Alkylation of α,β-Unsaturated Ketones with Polymethylene Dibromides[1]

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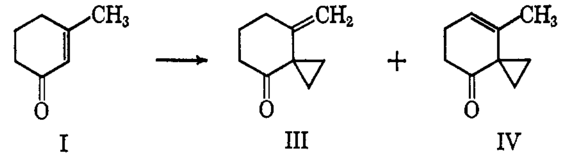
Alkylation of 3-methyl-2-cyclohexenone (I) in liquid ammonia containing sodium amide with 1,2-dibromoethane affords mixtures of 8-methylenespiro[2.5]octan-4-one (III) and 8-methylspiro[2.5]oct-7-en-4-one (IV) in which III predominates, although IV is the stable isomer. Alkylation of I with 1,3-dibromopropane yields 5-methylene-5,6,7,8-tetrahydrochroman (V). When 1,4-dibromobutane is used, 10-methylenespiro[4.5]decan-6-one (VII) is formed. When the alkylating agent is 1,5-dibromopentane, 5-methylenespiro[5.5]-undecan-1-one (VIII) is the only product. Both VII and VIII are the stable isomers. Alkylation of cholest-5-en-3-one with 1,4-dibromobutane in *t*-butyl alcohol containing potassium *t*-butoxide affords spiro[cholest-5-ene-4,1'-cyclopentan]-3-one (IX).

Alkylation of cyclic α,β-unsaturated ketones generally results mainly in the formation of α,α-dialkyl-β,γ-unsaturated ketones.[4] However, alkylation of such ketones with dihalides of the type $X(CH_2)_nX$ has not been studied. Such dihalides have been used in the alkylation of acetoacetic,[5] malonic,[5,6] and cyanoacetic esters,[6] and of phenylacetonitrile.[6] In this paper we report alkylation of 3-methyl-2-cyclohexenone (I) and cholest-5-ene-3-one (II) with certain polymethylene dibromides. Ketone I was chosen in preference to 2-cyclohexenone because I is readily prepared[7] and would be less likely to undergo Michael-type side reactions. Ketone II was selected as a readily available steroidal ketone[8] which reacts more rapidly with base than does the isomeric, conjugated cholest-4-ene-3-one.[9] The same resonating enolate anion is obtained from both II and cholest-4-ene-3-one.

After initial attempts to alkylate I with ethylene dibromide in ether using sodium amide (expt 7) or sodium hydride (expt 8) and in *t*-butyl alcohol containing potassium *t*-butoxide failed, all subsequent studies were carried out in liquid ammonia. The only alkylation products obtained were 8-methylenespiro[2.5]-octan-4-one (III) and 8-methylspiro[2.5]oct-7-en-7-one (IV) although 21 isomeric structures can be written for possible alkylation products. The combined yield[10] of III and IV never exceeded 48% and appreciable amounts, 37–47%, of unchanged I were present in the product. Because of the close boiling points of I, III, and IV all analyses of the reaction products were made by gas–liquid partition chromatography. Pure samples of III and IV were obtained by preparative glpc; the structures were established by nmr, ultraviolet and infrared spectral analysis (see Experimental Section). Catalytic reduction of a mixture of III and IV afforded 8-methylspiro[2.5]octan-4-one. Some results of the alkylation studies are present in Table I.



I III IV

TABLE I

ALKYLATION OF 3-METHYL-2-CYCLOHEXENONE (I) WITH 1,2-DIBROMOETHANE

Expt[a]	Time, hr	% crude[b]	% I[c]	% III[c]	% IV[c]
1	2	31	42	31	25
2[d]	4	93	47	26	15
3[e]	7	54	21	42	23
4[f]	12	68	76	10	5
5[g]	4	29	95	2	1
6[h]	5	38	76	13	11
7[i]	2	7	98	2	..
8[j]	3	43	99	..	..
9[k]	5	20	95	..	..
10[l]	1	85	47	26	22
11[m]	2	76	76	14	5
12[n]	1	..	74	..	..

[a] Typical experimental conditions involved sodium amide in liquid ammonia at reflux (−33°). The ratio of I, sodium amide, and ethylene dibromide was 1:3:3 unless otherwise stated. For further details see the Experimental Section. [b] This column represents distilled product. The per cent yield was calculated by assuming that the product was entirely product containing an added CH_2CH_2 group in place of two hydrogens in I. The difference between the per cent reported and 100 was always nondistillable resinous material which remained in the distilling flask. [c] The per cent reported was determined by glpc on crude distilled product. [d] This represents the average of several similar experiments in which the best yield of III and IV was obtained. [e] The ratio of I:$NaNH_2$:$BrCH_2CH_2Br$ was 1:12:6. [f] The temperature was held at −78° for the entire reaction period. [g] The sodium amide was added in portions to a solution of I and 1,2-dibromoethane in liquid ammonia. [h] A mixture of 1,2-dibromoethane and I was added to sodium amide in ammonia. [i] Standard conditions except that the reaction was carried out at 20° in ether with powdered sodium amide. [j] As in *i* but at 25° using sodium hydride instead of sodium amide. [k] Average values of three experiments involving 1-bromo-2-chloroethane, 1,2-diiodoethane, and ethylene glycol bismethanesulfonate. [l] Ratio of I to sodium amide to ethylene dibromide was 1:2.6. [m] Ratio of reactants was the same as in *l*, but temperature was −70°. [n] No ethylene dibromide was used. The ratio of I to sodium amide was 1:2.6. Undistilled resin (26%) remained in the distillation flask.

The failure to obtain higher yields of alkylation products may be explained by two side reactions: self-condensation of the ketone[11] (see expt 12, Table I);

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[2] Kettering Foundation Fellow, 1962–1963; Union Carbide Corp. Fellow, 1964–1965.

[3] Postdoctoral Fellow, 1964–1965, supported by National Science Foundation Grant GP-3178.

[4] For a general discussion, see J. M. Conia, *Rec. Chem. Progr.*, **24**, 43 (1963).

[5] See E. Eliel, "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p 115.

[6] A. C. Cope, H. L. Holmes, and H. O. House, *Org. Reactions*, **9**, 107 (1957).

[7] M. W. Cronyn and G. H. Riesser, *J. Am. Chem. Soc.*, **75**, 1664 (1953).

[8] L. F. Fieser, *ibid.*, **75**, 5421 (1953).

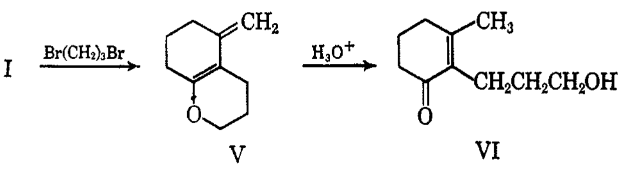
[9] H. J. Ringold and S. K. Malhotra, *ibid.*, **84**, 3402 (1962); *Tetrahedron Letters*, 669 (1962).

[10] The yields reported are those determined by gas–liquid partition chromatography (glpc).

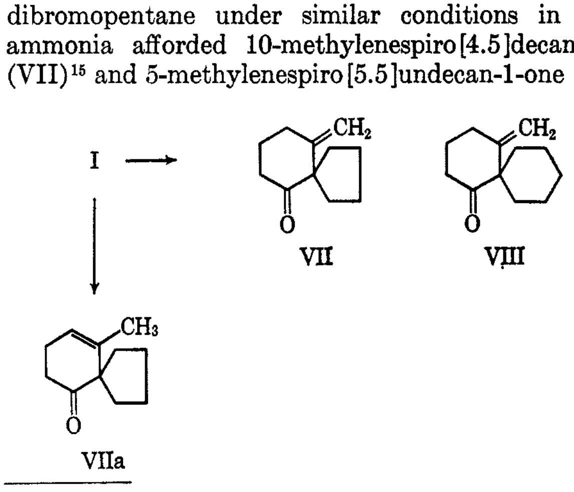
[11] G. Buchi, J. H. Hansen, D. Knutson, and E. Koller, *J. Am. Chem. Soc.*, **80**, 5517 (1958).

and dehydrohalogenation of the ethylene dibromide.[12] The success of our alkylations in liquid ammonia contrasted to those in ether may be due to the change in solvent or to a tendency of the carbanion to favor alkylation over proton extraction (as preliminary to dehydrohalogenation) at lower temperatures.[13] However, when the alkylation of I was carried out at −78 to −70° smaller yields were obtained than at −33° (see expt 2, 4, and 11, Table I). When 1-bromo-2-chloroethane, 1,2-diiodoethane, and ethylene glycol bismethanesulfonate were substituted for ethylene dibromide, no alkylation was observed (expt 9).

Alkylation of I with 1,3-dibromopropane yielded 5-methylene-5,6,7,8-tetrahydrochroman (V) in 53–56% yield.[14] Only alkylations in liquid ammonia were studied. The yield of V was not greatly dependent on the amount of excess sodium amide and dibromide used. Since only a few per cent more of V was obtained with large excess of reagents, the stoichiometric amounts were used in most experiments. A reaction time of about 4 hr was best, although this variable was not studied in detail. Structure V was established by nmr, ultraviolet, and infrared spectral analyses (see Experimental Section). Hydrolysis of V to 2-(3-hydroxypropyl)-3-methyl-2-cyclohexenone (VI) undoubtedly occurred but we were unable to isolate VI as cyclization and dehydration to yield V occurred so easily. However, both the oxime VIa and the 2,4-dinitrophenylhydrazone (VIb) (of unknown stereochemistry) of VI were obtained.



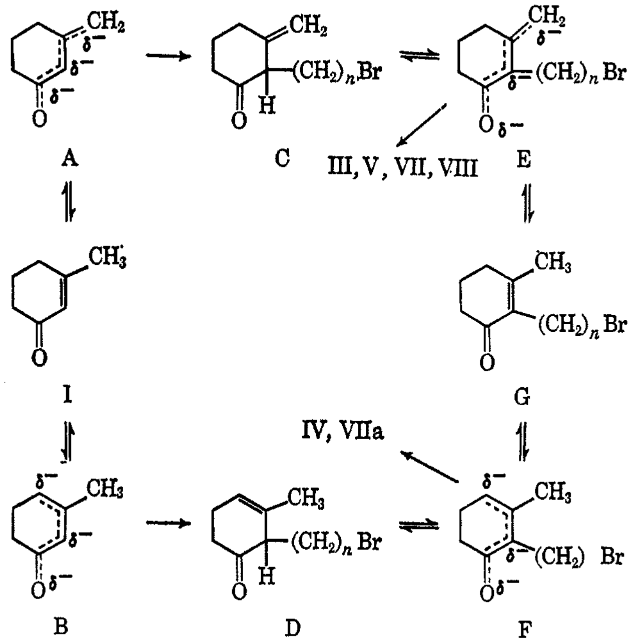
Alkylations of I with 1,4-dibromobutane and 1,5-dibromopentane under similar conditions in liquid ammonia afforded 10-methylenespiro[4.5]decan-6-one (VII)[15] and 5-methylenespiro[5.5]undecan-1-one (VIII) in about 42 and 35% yield, respectively.[16] Stoichiometric amounts of sodium amide (2 equiv), ketone, and dibromide were used. The reactions afforded VII and VIII in about the same quantity after 1- and 4-hr reaction times. The structures of VII and VIII were established by nmr, ultraviolet, and infrared spectral analysis (see Experimental Section).



The stabilities of ketones III, IV, VII, and VIII are of interest. Both VII and VIII are stable to isomerization under acidic conditions. *E.g.*, when treated in the following ways VII was recovered unchanged: (A) *p*-toluenesulfonic acid in ethanol at reflux for 24 hr; (B) heated neat at 180° for 2 hr; (C) *p*-toluenesulfonic acid in xylene at reflux for 24 hr; (D) methanesulfonic acid in benzene at reflux for 24 hr. Similarly, VIII was recovered unchanged after treatment comparable to A and D above. Thus, in these cases the stable isomer was formed in the alkylation experiments. On the other hand, IV proved to be more stable than III and, on treatment with *p*-toluenesulfonic acid in ethanol at reflux, III was completely isomerized to IV in 5 hr. Thus, in the case of alkylation of I with ethylene dibromide, in general greater amounts of the unstable isomer, III, were formed than IV (see Table I).

The alkylation of I with bromides of structure $Br(CH_2)_nBr$, when $n = 2–5$, may best be understood by consideration of the rates and equilibria pictured in Chart I.

CHART I



The amide ion abstracts a proton from I to give anions A and B, each of which is alkylated preferentially at the carbon α to the carbonyl to give monoalkylation products C and D, respectively. Amide ion abstracts the α proton from C and D to yield anions E and F, respectively. When $n = 2$ the rate of ring closure to ketones III and IV is rapid relative to the rate of interconversion of E to F and *vice versa* through G and the yields of III and IV reflect the tendency of the starting ketone, I, to yield anions A and B.

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[12] V. V. Korshak, K. K. Samplavskaya, and N. M. Dovolskaya, *Zh. Obsch. Khim.*, **20**, 2080 (1950); *Chem. Abstr.*, **45**, 5604^e (1951); V. V. Korshak and N. G. Matveea, *Izv. Akad. Nauk SSSR*, 334 (1953); *Chem. Abstr.*, **48**, 5788^e (1954).

[13] The alkylation of the anion of methylphenylacetonitrile by 4-bromobutyronitrile proceded in 85% yield at −78°, whereas the same reactants at room temperature afforded mainly cyclopropyl cyanide, the 1,3-elimination product. See M. S. Newman and R. D. Closson, *J. Am. Chem. Soc.*, **66**, 1553 (1944).

[14] This result is comparable with that obtained on alkylation of ethyl acetoacetate by W. H. Perkin Jr. [*J. Chem. Soc.*, 1347 (1929)] who isolated 6-methyl-5-carboethoxy-2,3-dihydro-4-pyran.

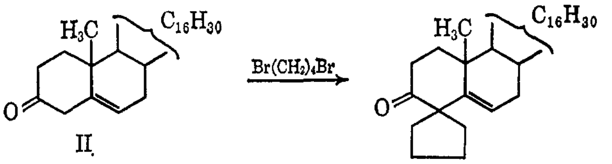
[15] In one experiment the alkylation product was mainly 10-methylspiro[4.5]dec-9-en-6-one (VIIa). However, in all other runs VII was produced. We are unable to account for this result.

[16] Insignificant amounts of spiro ketone were obtained in experiments using 1,6-dibromohexane. Higher dibromides were not studied.

When $n = 4$ and 5 the rate of ring closure of E and F is slow relative to the interconversions *via* G. The formation of the thermodynamically stable ketones VII and VIII is most likely due to the influence of the relative stabilities of the products on the transition states involved, since it is hard to see how there could be much difference in the relative stabilities or nucleophilicities of the anions E and F in the cases where $n = 4$ or 5.

When $n = 3$, the anions E and F would be expected to form as discussed above. Here again, equilibration *via* G must be more rapid than cyclization. When cyclization does occur, oxygen alkylation predominates. We presume that the compound, V, is more stable than the isomeric *endo* cyclic diene, although we have not established the relative stabilities.

The alkylation of cholest-5-en-3-one (II) with 1,4-dibromobutane in liquid ammonia, failed because of the insolubility of II in the solvent. When this alkylation was carried out in *t*-butyl alcohol with potassium *t*-butoxide, a 75% yield of spiro[cholest-5-ene-4,1^1-cyclopentan]-3-one (IX) was obtained. Because of this result, higher yields of the alkylation products of I, namely, V, VII, and VIII, might be obtained if the corresponding alkylations were run in *t*-butyl alcohol.



II

IX

Experimental Section[17]

8-Methylenespiro[2.5]octan-4-one (III) and 8-Methylspiro[2.5]oct-7-en-4-one (IV).—In the best of many reactions (see Table I), 110 g (1 mole) of 3-methyl-2-cyclohexenone[7] (I) was added to a refluxing suspension of 117 g (3 moles) of sodium amide in 1.5 l. of liquid ammonia and the mixture was stirred for 1 hr. During 30 min, 564 g (3 moles) of 1,2-dibromoethane was added and after 4 hr the reaction was stopped by the addition of 161 g of ammonium chloride. When the ammonia had evaporated the residue was worked up as usual.[18] Distillation afforded 126 g of a clear, colorless liquid: bp 70–83° (9 mm). Analysis of the distillate by glpc with a 2 ft × 0.25 in. 20% SE-30 silicone oil on Chromosorb W column at 125° indicated that it contained 12% 1,2-dibromoethane, 47% I, 26% III, and 15% IV. Separation of the components of this mixture by fractional distillation with a 30-cm spinning-band column proved unsuccessful. The ketonic components of this mixture were isolated by preparative glpc with a 20 ft × $^3/_8$ in. 30% SE-30 silicone oil on Chromosorb W column.

The infrared (C=O, 5.88 μ; =CH$_2$, 11.3 μ), near-infrared [$\lambda_{\max}^{\mathrm{CCl_4}}$, 1.629 μ[19] (ϵ 0.86)], and nmr spectra [τ 5.4 (1 H), 5.6 (1 H), 7.6 multiplet (4 H), 8.1 multiplet (2 H), and 8.8 multiplet (4 H)] confirm[20] the structure of III.

The infrared (C=O, 5.88 μ), near-infrared [$\lambda_{\max}^{\mathrm{CCl_4}}$, 1.628 μ[19] (ϵ 0.64)], and nmr spectra [τ 4.3 (1 H), 7.6 multiplet (4 H), 8.5 (3 H), and 8.8 multiplet (4 H)] confirm[20] the structure of IV.

Anal. Calcd for C$_9$H$_{12}$O: C, 79.4; H, 8.9. Found for III: C, 79.2; H, 8.9; for IV: C, 79.1; H, 9.0.

The semicarbazones of III, mp 179–180°, and of IV, mp 196–199°, were prepared.

Anal. Calcd for C$_{10}$H$_{15}$N$_3$O: C, 62.2; H, 7.8; N, 21.8. Found for III: C, 62.1; H, 7.8; N, 21.9. Found for IV: C, 62.0; H, 7.9; N, 21.8.

Hydrogenation of III and IV.—A solution of 20.0 g of a distilled portion of the above alkylation product in 150 ml of 95% ethanol was hydrogenated at 10 psi over 0.1 g of platinum oxide on kieselguhr. Fractional distillation with a 30 × 0.5 cm spinning-band column afforded 5.1 g (62% yield based on III and IV in the original mixture) of 8-methylspiro[2.5]octan-4-one: bp 76–78° (10 mm). Additional saturated ketone was present in the next lower boiling fraction.

Anal. Calcd for C$_9$H$_{14}$O: C, 78.2; H, 10.2; O, 11.6. Found: C, 78.0; H, 10.3; O, 11.7.

The infrared (C=O, 5.89 μ), near-infrared [$\lambda_{\max}^{\mathrm{CCl_4}}$, 1.632 μ[19] (ϵ 0.43)], and nmr spectra (no vinyl hydrogen) were consistent with the assigned structure. The semicarbazone, mp 199–200°, was prepared.

Anal. Calcd for C$_{10}$H$_{17}$N$_3$O: C, 61.5; H, 8.8; N, 21.5. Found C, 61.6; H, 8.8; N, 21.8.

Isomerization of III.—A solution containing 1.0 g of a mixture containing 29% I, 31% III, and 40% IV (by glpc) and 0.1 g of *p*-toluenesulfonic acid in 10 ml of 95% ethanol was refluxed. Analyses (glpc) after various intervals showed that only after 5 hr had all III been converted to IV. There was no change in the amount of I present.

5-Methylene-5,6,7,8-tetrahydrochroman (V).—A mixture of 80.0 g (2 moles) of sodium amide, 110 g (1 mole) of 3-methyl-2-cyclohexenone, and 1.0 l. of liquid ammonia was stirred at reflux for 30 min. During 1 hr, 202 g (1 mole) of 1,3-dibromopropane was added and after a total of 3 hr the reaction was stopped by the addition of 54 g of ammonium chloride. When the ammonia had evaporated the residue was worked up as usual and distillation afforded 104 g of crude V: bp 70–96° (6 mm). The distillate was added to a solution of 35 g of hydroxylamine hydrochloride, 40 g of sodium hydroxide, and 10 ml of 95% ethanol in 300 ml of water and the mixture was refluxed 10 min. The mixture was extracted twice with 100 ml of ether and the ethereal solution was dried over anhydrous magnesium sulfate and concentrated. Distillation of the residue afforded 59.3 g (40%) of V: bp 83–91° (10 mm). Distillation on a spinning-band column afforded material homogenous by glpc with little loss.

Anal. Calcd for C$_{10}$H$_{14}$O: C, 80.0; H, 9.4; O, 10.7. Found: C, 80.0; H, 9.3; O, 10.9.

The infrared (=CH$_2$, 11.5 μ medium), near-infrared [$\lambda_{\max}^{\mathrm{CCl_4}}$, 1.620 μ (ϵ 0.37)], ultraviolet [$\lambda_{\max}^{\mathrm{ethanol}}$, 251 m$\mu$ [ϵ 12.700)],[21] and nmr spectra [τ 5.6 (1 H), 5.7 (1 H), 6.2 triplet (2 H), and 8.1 multiplet (10 H)] were consistent with the assigned structure.

Oxime of 2-(3-Hydroxypropyl)-3-methyl-2-cyclohexenone (VIa).—A solution containing 8.0 g of hydroxylamine hydrochloride, 4.0 g of sodium hydroxide, 5.0 ml of water, 9.0 g of V, and 5.0 ml of 95% ethanol was refluxed for 10 min. The mixture was extracted twice with 25 ml of ether and the extract was dried over anhydrous magnesium sulfate and concentrated. The residue was crystallized from petroleum ether, bp 30–60°, to yield 10.3 g (94%) of VIa: mp 78–80°; ultraviolet absorption, $\lambda_{\max}^{\mathrm{ethanol}}$ 240 mμ (ϵ 27,000).

Anal. Calcd for C$_{10}$H$_{17}$NO$_2$: C, 65.5; H, 9.3; N, 7.7. Found: C, 65.4; H, 9.4; N, 7.7.

2,4-Dinitrophenylhydrazone of 2-(3-Hydroxypropyl)-3-methyl-2-cyclohexenone (VIb).—A solution of 1.0 g of V and 0.1 ml of acetic acid in 40 ml of 95% ethanol was added and after 10 min the mixture was filtered to yield 2.1 g (99%) of VIb: mp 182–

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[17] All melting points are corrected. Microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn., and by Microanalysis, Wilmington, Del. Infrared spectra were determined in carbon tetrachloride solution with a Perkin-Elmer Infracord. Ultraviolet and near infrared spectra were determined with a Cary 14 spectrophotometer. Nmr spectra were determined with a Varian A-60 spectrometer using tetramethylsilane as an internal standard. Analytical glpc was done with an F & M 609 and a Barber-Coleman 5000 gas chromatograph. Preparative glpc was done with a Wilkins A-700 Autoprep gas chromatograph.

[18] The phrase "worked up as usual" means that a methylene chloride solution of the products was washed with water and 20% ammonium chloride solution, dried over anhydrous magnesium sulfate, and concentrated on a rotary evaporator under reduced pressure.

[19] P. G. Gassman [*Chem. Ind.* (London), 740 (1962)] reported that each of 16 compounds containing cyclopropyl rings has absorption in the 1.624–1.650-μ region.

[20] See ref 1 for a detailed discussion of the evidence supporting the structures of all new compounds.

[21] Although $\lambda_{\max}$ for V cannot be predicted accurately, the difference between the observed ultraviolet spectrum and that reported[22] for 2,3-dihydrooxepine [$\lambda_{\max}$, 260 mμ ($\epsilon_{\max}$ 8900)] is in accord with the general rule[23] that transoid dienes exhibit a decrease in $\lambda_{\max}$ and an increase in $\epsilon_{\max}$ relative to cisoid dienes.

[22] J. Meinwald, D. W. Dicker, and N. Danieli, *J. Am. Chem. Soc.*, **82**, 4087 (1960).

[23] L. F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, p 16.

186°. Recrystallization from ethanol–ethyl acetate yielded the analytical sample: mp 192–193°; ultraviolet absorption, $\lambda_{\max}^{\text{ethanol}}$ 390 mμ (ϵ 29,500).

Anal. Calcd for $C_{16}H_{20}N_4O_5$: C, 55.2; H, 5.8; N, 16.1. Found: C, 55.5; H, 5.9; N, 16.3.

5-Methylenespiro[4.5]decan-1-one (VII).—In the best of five runs, 5.2 g (0.047 mole) of 3-methyl-2-cyclohexenone (I) was added to a refluxing suspension of 5.0 g (0.128 mole) of sodium amide in 250 ml of liquid ammonia. After 0.5 hr 13.8 g (0.064 mole) of 1,4-dibromobutane was added over a 1-hr period. After an additional 1.5 hr, the reaction was stopped by the addition of 3.5 g of ammonium chloride. When the ammonia had evaporated the residue was worked up as usual. Distillation afforded 6.8 g of a colorless liquid: bp 55–75° (1 mm). Analysis of the distillate by glpc with a 2 ft × 0.25 in. 20% SE-30 silicone oil on Chromosorb W column at 125° indicated that it contained 27% I and 73% VII. Fractional distillation with a 30 × 0.5 cm spinning-band column afforded 4.4 g (58%) of VII: bp 54–58° (0.3 mm).

The infrared (C=O, 5.80 μ; =CH_2, 11.2), near-infrared [$\lambda_{\max}^{CCl_4}$, 1.630[24] (ϵ 0.37)], and nmr spectra [τ 5.3 singlet (2 H), 7.6 multiplet (6 H), and 8.4 multiplet (8 H)] were consistent with the assigned structure.

Anal. Calcd for $C_{11}H_{16}O$: C, 80.4; H, 9.8. Found: C, 80.2; H, 9.9.

The semicarbazone, mp 204–205°, and the 2,4-dinitrophenylhydrazone, mp 113–114°, of VII were prepared.

Anal. Calcd for $C_{12}H_{19}N_3O$: C, 65.1; H, 8.7. Found: C, 65.4; H, 8.8.

Anal. Calcd for $C_{17}H_{20}N_4O_4$: C, 59.3; H, 5.9. Found: C, 59.5; H, 6.0.

Ozonization of VII in methylene chloride afforded spiro[4.5]-decane-1,5-dione in 56% yield. This material was only *ca.* 87% pure by glpc analysis. The impurity was VII. The infrared (2 C=O, 5.75 μ and 5.83, no peak at 11.2 or near 1.630[21]) and nmr spectra [τ 7.4 triplet (4 H), 8.1 multiplet (6 H), and 8.4 triplet (4 H)] were consistent with the assigned structure. A disemicarbazone, mp 223–224°, and a mono-2,4-dinitrophenylhydrazone, mp 209–210°, were prepared.

Anal. Calcd for $C_{12}H_{20}N_6O_2$: C, 51.4; H, 7.4. Found: C, 51.3; H, 7.3.

Anal. Calcd for $C_{16}H_{18}N_4O_5$: C, 55.5; H, 5.2. Found: C, 55.5; H, 5.4.

In one experiment (see below) the formation of 10-methylspiro-[4.5]dec-9-en-6-one was obtained as the only product from the reaction of I, 4,5-dibromobutane, sodium amide, and liquid ammonia. This experiment could not, however, be duplicated.

Hydrogenation of VII.—A solution of 3.5 g of VII in 50 ml of 95% ethanol was hydrogenated at 20 psi over 0.05 g of 86% platinum oxide on kieselguhr. Distillation afforded 3.0 g (85%) of 10-methylspiro[4.5]decan-6-one: bp 92–97° (5 mm). The infrared (C=O, 5.83 μ) and nmr spectra [τ 8.2 multiplet (15 H) and 9.1 doublet (3 H)] were consistant with the assigned structure. The compound gave a 2,4-dinitrophenylhydrazone that had a melting point of 112–113°. A mixture melting point with the 2,4-dinitrophenylhydrazone obtained from the hydrogenated compound of VIIa gave no depression.

10-Methylspiro[4.5]dec-9-en-6-one (VIIa).—A mixture of 80.0 g (2 moles) of sodium amide, 110 g (1 mole) of 3-methyl-2-cyclohexenone, and 1.0 l. of liquid ammonia was stirred at reflux for 1 hr. During 30 min, 216 g (1 mole) of 1,4-dibromobutane was added and after 1 hr the reaction was stopped by the addition of 54 g of ammonium chloride. When the ammonia had evaporated, the residue was worked up as usual. Distillation afforded 105 g of crude VIIa: bp 65–105° (3 mm). Fractional distillation with a 30 × 0.5 cm spinning-band column afforded 51 g (31%) of VIIa: bp 88–90° (3 mm).

Anal. Calcd for $C_{11}H_{16}O$: C, 80.4; H, 9.8; O, 9.7. Found: C, 80.6; H, 9.9; O, 9.9.

The infrared (C=O, 5.84 μ) and nmr spectra [τ 4.5 (1 H) and 8.1 multiplet (15 H)] were consistent with the assigned structure. The 2,4-dinitrophenylhydrazone, mp 150–151°, and semicarbazone, mp 180–181°, were prepared.

Anal. Calcd for $C_{17}H_{20}N_4O_4$: C, 59.3; H, 5.9; N, 16.3. Found: C, 59.4; H, 5.8; N, 16.1.

Anal. Calcd for $C_{12}H_{19}N_3O$: C, 65.1; H, 8.7; N, 19.0. Found: C, 65.3; H, 8.7; N, 18.7.

Hydrogenation of VIIa.—A solution of 10.0 g of VIIa in 150 ml of 95% ethanol was hydrogenated at 10 psi over 0.1 g of platinum oxide on kieselguhr. Distillation afforded 8.1 g (80%) of 10-methylspiro[4.5]decan-6-one: bp 90–96° (5 mm). The infrared (C=O, 5.84 μ) and nmr spectra [τ 8.2 multiplet (15 H) and 9.1 doublet (3 H)] were consistent with the assigned structure. The 2,4-dinitrophenylhydrazone, mp 112–113°, was prepared.

Anal. Calcd for $C_{11}H_{18}O$: C, 79.5; H, 10.9. Found: C, 79.5; H, 10.8.

Anal. Calcd for $C_{17}H_{22}N_4O_4$: C, 58.9; H, 6.4; N, 16.2. Found: C, 59.1; H, 6.6; N, 15.9.

5-Methylenespiro[5.5]undecan-1-one (VIII).—A mixture of 39.0 g of sodium amide, 55.0 g of 3-methyl-2-cyclohexenone, and 1.0 l. of liquid ammonia was stirred at reflux for 30 min. During 30 min, 155 g of 1,5-dibromopentane was added and after 1 hr the reaction was stopped by the additon of 54 g of ammonium chloride. When the ammonia had evaporated, the residue was worked up as usual. Distillation afforded 41.0 g (35%) of crude VIII: bp 72–95° (3 mm). Fractional distillation with a 30 × 0.5 cm spinning-band column afforded 20 g (22%) of VIII: bp 102–103° (3 mm). The infrared (C=O, 5.85 μ; =CH_2, 11.1 μ), near-infrared [=CH_2, 1.627 μ (ϵ 0.84)], and nmr spectra [τ 5.1 (1 H), 5.3 (1 H), and 8.2 multiplet (16 H)] were consistent with the assigned structure. The semicarbazone, mp 225–226°, was prepared.

Anal. Calcd for $C_{12}H_{18}O$: C, 80.8; H, 10.2; O, 9.0. Found: C, 80.5; H, 10.1; 0, 9.1.

Anal. Calcd for $C_{13}H_{21}N_3O$: C, 66.4; H, 9.0; N, 17.9. Found: C, 66.2; H, 9.1; N, 17.8.

Hydrogenation of VIII.—A solution of 5.0 g of VIII in 150 ml of 95% ethanol was hydrogenated at 20 psi over 0.1 g of platinum oxide on kieselguhr. Distillation afforded 3.9 g (77%) of 5-methylspiro[5.5]undecan-1-one: bp 100–102° (3 mm). The infrared (C=O, 5.83 μ) and nmr spectra [τ 8.3 multiplet (17 H) and 9.2 doublet (3 H)] were consistent with the assigned structure. The 2,4-dinitrophenylhydrazone, mp 104–105°, was prepared.

Anal. Calcd for $C_{12}H_{20}O$: C, 79.9; H, 11.2; O, 8.9. Found: C, 79.8; H, 11.0; O, 9.0.

Anal. Calcd for $C_{18}H_{24}N_4O_4$: C, 60.0; H, 6.7; N, 15.6. Found: C, 60.0; H, 6.6; N, 15.4.

Spiro[cholest-5-ene-4,1^1-cyclopentan]-3-one (IX).—A stirred suspension of 10.0 g of cholest-5-en-3-one[8] and 12.0 g of potassium *t*-butoxide in 500 ml of anhydrous *t*-butyl alcohol was heated. When the mixture became homogeneous 10.0 g of 1,4-dibromobutane was added. Concentration yielded a partly solid residue which was dissolved in 300 ml of ether and washed twice with 200 ml of 5% sulfuric acid and twice with 200 ml of water. The ether solution was concentrated to 100 ml and 50 ml of warm methanol was added. Crystallization yielded 7.1 g (62%) of IX: mp 134–135°. A second crop (1.4 g) of slightly less pure product, mp 129–133°, brought the total yield to 75%. The infrared (C=O, 5.83 μ) and nmr spectra [τ 4.4 (1 H) and 8.3 multiplet (49 H)] were consistent with the assigned structure. The 2,4-dinitrophenylhydrazone, mp 171–172°, was prepared.

Anal. Calcd for $C_{31}H_{50}O$: C, 84.9; H, 11.5; O, 3.7. Found: C, 84.6; H, 11.4; O, 4.0.

Anal. Calcd for $C_{37}H_{54}N_4O_4$: C, 71.8; H, 8.8; N, 9.1. Found: C, 72.0; H, 8.7; N, 8.8.

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(24) H. Weitkamp and F. Korte [*Tetrahedron*, **20**, 2125 (1964)] gave near-infrared absorption for =CH_2 at *ca.* 1.630 μ and of low intensity.