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(24) It has been found[25] that with heterogeneized phase-transfer catalysts in a fixed-bed reactor external diffusion may be rate limiting at low temperatures and low liquid fluxes. A comparison between fixed-bed and suspended catalysts indicates that, as the temperature increases, conversions tend to approach one another, probably coinciding above 90 °C.
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(31) Elemental composition of resins **4–11** was calculated from $[-CH(C_6H_4CH_2X)CH_2(CHPhCH_2)_n-]$, where X is the functionalized chain and $n = 1.28$, 6.0, and 1.13 for titers of 3.5, 1.29, and 3.6 mequiv Cl/g in the original chloromethylpolystyrene, respectively. Influence of cross-linking by *p*-divinylbenzene was neglected. Analyses of resins not obtained with quantitative conversions have not been reported.
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Stereoelectronic Control in the Electrochemical and Mercury-Promoted Reductive Acetoxylation of α,α′-Dibromobicycloalkanones

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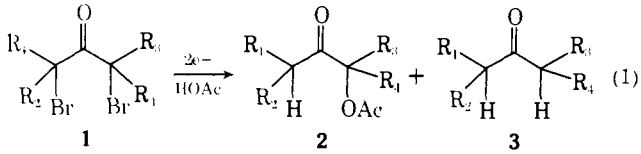
Abstract: Reductions in acetic acid of the stereochemically well-defined α,α′-dibromo ketones *cis*-2,6-dibromo-3,3,5,5-tetramethylcyclohexanone, *cis*-2,6-dibromo-4-*tert*-butylcyclohexanone, 2,4-dibromobicyclo[3.2.1]octan-3-one (and its 2,4-dimethyl derivative), and dibromoisopinocamphone were carried out both electrochemically and by finely dispersed mercury. The results are consistent with a previously proposed mechanism for such reactions involving as its key step the ionization of an enol allylic bromide to a 2-hydroxyallyl cation.

We have previously reported[2] that electrochemical reduction of α,α′-dibromo ketones (**1**) in acetic acid affords α-acetoxy ketones (**2**) in good yield when at least three of the alkyl groups flanking the carbonyl group are alkyl, and that otherwise the principal products are the so-called "parent" ketones (**3**) (eq 1). More recently, we found that dibromo ketones **1** are



(1)

1 **2** **3**

also converted to **2** and **3** by ultrasonically dispersed mercury in acetic acid.[3] The mercury reaction appears to be mechanistically similar to the electrochemical process, in that increasing α-alkyl substitution favors formation of **2** over **3**, but there are differences between the two processes: (a) for a given dibromo ketone, the ratio of **2** to **3** is generally higher in the mercury reaction; (b) total yields are lower in the mercury reaction; (c) with unsymmetrical dibromo ketones the ratio of isomeric α-acetoxy ketones is generally somewhat different between the two processes.[3-5] We have outlined our reasons for believing the reductive substitution process embodied in the conversion **1** → **2** to be of synthetic utility.[2,3,5]

Our attention has recently turned to consideration of the mechanism of formation of **2** from **1**. We had originally suggested[2] that electron transfer to **1** results in formation of enolate **4**, which is immediately protonated to enol allylic bromide

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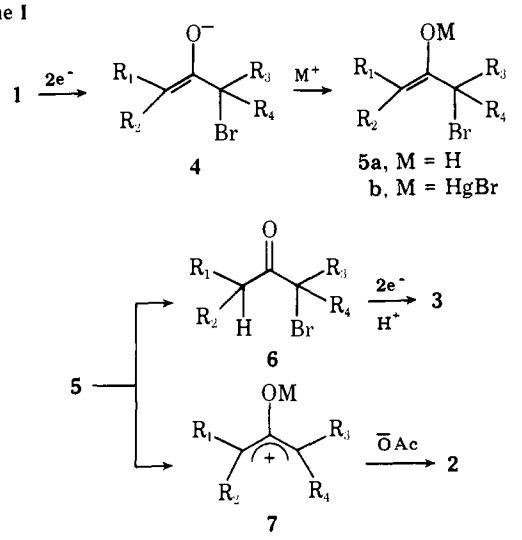
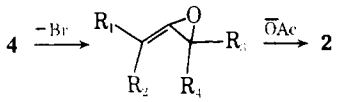
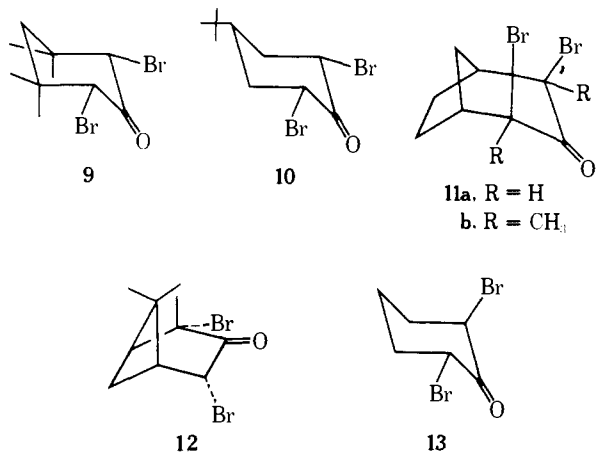
Scheme I



5a, and that **5** might undergo two processes: tautomerization to monobromide **6** (subsequently reduced to **3**) and/or ionization to a 2-hydroxyallyl cation (**7a**), which would then suffer nucleophilic attack by acetate or acetic acid to afford, ultimately, **2** (Scheme I). The mercury reaction has been suggested by us[3] to proceed by a similar mechanism involving intermediates **5b** and **7b** rather than **5a** and **7a**. The principal consideration impelling us to advance the mechanism shown in Scheme I has been the marked increase of the ratio of **2** to **3** as the number of α-alkyl groups is increased.[2-4] We feel that the considerable body of data[2-6] obtained by us to date strongly supports this mechanism. We recognize, however, that alternative interpretations of the data are possible. For example, enolate **4** might cyclize to an allene oxide (**8**), which could undergo ring opening in known fashion[7] to afford **2**. As part of a program designed to distinguish between these two mechanistic possibilities (**5** → **7** or **4** → **8**),[6] we have examined



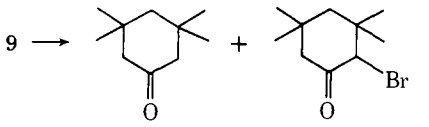
the reduction, both electrochemically and by ultrasonically dispersed mercury, of a series of cyclic and bicyclic α,α'-dibromo ketones of closely defined geometry. We now wish to report the results of that study, which are fully consistent with the mechanism advanced in Scheme I. The substances examined were *cis*-2,6-dibromo-3,3,5,5-tetramethylcyclohexanone (**9**),[8] *cis*-2,6-dibromo-4-*tert*-butylcyclohexanone (**10**),[9] 2α,4α-dibromobicyclo[3.2.1]octan-3-one (**11a**)[10] and its 2,4-dimethyl derivative (**11b**), and 2α,4α-dibromo-2β,6,6-trimethylbicyclo[3.1.1]heptan-3-one[11] (dibromoisopinocamphone) (**12**) (steroid nomenclature is used throughout this paper to indicate stereochemical relationships).



The dibromo ketones used in this study were chosen because (a) they are stereochemically well defined and (b) the bromine atoms are disposed stereochemically quite differently in the various dibromides. Thus, in **9** the two bromine atoms are diequatorial as a consequence of the so-called conformational "reflex effect",[12] while **10** is also a diequatorial dibromide, though it appears that in this case it is isolated because of its much lower solubility[9] than the initially formed (and presumably more stable) trans 2,6-dibromide.[13] On the other hand, the bromine atoms in **11a** and **11b** are diaxial as a consequence of the inverse operation of the reflex effect.[12] Dibromo ketone **12** represents an intermediate case: while the two-carbon bridge in **11a** and **11b** holds the six-membered ring in a rather well-defined chair, its contraction to a one-carbon bridge in **12** results in distortion of the cyclohexanone ring such that the two bromine atoms favor an orientation intermediate between axial and equatorial.[15] We anticipated (and found—see Discussion) that the stereochemical differences between the bromine atoms in **9**–**12** would result in major differences in their behavior upon reduction.

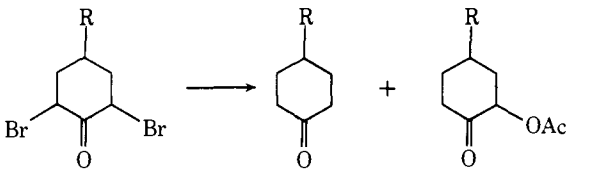
Results

Reduction of dibromotetramethylcyclohexanone **9** afforded only the parent ketone (**14**) and a small amount of monobromide (**15**). Significantly, no acetoxy ketone could be detected (singlet at δ 2.0) by NMR spectroscopy; this is in distinct contrast with the reduction of 2,6-dibromocyclohexanone (**13**), in which the major product is α-acetoxycyclohexanone (ratio of **2** to **3** = 78:18).[6]



	14	**15**
electrochemical:	80%	1%
mercury:	76%	5%

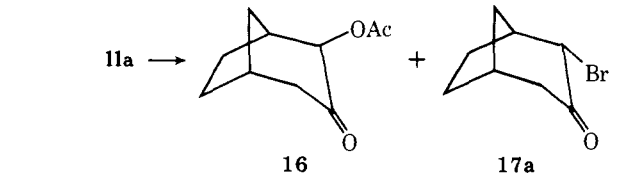
Likewise, as we have reported previously,[2] electrochemical reduction of **10** affords only a trace of α-acetoxy ketone, and reduction by mercury affords a considerably diminished proportion of acetoxy ketone relative to **13**.



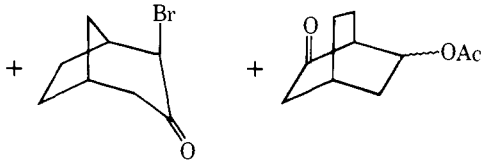
	R = H	R = *t*-Bu	R = H	R = *t*-Bu
electrochemical:		99%		1%
mercury:	18	65%	78	24%

In contrast to the preceding results, electrochemical reduction of **11a** afforded as the major product the α-acetoxy ketone (**16**), accompanied by small amounts of two monobromo ketones (**17**) and a substance isomeric with **16**, isolated in quantities insufficient for full characterization but believed on mechanistic grounds (see Discussion) to be 6-acetoxybicyclo[2.2.2]octan-2-one (**18**).

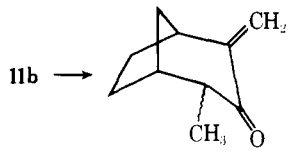
In similar contrast with the behavior of **9** and **10**, reduction of **11b** afforded a single product (homogeneous by VPC), assigned the structure 2-methylene-4-methylbicyclo[3.2.1]-octan-3-one (**19**) on the basis of its NMR and mass spectra, especially the presence of two doublets, each with a homoallylic coupling constant of 1.5 Hz, at δ 5.00 and 5.65. A control experiment showed that **11b** is not dehydrohalogenated under the conditions in which **19** is produced.



	16	17a
electrochemical:	73%	9%
mercury:	43%	25%

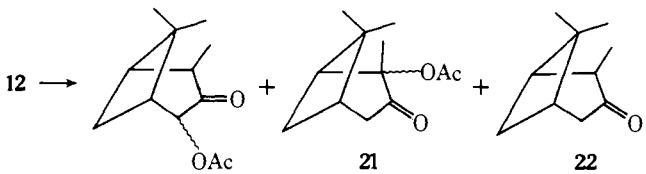


	17b	18 (?)
electrochemical:	7%	6%
mercury:	20%	4%

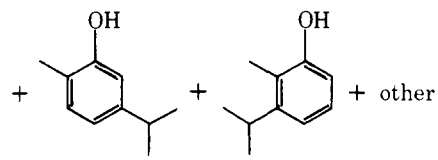


	19
electrochemical:	94%
mercury:	83%

Reduction of dibromoisopinocamphone (**12**) afforded five principal products: two acetoxy ketones (**20** and **21**),[16] isopinocamphone (**22**), and two substances whose NMR and mass spectra indicated them to be isomeric methylisopropylphenols. For mechanistic reasons structures **23** and **24** were assigned



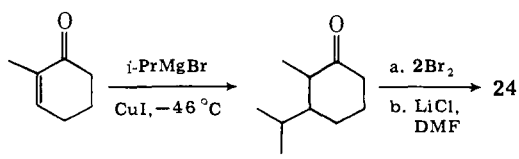
20 **21** **22**



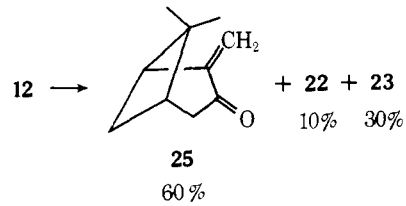
23 **24**

	20	21	22	23	24	other
electrochemical:	37%	7.5%	22%	17%	11.5%	0%
mercury:	24%	5%	14%	25%	14%	6%

to the two phenols; these structural assignments were subsequently confirmed on the one hand for **23** (carvacrol) by comparison with an authentic commercial sample and on the other hand for **24** by unambiguous independent synthesis.[17]



When **12** was reduced electrochemically in dimethylformamide containing *p*-toluenesulfonic acid (to serve as a proton source toward enolate **4**) in an attempt to maximize the yields of phenols **23** and **24**, the major product was the α-methylene ketone **25** (pinocarvone),[18] whose structure was established inter alia by resonances in its NMR spectrum at δ 5.97 and 4.98[18] and by comparison of its 2,4-DNP derivative with authentic material. Surprisingly, only one phenol (**23**) was formed in this reaction.

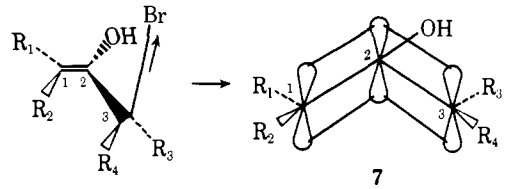


25

60%

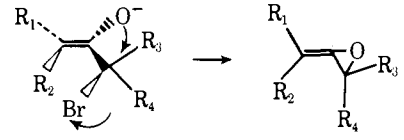
Discussion

The results presented above clearly demonstrate that in rigid dibromo ketones the stereochemistry of the bromine atoms has a dominant effect upon the course of the reductive substitution process. Furthermore, the results are exactly those which could have been predicted on the basis of the mechanism outlined in Scheme I. We first note that the key step in this mechanism is the ionization of enol allylic bromide **5** to carbonium ion **7**, as opposed to tautomerization of **5** to monobromide **6**, which would generally, though not necessarily, suffer further reduction to "parent" ketone **3**.[19] *We believe that **5** is converted to **7** most readily when the carbon-bromine bond of **5** is perpendicular to the plane defined by the carbon-carbon double bond and the sp^3-hybridized carbons attached to that bond*, that is, that ionization proceeds best from geometry **26a**.



26a **7**

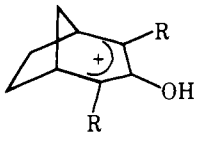
In this geometry the incipient p orbital at C-3 of **26a** can grow in smoothly as the C-Br bond begins to break. On the other hand, formation of allene oxide **8** ought to occur most readily when the carbon-bromine lies close to the aforementioned plane, i.e., geometry **26b**. Inspection of dibromo ketones **9–12**



26b **8**

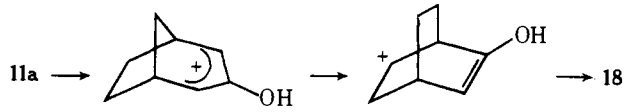
indicates that geometry **26a** is that resulting when diaxial dibromides **11a** and **i1b** are reduced to their enol bromides, and that diequatorial bromides **9** and **10** afford enol bromides approximating **26b** in geometry; hence **11a** and **11b** should favor carbonium ion formation as compared to **9** and **10**. Dibromo ketone **12** is sufficiently distorted from idealized cyclohexanone geometry (as inspection of models and empirical force field calculations[15] both show) that the enol allylic bromide derived from it should exhibit intermediate behavior.

These stereoelectronic predictions are confirmed by experiment. Dibromide **9** affords no detectable amount of acetoxy ketone, and **10**, the enol bromide of which is, unlike **9**, somewhat flexible,[20] affords a proportion of acetoxy ketone which is considerably diminished relative to dibromocyclohexanone **13**. Reduction of the diaxial dibromides **11a** and **11b** affords, as predicted, substantial amounts of products derived from intermediate 2-hydroxyallyl cations. Dibromide **11b**, possessing four α-alkyl substituents, is inherently predisposed toward cation formation already,[2] but **11a** also forms a very substantial amount of α-acetoxy ketone. Isolation of methylene ketone **19** rather than an α-acetoxy ketone from **11b** is understandable, since models demonstrate that nucleophilic at-



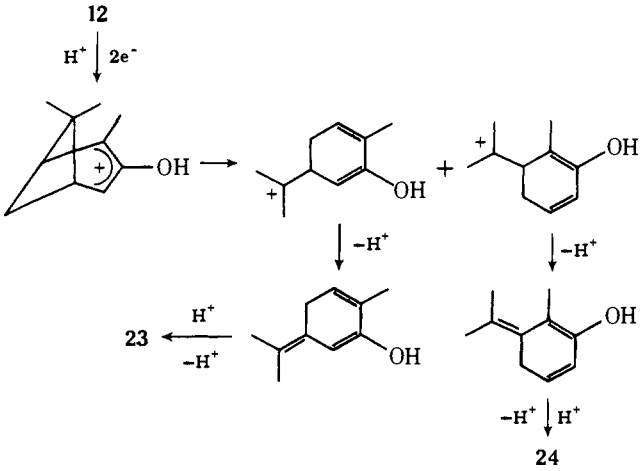
27

tack on cation **27b** by acetate engenders substantial torsional interaction with the bridgehead proton; hence proton loss from **27b** can compete successfully. Isolation of rearranged acetate **18** from **11a** is further evidence for the intermediacy of cation



27a; this type of rearrangement is well precedented in bicyclo[3.2.1]oct-2-yl cations.[21]

Again as expected, pinanone derivative **12** exhibits intermediate behavior: a substantial amount of parent ketone is formed upon reduction in the presence of acetic acid even though the ketone has three α-alkyl substituents, and yet most of the products derive from the corresponding 2-hydroxyallyl cation. Ring-opened phenols **23** and **24** afford especially convincing evidence of a carbonium ion intermediate in the reduction.



Reduction of **12** in DMF/toluenesulfonic acid afforded pinocarvone (**25**) in good yield. It appears that proton loss from the intermediate 2-hydroxyallyl cation is more rapid than ring opening. Isolation of α-methylene ketones **19** and **25** from reductions of **11b** and **12** suggests that reduction of dibromo ketones in the presence of *p*-toluenesulfonic acid may be a synthetically useful route to such species; we intend to explore this possibility. It is not clear to us at this time why only one phenol, **23**, is isolated from **12** under these conditions.

Experimental Section

General. Melting points (uncorrected) were determined on a Fisher-Johns apparatus. NMR spectra were recorded on Varian A-60A and HA-100 spectrometers. VPC analyses were carried out on either a Varian 90-P instrument with 1.5 m × 6 mm column packed with 3% SE-30 on Chromosorb P (column A) or Varian Model 1700 chromatograph with 1.5 m × 6 mm columns: 12.5% Carbowax 20M on Chromosorb P (column B) or 20% SE-30 on Chromosorb P (column C). High-pressure liquid chromatographic (LC) separations were made on a Waters Associates ALC/GPC-201 liquid chromatograph, using a 4-ft Corasil II column. Mass spectra were recorded at 70 eV on a Perkin-Elmer Hitachi RMU-6L spectrometer, and calibrated against perfluorokerosene. Electrochemical experiments were carried out using a Princeton Applied Research Model 170 electrochemistry system, equipped with a Koslow Model 541 digital coulometer.

Bicyclo[3.2.1]octan-3-one was prepared by the method of Jefford et al.[22] Final purification is more simply carried out by steam distillation of the crude ketone, instead of vacuum sublimation as recommended[22] previously.

2,4-Dimethylbicyclo[3.2.1]oct-6-en-3-one. The procedure[23a] of Noyori, Makino, and Takaya for synthesis of this compound was found unsatisfactory, and the following procedure was developed. To 500 mL of dry tetrahydrofuran (THF) in a 1-L three-neck flask equipped with reflux condenser, thermometer, pressure-equalizing addition funnel, and nitrogen purge was added 45.9 g (0.12 mol) of diiron nonacarbonyl. The solution was stirred for 4 h to complete formation of the THF–iron tetracarbonyl complex,[24] and the solution was then heated to reflux. A mixture of 2,4-dibromo-3-pentanone (25.6 g, 0.10 mol) and cyclopentadiene (36 g, 1.0 mol) was diluted with an equal volume of THF and added dropwise to the refluxing iron carbonyl solution over a period of 3 h. After 12 h, TLC showed the absence of starting dibromo ketone. At this time a mixture of 10 g (0.04 mol) of the dibromo ketone and 14.7 g (0.4 mol) of cyclopentadiene was added dropwise to the flask, and reflux was continued for an additional 8 h. The solution was then allowed to cool and crystalline ceric ammonium nitrate was cautiously added till all bubbling had ceased. Water (200 mL) was added and the mixture extracted with 200 mL of ether. The aqueous THF layer was extracted with five 200-mL portions of ether, the combined ether extracts were dried over sodium sulfate, and the ether was removed at the rotary evaporator. Distillation in vacuo (20-cm Vigreux column) afforded, after an initial forerun consisting of dicyclopentadiene, 17.1 g of 2,4-dimethylbicyclo[3.2.1]oct-6-en-3-one (81% yield based on dibromo ketone), bp 54–58 °C (6.8 mm); the presence of two doublets (J = 7 Hz) at δ 1.10 and 0.9 in the ratio of ca. 2:1 in the NMR spectrum demonstrated this to be a mixture of stereoisomers.[23b]

2β,4β-Dibromo-2α,4α-dimethylbicyclo[3.2.1]octan-3-one (11b). A solution of 15.0 g of 2,4-dimethylbicyclo[3.2.1]oct-6-en-3-one in 100 mL of ethanol containing 0.1 g of 10% palladium on carbon was shaken in a Parr hydrogenation apparatus at an initial hydrogen pressure of 50 lb/in^2. After removal of catalyst by filtration through diatomaceous earth and solvent, by rotary evaporation, a yellow oil was obtained, which afforded upon distillation 12.4 g (82%) of 2,4-dimethylbicyclo[3.2.1]octan-3-one as a colorless liquid, bp 78–80 °C (6.8 mm). To a suspension of 10 g (0.065 mol) of this material in 25 mL of 48% hydrobromic acid at room temperature was added dropwise 10.5 g (0.065 mol) of bromine. The solution was then heated to 55 °C, and another 10.5-g portion of bromine was added. The mixture was kept at this temperature for 3 h, at which point the contents of the flask were extracted with 100 mL of carbon tetrachloride. The organic extracts were washed with water (twice), 10% sodium bisulfide, 10% sodium bicarbonate, and water and dried over $MgSO_4$. Removal of solvent afforded a solid, which was recrystallized from carbon tetrachloride to afford dibromide **11b** in 39% yield, mp 125–127 °C.

Reductions. The procedures employed for electrochemical[2] and mercury[3-5] reductions have been described elsewhere. All electrolyses were carried out at −1.3 V vs. SCE. Crude reaction mixtures were analyzed by VPC and NMR spectroscopy, and products were separated for NMR and mass spectral characterization by preparative VPC, or, in the case of **11a** reductions, by LC.

Reduction of *cis*-2,6-Dibromo-3,3,5,5-tetramethylcyclohexanone (9). Controlled-potential electrochemical reduction of 2.95 g of **9** in 50 mL of a solvent system consisting of 0.2 M sodium acetate in 9:1 (v/v) DMF/acetic acid consumed 2.1 Faradays/mol of **9**. Workup in the usual manner[2] afforded 1.21 g of crude product. Analysis by VPC (column A, 140 °C, helium flow rate 50 mL/min) indicated the presence of two products in ca. 99:1 ratio. The major product was shown to be 3,3,5,5-tetramethylcyclohexanone by comparison with an authentic sample. The minor product was shown to be 2-bromo-3,3,5,5-tetramethylcyclohexanone: NMR δ 4.15 (s);[27] mass spectrum *m/e* 230 and 232 (parent).

Reduction of 2.95 g of **9** by ultrasonically dispersed mercury followed by the customary workup[3-5] afforded 1.7 g of product consisting of a 94:6 mixture of the same products.

Reduction of *cis*-2,6-dibromo-4-*tert*-butylcyclohexanone (10) (2.95 g) by ultrasonically dispersed mercury afforded a 27:73 mixture of 2-acetoxy-4-*tert*-butylcyclohexanone (2:1 ratio of isomers) and 4-*tert*-butylcyclohexanone, whose structures were proven by NMR and mass spectroscopic measurements on samples isolated by preparative VPC and, for the latter compound, comparison with an authentic sample.

Reduction of 2,4-Dibromobicyclo[3.2.1]octan-3-one (11a). Controlled-potential electrochemical reduction of 3.10 g of **11a** in 50 mL

of acetic acid containing 1.0 M sodium acetate consumed 2.5 Faradays/mol of **11a**. Workup[2] afforded 1.83 g of product mixture. Analysis and preparative separation by LC (elution with 10% hexane–90% dichloromethane) demonstrated this to be a mixture of α-2-bromobicyclo[3.2.1]octan-3-one (**17a**, 9%),[27] β-2-bromobicyclo[3.2.1]octan-3-one (**17b**, 8%),[27] 2-α-acetoxybicyclo[3.2.1]octan-3-one (**16**, 76%), and a fourth substance believed to be 5-acetoxybicyclo[2.2.2]octan-2-one (**18**). Acetoxy ketone **16** exhibited a broad doublet at δ 4.75 (1 H) and singlet (δ 2.07, 3 H) in its NMR spectrum, and a parent peak at *m/e* 182 in its mass spectrum. The compound believed to be **18** also exhibited a mass spectral parent peak at *m/e* 182, broad triplets at δ 3.38 and 4.05 (C*H*OAc), and a sharp singlet (δ 2.00) in the acetoxy region of the NMR spectrum.

Reduction of **11a** by ultrasonically dispersed mercury in acetic acid afforded the same products: **17a** (27%), **17b** (23%), **16** (45%), and **18** (?) (5%).

Reduction of 2,4-Dibromo-2,4-dimethylbicyclo[3.2.1]octan-3-one (11b). Controlled-potential electrochemical reduction of 2.95 g of **11b** in 50 mL of acetic acid containing 1.0 M sodium acetate resulted in consumption of 2.01 Faradays/mol of **11b**. Workup[2] afforded 1.34 g (94%) of a colorless oil, shown by VPC (column B, 200 °C, helium flow rate 50 mL/min) to be a single substance, 2-methyl-4-methylenebicyclo[3.2.1]octan-3-one (**19**): NMR ($CDCl_3$) δ 1.15 (d, 3H), 1.5–2.6 (m, 8 H), 3.10 (broad s, 1 H), 5.00 (d, J = 1.5 Hz, 1 H), and 5.65 (d, J = 1.5 Hz, 1 H); mass spectrum *m/e* (intensity) 150 (62), 122 (50), 121 (65), 119 (42), 117 (42), 107 (40), 94 (45), 93 (100), 91 (40), 80 (39), 79 (78), 77 (42), 67 (40), 41 (70), 39 (62).

Reduction of 2.95 g of **11b** in 15 mL of acetic acid afforded 1.18 g of **19** (83%), homogeneous by VPC.

Reduction of Dibromoisopinocamphone (12). Controlled-potential electrochemical reduction of 2.95 g of **12** in 50 mL of 9:1 (v/v) DMF/acetic acid containing 0.2 M sodium acetate consumed 2.8 Faradays/mol of **12**. Workup in the usual manner[3-5] afforded 1.90 g of a mixture shown by VPC analysis (column B, 230 °C, helium flow rate 50 mL/min) to be a mixture of isopinocamphone (**22**, 23%), 2-methyl-5-isopropylphenol (carvacrol, **23**, 18%) (identified by comparison of VPC retention time and NMR and mass spectra with a commercial sample, 2-methyl-3-isopropylphenol (**34**, 12%) (for spectral properties, vide infra), and an inseparable mixture of acetoxy ketones **20** and **21** (47%). The NMR spectrum of this mixture exhibited a broad doublet at δ 5.3 due to the methyne proton of **20**; integration of this proton relative to the upfield resonances indicated the ratio of **20** to **21** to be ca. 5:1.

Reduction of 2.95 g of **12** by ultrasonically dispersed mercury in acetic acid afforded 1.78 g of a mixture of the same products: isopinocamphone (16%), 2-methyl-5-isopropylphenol (28%), 2-methyl-3-isopropylphenol (14%), and a mixture of the acetoxy ketones **20** and **21** (33%) (shown to be a 4.5:1 mixture of **20** and **21**).

Reduction of 2.95 g of **12** by mercury in 25 mL of DMF containing 3.27 g (2 equiv) of *p*-toluenesulfonic acid afforded 1.74 g of a mixture shown by VPC (column B, 230 °C) to be a mixture of phenol **23** (30%), isopinocamphone (10%), and pinocarvone (**25**, 60%). The 2,4-dinitrophenylhydrazone of **25** melted at 165–166 °C. The NMR spectrum of this substance was found to be identical with that of the corresponding derivative of authentic pinocarvone, which was prepared by oxidation of pinocarveol.[28] An analytical sample was prepared by chromatography over alumina (elution with chloroform) and four recrystallizations from ethanol. Anal. Calcd for $C_{16}H_{18}N_4O_4$: C, 58.17; H, 5.49; N, 16.96. Found: C, 58.47; H, 5.38; N, 17.22.

2-Methyl-3-isopropylphenol (24). To a suspension of 29.7 g of magnesium in 50 mL of dry ether was added 10 drops of isopropyl bromide. When reaction began, a solution of 136.8 g of isopropyl bromide in 100 mL of ether was added dropwise over 1 h, and stirring was then continued for 2 h. The Grignard solution was then placed in a dropping funnel and added dropwise to a suspension of 30.7 g of copper(I) iodide in 75 mL of ether containing 28.9 g of 2-methylcyclohexenone maintained at −46 °C. After addition stirring was continued for 1 h at −46 °C and 2 h at 25 °C. Saturated aqueous ammonium chloride (50 mL) was then added cautiously, and the ether layer was separated, washed with water, and dried over magnesium sulfate. Solvent removal at the rotary evaporator afforded ca. 20 g of colorless oil. Distillation of this material in vacuo was unsuccessful because of foaming, so it was filtered through a silica gel column (elution with chloroform). Evaporation of solvent and VPC analysis (Carbowax) showed the presence of four constituents in ca. 1:1:1:8 ratio. The largest (and slowest moving) peak was isolated by preparative VPC. Its NMR and mass spectrum (NMR δ 0.8–2.3, complex; *m/e* 154) demonstrated it to be 2-methyl-3-isopropylcyclohexanone. A 2,4-dinitrophenylhydrazone, mp 146–149 °C, was prepared and purified by chromatography over alumina (elution with chloroform) and four recrystallizations from ethanol. Anal. Calcd for $C_{16}H_{22}N_4O_4$: C, 57.47; H, 6.63. Found: C, 57.79; H, 6.77.

To a solution of 10 g of 2-methyl-3-isopropylcyclohexanone in 50 mL of carbon tetrachloride at 0 °C was added 21 g of bromine, dropwise over 1 h. After stirring for an additional 7.5 h, the mixture was poured into 50 mL of distilled water. The organic layer was separated, washed with 125 mL each of aqueous sodium bisulfite, aqueous sodium bicarbonate, and water, and dried over magnesium sulfate. Removal of solvent at the rotary evaporator afforded 10 g of crude product, which was added to a suspension of 22 g of lithium chloride in 50 mL of DMF and heated at 100 °C under nitrogen for 40 min. After standing overnight, 50 mL of ether was added, and the mixture was washed with distilled water. The ether layer was then extracted with 0.1 M aqueous sodium hydroxide, and the aqueous extracts were then acidified (concentrated HCl) and extracted with ether. The ether extracts were dried over magnesium sulfate, and the ether was removed at the rotary evaporator to afford 1.0 g (10%) of 2-methyl-3-isopropylphenol (**24**), whose VPC retention time and NMR and mass spectra were identical with those of **24** isolated from the reduction of **12**.

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Study of the Highly Strained Bicyclo[1.1.1]pentyl Cations under Stable Ion Conditions[1]

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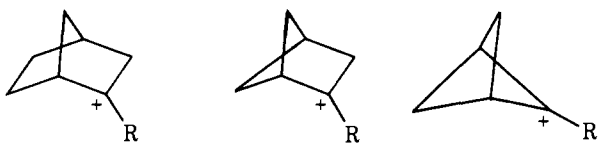
Abstract: 2-Chlorobicyclo[1.1.1]pentane in SbF_5/SO_2ClF solution, even at −140 °C, upon ionization, immediately rearranges to the 3-cyclopentenyl cation. The parent 2-bicyclo[1.1.1]pentyl cation, thus, could not be directly observed. In contrast, 2-phenyl-2-bicyclo[1.1.1]pentanol, under similar conditions, gives the stable 2-phenyl-2-bicyclo[1.1.1]pentyl cation, which is observed together with the 3-phenyl-3-cyclopentenyl cation, formed in the rearrangement reaction. The structures of these ions were studied by ^1H and ^{13}C NMR spectroscopy.

Introduction

2-Bicyclo[2.2.1]heptyl and 2-bicyclo[2.1.1]hexyl cations **1** and **2** are well studied and characterized.[2,3] The degree of

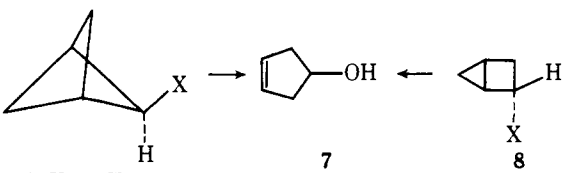


1 **2** **3**

charge delocalization into the neighboring C–C bonds in these ions depends on the nature of the substituent (R) and geometric arrangements. The considerably more strained 2-bicyclo[1.1.1]pentyl cations, **3**, have not yet been directly observed in solution. Interested in the effect of strain on carbocations, we report now the study of 2-bicyclo[1.1.1]pentyl cations in superacidic solutions.

Results and Discussion

Wiberg and Williams[4] first prepared 2-chlorobicyclo[1.1.1]pentane (**4**) and 2-bicyclo[1.1.1]pentanol (**5**). Subsequently, the solvolysis of the dinitrobenzoate (ODNB)

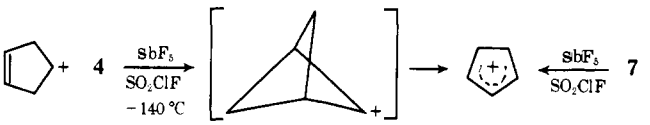


7 **8**

4, X = Cl
5, X = OH
6, X = OPNB

6 in 60% aqueous acetone was studied.[5] The sole product **7**[6] derived from **6** had also been observed starting with 2-bicyclo[2.1.0]pentyl derivatives.[5]

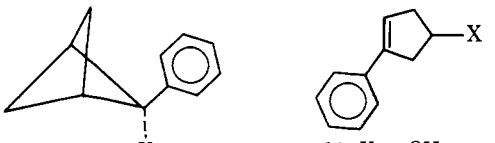
When chloride **4** was ionized in SbF_5/SO_2ClF solution at −140 °C (cooled with liquid N_2–pentane slush), the ^1H and ^{13}C NMR spectrum of the solution, thus obtained, showed the exclusive presence of only the allylic 3-cyclopentyl cation **10**.[7] Ion **10** has been previously prepared by ionization of **7**. There was no observation of any of the secondary 2-bicyclo[1.1.1]-pentyl cation **9**. The results obtained from both the solvolysis



11 **9** **10**

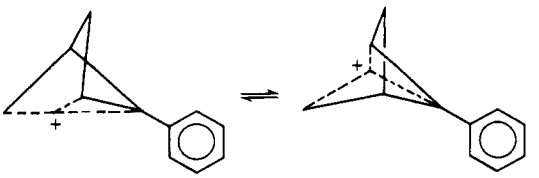
and stable ion studies agree with each other, indicating the extreme instability of the very strained 2-bicyclo[1.1.1]pentyl cation. The expected rearrangement of the ion **9** to **10** apparently involves the 4-cyclopentenyl ion **11** as the transient species, as the latter was quenched under solvolytic conditions.

Padwa has extended the study of the bicyclo[1.1.1]pentyl system to the preparation of 2-phenyl-2-bicyclo[1.1.1]pentanol (**12**)[8,9] and the solvolysis of its *p*-nitrobenzoate derivative **13**.[10] The alcohol **12** was found to be extremely labile to acidic



12, X = OH
13, X = OPNB

14, X = OH
15, X = OPNB



16

conditions and rearranged readily to 3-phenyl-3-cyclopenten-1-ol (**14**) through an assumed bicyclo[2.1.0]pentyl cation intermediate. Kinetic evidence obtained from the solvolysis of the *p*-nitrobenzoate ester **13** suggested that the ionization proceeded with participation of the one-carbon bridge adjacent to the departing *p*-nitrobenzoate group (**16**). These results lead

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