[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Synthesis and Properties of Derivatives of Spiro[4.4]nonane[1]

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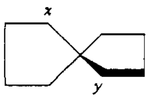
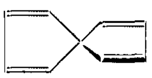
Methods have been developed for the preparation of compound I in which X = Y = O═; X = Y = HON═; X = Y = HO—(all three racemates); X = O═, Y = HO—; X = H—, Y = O═; X = H—, Y = HO—; X = H—, Y = NH_2—. The unusual spectral properties of the diketone (I, X = Y = O═) are discussed.

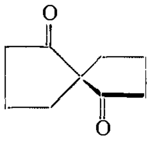
The objectives of this and subsequent publications on this subject are to explore the chemistry of a number of carbocyclic compounds of rigid geometry, with particular emphasis on those systems with unique symmetry properties. This paper reports the synthesis and properties of a number of derivatives of spiro[4.4]nonane which it is hoped will ultimately be convertible into compound II. The key intermediate in the synthesis of II and a number of other interesting bifunctional spirans is the diketone III, whose preparation has been reported without the benefit of experimental documentation.[2]



I

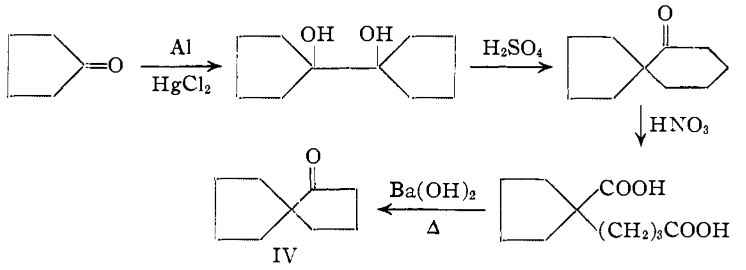


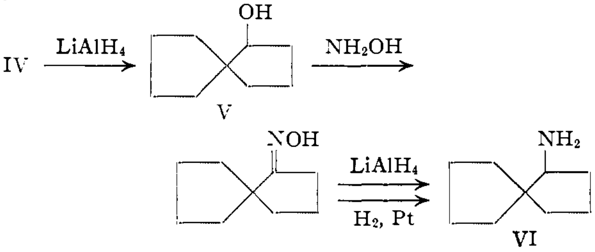
II



III

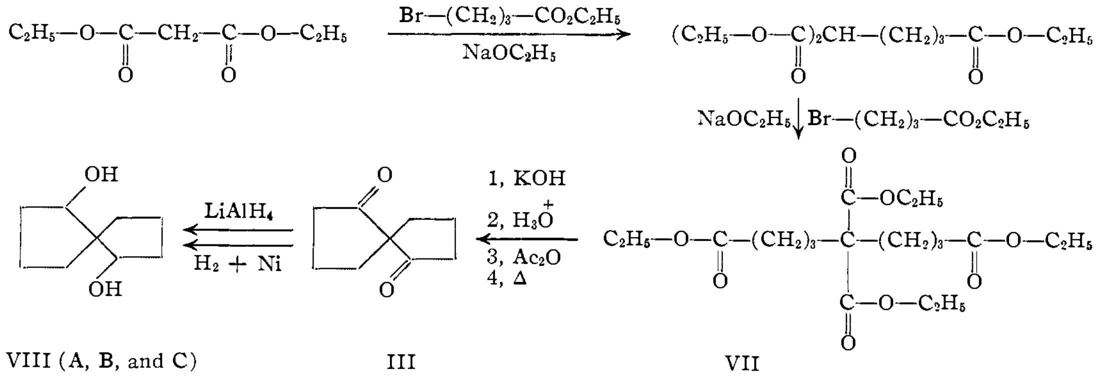
In the present work, 1-ketospiro[4.4]nonane (IV)[3] was prepared as a model by the sequence shown, the over-all yield amounting to 15%. This compound was reduced with lithium aluminum hydride to 1-hydroxyspiro[4.4]nonane (V), and the corresponding 1-aminospiro[4.4]nonane (VI) was prepared from the oxime of IV by reduction with lithium aluminum hydride (34% yield) and by a superior catalytic hydrogenation method (83% yield).





The bifunctional spiran III was obtained by a four-step sequence involving two successive malonic ester alkylations followed by hydrolysis and pyrolysis to give a 9% over-all yield. An attempted Diekmann condensation of the tetraester VII was unsuccessful.

The ethyl γ-bromobutyrate employed in the malonic ester alkylation reactions was prepared by three independent paths: A six-step sequence involving intermediary preparations of phenoxypropyl bromide and phenoxybutyronitrile[4]; a less arduous path involving the half substitution of trimethylene bromide with potassium cyanide[5]; an extremely expedient method involving the treatment of butyrolactone with hydrogen bromide followed by methanol.[6]



VIII (A, B, and C) III VII

The diketone III (characterized as its dioxime)

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[1] This research was conducted under contract AF 33(616)-146 with the United States Air Force, the sponsoring agency being the Aeronautical Research Laboratory of the Wright Air Development Center, Air Research and Development Command.

[2] A. Horeau, *Compt. rend.*, **228**, 2039 (1949).

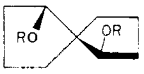
[3] N. D. Zelinskii and H. V. Elagina, *Compte rend. acad. sci., U.S.S.R.*, **49**, 568 (1945); *C. A.*, **40**, 6058 (1946).

[4] (a) C. S. Marvel and A. L. Tannenbaum, THIS JOURNAL, **44**, 2645 (1922); (b) C. S. Marvel and E. R. Birkheimer, *ibid.*, **51**, 260 (1929).

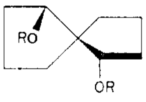
[5] (a) C. G. Derick and R. W. Hess, *ibid.*, **40**, 537 (1918); (b) E. A. Prill and S. M. McElvain, *ibid.*, **55**, 1233 (1933).

[6] (a) J. F. Tinker, *J. Org. Chem.*, **16**, 1417 (1951); (b) R. O. Clinton and S. C. Laskowski, THIS JOURNAL, **70**, 3135 (1948).

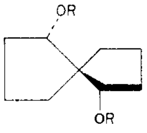
was reduced both catalytically and with lithium aluminum hydride to the glycol VIII, which is theoretically capable of existing in three different racemic forms, *cis–cis*, *cis–trans* and *trans–trans*. Although these three stereomers were not separated as glycols, they were each isolated in a pure state as their respective bis-*p*-nitrobenzoates through the use of chromatographic and fractional crystallization techniques. The isolation of these three racemates marks the third example of the separation of stereomers in a system possessing the same symmetry as VIII. Thus, Leuchs and Gieseler[7] isolated the three forms of IX, and Sutter and Wijkman[8] prepared the three racemates of the structurally similar compound X.



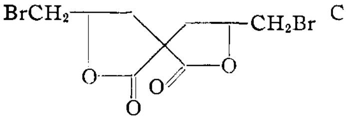
cis–cis



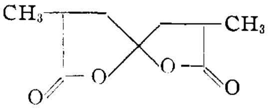
cis–trans



trans–trans



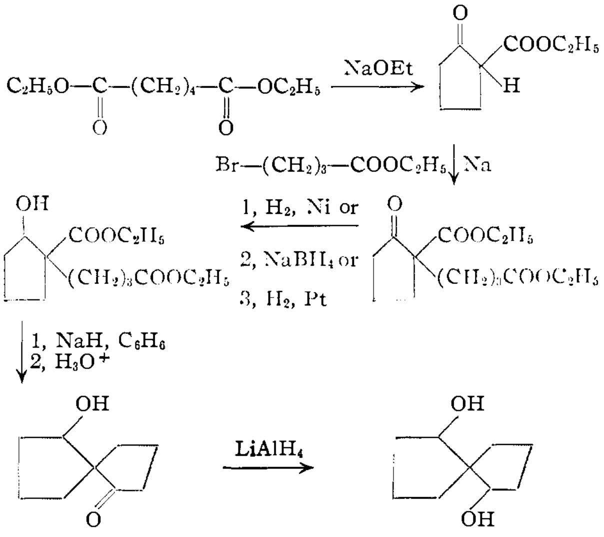
IX



X

Although the stereochemical structure of each of these three racemates[9] (A, B and C) cannot be assigned on the basis of the current data, a number of hints regarding the structures are available. Isomer A appears to predominate in the glycol mixtures coming from ketone by both the catalytic and lithium aluminum hydride reductions. If the hydrogens come in from the least hindered sides, the *cis–cis* isomer might be expected to predominate. Weak evidence supporting the above implication that A possesses the *cis–cis* configuration is found in the small but reproducible differences between the ultraviolet absorption spectra of the three isomeric esters and that of the *p*-nitrobenzoate of V (the monofunctional model compound). The spectra in 95% ethanol are as follows: isomer A, $\lambda_{\max}$ 258 mμ (ϵ 27,100); isomer B, $\lambda_{\max}$ 260 mμ (ϵ 26,600); isomer C, $\lambda_{\max}$ 260 mμ (ϵ 28,100); *p*-nitrobenzoate of V, $\lambda_{\max}$ 260 mμ (ϵ 13,600). Whatever differences exist must be due to the differences in steric situations in the four molecules. Since molecular models of three of the isomers (*cis–trans*, *trans–trans*, and the ester of V) are relatively unconstrained as compared to the fourth (*cis–cis*), and since three of the substances have the same $\lambda_{\max}$ (B, C and the ester of V) which is different from that of the fourth (A), then the data suggest that isomer A possesses the *cis–cis* configuration.[10]

A second, five-step approach to the preparation of the diols VIII was developed (16% over-all yield), the reactions of which are formulated. The ketol XI is theoretically capable of existing in two racemic forms. Although each form was not isolated, the liquid ketol was characterized as its *p*-nitrobenzoate (single pure compound) and its 2,4-dinitrophenylhydrazone (probably a mixture of racemates). The only bis-*p*-nitrobenzoate of VIII isolated from the esterified reduction product proved to be the A isomer, identical with that prepared from the reduction product of diketone III.



XI VIII

Figure 1 records the ultraviolet absorption spectra in the region of 300 mμ of the three ketones prepared in this investigation (III, IV and XI) as well as that of cyclopentanone. The differences in the spectra of cyclopentanone and the two spiro-monoketones (IV and XI) are rather small compared to the differences between the spectra of these three compounds on the one hand and that of diketone III on the other. For instance, ϵ for the three monoketones in the region of 300 mμ range from 19 to 24 and in the region of 310 mμ from 15 to 21. In contrast, ϵ for the diketone III is 121 at both 300 and 310 mμ, and even if this extinction coefficient is halved (ϵ for a single carbonyl), the resulting value is higher than those of the three model compounds by at least a factor of 3. This result constitutes still another case where chromophores insulated by saturated carbon but held in rigid proximity to one another modify each other's ultraviolet absorption spectra.[11] The present case is unique because the π-orbitals of each carbonyl group are orthogonal to one another, and nevertheless appear to interact.

A comparison of the infrared spectra (in carbon tetrachloride) of cyclopentanone, 1-ketospiro[4.4]-nonane (IV) and 1,6-diketospiro[4.4]nonane (III), reveals that the band associated with carbonyl stretching moves from 5.67 to 5.71 to 5.83 μ for the three compounds, respectively. Apparently the π-orbital interaction between the two carbonyl

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(7) H. Leuchs and E. Gieseler, *Ber.*, **45**, 2114 (1912).

(8) H. Sutter and N. Wijkman, *Ann.*, **519**, 97 (1935).

(9) For purposes of discussion, these isomeric esters are identified as A (m.p. 192.6–193.6°), B (m.p. 210–210.3°) and C (m.p. 223–224°).

(10) These small differences in spectra are attributable to small differences in steric inhibition of resonance of the ester function with the benzene ring which characterize the geometry of the *cis–cis* isomer on the one hand as compared to the other two isomers on the other. The above correlation is weakened by the lack of a clear-cut correlation between the ϵ's. For other correlation between spectra and configuration, see F. Hawthorne and D. J. Cram, THIS JOURNAL, **74**, 5859 (1952).

(11) See D. J. Cram and H. U. Daeniker [THIS JOURNAL, **76**, 2743 (1954)] *for a summary of references.*

groups of III is such as to increase the single bond character of the carbonyl functions.

Experimental Part

1-Ketospiro[4.4]nonane (IV).—From 200 g. of cyclopentanone, 20 g. of mercuric chloride, 40 g. of aluminum shavings, 5 ml. of benzene and 170 ml. of water was obtained 60 g. (30% yield) of 1,1′-dihydroxybicyclopentyl (m.p. 108.5–110°) according to the procedure of Zelinskii and Elagina[3] (32%, m.p. 108–109°). From 59 g. of this diol, 100 ml. of concentrated sulfuric acid and 100 ml. of water was obtained 45.5 g. (86% yield) of 6-ketospiro[4.5]decane, b.p. 105–110° (20 mm.), n^{25}_{D} 1.4869 (lit.[3] b.p. 120° at 45 mm., n^{25}_{D} 1.4848, yield 78%). This spiran (57 g.) was oxidized[3] by adding it dropwise to a solution of 170 ml. of concentrated nitric acid, 75 ml. of water and 2 g. of ammonium vanadate stirred at 55°. The γ-(1-carboxy-1-cyclopentyl)-butyric acid product was obtained in 71% yield (53 g.), m.p. 86.5–90.5 (lit.[3,12] 68% yield, m.p. 91–92°). This diacid (53 g.) was heated with 3 g. of barium hydroxide to give 30 g. (82% yield) of crude 1-ketospiro[4.4]nonane (IV), b.p. 88–89° (17 mm.) (lit.[3] b.p. 202–203°, n^{20}_{D} 1.4770, 90% yield). A small sample of ketone (1 g.) was absorbed on a column of 25 g. of activated alumina (basic), and the column was developed with pure pentane. The first 0.6 g. of ketone appearing in the column eluates was distilled, and a middle fraction (b.p. 90° at 22 mm., n^{25}_{D} 1.4737) was used for the spectra.

The 2,4-dinitrophenylhydrazone of IV was prepared in the usual way (87% yield), m.p. 155–157° (flat yellow needles from ethanol–ethyl acetate).

Anal. Calcd. for $C_{15}H_{18}O_4N_4$: C, 56.59; H, 5.70. Found: C, 56.33; H, 5.50.

1-Hydroxyspiro[4.4]nonane.—A solution of 4 g. of ketone IV in 30 ml. of anhydrous ether was added dropwise (ten minutes) to a mixture of 1.9 g. of lithium aluminum hydride and 30 ml. of dry ether. The mixture was stirred for thirty minutes, cooled, and 7.5 ml. of ethyl acetate was added dropwise followed by 60 ml. of 10% sulfuric acid. The ether layer was washed with water, dilute base and again with water, dried and evaporated. The residual oil was distilled to give 4.03 g. (99% yield) of colorless oil, b.p. 105° (20 mm.). Redistillation of this material (V) gave product of the same boiling point, n^{25}_{D} 1.4885.

Anal. Calcd. for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.04; H, 11.37.

A *p*-nitrobenzoate of this alcohol (1-hydroxyspiro[4.4]-nonane) was prepared by the usual method in 87% yield, m.p. 67.8–68.8° (methanol, white plates).

Anal. Calcd. for $C_{16}H_{19}O_4N$: C, 66.42; H, 6.62. Found: C, 66.36; H, 6.35.

1-Oximospiro[4.4]nonane.—A mixture of 5 g. of 1-ketospiro[4.4]nonane, 5 g. of hydroxylamine hydrochloride, 25 ml. of absolute ethanol and 25 ml. of anhydrous pyridine was heated at reflux on a steam-bath for one hour. The solvents were removed under reduced pressure leaving a colorless oil that crystallized when cooled. The solid was triturated with water, filtered and dried to give 5.2 g. (94% yield) of white granules, m.p. 42–46°. Two recrystallizations of a small portion of the crude material from pentane gave white platelets, m.p. 47.2–48.4°.

Anal. Calcd. for $C_9H_{15}ON$: C, 70.55; H, 9.87. Found: C, 70.39; H, 9.84.

1-Aminospiro[4.4]nonane. Method A.—A solution of 4.96 g. of the above oxime in 25 ml. of dry ether was added dropwise (13 minutes) to a stirred mixture of 2.46 g. of lithium aluminum hydride and 65 ml. of dry ether. The reaction mixture was stirred at reflux temperature for 90 minutes, cooled, and the excess reagent was destroyed with 9.5 ml. of ethyl acetate and 75 ml. of 10% sulfuric acid. The ether layer was washed with two 20-ml. portions of 3 *N* hydrochloric acid, the acid fractions were combined and first washed with ether and then made basic with 20% sodium hydroxide solution. This milky mixture was extracted four times with ether, the extracts were washed with water, dried and evaporated. The resulting yellow oil was distilled twice to give 1.52 g. (34%) of a colorless oil (VI), b.p. 90° (19 mm.), n^{25}_{D} 1.4822.

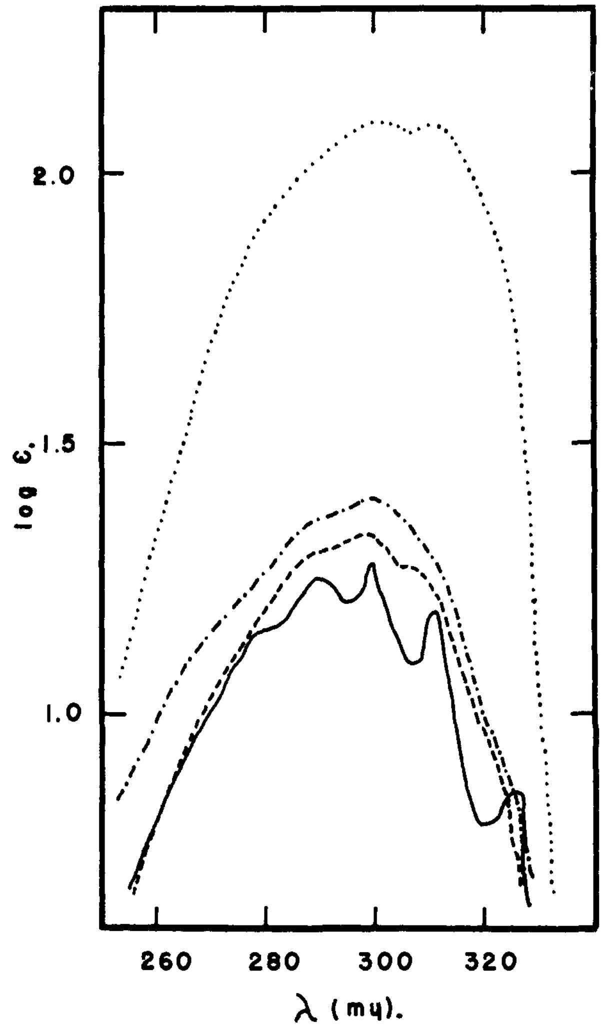

Fig. 1.—Ultraviolet absorption spectra of 95% ethanol (Cary recording spectrophotometer, model 11 PMS, quartz cells): —, cyclopentanone; – – –, compound IV; –·–·, compound XI; . . . . , compound III.

Anal. Calcd. for $C_9H_{17}N$: C, 77.63; H, 12.31. Found: C, 77.78; H, 12.29.

All of the aqueous layers were combined and continuously extracted with ether, and from the ether extracts was obtained an additional 0.23 g. of amine. From the original ether layer was isolated 2.0 g. of the original oxime, m.p. 46–48.4° (undepressed by admixture with an authentic sample).

Method B.—A mixture of 2.0 g. of oxime, 0.5 g. of Raney nickel catalyst and 60 ml. of 95% ethanol was rocked in a bomb at 70° under 1520 lb./in.^{2} of hydrogen for three hours. The resulting mixture was filtered, and the filtrate was evaporated to give a yellow oil that was twice distilled to give 1.4 g. of colorless amine VI, b.p. 88° (19 mm.), n^{25}_{D} 1.4850.

Anal. Calcd. for $C_9H_{17}N$: C, 77.63; H, 12.31. Found: C, 77.86; H, 12.09.

Ethyl α-Bromobutyrate. Method A.—The substance γ-phenoxypropyl bromide[13] was converted to γ-phenoxybutyronitrile[4a] in 92% yield which in turn gave a 41% yield of α-bromobutyric acid.[4b] Esterification[5b] of this material gave the desired ethyl γ-bromobutyrate in 76% yield, b.p. 116–120° (52–58 mm.), n^{25}_{D} 1.4564.

Method B.—The compound γ-bromobutyronitrile was prepared from trimethylene bromide and potassium cya-

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[12] M. Qudrat-i-Khuda and A. Mukherjee, *J. Indian Chem. Soc.*, **16**, 532 (1939).

[13] "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1947, p. 435.

nide[5a] in 57% yield (based on unrecovered bromide), which was hydrolyzed with 48% hydrobromic acid to γ-bromobutyric acid in 68% yield, b.p. 153–160° (45 mm.).

Method C.[6a]—From γ-butyrolactone was obtained a 93% yield of ethyl γ-bromobutyrate, b.p. 96–100° (20 mm.), n^{25}D 1.4546.

1,4,4,7-Tetracarbethoxyheptane.—From 300 ml. of absolute ethanol, 5.9 g. of sodium, 42.2 g. of malonic ester and 50 g. of ethyl γ-bromobutyrate was obtained 46 g. (65% yield) of 1,1,4-tricarbethoxybutane,[14] b.p. 113–129° (0.35 mm.), n^{25}D 1.4350, and 5.0 g. (10% yield) of 1,4,4,7-tetracarbethoxyheptane, b.p. 164–168° (0.35 mm.), n^{25}D 1.4455. An attempted preparation of the tetraester directly from malonic ester using two moles of ethyl γ-bromobutyrate gave a 13% yield of the product. The stepwise substitution of malonic ester proved to give better yields. Horeau[2] reported that this approach had been employed, without giving experimental details.

To a stirred solution of sodium ethoxide (37 g. of sodium plus 1 l. of absolute ethanol) was added dropwise (30 minutes) 441.5 g. of 1,1,4-tricarbethoxybutane followed by 314 g. (30 minutes) of ethyl γ-bromobutyrate. The mixture was then held at reflux for three hours, the ethanol was evaporated under reduced pressure, and the residue was shaken with 1 l. of water and 1.5 of ether. The ether layer was washed thoroughly with water, dried and the solvent was evaporated. The residual oil was distilled to give 196 g. (44% recovery) of 1,1,4-tricarbethoxybutane, b.p. 128–133° at 0.41 mm., and 252 g. (41% yield) of colorless tetraester, b.p. 167–181° (0.46 mm.), n^{25}D 1.4470. This material solidified when cooled, m.p. 26.5° (lit.[2] 28.5–29°).

The use of potassium in toluene gave an 11% yield of the tetraester, whereas sodium in benzene gave a 53% recovery of the starting triester and 27% of the tetraester.

1,4,4,7-Tetracarboxyheptane.—Horeau[2] reported this substance without giving experimental details for its preparation. The procedure is therefore recorded.

A mixture of 10 g. of 1,4,4,7-tetracarbethoxyheptane, 7.6 g. of potassium hydroxide and 40 ml. of water was held at reflux for 12 hours, cooled to 0° and acidified with 12 ml. of concentrated hydrochloric acid. The solvent was evaporated at 40° (30 mm.) and finally at 30° (1 mm.). The solid residue was triturated with anhydrous ether, filtered and air-dried. The mixture of product and potassium chloride was mixed with 100 ml. of boiling acetone, and the mixture was filtered. The solid was similarly treated with acetone, and the combined acetone filtrates were evaporated to give 5.1 g. (72% yield) of a white amorphous tetraacid, m.p. 169–175° (with gas evolution). The product from a similar run gave m.p. 177–179° (gas evolution). The yield could not be improved by employing aqueous ethanol or pure ethanol as solvent. In larger runs the potassium chloride was not removed, the solid material being used directly in the next step (see below).

1,6-Diketospiro[4.4]nonane (III).—The following procedure is adopted from that of Horeau.[2] A mixture of 41.5 g. of 1,4,4,7-tetracarboxyheptane and 270 ml. of acetic anhydride was gently stirred and heated at 60° for 80 minutes by which time the acid had completely dissolved. The clear yellow solution was kept for 20 hours at 60° (when potassium chloride was present, the mixture was filtered), and then about 200 ml. of acetic anhydride was evaporated at 80° and 25 mm. The residual tan oil was heated to 90° at 25 mm. (in a 200-ml. flask equipped with a short path still) until a puffy brown resin remained in the flask. The receiver was changed and the resin was heated slowly to 250° and kept there for 45 minutes. The receiver (−78°) contained 19.9 g. of a tan solid that melted to a brown liquid at room temperature. Redistillation of this material gave 12.03 g. of colorless product, b.p. 128–131° (23 mm.). This material was crystallized and recrystallized from methanol to give 10.66 g. (48% yield) of large white crystals of III, m.p. 35–38°. The sample used for the spectral examinations was recrystallized three more times from methanol, m.p. 37.2–37.8° (lit.[2] m.p. 41–42°).

The oxime of this diketone was prepared by the method reported for the model compound, 1-ketospiro[4.4]nonane. From 5.0 g. of the diketone was obtained 5.46 g. of small prisms (methanol) of oxime, m.p. 227–231° dec., recrystallization of which gave m.p. 132–134° (lit.[2] 134–135°).

1,6-Dihydroxyspiro[4.4]nonane (VIII). **Method A**.—To a mixture of 2.5 g. of lithium aluminum hydride and 40 ml. of anhydrous ether was added dropwise a solution of 5.0 g. of diketone III in 40 ml. of anhydrous ether. The mixture was stirred an additional hour, treated first with ethyl acetate (10 ml.) and then with 80 ml. of 10% sulfuric acid. The layers were separated, the ether layer was washed with 10 ml. of 5% solution of sodium hydroxide and two 15-ml. portions of water. The ether solution was dried and evaporated to give a yellow oil that upon distillation provided 3.7 g. of colorless glycol, b.p. 159–160° (20 mm.).

All of the aqueous layers and washes were combined and continuously extracted with ether for 24 hours. An additional 0.93 g. of diol was obtained, b.p. 159–162° (21 mm.), to bring the total yield to 90%. An analytical sample was prepared by redistillation of the oil, b.p. 160–161° (23 mm.), n^{25}D 1.5025.

Anal. Calcd. for $C_9H_{16}O_2$: C, 69.19; H, 10.33. Found: C, 69.32; H, 10.53.

Method B.—A mixture of 5.0 g. of diketone III, 100 ml. of 95% ethanol and 5 ml. of Raney nickel catalyst was shaken in a bomb at 100° for 16 hours under a pressure of 1650 lb./sq. in. of hydrogen. The resulting mixture was cooled, filtered and solvent was evaporated. The residual orange oil was distilled to give 4.88 g. (95% yield) of colorless glycol product, b.p. 159–161° (23 mm.), n^{25}D 1.5020.

Bis-*p*-nitrobenzoate of 1,6-Dihydroxyspiro[4.4]nonane.—The diol VIII (0.56 g.) prepared by method A (see above) was mixed with 1.5 g. of *p*-nitrobenzoyl chloride and 5 ml. of dry pyridine, and heated to 100° for 40 minutes. The mixture was then cooled and shaken with a mixture of 20 ml. of benzene, 40 ml. of chloroform and 25 ml. of 3 *N* hydrochloric acid. The organic layer was washed with dilute acid, dilute base, water, was dried and evaporated. The yellow amorphous solid (1.52 g., m.p. 155–177°) thus obtained was crystallized from ethyl acetate and cooled to give 0.82 g. of white crystalline material, m.p. 184–192°, and filtrates (a). This solid was recrystallized twice from acetone to give 0.65 g. or 39% yield of racemate A, m.p. 192.6–193.6°.

Anal. Calcd. for $C_{23}H_{22}O_8N_2$: C, 60.78; H, 4.88. Found: C, 61.07; H, 5.16.

The original filtrate (a) was evaporated to dryness, dissolved in 10 ml. of benzene and chromatographed on a column of 17 g. of activated alumina. The column was developed with benzene, the column filtrates being cut into thirty-one 15-ml. fractions, each of which was evaporated. Fractions 2–9 were combined and the material was crystallized and recrystallized from acetone to give 0.070 g. of white needles, m.p. 210–211.5°, of racemate B. A mixture of racemates A and B gave m.p. 173–189°.

Anal. Calcd. for $C_{23}H_{22}O_8N_2$: C, 60.78; H, 4.88. Found: C, 60.79; H, 4.96.

The same esterification procedure was applied to 4.63 g. of glycol VIII prepared by reduction method A to give 11.58 g. of a tan yellow powder, m.p. 169–181°. From 8.2 g. of this material was obtained 4.95 g. of racemate A by crystallization from ethyl acetate and recrystallization from acetone, m.p. 191–193°. The filtrates were combined and evaporated, and the residual solid was dissolved in a minimum amount of dry acetone. The resulting solution was cooled to room temperature and 13 fractions of the product that crystallized were taken by decantation of the supernatant liquor every few minutes. Fraction 9 consisted of a mixture of granules and large polyhedra which were separated manually to give after recrystallization from acetone 1.3 g. of racemate A, m.p. 192–193° and 0.10 g. of racemate B, m.p. 210–211°, respectively. Fraction 10 gave after recrystallization from acetone 0.65 g. of racemate B, m.p. 210–211°. Fractions 2–6 (0.63 g. of needles, m.p. 220–222°) were combined and recrystallized from acetone at room temperature to give 0.48 g. of needles, m.p. 222.6–223.6°, of racemate C. Admixture of racemate C with B gave m.p. 186–195°.

Anal. Calcd. for $C_{23}H_{22}O_8N_2$: C, 60.78; H, 4.88. Found: C, 60.90; H, 5.11.

All filtrates from the above separations were combined and the above processes repeated exhaustively (utilizing manual separation whenever possible) to produce a total of 5.21 g. (39%) of racemate A, 0.92 g. (7%) of B and 1.3 g. (10%) of C.

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[14] J. Braun and F. Meyer, *Ber.*, **74**, 19 (1941). See also M. D. Potter and E. P. Taylor, *J. Chem. Soc.*, 3513 (1951).

Ethyl γ-(1-Carbethoxy-2-hydroxy-1-cyclopentyl)-butyrate. The preparation of ethyl γ-(1-carbethoxy-2-keto-1-cyclopentyl)-butyrate was accomplished by a modification of the procedure of Bachmann and Struve,[15] and is recorded here. A mixture of 64 g. of clean sodium and 2170 ml. of pure toluene was heated to reflux temperature, and the sodium was dispersed through violent stirring. The resulting mixture was cooled in an ice-bath and 433 g. of 2-carbethoxycyclopentanone[16] was added dropwise but rapidly. The ice-bath was replaced with a steam-bath, and the reaction mixture was heated *cautiously* with good stirring. After 16 minutes a spontaneous reaction set in, and the flask was *immediately* cooled in an ice-bath. When the reaction had subsided, the thick pasty reaction mixture was heated for one hour on the steam-bath, cooled in an ice-bath, and 541 g. of ethyl γ-bromobutyrate was added. The mixture was then held at reflux temperature for 17 hours.

The suspension of sodium bromide in a yellow solution was then cooled in an ice-bath and cautiously acidified with 1 l. of 1 *N* hydrochloric acid. The layers were separated, the toluene layer was washed thoroughly with water, dried and evaporated at 100° under reduced pressure. The tan oil remaining was distilled to give 562 g. of oil, b.p. 130–163° (0.8 to 1.0 mm.), which was redistilled to give 525 g. (70% yield) of colorless oil, b.p. 136–142° (0.20 mm.), $n^{25}D$ 1.4573. This material was used directly in the next step.

A mixture of 60 g. of the above ethyl γ-(1-carbethoxy-2-keto-1-cyclopentyl)-butyrate, 100 ml. of 95% ethanol and 1.0 g. of platinum oxide was shaken in an atmosphere of hydrogen for 24 hours. The up-take of hydrogen leveled at a calculated value of 82–89% of theory. The catalyst was removed by filtration of the mixture through a cake of Celite, the ethanol was evaporated from the filtrate under vacuum, and the residual oil was distilled to give 51 g. (91% yield) of product, b.p. 128–130° (0.4 mm.), $n^{25}D$ 1.4619.

Anal. Calcd. for $C_{14}H_{24}O_5$: C, 61.74; H, 8.88. Found: C, 61.70; H, 9.03.

A *p*-nitrobenzoate derivative of this alcohol was prepared by the usual method to give only one readily isolable diastereomer in 39% yield, m.p. 84–86° (fine needles from methanol).

Anal. Calcd. for $C_{21}H_{27}O_8N$: C, 59.85; H, 6.46. Found: C, 59.79; H, 6.39.

1-**Keto-6-hydroxyspiro**[**4.4**]**nonane** (**XI**).—To a mixture of 7.7 g. of sodium hydride and 60 ml. of pure benzene was added 0.2 ml. of pure methanol, and the mixture was heated to reflux temperature. To the stirred mixture was added dropwise (two hours) a solution of 20 g. of ethyl γ-(1-carbethoxy-2-hydroxy-1-cyclopentyl)-butyrate. The resulting brown, pasty reaction mixture was held at reflux with stirring for 12 hours. Butyl ether (4 ml.) and 13 ml. of toluene were then added, the condenser was replaced with a thermometer, and the mixture was cooled to −5° in an ice-salt-bath as 13.5 ml. of methanol was added dropwise, followed by the dropwise addition of 140 ml. of ice-water. The mixture was then heated to reflux and stirred for 30 minutes, again cooled to 0° and acidified by the dropwise addition of 16 ml. of 30% sulfuric acid solution. The mixture was heated to reflux for one hour, cooled, and the layers were separated. The water layer was extracted with three 100-ml. portions of ether, the organic layers were combined and washed with two 50-ml. portions of 3% sodium carbonate solution and three 50-ml. portions of water. The organic layer was dried, evaporated and the residual oil was distilled to give two fractions, b.p. 135–146° (18 mm.), wt. 3.77 g., and b.p. 146–160° (18 mm.), wt. 1.0 g. Fraction 1 was redistilled for analysis, 3.0 g., b.p. 70–76° (0.07 mm.), $n^{25}D$ 1.4909.

Anal. Calcd. for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.81; H, 9.26.

The 2,4-dinitrophenylhydrazone of this material was prepared by the usual method, a 93% yield of what appears to be a mixture of diastereomers resulting, m.p. 114–118°. Three recrystallizations of this material from ethanol gave rust colored granules, m.p. 138–144°.

Anal. Calcd. for $C_{15}H_{18}O_5N_4$: C, 53.88; H, 5.43. Found: C, 53.80; H, 5.43.

The *p*-nitrobenzoate of the ketol was prepared by the usual method, a brown pasty product resulting. The material was triturated with methanol, filtered, and the filtrate was concentrated and cooled. The solid that separated was recrystallized five times from methanol to give a 15% yield of one diastereomer, m.p. 90.5–92° (yellow plates).

Anal. Calcd. for $C_{16}H_{17}NO_5$: C, 63.35; H, 5.65. Found: C, 63.48; H, 5.50.

Conversion of 1-**Keto-5-hydroxyspiro**[**4.4**]**nonane** (**XI**) **to** 1,**5-Dihydroxyspiro**[**4.4**]**nonane** (**VIII**).—Reduction of XI with lithium aluminum hydride by the same method used with diketone III as starting material (see above) gave an 86% yield of glycol, b.p. 159–161° (21 mm.), $n^{25}D$ 1.5026. This material (2.60 g.) was converted to a mixture of diastereomeric bis-*p*-nitrobenzoates of VIII by the method reported above. Fractional crystallization of this material from acetone gave 1.6 g. of racemate A, m.p. 192–194° undepressed by admixture with an authentic sample.

LOS ANGELES, CALIFORNIA

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[15] W. E. Bachmann and R. S. Struve, THIS JOURNAL, **63**, 2589 (1941).

[16] "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1947, p. 119.

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

Cyclic Polyolefins. XXXII. *cis*- and *trans*-1,3-Diphenylcycloöctane[1]

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Authentic samples of the two geometric isomers of 1,3-diphenylcycloöctane have been prepared and proved to be identical with the two isomers previously obtained from carbonyl-bridged intermediates. The synthetic route involved Friedel–Crafts addition of benzene to 2-cycloöcten-1-one (III), followed by reaction of the resulting 3-phenylcycloöctanone (IV) with phenyllithium, dehydration of the tertiary alcohol, and reduction of the mixture of olefins that was formed. 2-Cycloocten-1-one was prepared by Oppenauer or chromic acid oxidation of 2-cycloöcten-1-ol (II), obtained from the acetate I, which in turn was prepared from 3-bromocycloöctene and silver acetate or *cis*-cycloöctene and mercuric acetate.

Convenient routes for the synthesis of eight-membered ring compounds from carbonyl-bridged intermediates have been described for the preparation of 2,4-diphenylcycloöcta-1,4-diene, 2,4-diphenylcycloöctene and 3,5-diphenylcycloöctene.[3] Evidence for the structure of these compounds was based on ultraviolet absorption spectra, oxidative degradation, analogy with a similar synthesis of 1-phenylcycloöcta-1,3-diene,[4] and reduction to one or both of two solid hydrocarbons, believed to be the two geometric isomers of 1,3-diphenylcycloöctane.[3] The presence of an eight-membered ring in the

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[2] du Pont Fellow, 1950–1951.

[3] A. C. Cope, F. S. Fawcett and G. Munn, THIS JOURNAL, **72**, 3399 (1950).

[4] A. C. Cope and E. C. Hermann, *ibid.*, **72**, 3405 (1950); D. F. Rugen, Ph.D. Thesis, Massachusetts Institute of Technology, 1952.