The Tricyclo[6.3.0.0^{4,8}]undecane System[1]

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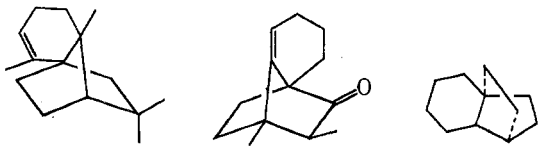
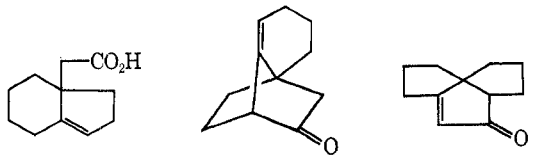
Cyclodehydration of bicyclo[4.3.0]non-1(9)-ene-6-acetic acid (**4**) or a mixture of *syn*- and *anti*-tricyclo[4.3.1.0^{1,6}]-decane-10-carboxylic acid (**15**) with polyphosphoric acid yields tricyclo[6.3.0.0^{4,8}]undec-3-en-2-one (**6**) as the sole volatile product. The structure of **6** is established by conversion into methyl spiro[4.4]nonanecarboxylate (**9**). Some transformations of **6** are discussed.

Acid-catalyzed isomerizations have provided the only examples of the tricyclo[5.2.2.0^{1,6}]undecane skeleton, neoclovene (**1**)[2] and ketone **2**.[3] One synthetic approach to this carbon skeleton involves recognition of the objective as an ethano-bridged hydrindan, **3**. Here we report the discovery of a rearrangement in the cyclodehydration of acid **4**, which led to the new tricyclo[6.3.0.0^{4,8}]undecenone (**6**), rather than the desired tricyclo[5.2.0.0^{1,6}]undecenone (**5**).



1 **2** **3**

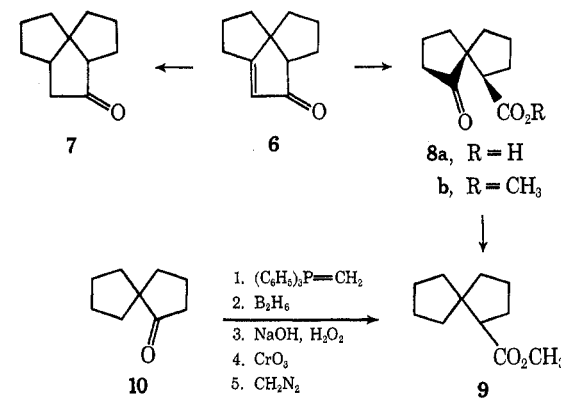
Cyclodehydration of acid **4** seemed a reasonable candidate for the preparation of ketone **5**. In the event, treatment of **4** with polyphosphoric acid (PPA) provided a single unsaturated ketone in 31% yield. The new ketone was assigned structure **6** after consideration of the spectral data,[4] which show the presence of a cyclopentenone bearing a single vinyl hydrogen, and that at the α position.



4 **5** **6**

Subsequent chemical degradation confirmed our assignment. Catalytic hydrogenation of **6** yields a cyclopentanone (**7**), and oxidation (periodate–permanganate) yields a C_{10} keto acid (**8a**) in which the ketone function is a cyclopentanone. Wolff–Kishner reduction of the keto acid followed by esterification provides the new ester **9**,[5] which was identified by comparison with an authentic sample prepared from ketone **10**,[6] as is outlined in Scheme I. The conversion of the new ketone **6** into ester **9** by the sequence described defines the positions of 10 of the 11 carbons unambiguously. To reconstruct mentally the unknown ketone from ester **9** we need only consider that one trigonal carbon

SCHEME I

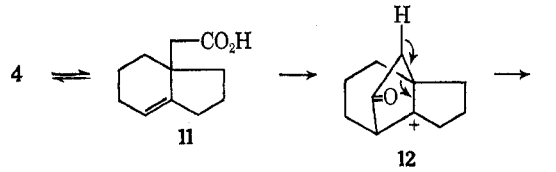


7 **6** **8a**, R = H; **b**, R = CH_3 **10** **9**

(corresponding to the trigonal C_α removed by oxidation) must be attached to the spiran through a carbon–carbon double bond as well as to the carboxyl at C_1, such that a normal α,β-unsaturated ketone results. Only at C_2 and C_6 is this possible.[7] The former position is eliminated by the evidence already presented; therefore, structure **6** is firmly established.

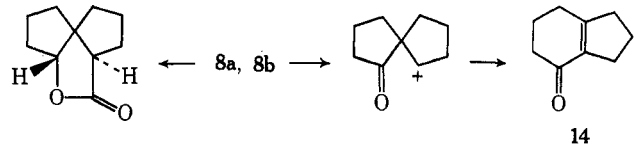
Ketone **6** evidently arises by isomerization of acid **4** to the more stable **11**, which then undergoes intramolecular acylation followed by a Wagner–Meerwein shift and proton elimination as is depicted in Scheme II.

SCHEME II



11 **12**

Keto ester **8b** was further characterized by reduction with sodium borohydride to yield lactone **13**; oxidative decarboxylation of **8a** with lead tetraacetate yielded the rearranged ketone **14**. The latter may be considered to arise *via* an acyl shift in the carbonium ion formed by the decarboxylation of **8a**.[8]



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(1) We thank the National Science Foundation for generous support of this research.

(2) (a) W. Parker, R. A. Raphael, and J. S. Roberts, *Tetrahedron Lett.*, 2313 (1965); (b) T. F. W. McKillop, J. Martin, W. Parker, and J. S. Roberts, *Chem. Commun.*, 162 (1967).

(3) R. L. Cargill, M. E. Beckham, and J. R. Damewood, Abstracts, 155th National Meeting of the American Chemical Society, San Francisco, Calif., April 1968, No. P179.

(4) See Experimental Section for spectral data.

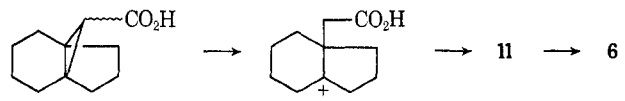
(5) The acid corresponding to **9** was reported as an uncharacterized oil: N. N. Chatterjee, *J. Indian Chem. Soc.*, **14**, 259 (1937).

(6) R. K. Hill and R. T. Conley, *J. Amer. Chem. Soc.*, **82**, 645 (1960).

(7) Bicyclic olefins having double bonds at the bridgeheads have been prepared, but the bicycloheptenes and bicyclooctenes remain fugitive. See J. A. Marshall and H. Faubl, *ibid.*, **89**, 5965 (1967); J. R. Wiseman, *ibid.*, **89**, 5966 (1967); J. R. Wiseman, H. F. Chan, and C. J. Ahola, *ibid.*, **91**, 2812 (1960).

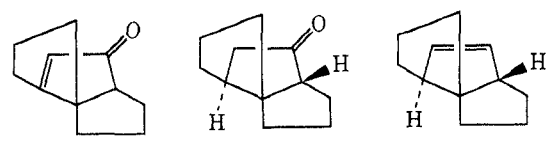
(8) (a) E. J. Corey and J. Casanova, *ibid.*, **85**, 165 (1963); (b) G. Buchi, R. E. Erickson, and N. Wakabayashi, *ibid.*, **83**, 927 (1961).

Our interest in the chemistry of the tricyclic system represented by ketone **6** led us to develop a route to that enone which is somewhat more efficient than is the cyclodehydration of **4** or **11**. Acids **4** and **11** may be prepared by the method developed by Burgstahler,[9] an elegant but somewhat time-consuming sequence. Since isomerization of **4** to **11** must proceed *via* ion **16**, we considered that the cyclopropyl acids **15**,[10] which are more readily available than are acids **4** or **11**, would undergo acid-catalyzed ring opening to yield acid **11** and subsequent ring closure to give ketone **6**. Indeed, ketone **6** was obtained in 60% yield when acids **15** were heated in PPA at 100° for 45 min. The cyclodehydration of acids **15** provides another example of the utilization of a cyclopropane ring to introduce an angular substituent on a polycyclic nucleus.[11]



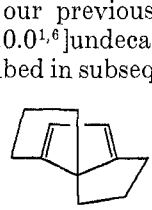
15 16

Saturated ketone **7** is readily converted into the monoolefin **17** by the method of Shapiro.[12] The nmr spectrum of olefin **17** (see Experimental Section), which strongly indicates C_2 molecular symmetry in that olefin, provides support for the stereochemical assignments shown in formulas **7** and **17**.



6 7 17

The transformations of ketone **6** described here provide paths to 1,6-disubstituted spiro[4.4]nonanes as well as the basis for further exploration of the chemistry of the tricyclo[6.3.0.0^{4,8}]undecane system, including the synthesis of the chiral diene **18**. We shall report further on our efforts to prepare diene **18**. In addition, other variations of our previously outlined approach to the tricyclo[5.2.0.0^{1,6}]undecane system (see formula **3**) will be described in subsequent papers.



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Experimental Section[13]

Bicyclo[4.3.0]non-1(9)-ene-6-acetic Acid (4).—The corresponding aldehyde was prepared through an angular alkylaton adapted from the procedure of Burgstahler and Nordin.[9] The overall yield of bicyclo[4.3.0]non-1(9)-ene-6-acetaldehyde from bicyclo[4.3.0]non-1(6)-en-7-one was 30%: ir (CCl_4) 3020, 2700, and 1720 cm^{-1}; nmr (CCl_4) δ 9.50 (t, 1, J = 2.5 Hz, $-CH_2-CHO$), 5.2 (m, 1, $-CH=C$).

Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.83. Found: C, 80.39; H, 9.89.

To a solution of 3.43 g of the above aldehyde in 300 ml of acetone and 100 ml of water was added 12 ml of stock chromic anhydride solution (prepared from 27 g of chromic anhydride and 23 ml of sulfuric acid diluted to 100 ml with water) and the resulting mixture was stirred at 25° for 7 hr. Aqueous sodium carbonate solution was added and the mixture was washed twice with pentane. The aqueous portion was acidified with hydrochloric acid, saturated with sodium chloride, and extracted three times with ether. The combined ethereal extracts were dried and concentrated to yield 3.16 g of crude bicyclo[4.3.0]non-1(9)-ene-6-acetic acid (**4**): ir (neat) 3600–2600 and 1710 cm^{-1}. Esterification with diazomethane gave the methyl ester (single compound by glpc): ir (neat) 3030 and 1735 cm^{-1}; nmr (CCl_4) δ 5.14 (m, 1, $-CH=C$) and 3.53 (s, 3, $-CO_2CH_3$).

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.35. Found: C, 74.22; H, 9.23.

Periodate–Permanganate Cleavage of Acid 4.—To a solution of 1.44 g of sodium periodate, 0.0179 g of potassium permanganate, 0.350 g of potassium carbonate, and 340 ml of water was added 0.152 g of **4** in 1 ml of ether. The mixture was stirred at 25° for 2 days, 0.1 g of sodium hydroxide was added, and the alkaline solution was washed twice with pentane. The aqueous solution was acidified with sulfuric acid, saturated with sodium chloride, and extracted three times with ether. The ethereal solution was dried and concentrated to afford 0.258 g of crude 1-(carboxymethyl)-2-oxocyclohexanepropionic acid: ir (CCl_4) 3600–2500 and 1715 cm^{-1}. Esterification with diazomethane gave the keto diester (purity greater than 90% by glpc): ir (CCl_4) 1735 and 1710 cm^{-1}; nmr (CCl_4) δ 3.55 (s, 6, $-CO_2CH_3$).

Anal. Calcd for $C_{13}H_{20}O_5$: C, 60.92; H, 7.87. Found: C, 60.91; H, 8.14.

Tricyclo[6.3.0.0^{4,8}]undec-3-en-2-one (6).—A mixture of 2.78 g of crude **4** and 53 g of polyphosphoric acid was heated at 100° for 2 hr with occasional stirring. The reaction mixture was quenched with ice and extracted three times with pentane. The organic portion was washed with sodium bicarbonate and saturated sodium chloride solutions, dried, concentrated, and chromatographed over alumina with 25% ether in pentane. The eluate was concentrated and distilled to give 0.784 g (31%) of tricyclo[6.3.0.0^{4,8}]undec-3-en-2-one (**6**): bp 80° (0.5 Torr); ir (CCl_4) 1710 and 1635 cm^{-1}; nmr (CCl_4) δ 5.61 (br s, 1, $-CH=C$]; uv max (95% C_2H_5OH) 235 mμ (ϵ 11,300).

Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.49; H, 8.59.

Tricyclo[6.3.0.0^{4,8}]undecan-2-one (7).—Catalytic hydrogenation (5% palladium on charcoal) of 1.10 g of **6** yielded 0.99 g of distilled tricyclo[6.3.0.0^{4,8}]undecan-2-one (**7**): bp 61° (0.3 Torr); ir (CCl_4) 1735 cm^{-1}.

Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.83. Found: C, 80.54; H, 9.67.

Periodate–Permanganate Cleavage of 6.—To a solution of 3.80 g of sodium periodate, 0.050 g of potassium permanganate, 0.913 g of potassium carbonate, and 890 ml of water was added 0.353 g of **6** in 0.5 ml of ether. After 2.5 days the reaction was worked up as previously described. The crude product was crystallized from *n*-hexane (charcoal), giving 0.208 g of *cis*-6-oxospiro[4.4]nonanecarboxylic acid (**8a**), mp 70–72°. A pure sample was obtained after two recrystallizations from *n*-hexane: mp 71–71.5°; ir (CCl_4) 3600–2400, 1740, and 1715 cm^{-1}.

Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 65.95; H, 7.72.

Esterification with diazomethane gave the corresponding methyl ester **8b**: ir (CCl_4) 1740 and 1735 cm^{-1}; nmr (CCl_4) δ 3.52 (s, 3).

Anal. Calcd for $C_{11}H_{18}O_3$: C, 67.32; H, 8.22. Found: C, 67.46; H, 8.47.

(9) A. W. Burgstahler and I. C. Nordin, *J. Amer. Chem. Soc.*, **83**, 198 (1961).

(10) H. O. House and C. J. Blankley, *J. Org. Chem.*, **33**, 47 (1968).

(11) For some examples see (a) ref 10; (b) J. J. Sims, *ibid.*, **32**, 1751 (1967); (c) J. J. Sims, *J. Amer. Chem. Soc.*, **87**, 3511 (1965); (d) T. Hanafusa, L. Birladeanu, and S. Winstein, *ibid.*, **87**, 3510 (1965); (e) D. J. Beames and L. N. Mander, *Chem. Commun.*, 498 (1969); (f) R. D. Stiptanovic and R. B. Turner, *J. Org. Chem.*, **33**, 3261 (1968), and J. J. Sims and V. K. Honwad, *ibid.*, **34**, 496 (1969).

(12) R. H. Shapiro and M. J. Heath, *J. Amer. Chem. Soc.*, **89**, 5734 (1967).

(13) All boiling points and melting points are uncorrected. Microanalyses were performed by Bernhardt Microanalytisches Laboratorium, West Germany, or by Gailbraith Laboratories, Inc., Knoxville, Tenn. Infrared spectra were determined in carbon tetrachloride unless otherwise stated, using either a Perkin-Elmer Model 337 or 257 grating spectrophotometer. All nmr spectra were determined in carbon tetrachloride containing 5% tetramethylsilane as an internal standard using a Varian A-60 nmr spectrometer. Analytical gas–liquid partition chromatograms were determined using a Varian Aerograph Model 1200 chromatograph, and preparative glpc separations were conducted using a Varian Aerograph 90-P-3 chromatograph. Liquid samples were purified for combustion analysis by glpc followed by vacuum distillation onto a cold finger.

Modified Wolff–Kishner Reduction of Keto Acid 8a.—To a solution of 0.21 g of potassium hydroxide, 0.15 ml of hydrazine hydrate, and 1.5 ml of diethylene glycol was added 0.20 g of **8a**. The solution was heated under reflux for 1 hr, and then the temperature was raised to 190–200°. After an additional 2 hr the volatile material had been removed and the reaction was cooled, dilute hydrochloric acid was added, and the mixture was extracted with ether. The ethereal extract was dried and concentrated to give 0.18 g of crude spiro[4.4]nonanecarboxylic acid. Esterification with diazomethane gave methyl spiro[4.4]-nonanecarboxylate (**9**) (see below).

Methylenespiro[4.4]nonane.—The conversion of 11.06 g of spiro[4.4]nonanone[14] (**10**) into the methylene analog was carried out with methylenetriphenylphosphorane in dimethyl sulfoxide according to the procedure of Corey.[15] A yield of 8.02 g of methylenespiro[4.4]nonane was obtained: bp 78° (25 Torr); ir (CCl_4) 3069, 1655, and 880 cm^{-1}; nmr (CCl_4) δ 4.67 (s, 2, >C=CH_2), 2.28 (m, 2), and 1.56 (s, 12).

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 88.38; H, 11.61.

Hydroxymethylspiro[4.4]nonane.—To a solution of 4.0 g of methylenespiro[4.4]nonane and 0.42 g of sodium borohydride in 25 ml of diglyme maintained at 0° was added dropwise with stirring 1.85 ml of boron trifluoride etherate. The reaction mixture was warmed to 25° and stirring was continued for 1 hr. Then 3.1 ml of 3 *N* sodium hydroxide was added followed by 3.1 ml of 30% hydrogen peroxide and the solution was stirred for 30 min. The resulting mixture was poured into 100 ml of water and was extracted with ether. The organic portion was washed twice with ice water, dried, and concentrated to give 5.47 g of crude hydroxymethylspiro[4.4]nonane: bp 60° (0.5 Torr); ir (CCl_4) 3610 and 3500–3200 cm^{-1}; nmr (CCl_4) δ 3.40 (m, 2 CH_2OH) and 3.35 (s, 1, -OH).

Anal. Calcd for $C_{10}H_{18}O$: C, 77.86; H, 11.76. Found: C, 77.74; H, 11.92.

Methyl Spiro[4.4]nonanecarboxylate (**9**).—To an ice-cooled solution of 1.46 g of hydroxymethylspiro[4.4]nonane in 9.3 ml of aqueous sulfuric–acetic acid (prepared from 5 ml of sulfuric acid and 10 ml of water diluted to 50 ml with acetic acid) was added at once 8.2 ml of chromic anhydride solution (prepared from 12.5 g of chromic anhydride in 12.5 ml of water diluted to 50 ml with acetic acid). The mixture was stirred at 25° for 4 hr and and then heated to 100° for 0.5 hr. Approximately 50 ml of water was added and the mixture was extracted three times with ether. The ethereal portion was extracted three times with 1 *N* sodium hydroxide, and the alkaline solution was washed with hexane and then acidified with sulfuric acid. The resulting emulsion was extracted twice with pentane and the organic portion was dried and concentrated to yield 0.725 g (40% from **10**) of spiro[4.4]nonanecarboxylic acid. Esterification with diazomethane gave methyl spiro[4.4]nonancarboxylate (**9**) (single compound by glpc): ir (CCl_4) 1735 cm^{-1}; nmr (CCl_4) δ 3.52 (s, 3).

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.67; H, 9.90.

(14) R. K. Hill and R. T. Conley, *J. Amer. Chem. Soc.*, **82**, 645 (1960).

(15) R. Greenwald, M. Chaykovsky, and E. J. Corey, *J. Org. Chem.*, **28**, 1128 (1963).

Lithium aluminum hydride reduction of **9** regenerated hydroxymethylspiro[4.4]nonane.

Oxidative Decarboxylation of Keto Acid 8a.—A solution of 0.100 g of **8a**, 0.07 ml of pyridine, and 0.211 g of lead tetraacetate in 1.5 ml of benzene was stirred with gentle refluxing under a nitrogen atmosphere for 7 hr. The reaction mixture was eluted from alumina with ether and the eluate was washed twice with 1 *N* sodium hydroxide, twice with brine, twice with 1 *N* hydrochloric acid, and twice again with brine. Removal of solvent gave exclusively the known bicyclo[4.3.0]non-1(6)-en-2-one (**14**).[16]

Cyclodehydration of Acids 15.[10]—A mixture of 4.60 g of acids **15** and 90 g of polyphosphoric acid was stirred at 100° for 45 min. The reaction was worked up as previously described, yielding 2.41 g of distilled tricyclo[6.3.0.0^{4,8}]undec-3-en-2-one (**6**).

Tricyclo[6.6.0.0^{4,8}]undec-2-ene (**17**).—A solution of 0.627 g of tricyclo[6.3.0.0^{4,8}]undecan-2-one (**7**), 0.760 g of tosylhydrazide, and 0.03 ml of hydrochloric acid in 3 ml of ethanol was refluxed for 1 hr and then allowed to stand at 25° overnight. Removal of solvent gave crude tosylhydrazone, which was dissolved in 25 ml of ether and treated with 7.6 ml of 2.0 *M* *n*-butyllithium. Gas evolution was evident; after 10 min 25 ml of water was added and the mixture was extracted twice with pentane. The dried organic portion was concentrated and the residue was distilled (0.5 Torr, bath temperature 90°) to give 0.232 g (41%) of tricyclo[6.3.0.0^{4,8}]undec-2-ene (**17**): ir (CCl_4) 3025 cm^{-1}; nmr (CCl_4) δ 5.31 (s, 2, HC=CH), 2.59 (m, 2), and 1.51 (br s, 12).

Anal. Calcd for $C_{11}H_{16}$: C, 89.12; H, 10.88. Found: C, 89.05; H, 11.00.

***cis,cis*-6-Hydroxyspiro[4.4]nonane-1-carboxylic Acid Lactone** (**13**).—To a stirred solution of 0.22 g of keto ester **8b** in 3.2 ml of methanol at 0° was added 25 mg of sodium borohydride. After 30 min 3 ml of dilute hydrochloric acid was added and the mixture was extracted with ether. The ethereal extract was concentrated to give crude *cis,cis*-6-hydroxyspiro[4.4]nonane-1-carboxylic acid lactone (**13**) containing an uncharacterized ester impurity. The crude product was refluxed for 5 hr in 10% aqueous sodium hydroxide. The mixture was neutralized with dilute hydrochloric acid and extracted with ether. The organic layer was washed twice with sodium bicarbonate, dried, concentrated, and collected by glpc (DEGS) to give 0.079 g of *cis,cis*-hydroxyspiro[4.4]nonane-1-carboxylic acid lactone (**13**): ir (CCl_4) 1775 cm^{-1}; nmr (CCl_4) δ 4.27 (m, 1, HCO).

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.47; H, 8.57.

Registry No.—Bicyclo[4.3.0]non-1(9)-ene-6-acetaldehyde, 24097-40-3; 1-(carboxymethyl)-2-oxocyclohexanepropionic acid dimethyl ester, 24097-42-5; methylenespiro[4.4]nonane, 19144-06-0; hydroxymethylspiro-[4.4]nonane, 24097-45-8; methyl ester of **4**, 24097-41-4; **6**, 24097-43-6; **7**, 24215-67-6; **8a**, 24097-75-4; **8b**, 24097-76-5; **9**, 24097-46-9; **13**, 24097-77-6; **17**, 24097-78-7.

(16) R. K. Hill and R. T. Conley, *Chem. Ind.* (London), 1314 (1956).