thus need not require the formal breaking of a double bond. If this argument were accepted, it would not be possible to employ the relative rotational barriers of $^{-}CH_2SH$ and $^{-}CH_2OH$ to rule out $(p \rightarrow d)_{\pi}$ conjugation in $^{-}CH_2SH$.
(61) (a) R. D. Baechler and K. Mislow, *J. Am. Chem. Soc.*, **93**, 773 (1971); (b) R. D. Baechler, J. P. Casey, R. J. Cook, G. H. Senkler, Jr., and K. Mislow, *ibid.*, **94**, 2859 (1972).
(62) A. L. Allred, *J. Inorg. Nucl. Chem.*, **17**, 215 (1961).
(63) The computed inversion barrier of CH_3^- with the double zeta basis set is 13.8 kcal/mol.[19a]
(64) A. Liberles, A. Greenberg, and J. E. Eilers, *J. Chem. Educ.*, **50**, 676 (1973).
(65) F. Bernardi, W. Cherry, N. D. Epiotis, M. H. Whangbo, and S. Wolfe, to be published.
(66) NOTE ADDED IN PROOF. For a similar interpretation, see A. Streitwieser, Jr., and J. E. Williams, Jr., *J. Am. Chem. Soc.*, **97**, 191 (1975).

New Synthetic Reactions. Geminal and Reductive Alkylations

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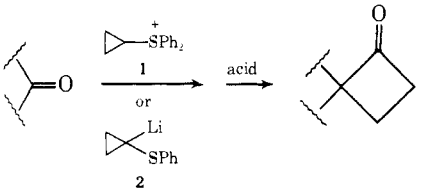
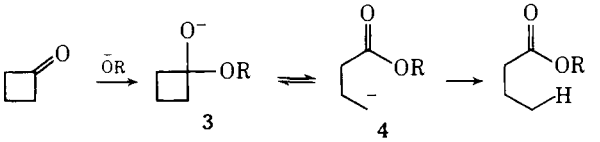
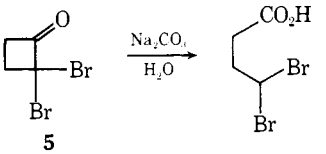
Abstract: Anion-stabilizing groups at the α position of a cyclobutanone facilitate ring cleavage. In conjunction with the cyclobutanone annelation utilizing sulfonium cyclopropylides and lithiated phenyl cyclopropyl sulfides, this method achieves a net replacement of the carbon–oxygen bonds of a carbonyl group by either C–H or C–R bonds (reductive alkylation) or by two C–R bonds (geminal alkylation) in a highly stereoselective fashion. A 2-aryl substituent is a sufficient anion-stabilizing group. Geminal bromine substitution at the α position of a cyclobutanone offers unusual versatility after ring cleavage since the bromines can be substituted or eliminated. In this way, one of the carbon–oxygen bonds of a C=O of an aldehyde or ketone has been replaced by a carboxyl group and the second by a methyl, ethyl, vinyl, 2-hydroxyethyl, or 2-oxoethyl substituent.

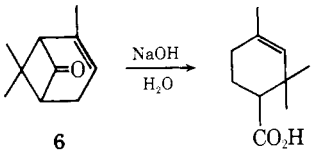
Although small strained rings have fascinated physical organic chemists for many years, their applications in synthesis remained quite limited until recently. Their strain energy provides a strong driving force for chemical reactions. The use of this potential energy to modify structure allows novel ways to develop molecular architecture. Most work focused on cyclopropanes because of their ready availability by alkylidene transfer.[2] The difficulty in obtaining cyclobutanes restricted their application. The recent discoveries[3] for making cyclobutanones readily available especially by condensing carbonyl compounds with diphenylsulfonium cyclopropylide (**1**)[4] or 1-lithiocyclopropyl phenyl sulfide (**2**)[5] initiated an investigation into the scope of such intermediates in creating various carbon fragments.[6] It might be envisioned that such cyclobutanones would undergo cleavage initiated by base. This simple scheme cannot be realized



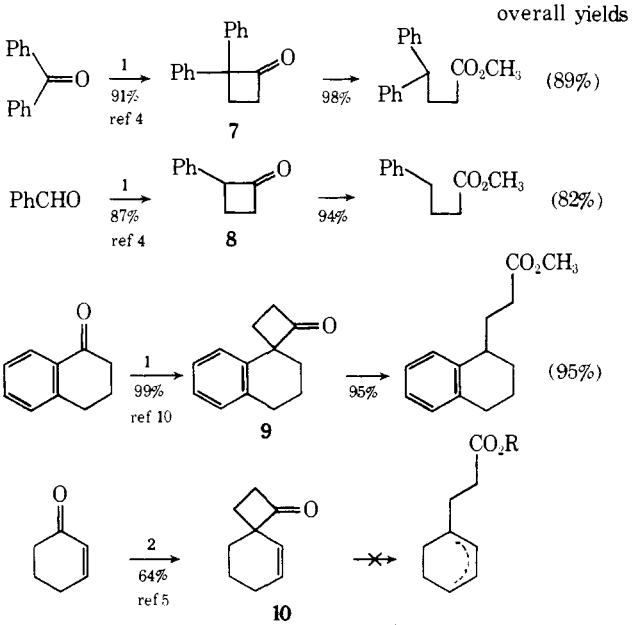


presumably because of the high endothermicity in going from the oxygen anion **3** to the carbanion **4**. Stabilization of the developing negative charge in **4** should facilitate this process. Indeed, isolated examples exist. For example, dibromocyclobutanone **5** undergoes facile cleavage in aqueous carbonate,[7] and chrysanthenone **6** undergoes ring cleavage with aqueous hydroxide.[8] To investigate the applicability of such methods, we undertook an investigation of the chemistry of the cyclobutanones available by our annelation procedure as a method of elaborating a carbonyl group.[9,10]

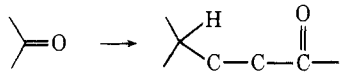




Initial work centered on the cyclobutanones **7–10**. Huisgen et al. reported the cleavage of 2,2-diphenyl-3-vinylcyclobutanone with hydroxylic base.[11] In agreement with this observation, we find that **7** undergoes smooth cleavage in

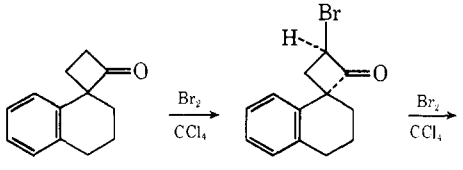


refluxing methanolic sodium methoxide. Two phenyl groups are not required. Both **8** and **9** undergo ring cleavage under comparable conditions. On the other hand, a simple double bond is not sufficient. Cyclobutanone **10** resists cleavage under these conditions.[12] This result is a little surprising considering that toluene (pK_a = 35) and propylene (pK_a = 35.5) have almost identical pK_a's.[13] It is clear that the driving force for cleavage of these ketones results from a combination of ring strain and stabilization imparted by the π orbitals of the double bond to a developing carbanion in the transition state. Synthetically, the overall process from the cyclobutanone precursor results in the replacement of two C-O bonds of the carbonyl group with a C-H and C-C

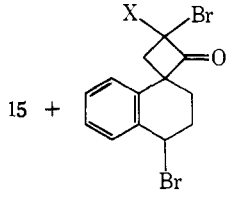


bond, i.e., a net reductive alkylation in 82-95% yields. In principle, other nucleophiles could initiate the ring cleavage.

An alternative approach involves the direct introduction of anion-stabilizing groups. The ability of bromine to serve as an anion-stabilizing atom is demonstrated by the classical haloform cleavage of methyl ketones. Geminal bromination of cyclobutanones has not been generally studied.[7] Bromination of the spirocyclobutanone **11** proceeded smoothly in quantitative yield with excess molecular bromine in carbon tetrachloride (see Table I). Monobromination is fast; whereas, dibromination proceeds more slowly. However, this procedure is not general. Cyclobutanone **12** is inert. Cyclobutanone **9** monobrominates rapidly as determined by the appearance of a doublet of doublets at δ 5.0 (J = 10, 7 Hz) for the CHBr proton in the NMR spectrum (apparently a single isomer is produced). However, increased reaction time leads to benzylic bromination as well as geminal bromination. On the other hand, pyridinium



9

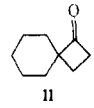
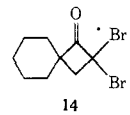
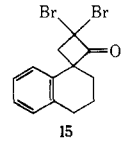
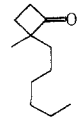
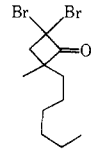
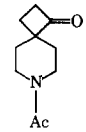
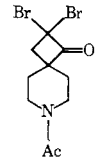


(X = H, Br)

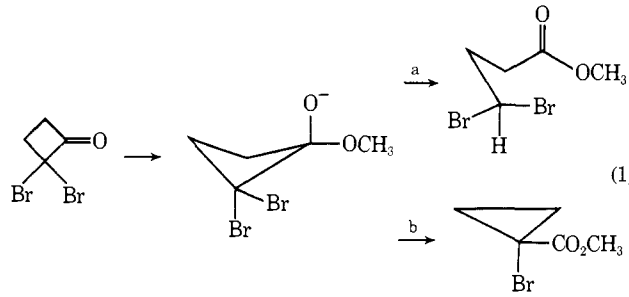
bromide perbromide in acetic acid[14] overcomes these problems and geminally brominates both **9** and **12** in over 90% yields. Cyclobutanone **13,** derived from 1-acetyl-4-piperidone in 77% yield, brominates by both methods, although the latter method gives cleaner results. The geminal bromides exhibit a characteristic high-energy carbonyl stretch at 1799 ± 4 cm^{-1} and a downfield shift for the remaining methylene group of the cyclobutane ring in the NMR spectrum to δ 3.1 ± 0.2.

Two reactions may be envisioned for the dibromocyclobutanones upon treatment with base, ring cleavage (eq 1, path a) or semibenzylic acid rearrangement[15] (eq 1, path b). Dissolution of dibromocyclobutanones **14, 15,** and **17** in methanolic sodium methoxide led to smooth cleavage. On the other hand, treatment of **15** under similar conditions led to the desired ring-cleaved product only in low yield. The major products have been identified as the ring-contracted cyclopropanes. The relative yields of **18, 19,** and **20** were

Table I. Bromination of Cyclobutanones

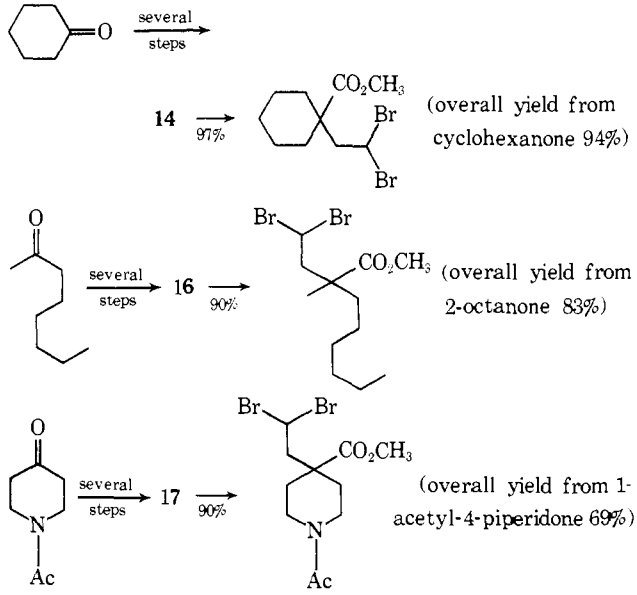
Cyclobutanone	Product	Method[a]	Yield
 **11**	 **14**	A	100
9	 **15**	B	92
 **12**	 **16**	B	100
 **13**	 **17**	B	100

[a] Method A: bromine in carbon tetrachloride. Method B: pyridinium bromide perbromide in acetic acid.

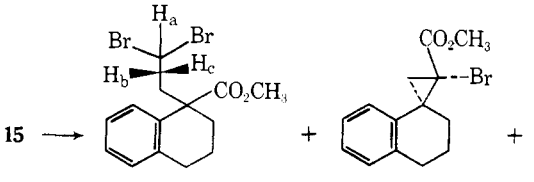


(1)

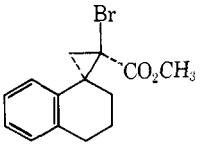
determined by NMR integration of the three methyl ester singlets at δ 3.75, 3.22 and 3.62, respectively. The major product was separated by preparative TLC and exhibited the abnormally high-field methyl ester singlet (δ 3.22) in the NMR spectrum as a result of shielding by the aromatic ring. The two minor products coeluted and were tentatively identified as **18** and **20** on the basis of the NMR spectrum of the mixture. Three doublets of doublets at δ 5.68 (J =



6.5, 5.5 Hz), 3.48 (J = 16, 6.5 Hz), and 2.99 (J = 16, 5.5 Hz) characterize a $-CCH_2CHBr_2$ system. Thus, these absorptions which were assigned to H_A, H_B, and H_C, respectively, as well as the methyl ester singlet at δ 3.75, indicate structure **18**. The AB pattern at δ 1.87 and 2.05 (J = 7 Hz) in conjunction with the methyl ester singlet at δ 3.62 was assigned to the cyclopropane **20**.

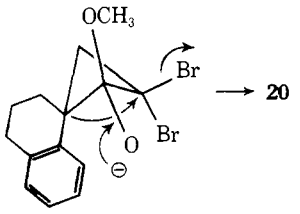


18 (12%) **19** (70%)

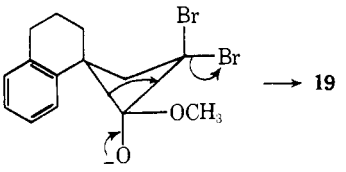


20 (18%)

The stereochemical preference for **19** in the ring contraction can be understood in terms of the conformations for rearrangement. The ring contraction is envisioned to be concerted with expulsion of the equatorial-like bromine. Of the two conformers, the unfavorable bromine aryl eclipsing interaction (1,3-diaxial-like interaction) in **21** destabilizes this conformer relative to **22**.



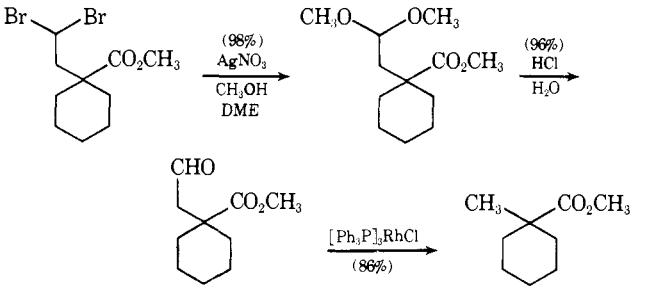
21



22

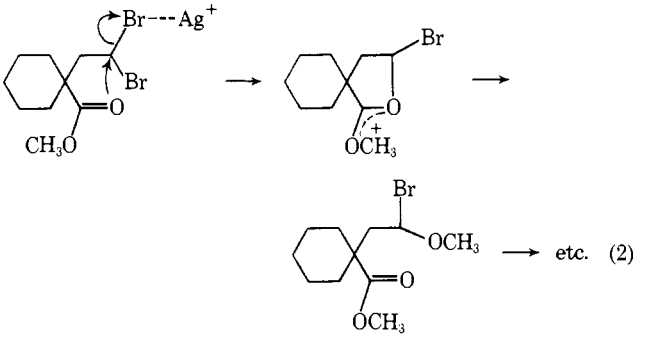
The preference for ring contraction rather than cleavage in **15** compared with **14, 16,** and **17** may arise because of the substitution pattern. In the ring contraction, the migrating carbon presumably develops negative charge. In the case of **15**, this carbon is benzylic; whereas, in the other cases, it is simply tertiary. The greater ability of the benzylic carbon to bear negative charge would therefore lower the activation energy for ring contraction relative to cleavage.

The advantages of this geminal alkylation method lie in the versatility of the dibromo substitution. Thus, a geminal bromide unit can be recognized as a masked carbonyl group. Unmasking can be effected by solvolyzing the dibromo compound in methanol aided by silver nitrate. The facility of the solvolysis may in part derive from a neighboring-group effect of the ester carbonyl (see eq 2). The resulting acetal upon aqueous acid treatment completes the unmasking process. The functionality available in **23** offers a wide variety of possible transformations. The carbon chains differ not only in length, but also in oxidation level. One reaction illustrating this utility is the decarbonylation with

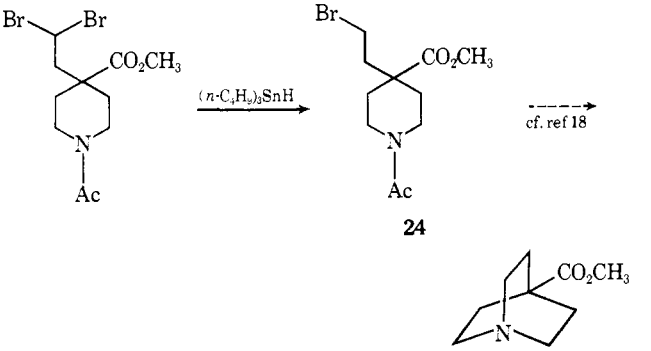


23

Wilkinson's catalyst which creates an α-methyl carboxylic ester.[16] In an unsymmetrical ketone, the stereochemistry of these substituents depends upon the stereoselectivity of the cyclobutanone annelation procedure. Since the latter proceeds with delightfully high stereoselectivity,[4,6] this method becomes a useful stereoselective geminal alkylation. It should be noted that, although this is a five-step sequence from a carbonyl group, the overall yield is high. In the above case, the yield of **23** from cyclohexanone is 88%.

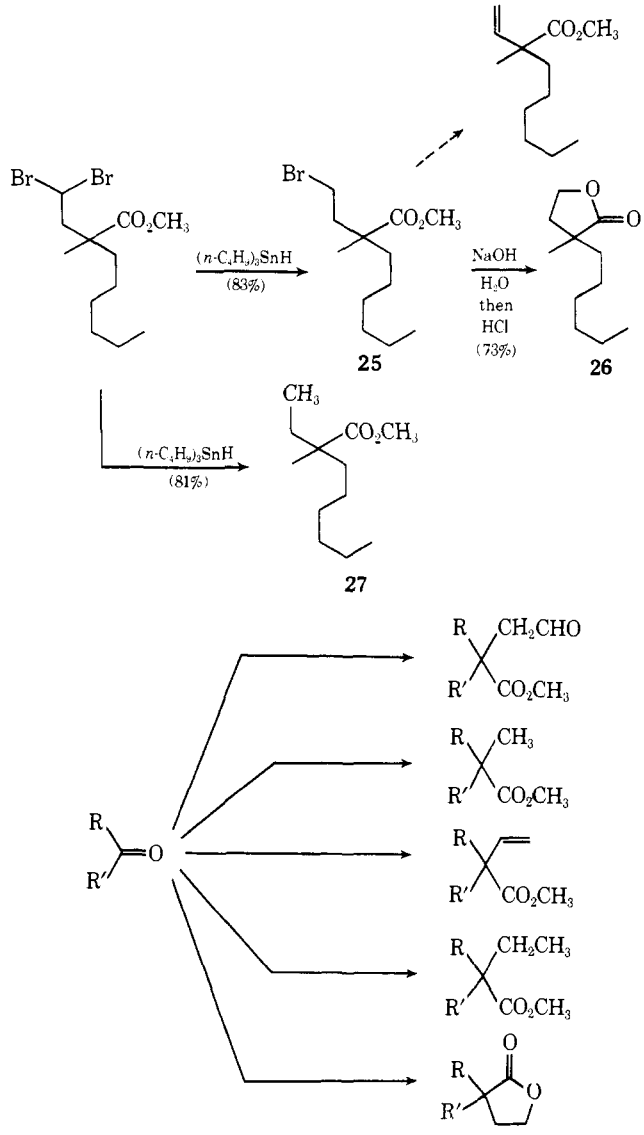


Alternatively, the bromines can be reductively removed in a sequential fashion. Treatment with tri-*n*-butyltin hydride[17] at room temperature produces the monobromo compound. The production of **24** in this way can serve as a facile entry into the quinuclidine system. Alternatively, hydrolysis of the ester effects lactonization to a 2,2-disubstituted γ-butyrolactone (see **25** → **26**). In principle, dehydrohalogenation would create a vinyl unit. Finally, reduction of the dibromo compounds with tri-*n*-butyltin hydride at 80° completely dehalogenates the substrate and produces an α-ethyl carboxylic ester (see formation of **27**).



24

The methodology outlined effects the net replacement of both carbon-oxygen bonds of a carbonyl group with new carbon-carbon bonds—a process we have termed geminal alkylation.[2a,19] Scheme I summarizes the net accomplishments achievable by this methodology. The fact that cyclobutanone annelation is stereoselective makes this overall process also stereoselective. Obviously, the limitations imposed by bromination conditions will also limit this approach to alkylation. For example, an isolated double bond may not survive the geminal halogenation reaction. To obviate these and other difficulties, an alternative approach



based on sulfur chemistry has been developed and is reported in the accompanying article.[10]

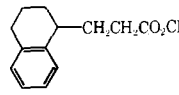
Experimental Section

Infrared spectra were determined on a Beckman IR-8 spectrophotometer, and ultraviolet spectra were recorded on Cary Model 11 and Model 15 spectrophotometers. NMR spectra were determined on a Varian Associates Model A-60A spectrometer fitted with a variable-temperature probe. Chemical shifts are given in parts per million relative to Me_4Si as an internal standard. Mass spectra were taken on a CEC 103 C or a MS-902 mass spectrometer at an ionizing current of 40 mA and ionizing voltage of 70 V. VPC analyses were performed on an Aerograph Model 90P instrument.

All reactions were performed under an atmosphere of nitrogen. Chromatography employed Merck silica gel PF254. The NMR abbreviations include m = multiplet, s = singlet, ps = pseudosinglet, d = doublet, pd = pseudodoublet, t = triplet, pt = pseudotriplet.

Starting Materials. The cyclobutanones **7**, **8**, **9**, **10**, **11**, and **12** were prepared as previously described.[4,10] The cyclobutanone **13** was prepared as follows. A suspension of 6.24 g (19.8 mmol) of cyclopropyldiphenylsulfonium fluoroborate[4] in 200 ml of DME (freshly distilled from sodium benzophenone ketyl) was cooled to −40°. A solution of dimsylsodium (13.0 ml of a 1.77 *M* solution, 23.0 mmol) in dimethyl sulfoxide was added all at once. After the solution was stirred for 5 min, 3.00 g (21.2 mmol) of 1-acetyl-4-piperidone[20] was added. Stirring continued at −40° for 20 min and then for an additional hour after removal of the cooling bath. Addition of 200 ml of saturated aqueous sodium chloride solution quenched the reaction. The resulting mixture was extracted with 3 × 100 ml of ether and 1 × 100 ml of ethyl acetate. After drying (Na_2SO_4) and evaporation, 7.24 g of a yellow oil which is a mixture of the oxaspiropentane and diphenyl sulfide was obtained. Infrared analysis revealed the absence of starting ketone. The crude mixture was dissolved in 100 ml of benzene (distilled from calcium hydride) and 0.155 g (1.65 mmol) of anhydrous lithium fluoroborate[10,21] added. After refluxing for 3 hr, 50 ml of saturated aqueous sodium chloride solution was added, and the layers were separated. The aqueous layer was washed with 2 × 100 ml of ether and 2 × 100 ml of ethyl acetate. The combined organic extracts were dried (Na_2SO_4) and evaporated in vacuo. This oil was chromatographed on 100 g of silica gel. Elution with 250 ml of hexane removed the diphenyl sulfide. Increasing the solvent polarity by utilizing 100 ml of 3:1, 100 ml of 1:1, and 100 ml of 1:3 hexane:ether and finally 250 ml of ether allowed recovery of 2.75 g (77% yield) of colorless product which was a single spot on TLC (9:1 ether:methanol): ir ($CHCl_3$) 1765 and 1630 cm^{-1}; NMR ($CDCl_3$) δ 1.8 (m, 4 H), 1.83 (t, J = 8.5 Hz, 2 H), 1.95 (s, 3 H), 2.97 (t, J = 8.5 Hz, 2 H), 3.45 (m, 4 H); MS *m/e* (rel %) 181 (30), 153 (22), 139 (59), 124 (45), 82 (90), 72 (25), 56 (39), 43 (100), 42 (87); mol wt 181.11049 (calcd for $C_{10}H_{15}NO_2$, 181.11033).

Table II. Reductive Alkylation

Cyclobutanone	Wt (mmol)	Product	Wt (% yield)
7	1.43 g (6.45)	$Ph_2CHCH_2CH_2CO_2CH_3$	1.60 g (98)
8	150 mg (0.97)	$PhCH_2CH_2CH_2CO_2CH_3$	162 mg (94)
9	500 mg (2.68)		558 mg (95)

Ring Cleavage of Arylcyclobutanones. A solution of the cyclobutanone in 5 ml of methanol was treated with 1 ml of a 1 *M* (1.0 mmol) methanolic solution of sodium methoxide. After 3–4 hr of reflux, 100 ml of ether and 50–100 ml of water were added. The ether layer was separated and the water layer extracted with an additional 100 ml of ether. The combined ether extracts were dried ($MgSO_4$) and evaporated in vacuo to yield the product. In each case, purity was established by chromatography on silica gel. Table II summarizes the details of each experiment.

Spectral Properties. Methyl 4,4-diphenylbutanoate:[22] ir (CCl_4) 1742 cm^{-1}; NMR (CCl_4) δ 2.0–2.4 (m, 4 H), 3.50 (s, 3 H), 3.8 (m, 1 H), 7.1 (ps, 10 H); MS *m/e* (rel %) 254 (0.3), 223 (0.2), 222 (0.3), 182 (20), 106 (4), 105 (43), 78 (100), 77 (35), 52 (17), 51 (20), 44 (11); mol wt 254.13201 (calcd for $C_{17}H_{18}O_2$, 254.13067).

Methyl 4-phenylbutanoate: ir (CCl_4) 1742 cm^{-1}; NMR (CCl_4) δ 1.7–2.4 (m, 4 H), 2.62 (t, J = 6.5 Hz, 2 H), 3.59 (s, 3 H), 7.11 (ps, 5 H); MS *m/e* (rel %) 178 (28), 147 (26), 146 (25), 117 (9), 105 (46), 104 (85), 91 (68), 74 (100), 43 (37); mol wt 178.09904 (calcd for $C_{11}H_{14}O_2$, 178.09937).

1-(2′-Carbomethoxyethyl)tetralin: ir (CCl_4) 1739 cm^{-1}; NMR (CCl_4) δ 1.5–2.4 (m, 8 H), 2.4–2.9 (m, 3 H), 3.56 (s, 3 H), 6.8–7.1 (m, 4 H); MS *m/e* (rel %) 218 (15), 187 (10), 186 (22), 144 (100), 131 (76), 129 (48), 115 (23), 91 (23), 77 (13), 59 (12); mol wt 218.12949 (calcd for $C_{14}H_{18}O_2$, 218.13067).

Preparation of 2,2-Dibromospiro[3.5]nonan-1-one. A carbon tetrachloride solution (20 ml) of spiro[3.5]nonan-1-one (0.635 g, 4.6 mmol) was stirred at 25° and 1.5 g (18.5 mmol) of liquid bromine added all at once. After stirring at 25° for 1 hr, the excess bromine and carbon tetrachloride were evaporated in vacuo, and the resulting product weighed 1.35 g (100%). Its purity was established by chromatography on silica gel (10% ether in hexane): ir (CCl_4) 1799 cm^{-1}; NMR (CCl_4) δ 1.55 (broad, 6 H), 1.83 (broad, 4 H), 3.04 (s, 2 H); MS *m/e* (rel %) 294 (0.4), 135 (4), 133 (4), 110 (100), 82 (42), 81 (12), 79 (12), 67 (45); mol wt 293.92814 (calcd for $C_9H_{12}Br_2O$, 293.92559).

Geminal Bromination with Pyridinium Bromide Perbromide. To a solution of the cyclobutanone in glacial acetic acid was added solid pyridinium bromide perbromide.[14] After stirring for the specified time at 50°, the solution was cooled to room temperature and diluted with 100 ml of ether (in the case of **12**, hexane was employed). The resulting mixture was washed twice with 100 ml of water and then once with aqueous saturated sodium bicarbonate solution. Upon drying ($MgSO_4$) and evaporation in vacuo, the product whose purity was established by chromatography (10%

Table III. Germinal Bromination

Cyclobutanone (wt, mmol)	Acetic acid, ml	Pyridinium bromide Perbromide, wt (mmol)	Reaction time, hr	Product (wt, % yield)
9 (550 mg, 3.16)	10	1.92 g (6.0)	3.0	15 (0.99 g, 92%)
12 (750 mg, 4.46)	12	3.20 g (10.0)	1.0	16 (1.53 g, 100%)
13 (1.23 g, 6.79)	50	6.50 (20.3)	30	17 (2.69 g, 100%)

ether in hexane) was isolated as a pale-yellow oil. Table III summarizes the details of each run. Instability in most cases precluded elemental analysis or mass spectrum. However, confirmation of molecular composition arises from the full characterization of their methoxide cleavage products.

Spectral Properties. **15**: ir (CCl_4) 1804 cm^{-1}; NMR (CCl_4) δ 1.6–2.0 (m, 2 H), 2.0–2.4 (m, 2 H), 2.73 (bt, J = 6 Hz, 2 H), 3.33 (s, 2 H), 6.9–7.3 (m, 4 H).

16: ir (CCl_4) 1803 cm^{-1}; NMR (CCl_4) δ 0.90 (pt, J = 7 Hz, 3 H), 1.1–2.0 (m, 10 H), 1.46 (s, 3 H), 2.89 (d, J = 16 Hz, 1 H), 3.16 (d, J = 16 Hz, 1 H).

17: ir ($CHCl_3$) 1795 cm^{-1}; NMR ($CDCl_3$) δ 2.07 (ps, 7 H), 3.2 (s, 2 H), 3.64 (m, 4 H).

Methoxide Cleavage of Dibromocyclobutanones. To a solution of the dibromocyclobutanone in methanol was added a 1.0 M methanolic solution of sodium methoxide. After stirring for 2–15 min at room temperature, 100–200 ml of ether (in the case of **16**, hexane was employed) and a corresponding volume of water were added consecutively. The aqueous layer was separated and washed with an additional 100 ml of the organic solvent. The combined organic layers were dried ($MgSO_4$) and evaporated in vacuo. Further purification was effected by chromatography (10% ether in hexane). Table IV summarizes the details for each experiment.

Spectral Properties. Methyl 1-(2′,2′-dibromoethyl)cyclohexan-1-carboxylate: ir (CCl_4) 1730 cm^{-1}; NMR (CCl_4) δ 1.42 (m, 8 H), 2.1 (m, 2 H), 2.85 (d, J = 6.5 Hz, 2 H, 3.69 (s, 3 H), 5.74 (t, J = 6.5 Hz, 1 H); MS *m/e* (rel %) 330 (1.5), 328 (2.5), 326 (1.4), 299 (0.5), 297 (0.8), 295 (0.5), 275 (6), 273 (11), 271 (7), 260 (6), 249 (18), 247 (18), 189 (15), 187 (15), 168 (28), 155 (35), 142 (92), 81 (100), 67 (100), 41 (95); mol wt 327.94939 (calcd for $C_{10}H_{16}O_2Br_2$, 327.94983).

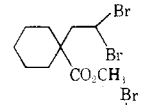
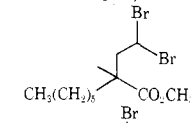
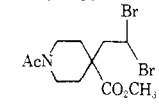
Methyl 2-(2′,2′-dibromoethyl)-2-methyloctanoate: ir (CCl_4) 1730 cm^{-1}; NMR (CCl_4) δ 0.91 (pt, J = 7 Hz, 3 H 1.23 (s, 3 H), 1.3 (bs, 10 H), 2.60 (dd, J = 18, 6 Hz, 1 H), 3.10 (dd, J = 18, 8 Hz, 1 H), 3.68 (s, 3 H), 5.75 (dd, J = 8, 6 Hz, 1 H); MS *m/e* (rel %) 360 (16), 358 (25), 356 (16), 315 (10), 313 (15), 311 (10), 196 (30), 194 (31), 177 (14), 175 (10), 128 (30), 127 (15), 101 (45), 100 (30), 83 (22), 41 (100); mol wt 355.99001 (calcd for $C_{12}H_{22}O_2Br_2$, 355.99875).

Methyl 1-acetyl-4-(2′,2′-dibromoethyl)piperidine-4-carboxylate: ir ($CHCl_3$) 1720 and 1627 cm^{-1}, NMR ($CDCl_3$) δ 1.2–1.7 (m, 2 H), 1.9–2.3 (m, 2 H), 2.00 (s, 3 H), 2.79 (bt, J = 12 Hz, 1 H), 2.89 (d, J = 6 Hz, 2 H), 3.24 (bt, J = 12 Hz, 1 H), 3.65 (m, 1 H), 3.76 (s, 3 H), 4.20 (m, 1 H), 5.82 (t, J = 6 Hz, 1 H); MS *m/e* (rel %) 373 (4), 371 (7), 369 (4), 330 (10), 328 (24), 326 (12), 211 (22), 185 (56), 168 (26), 110 (27), 83 (21), 82 (49), 58 (55), 57 (39), 48 (49), 43 (100), 42 (59), 41 (31); mol wt 370.95510 (calcd for $C_{11}H_{17}NO_3Br$, 370.95532).

Reaction of 2,2-Dibromo-4,5-benzospiro[3.5]nonan-1-one (15) with Sodium Methoxide in Methanol. A methanol (50 ml) solution of 2,2-dibromo-4,5-benzospiro[3.5]nonan-1-one (510 mg, 1.48 mmol) was treated with commercial solid sodium methoxide (108 mg, 2.0 mmol). This mixture was stirred for 5 min, then 200 ml of hexane was added. After dilution with 200 ml of water, the hexane layer was separated. The hexane extract was washed with water (200 ml) and dried over anhydrous magnesium sulfate. The weight of the crude material upon evaporation of the hexane in vacuo was 426 mg. The NMR spectrum of this mixture showed three methyl ester singlets at δ 3.22, 3.62, and 3.75 in the relative amounts of 70:18:12, respectively.

The major isomer, *cis*-3,4-benzo-1-bromo-1-carbomethoxyspiro[2.5]octane (**19**), was separated with 4% tetrahydrofuran in hexane on a silica gel PF-254 thick-layer plate and possessed the highest R_f value. The other compounds, *trans*-3,4-benzo-1-bromo-1-carbomethoxyspiro[2.5]octane (**20**) and 1-carbomethoxy-1-(2′,2′-dibromoethyl)tetralin (**18**), are inseparable on TLC. Thus, 426 mg represents a 94% yield with absolute yields of **19**, 66%, **20**, 17%, **18**, 11%.

Table IV. Methoxide Cleavage of Dibromocyclobutanones

Dibromocyclobutanone (wt, mmol)	1.0 M $NaOCH_3$ (in CH_3OH), ml	Solvent, ml	Product (wt, % yield)	
14 (1.20 g, 4.05)	15	50		(1.30 g, 98)
16 (0.70 g, 2.15)	5	25		(0.69 g, 90)
17 (2.55 g, 7.52)	15	50		(2.53 g, 91)

***cis*-3,4-Benzo-1-bromo-1-carbomethoxyspiro[2.5]octane (19)**: ir (CCl_4) 3067, 1730, 1605, 1431, 1357, 1342, 1305, 1282, 1222, 1156, 1107, 1086, 964, 943, 888, 864, 837, 716, 703, 667 cm^{-1}; NMR (CCl_4) δ 1.28 (d, J = 8 Hz, 1 H), 1.8–2.2 (m, 4 H), 2.53 (d, J = 8 Hz, 1 H), 2.82 (m, 2 H), 3.22 (s, 3 H), 6.6–6.9 (m, 1 H), 6.9–7.1 (m, 3 H); MS *m/e* (rel %) 295 (2.5), 294 (2.5), 265 (1.0), 264 (0.9), 215 (30), 214 (27), 154 (100), 128 (31), 77 (10); mol wt 294.02410 (calcd for $C_{14}H_{15}O_2Br$, 294.02558).

The structures of **18** and **20** were assigned from a NMR spectrum of the mixture as presented in the Discussion section.

Conversion of a Geminal Dibromide to an Acetal. To a solution of methyl 1-(2′,2′-dibromoethyl)cyclohexane-1-carboxylate (170 mg, 0.518 mmol) in 30 ml of methanol was added silver nitrate (425 mg, 2.5 mmol). This mixture was stirred in the dark for 5 hr. The mixture was filtered, 50 ml of water added to the filtrate, and the filtrate extracted with 3 × 50 ml of hexane. The hexane was dried over anhydrous sodium sulfate and evaporated in vacuo to yield 117 mg (98%) of an oil whose purity was established by TLC on silica gel (10% ether in hexane). Spectral properties of methyl 1-(2′,2′-dimethoxyethyl)cyclohexane-1-carboxylate allow the assigned structure: ir (CCl_4) 1733 cm^{-1}; NMR (CCl_4) δ 1.35 (m, 8 H), 1.70 (d, J = 5.5 Hz, 2 H), 2.05 (m, 2 H), 3.18 (s, 6 H), 3.60 (s, 3 H), 4.30 (t, J = 5.5 Hz, 1 H); MS *m/e* (%) 230 (0.06), 229 (0.1), 199 (7), 139 (10), 89 (5), 81 (10), 75 (100), 71 (7), 59 (6), 58 (6), 41 (6); mol wt 199.13321 (calcd for $C_{11}H_{19}O_3$, 199.13341).

Hydrolysis of Methyl 1-(2′,2′-Dimethoxyethyl)cyclohexane-1-carboxylate to Methyl 1-(2′-Oxoethyl)cyclohexane-1-carboxylate (23). A solution of methyl 1-(2′,2′-dimethoxyethyl)cyclohexane-1-carboxylate (90 mg, 0.391 mmol) in 10 ml of a 1:1 v/v mixture of dioxane and water was treated with 5 drops of concentrated aqueous hydrochloric acid. After 5 hr of stirring at 25°, 150 ml of ether was added. The mixture was washed with 2 × 50 ml of water and subsequently the ether layer separated, dried over anhydrous magnesium sulfate, and evaporated in vacuo to yield 69.0 mg (96%) of an oil whose purity was established by TLC (10% ether in hexane), and whose spectral properties assign the structure methyl 1-(2′-oxoethyl)cyclohexane-1-carboxylate: ir (CCl_4) 2732, 1724 (broad) cm^{-1}; NMR (CCl_4) δ 1.44 (bs, 8 H), 2.0 (m, 2 H), 2.50 (d, J = 2.0 Hz, 2 H), 3.68 (s, 3 H), 9.63 (t, J = 2.0 Hz, 1 H); MS *m/e* (rel %) 184 (0.27), 156 (14), 141 (40), 125 (11), 124 (10), 113 (19), 96 (25), 81 (100), 74 (61), 55 (40); mol wt 184.11004 (calcd for $C_{10}H_{16}O_3$, 184.10994).

Decarbonylation of Methyl 1-(2′-Oxoethyl)cyclohexane-1-carboxylate (23). A solution of **23** (41.1 mg, 0.223 mmol) and tris(triphenylphosphine)rhodium chloride[16] (212 mg, 0.23 mmol) in acetonitrile (6 ml) was refluxed for 5 hr. The acetonitrile was removed in vacuo and the residue dissolved in hexane. 2-Octanone (15.0 mg) was added as an internal standard for VPC analysis utilizing a 6 ft × 0.25 in. 5% SE-30 on Chromosorb W at 90°. The retention times of methyl 1-methylcyclohexane-1-carboxylate and **23** are 9.2 and 17 min, respectively. Only a trace (<1%) of starting aldehyde was observed. Assuming a normalization factor of 1.00 for the de-

carbonylated material, the weight of product is 35.3 mg, 86%. The peak at 9.2 min was collected, and spectral data were obtained: ir (CCl_4) 1730 cm^{-1}; NMR (CCl_4) δ 1.10 (s, 3 H), 1.35 (m, 8 H), 2.0 (m, 2 H), 3.60 (s, 3 H); MS *m/e* (rel %) 156 (13), 141 (6), 125 (3), 101 (38), 97 (99), 96 (20), 88 (21), 55 (100); mol wt 156.11553 (calcd for $C_9H_{16}O_2$, 156.11502).

Monodebromination of Geminal Dibromides. The removal of one bromine atom from methyl 2-(2′,2′-dibromoethyl)-2-methyl octanoate (0.30 g, 0.84 mmol) was effected by dissolving this geminal dibromide in 0.49 g (1.68 mmol) of tri-*n*-butyltin hydride[17] without solvent. The reactants were allowed to stir at 25° for 15 min, after which 2 ml of ether was added. The ether mixture was placed on a silica gel PF-254 thin-layer plate and eluted with 5% ether in hexane to remove the tin species. An oil, 0.19 g (83%), was obtained from the plate. This oil was a single spot on TLC. Cooling to −20° overnight induced crystallization; however, warming to room temperature resulted in melting of the white needles: ir (CCl_4) 1736 cm^{-1}; NMR (CCl_4) δ 0.7–1.7 (m, 13 H), 1.14 (s, 3 H), 2.09 (m, AB part of ABMN, 2 H), 3.25 (m, MN part of ABMN, 2 H), 3.64 (s, 3 H); MS *m/e* (rel %) 279 (26), 172 (55), 101 (100), 69 (51), 55 (60); mol wt 278.08628 (calcd for $C_{12}H_{23}O_2Br$, 278.08818).

In like fashion, 1-acetyl-4-carbomethoxy-4-(2′,2′-dibromoethyl)piperidine was converted to 1-acetyl-4-carbomethoxy-4-(2′-bromoethyl)piperidine: ir ($CHCl_3$) 1730, 1635 cm^{-1}; NMR ($CDCl_3$) δ 4.11 (m, AB part of ABMN, 2 H), 3.75 and 3.66 (s, 3 H), 3.0–3.8 (m, 4 H), 2.00 (s, 3 H), 0.9–2.0 (m, 6 H); MS *m/e* (rel %) 293 (8), 291 (10), 250 (23), 248 (28), 211 (35), 185 (32), 170 (42), 168 (49), 110 (68), 82 (100); mol wt 291.04632 (calcd for $C_{11}H_{18}BrNO_3$, 291.04687).

Lactonization of Methyl 2-(2′-Bromoethyl)-2-methyloctanoate. To a solution of methyl 2-(2′-bromoethyl)-2-methyloctanoate (100 mg, 0.36 mmol) in 10 ml of methanol was added solid potassium hydroxide (56 mg, 1.0 mmol). This mixture was refluxed for 2 hr. Upon cooling, 50 ml of hexane was added followed by 50 ml of 3 *N* aqueous hydrochloric acid. This mixture was stirred 10 min, then the hexane was separated, washed with 50 ml of water, and dried over anhydrous magnesium sulfate. The hexane was evaporated to yield 48 mg (73%) of an oil, 2-*n*-hexyl-2-methyl-γ-butyrolactone, which was purified by chromatography: ir (CCl_4) 1776 cm^{-1}; NMR (CCl_4) δ 0.8–2.2 (m, 15 H), 1.18 (s, 3 H), 4.12 (t, J = 8 Hz, 2 H); MS *m/e* (rel %) 184 (0.4), 169 (0.4), 113 (14), 100 (100), 70 (18), 55 (20); mol wt 184.14553 (calcd for $C_{11}H_{20}O_2$, 184.14632).

Debromination of Methyl 2-(2′,2′-Dibromoethyl)-2-methyloctanoate. Methyl 2-(2′,2′-dibromoethyl)-2-methyloctanoate (197 mg, 0.55 mmol) and tri-*n*-butyltin hydride (0.640 g, 2.20 mmol) were mixed together without solvent. The mixture was heated to 80° for 3 hr, then cooled to 25° for 3 hr. The crude reaction mixture was purified by elution with hexane on a silica gel thin-layer plate. The tin species moved near the top of the plate, while the ketone moved only slowly. The material recovered, 89 mg (81%), was pure methyl 2-ethyl-2-methyloctanoate:[24] ir (CCl_4) 1729 cm^{-1}; NMR (CCl_4) δ 1.08 (s, 3 H), 0.7–1.7 (m, 18 H), 3.59 (s, 3 H); MS *m/e* (rel %) 200 (1), 185 (1), 172 (9), 141 (33), 116 (100), 101 (31), 85 (38), 71 (40), 57 (62), 55 (35), 43 (51), 41 (42); mol wt 200.17710 (calcd for $C_{12}H_{24}O_2$, 200.17762).

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