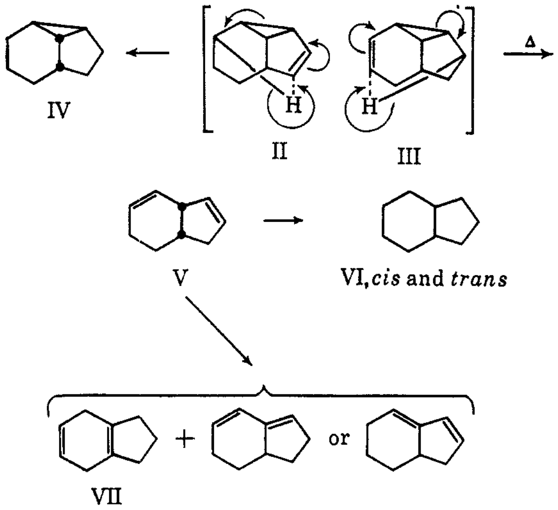
SCHEME II



sulting from insertion of the carbenoid intermediate on ether (solvent). The yield of intramolecular insertion products appears to be higher in this case than in any other studied to this time.[4,17]

Experimental Section

Reaction of 9.9-Dibromobicyclo[6.1.0]non-2-ene with Methyllithium.—A solution of 64 g (0.22 mole) of 9,9-dibromobicyclo-[6.1.0]non-2-ene (1)[18] in 200 ml of anhydrous ether was placed in a large, three-necked flask which was outfitted with a dropping funnel, stirrer, and a nitrogen-purge system. Ethereal methyllithium, prepared from 42.0 g (6.0 g-atoms) of lithium, 469 g (3.3 moles) of methyl iodide, and 1.1 l. of anhydrous ether, was filtered directly into the dropping funnel. The system was purged with nitrogen and cooled to −35 to −40°. The methyllithium solution was added dropwise with stirring while the temperature of the reaction mixture was maintained at −35°. When addition was complete the mixture was allowed to warm to room temperature. Water was added *very* cautiously from the dropping funnel to destroy excess methyllithium and the reaction mixture was then processed in the usual manner. Solvent was removed from the dried ethereal solution by fractional distillation and the residue was flash distilled under reduced pressure to give 13.5 g (51%) of a mixture of II and III. Varpor–liquid chromatography revealed that only trace contaminants were present. A preparative unit[19] was used to separate small samples of pure II and III for nmr studies (Figures 1 and 2).

Anal. Calcd for C_9H_{12}: C, 89.94; H, 10.06. Found: C, 89.80; H, 10.12.

Diimide Reduction of II and III.—A mixture of 6.2 g (0.051 mole) of a mixture of II and III (2:1), 20.0 g (0.10 mole) of dipotassium azodicarboxylate, and 175 ml of methanol was placed in a 1-l., three-necked flask outfitted with a dropping funnel. The system was purged with nitrogen and stirred magnetically while acetic acid (175 ml) was added at a rate of 4 drops/min. Stirring was continued for 2 days and the mixture was then poured into cold water and processed by pentane extraction. Solvent was removed using a fractionating column. The residue was examined by vapor–liquid chromatography and found to consist of a new compound and unreacted III (80:20). The mixture was recycled twice through the reduction procedure to produce only a minor improvement (85:15). This material (4.07 g, 65%) was finally separated by vapor–liquid chromatography to give pure tricyclo$[6.1.0.0^{5,9}]$nonane (IV) which, after sublimation at 30° (0.1 mm), melted at 43–45°.

Anal. Calcd for C_9H_{14}: C, 88.45; H, 11.55. Found: C, 88.61; H, 11.20.

Thermal Isomerization of II and III.—The 2:1 mixture of II and III (2.6 g) was sealed with a crystal of hydroquinone under nitrogen in a Pyrex ampoule. The tube was immersed in an oil bath and heated to 170° for 65 hr. Bulb-to-bulb distillation of this material afforded 1.9 g (73%) of *cis*-bicyclo[4.3.0]nona-2,8-diene (V) which appeared to be pure by vapor–liquid chromatography, $n^{24}{}_{\mathrm{D}}$ 1.5205.

Anal. Calcd for C_9H_{12}: C, 89.94; H, 10.06. Found: C, 89.72; H, 10.29.

Catalytic Hydrogenation of *cis*-Bicyclo[4.3.0]nona-2,8-diene (V).—To a presaturated mixture of 20 mg of 5% palladium-carbon and 5.0 ml of methanol contained in a microhydrogenator was added 91.1 mg of IV. The mixture was then stirred magnetically under 1 atm of hydrogen. One mole equivalent was absorbed rapidly and a second was absorbed much more slowly (1.95 total). Analysis by vapor–liquid chromatography, using several columns and authentic samples for comparison, showed the product to consist of 78% *cis*-bicyclo[4.3.0]nonane, 22% *trans*-bicyclo[4.3.0]nonane (VI), and smaller amounts of indan and an unidentified component.

Base-Catalyzed Isomerization of *cis*-Bicyclo[4.3.0]nona-2,8-diene (V).—Dry potassium *t*-butoxide, prepared from 0.33 g of potassium, was dissolved in 25 ml of dry dimethyl sulfoxide which had been purged with dry nitrogen. To the solution was added 0.88 g of V. The solution was stirred at 30° for 30 min and then quenched by pouring into cold water. The product was isolated in the usual way by ether extraction and evaporation of solvent through a fractionating column. Bulb-to-bulb distillation gave 0.50 g (57%) of a mixture which was shown by vapor–liquid chromatography to be bicyclo[4.3.0]nona-1(6),3-diene (VII) and a conjugated isomer in the ratio 27:73. The spectral properties of VII were identical with those of an authentic sample.[16] The same mixture was obtained by treatment of pure VII with base under the conditions described for the isomerization of V.

Registry No.—9,9-Dibromobicyclo[6.1.0]non-2-ene, 2570-08-3; methyllithium, 917-54-4; II, 7603-32-9; III, 7603-33-0; IV, 3103-88-6; V, 7603-35-2; *cis*-bicyclo-[4.3.0]nonane, 4551-51-3; VI, 3296-50-2; VII, 7603-37-4.

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[17] E. T. Marquis and P. D. Gardner, *Chem. Commun.*, 726 (1966).

[18] C. L. Osborn, T. C. Shields, B. A. Shoulders, J. F. Krause, H. V. Cortez, and P. D. Gardner, *J. Am. Chem. Soc.*, **87**, 3158 (1965).

[19] This separation could be effected only by use of a 12 ft × $^3/_8$ in. column containing 35% of a saturated solution of silver nitrate in tetraethylene glycol on Chromosorb P. Resolution was not complete and recycling was necessary.

Synthesis of Simple Tricyclo$[4.4.4.0^{1,6}]$ Compounds[1]

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Our interest in tricyclic systems of the $[n.n.n.0^{1,n+2}]$ type[2] and possession of some of the required compounds in connection with another synthesis has led us to examine, as simply constructed models of such systems, some 2,2-disubstituted cyclohexanones whose side chains are capable of forming additional rings by condensation at the ketone function.

As precursors, compounds of the general type of II and V are readily available because of the curious fact that unsymmetrical ketones usually undergo the Michael reaction at the more highly substituted α position;[3] consequently, two successive Michael condensations on cyclohexanone will tend to produce

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[1] Support for this work from the donors of The Petroleum Research Fund of The American Chemical Society and from the Rutgers Research Council is gratefully acknowledged.

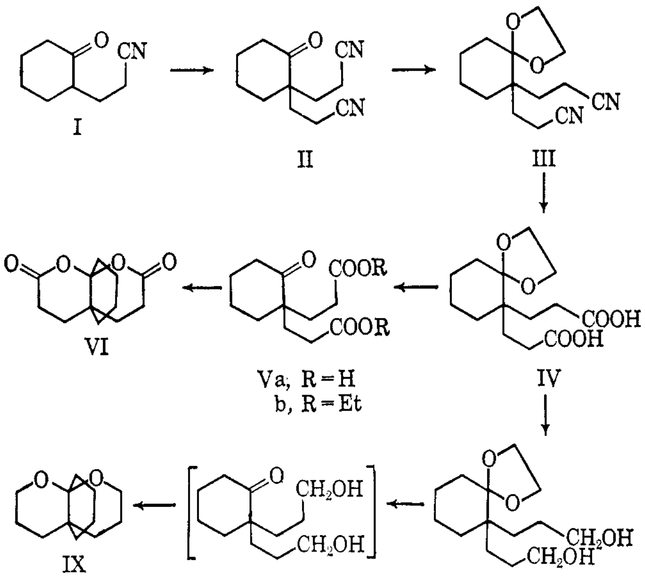
[2] (a) S. M. McElvain and G. R. McKay, Jr., *J. Am. Chem. Soc.*, **77**, 5601 (1955); (b) G. Snatzke and G. Zanati, *Ann.*, **684**, 62 (1965).

[3] H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, Inc., New York, N. Y., 1965, p 209, and references there cited.

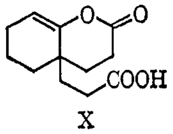
appreciable yields of 2,2-dialkylated products such as II.

Since it may also be difficult to stop such Michael condensations at intermediate stages of substitution, we chose to conduct our first condensation *via* the enamine, which can be made to give the monoalkylated cyclohexanone (I) cleanly.[4] Subsequent base-catalyzed reaction of I with acrylonitrile in *t*-butyl alcohol gave the known 2,2-di[β-cyanoethyl]cyclohexanone (II)[5] in 31% yield (based on unrecovered I) and ketalization of II in excess ethylene glycol with boron trifluoride etherate at room temperature[6] gave the ketal dinitrile III in 68% yield. Hydrolysis of the dinitrile in refluxing aqueous base[7] for 24 hr produced in 92% yield the ketal diacid (IV), which was reduced with excess lithium aluminum hydride in refluxing tetrahydrofuran to give, in 90% distilled yield, the liquid ketal diol (VII). The latter material, on hydrolysis with dilute mineral acid, gave directly in 95% yield 2,10-trioxatricyclo[4.4.4.0^{1,6}]tetradecane (IX) as pleasant-smelling sublimable needles, mp 53–53.5°. (See Scheme I.)

Scheme I



In considering as a synthetic route to IX the hydride reduction of X, the enol lactone of keto diacid Va, we became aware that the reported synthesis of X must be in error.[8] The authors who reported X hydrolyzed a liquid di(cyanoethyl)cyclohexanone to a keto diacid of mp 141–142°, which gave on esterification a keto diethyl ester, mp 61.5–62°, but which on heating either with or without barium hydroxide produced only an acidic enol lactone, assigned structure X.



X

The properties described, however, fit only the 2,6-disubstituted cyclohexanone series of compounds[4,9,10] (which structure is consistent with the fact that they can be produced by a double Michael reaction of the enamine of cyclohexanone).[4] Our keto dinitrile (II) melts at 66.5–68°[5] and our keto diacid Va (prepared in 91% yield from IV) melts sharply at 132–133°,[11] while diester Vb, which we prepared from Va in 96% yield and which gives thin layer and vapor phase chromatograms consistent with its being a single, pure compound, shows no sign of crystallinity at room temperature (see Table I).

Table I

Properties of Disubstituted Cyclohexanones

Substituent	Mp, °C 2,6-Disubstituted	Mp, °C 2,2-Disubstituted
CH_2CH_2CN	Liquid[a,b]	68[c,d]
CH_2CH_2COOH	143[a,b,d,e]	133[d,f]
CH_2CH_2COOEt	61[d,e]	Liquid, $n^{25}D$ 1.4695[d]

[a] Reference 4. [b] Reference 10. [c] Reference 5. [d] Data determined in this study. [e] Reference 9. [f] Reference 11.

Since the dehydration of keto diacid Va to dilactone VI, rather than only to X, therefore seemed possible, we attempted this reaction using a refluxing mixture of acetic anhydride and acetyl chloride[12] and obtained VI in 22% yield as needles from cyclohexane–ethyl acetate, mp 144–144.5°.

The two tricyclic compounds prepared may be contrasted in that IX exists completely in the dehydrated, ketal form, whereas dilactone VI is produced by dehydration of Va only with difficulty (*e.g.*, refluxing Va for 24 hr in toluene with water trapping gives no detectable dilactone in the absence of mineral acid). Since the steric situations in the two cases appear very nearly identical this difference presumably reflects the lower stability of δ-lactones compared with six-membered cyclic ethers. A quantitative study of hemiacetal formation of ω-hydroxy aldehydes has demonstrated a distinct preference for six-membered over five-membered rings.[13] The overwhelming reversal of this order of stability in lactonization of ω-hydroxy acids[14] may be attributable to steric inhibition of resonance stabilization in the nonplanar δ-lactones. These preferences are evidenced in the general tendency toward γ-lactone formation in the sugar acids but pyranose formation in the sugars themselves.

The reluctance of Va to undergo dilactonization may also be related to the general difficulty of forming *gem*-diacyloxy derivatives from ketones. While ketals are easily formed, ketone hydrate diesters, although stable, apparently cannot be formed directly from ketones (*cf.* aldehydes[15]) except internally in keto diacids such as Va and possibly in a few ketones which are known to form stable hydrates. A few cases are

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(4) G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Am. Chem. Soc.*, **85**, 207 (1963).

(5) A. D. Campbell and I. D. R. Stevens, *J. Chem. Soc.*, 959 (1956).

(6) W. J. Adams, D. N. Kirk, D. K. Patel, V. Petrow, and I. A. Stuart-Webb, *ibid.*, 2298 (1954).

(7) J. R. Ruhoff, "Organic Syntheses," Coll. Vol. II, A. H. Blatt, Ed., John Wiley and Sons, Inc., New York, N. Y., 1943, p 292.

(8) R. Y. Levina, N. P. Shusherina, and T. A. Kaminskaya, *Dokl. Akad. Nauk SSSR*, **86**, 79 (1952); *Chem. Abstr.*, **47**, 4849 (1953).

(9) H. T. Openshaw and R. Robinson, *J. Chem. Soc.*, 941 (1937).

(10) H. O. House, B. M. Trost, R. W. Magin, R. G. Carlson, R. W. Franck, and G. H. Rasmusson, *J. Org. Chem.*, **30**, 2513 (1965).

(11) R. H. Burnell and W. I. Taylor, *J. Chem. Soc.*, 3486 (1954).

(12) R. B. Turner, *J. Am. Chem. Soc.*, **72**, 579 (1950).

(13) C. D. Hurd and W. H. Saunders, *ibid.*, **74**, 5324 (1952).

(14) Data cited by F. G. Bordwell in "Organic Chemistry," The Macmillan Co., New York, N. Y., 1963, p 655.

(15) E. H. Man, J. J. Sanderson, and C. R. Hauser, *J. Am. Chem. Soc.*, **72**, 847 (1950).

known of spontaneous dilactonization of keto diacids at room temperature.[16]

Experimental Section[17]

Ketalization of Keto Dinitrile II.—Keto dinitrile II (8.30 g, 40.7 mmoles) was dissolved in 125 ml of ethylene glycol and to this was added, over a 15-min period with stirring and cooling, 25.0 ml (28.1 g, 198 mmoles) of freshly distilled boron trifluoride etherate. After standing for 8 days at room temperature, the mixture was worked up by pouring into excess aqueous potassium hydroxide. Extraction with ether gave a solution which, when dried and concentrated, yielded 6.95 g (68%) of white nuggets, mp 67–69°. Recrystallization from methyl acetate–hexane narrowed the melting range to 68–69°; $\nu_{\max}^{\mathrm{CCl_4}}$ 2245 cm^{-1}; nmr 4 H singlet at τ 6.07, 16 H complex at 7.4–8.6.

Anal. Calcd for $C_{14}H_{20}N_2O_2$: C, 67.71; H, 8.12. Found: C, 67.78; H, 8.22.

Basic Hydrolysis of Ketal Dinitrile III.—A mixture of 3.00 g of ketal dinitrile III (12.1 mmoles), 10 ml of ethanol, 50 ml of water, and 7.50 g (114 mmoles) of potassium hydroxide was refluxed under nitrogen for 24 hr and worked up by addition of excess aqueous oxalic acid and extraction with ether. Concentration of the dried extracts yielded a white solid which was recrystallized from xylene to give 3.19 g (92%) of diacid IV, as a white powder: mp 156–158.5°; $\nu_{\max}^{\mathrm{CHCl_3}}$ 3510, 3400–2200, 1710 cm^{-1}.

Anal. Calcd for $C_{14}H_{22}O_6$: C, 58.73; H, 7.74. Found: C, 58.78; H, 7.74.

Reduction of IV with Lithium Aluminum Hydride.—A solution of 700 mg (2.45 mmoles) of ketal diacid IV in 14 ml of tetrahydrofuran was added under nitrogen over a 2-min period to a stirred suspension of 350 mg (9.25 mmoles) of lithium aluminum hydride in 10 ml of tetrahydrofuran. The mixture was refluxed under nitrogen for 6 hr and worked up by addition of saturated aqueous sodium sulfate, addition of ether, and decantation of the organic solution. Concentration of the dried extracts gave a colorless oil, distilled in a Hickman still at 170° (0.03 mm) to yield 570 mg (90%) of viscous liquid: $n^{25}\mathrm{D}$ 1.5050; $\nu_{\max}^{\mathrm{CHCl_3}}$ 3630, 3430 cm^{-1}; nmr 4 H singlet at τ 6.13, 6 H double peak at 6.2–6.7, 16 H peak at 8.2–9.1 centered at 8.57.

Anal. Calcd for $C_{14}H_{26}O_4$: C, 65.08; H, 10.14. Found: C, 64.58; H, 10.11.

Acid Hydrolysis of Ketal Diol VII.—The distilled ketal diol VII (249 mg, 0.97 mmole) as a solution in a mixture of 5 ml of tetrahydrofuran and 13 ml of water was treated with 1 ml of concentrated hydrochloric acid and stirred for 1 hr at room temperature. The mixture was neutralized by addition of aqueous sodium bicarbonate and then saturated with potassium chloride. Extraction with pentane and concentration of the extracts gave crystalline material which was sublimed at *ca.* 50° (1 mm) to give 179 mg (95%) of white solid, mp 51.5–52°. Some crystals, formed by evaporation of a solution, melted at 53–53.5°. The infrared spectrum of this material lacks absorption in the 3- or 6-μ regions attributable to hydroxyl or carbonyl; nmr 4 H complex at τ 5.8–6.7, 16 H peak at 8.0–8.9 centered at 8.45.

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.43; H, 10.34.

Acid Hydrolysis of Ketal Diacid IV.—Ketal diacid IV (350 mg, 1.22 mmoles), dissolved in a mixture of 5 ml of tetrahydrofuran and 15 ml of water, was treated with 2 ml of concentrated hydrochloric acid and was allowed to stand for 2 hr. The mixture was worked up by neutralization of excess acidity, saturation with potassium chloride, and extraction with ether–methylene chloride. Concentration of the dried extracts gave a solid which, on recrystallization from toluene, yielded 270 mg (91%) of white platelets, mp 132–133° (lit.[11] mp 136°).

Preparation of Keto Diester Vb.—A solution of 500 mg (2.06 mmoles) of keto diacid Va in 15 ml of absolute ethanol containing 7 drops of concentrated sulfuric acid was refluxed under nitrogen for 1 hr and worked up by addition of excess solid sodium bicarbonate followed by water and extraction with ether–pentane. Concentration of the dried extracts gave a colorless oil distilled in a Hickman still at 145° (0.05 mm) to yield 593 mg (96%) of mobile liquid: $n^{25}\mathrm{D}$ 1.4695; $\nu_{\max}^{\mathrm{CCl_4}}$ 1728, 1708 cm^{-1}; nmr 4 H quartet at τ 3.96 (J = 7 cps), 16 H complex at 7.5–8.4, 6 H triplet at 8.79 (J = 7 cps).

Anal. Calcd for $C_{16}H_{26}O_5$: C, 64.41; H, 8.78. Found: C, 64.21; H, 8.61.

Dilactonization of Keto Diacid Va.—A mixture of 250 mg (1.03 mmoles) of keto diacid Va, 2 ml of acetyl chloride, and 5 ml of acetic anhydride was refluxed under nitrogen for 40 hr and worked up by removal of solvent under reduced pressure. Addition of ether to the residue produced 52 mg (22%) of crystals which were washed with ether and with aqueous sodium bicarbonate and sublimed at 130° (0.05 mm). Recrystallization from cyclohexane–ethyl acetate produced needles, mp 143.5–144.5°. The infrared spectrum of this material shows a single intense carbonyl band at 1750 cm^{-1} and absence of the usual carboxylic acid absorption in the 3–4-μ region; nmr 4 H triplet at τ 7.38 (J = 7.5 cps), 12 H complex at 7.8–8.7.

Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.26; H, 6.97.

Registry No.—III, 7641-49-8; IV, 7641-50-1; Va, 7641-52-3; Vb, 7677-62-5; VII, 7641-51-2; IX, 7666-49-1.

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[16] M. D. Soffer, R. A. Stewart, J. C. Cavagnol, H. E. Gellerson, and E. A. Bowler, *J. Am. Chem. Soc.*, **72**, 3704 (1950), and the references cited therein.

[17] Melting points were determined with a Mel-Temp apparatus and are uncorrected; infrared spectra were taken using a Beckman IR-10 spectrometer; nmr spectra were determined with a Varian A-60 spectrometer and utilizing an internal standard; microanalyses were performed by Micro-Tech Laboratories, Skokie, Ill.

Synthesis of Arylidene-2-methyl-2H-tetrazol-5-ylhydrazones *via* 1,3-Bis(2-methyl-2H-tetrazol-5-yl)triazene

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In our recent investigation[2] of the methylation reactions of arylidenetetrazol-5-ylhydrazones in basic medium we have found that, while direct methylation affords a satisfactory route to a number of methylated derivatives, it is not effective for the 2-alkylated derivatives (**4**) which are formed in very low yields and not at all in some instances depending on the arylidene substituent X. Because of these complications we were unable to present conclusive evidence for our proposed structure of these materials at that time. We now report data which confirm these earlier structural proposals and open a new route to workable yields of these hydrazones (**4**).

When 2-methyl-5-aminotetrazole (**1**) is treated with amyl nitrite in aqueous acetic acid solution at 0–5° the triazene (**2**)[3a] is formed along with some decomposition gums. This material, a stable, white, crystalline solid, does not show the deflagration and extreme hygroscopic properties of its unmethylated analog,[3b] which was formed by the reaction of aminoguanidine[4] with sodium nitrite in acetic acid. Mild reduction of

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[1] This author acknowledges a State Maintenance Grant for Research.

[2] R. N. Butler and F. L. Scott, *J. Org. Chem.*, **31**, 3182 (1966).

[3] (a) See K. Hattori, E. Lieber, and J. P. Horwitz, *J. Am. Chem. Soc.*, **78**, 411 (1956). (b) K. A. Hofmann and H. Koch, *Ber.*, **43**, 1866 (1910); K. A. Hofmann, H. Koch, and R. Roth, *ibid.*, **43**, 1087 (1910).

[4] J. Reilly, J. P. Teegan, and M. F. Carey, *Sci. Proc. Roy. Dublin Soc.*, **24**, 349 (1948); J. Reilly, J. P. Teegan, and M. F. Carey, *Nature*, **159**, 643, (1947). For a review of the synthesis of tetrazole derivatives from aminoguanidines, see F. Kurzer, *Angew. Chem. Intern. Ed. Engl.*, **2**, 468 (1963).