an improved preparation of this compound quite different from that described by Craig.[3] We find that 2,2-diphenylcyclopentanone is readily prepared through the reactions

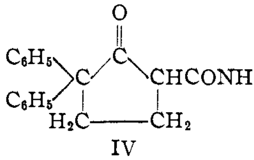


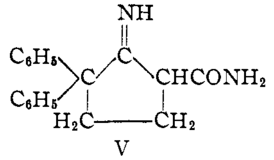
In the preparation of 2,2-diphenyladiponitrile (I) the cyclic product II is sometimes obtained along with the linear product, probably because of the presence of a slight excess of sodium amide. The reaction mixture in these cases is tarry and difficult to purify although yields of about 50% of the cyclized product (II) are obtained. The cyclization of 2,2 - diphenyladiponitrile goes smoothly in virtually quantitative yield when sodium *t*-butoxide in *t*-butyl alcohol is used as the condensing agent. Sodium amide in benzene gives a tarry reaction mixture and a lower yield of product, while sodium ethoxide in absolute alcohol does not catalyze the condensation.

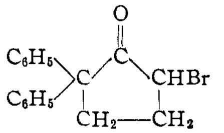
The cyclized product, 5-cyano-2,2-diphenylcyclopentanoneimine, is readily hydrolyzed and decarboxylated with dilute sulfuric acid. A yield of 81% is obtained based on the 2,2-diphenyladiponitrile. When the hydrolysis is incomplete two other products which analyzed for the 2,2-diphenylcyclopentanone-5-carboxamide (IV) and 2,2-diphenylcyclopentanoneimine-5-carboxamide (V) are obtained from the reaction mixture.

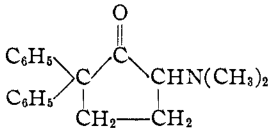
Although Burger[4] has reported that 2,2-diphenylcyclohexanone is brominated readily with bromine in carbon tetrachloride, we find that 2,2-diphenylcyclopentanone gives a variety of products which are very difficult to separate when brominated in this manner; however, excellent yields of VI are obtained when this bromination is carried out using the complex of ether and bromine. When this substance, which is an ether-insoluble oil, is added to an ether solution of the ketone, the bromo compound is obtained in 76% yield.

The amination of 5-bromo-2,2-diphenylcyclopentanone with dimethylamine is carried out in 95% alcohol. Yields of VII of about 33% are obtained when four moles of the amine are used, but these are increased to 81% when 20 moles are used.


IV


V


VI


VII

It has been reported[4] that 2,2-diphenylcyclohexanone undergoes the Mannich reaction very readily when formaldehyde and dimethylamine are used. We were unable to obtain any basic product under these conditions with 2,2-diphenylcyclopentanone.

Experimental

2,2-Diphenyladiponitrile.—A mixture of 110 ml. of sodium dried benzene, 18.4 g. (0.0953 mole) of diphenylacetonitrile and 3.90 g. (0.100 mole) of finely powdered

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[1] Abstracted in part from the thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

[2] P. N. Craig and I. H. Witt, THIS JOURNAL, **72**, 4925 (1950).

[3] Personal communication from P. N. Craig.

[4] A. Burger and W. B. Bennet, THIS JOURNAL, **72**, 5415 (1950).