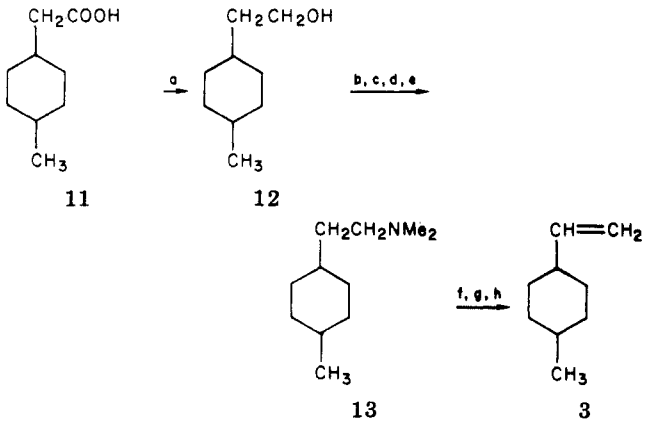
Scheme III[a]



[a] a, $LiAlH_4$/ether; b, TsCl/Py; c, NaN_3/Me_2SO–water; d, $LiAlH_4$–ether; e, HCHO–HCOOH; f, MeI/MeOH; g, Ag_2O; h, pyrolysis.

ring), 2.26–2.60 (m, 1 H, benzylic), 7.1–7.4 (m, 5 H, Ph).

***cis*-4-Methyl-1-vinylcyclohexane (3)** was prepared according to Scheme III. *cis*-4-Methylcyclohexylacetic acid (11) was prepared according to the procedure of Stork:[25] ^{1}H NMR ($CDCl_3$) δ 0.82–0.96 (d, J = 6 Hz, 3 H, Me), 1.04–1.8 (m, 9 H, ring), 1.8–2.2 (m, 1 H, β-CH), 2.2–2.38 (d, J = 5 Hz, 2 H, α-CH_2), 10.85–11.04 (s, 1 H, CO_2H); C-13 spectrum, see Table V.

Reduction of 9.36 g (0.06 mol) of 11 with 1.71 g of $LiAlH_4$ (0.045 mol) in 100 mL of absolute ether gave, after workup and distillation, 7 g (82%) of 2-(*cis*-4-methylcyclohexyl)ethanol, **12**: bp 95–100 °C (15 mm); ^{1}H NMR ($CDCl_3$) δ 0.82–0.94 (d, J = 6 Hz, 3 H, Me), 1.02–1.8 (m, 12 H, ring and β-CH_2), 3.4–3.66 (m, 2 H, CH_2O), 4.02 (s, 1 H, OH); C-13 spectrum; see Table V.

The alcohol **12** yielded an oily tosylate on treatment with *p*-toluenesulfonyl chloride–pyridine followed by workup.

***N,N*-Dimethyl-2-(*cis*-4-methylcyclohexyl)ethylamine[26-28] (13).** To a solution of 16.25 g of sodium azide (0.25 mol) in 100 mL of Me_2SO and 20 mL of water kept at 70 °C was added 13.3 g (0.045 mol) of the tosylate of **12** in 60 mL of Me_2SO followed by stirring at 70 °C overnight. The mixture was cooled and diluted with water and the product was extracted with ether. The ethereal solution was dried over anhydrous $MgSO_4$ and reduced without further purification by using 19 g (0.5 mol) of $LiAlH_4$ in 200 mL of absolute ether to give 2.75 g (42%) of 2-(*cis*-4-methylcyclohexyl)ethylamine. The amine was dimethylated by using 88% formic acid (10 g) and 37% formaldehyde (10 mL) and heating in an oil bath at 110°C for about 4 h followed by the usual workup to give 2.72 g (84%) of the tertiary amine **13**: bp 115–120 °C (25 mm); ^{1}H NMR ($CDCl_3$) δ 0.84–0.96 (d, J = 6 Hz, 3 H, Me), 1.2–1.8 (m, 12 H, ring and β-CH_2), 2.24 (s, 6 H, NMe_2); C-13 spectrum, see Table V.

Compound **13** (2.7 g, 0.016 mol) was quaternized[29] by using excess (15 g) methyl iodide in 40 mL of methanol and refluxing the solution for about 3 h. The resulting solution was concentrated and 200 mL of anhydrous ether was added to precipitate the solid methiodide (5 g; quantitative yield), mp 218–220 °C.

A solution of the methiodide (5 g) in 60 mL of distilled water and 10 mL of methanol was stirred with 0.033 mol of freshly prepared silver oxide for 2 h. The resulting quaternary ammonium hydroxide was filtered and concentrated below 40 °C to a yellow oil. This was heated under vacuum (50 mm) at 120 °C in an oil bath. *cis*-4-Methyl-1-vinylcyclohexane was distilled and collected in a dry ice–acetone trap. To the distillate was added 10 mL of 4 N hydrochloric acid and the olefin was extracted with pentane. After the solution was dried over anhydrous K_2CO_3, pentane was evaporated, and Kugelrohr distillation [140–145 °C (760 mm)] gave 1 g (50%) of **3**. Traces of pentane were removed by passing the olefin through a preparative GLC column (12 ft × 0.375 in. 30% SE-30 on 80/100 Chromosorb A) at 140 °C: ^{1}H NMR (CD_2Cl_2) δ 0.88–0.94 (d, J= 6.3 Hz, 3 H, Me), 1.21–1.41 (m, 2 H, ring), 1.42–1.68 (m, 7 H, ring), 2.13–2.26 (m, 1 H, allylic) (the olefinic region shows a well-resolved ABM part of an ABMX spectrum), 4.91–5.03 (AB part of ABMX system, 10 lines, J_t = 17.36, J_c = 10.5, J_{gem} = 2, $J_{allylic}$ = 1.65 Hz, 2 H, =CH_2), 5.81–5.95 (M part of ABMX spectrum, 8 lines, J_t = 17.36, J_c = 10.5, J_{vic} = 6.4 Hz, 1 H, —CH=).

Anal. Calcd for C_9H_{16}: C, 87.01; H, 12.99. Found: C, 87.27; H, 12.82.

Acknowledgment. We are indebted to the National Science Foundation (Grant CHE78-08713) for financial support.

Registry No. 1, 828-45-5; 2, 76833-24-4; 3, 34780-47-7; 4, 695-12-5; 5, 827-52-1; 6, 63007-33-0; *cis*-11, 7132-95-8; *trans*-11, 7132-93-6; *cis*-12, 76833-25-5; *cis*-12 tosylate, 76833-26-6; *trans*-12, 76833-27-7; 13, 76833-28-8; 13 methiodide, 76833-29-9; 13 quaternary ammonium hydroxide, 76833-30-2; 4-methyl-4-phenylcyclohexanone, 18932-33-7; *cis*-4-methyl-1-phenylcyclohexanol, 30689-83-9; *trans*-4-methyl-1-phenylcyclohexanol, 30689-84-0; 4-methyl-1-phenylcyclohexene, 16776-31-1; 2-(*cis*-4-methylcyclohexyl)ethylamine, 76833-31-3; $C_6H_{11}CH_2COOH$, 5292-21-7; $C_6H_{11}CH_2CH_2OH$, 4442-79-9; $C_6H_{11}CH_2CH_2NMe_2$, 2358-91-0.

Regioselective Synthesis of α-Alkoxy Ketones from α,α'-Dibromo Ketones

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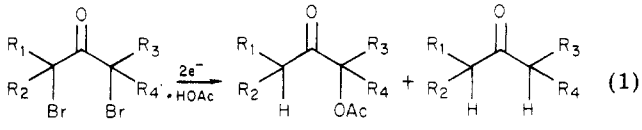
Received December 31, 1980

A series of reports from this laboratory has described our studies of the reduction of α,α'-dibromo ketones (**1**), either electrochemically or by ultrasonically dispersed mercury.[1-7] Usually, though not always, these experiments have been carried out in the presence of acetic acid, and in such cases the reaction affords primarily the corresponding α-acetoxy ketones (**2**) and/or the parent ketones (**3**) (eq 1).



1 2 3 (1)

We have adduced considerable evidence[1,3,4,7] that these products are formed via the mechanism shown in Scheme I, in which the key intermediate, enol allylic bromide **4**, is the precursor of both **2** and **3**. For present purposes, we note that in principle any nucleophile might replace acetic acid in this reaction, inasmuch as nucleophilic attack takes place at the end of the mechanistic sequence, resulting in generation of the critical precursor **6**. We have found in a few previous experiments that methanol[2] and some ketones[5] may indeed replace acetic acid in this re-

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Scheme I

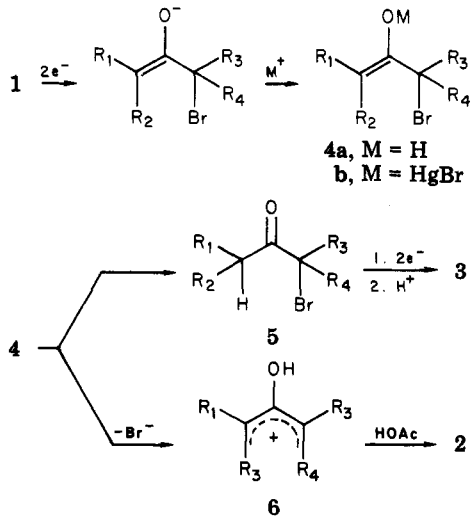
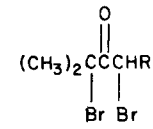


Table I. Reduction of Dibromo Ketones by Ultrasonically Dispersed Mercury in the Presence of Alcohols

run no.	dibromo ketone	solvent[a]	% yield[b] 9 + 10	9:10[c]	3
1	7a	MeOH	73	99:1	44
2	7a	EtOH	77	96:4	4
3	7a	*i*-PrOH	73	95:5	5
4	7b	MeOH	44	90:10	tr
5	7b	EtOH	56	89:11	tr
6	7b	*i*-PrOH	92	84:16	1
7	7b	*t*-BuOH	40	3:97	4
8	7c	MeOH	76	100:0	4[d]
9	7c	*i*-PrOH	54	94:6	2
10	7d	MeOH	82	95:5	tr
11	7d	*i*-PrOH	78	93:7	2[d]
12	7a	MeOH/DMF	16	100:0	17
13	7b	MeOH/DMF	26	87:13	tr
14	7b	*i*-PrOH/DMF	74	81:19	3
15	7c	MeOH/DMF	81	100:0	3[d]
16	7c	*i*-PrOH/DMF	75	92:8	1[d]
17	7d	MeOH/DMF	78	96:4	1
18	7d	*i*-PrOH/DMF	59	92:8	1[e]

[a] ROH/DMF = 1:9 (v/v) ratio of ROH to DMF. [b] Yields were obtained by VPC analysis (area integration). [c] The ratio of **9** to **10** was determined by NMR and, where the isomers were separable, VPC analysis. [d] 1–3% α,β-unsaturated ketone(s) produced. [e] Same as *d*, 8%.

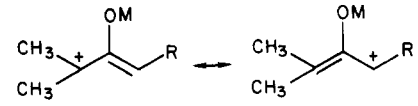
action. We had felt originally[1] that this "reductive substitution" process would necessarily be limited for synthetic purposes to symmetrical ketones, inasmuch as nucleophilic attack can occur at either terminus of allyl cation **6**, affording regioisomers with unsymmetrical ketones. We discovered subsequently, however, that introduction of α-acetoxy (and other carboxy) groups can be largely and often even cleanly regiospecific, depending upon both experimental conditions and the structures of the substrates.[6] The aims of the present study were twofold: (a) to explore the reduction of α,α'-dibromo ketones in the presence of alcohols as a synthetic route to α-alkoxy ketones, and (b) to examine the regioselectivity of the process with unsymmetrical ketones. The series of dibromo ketones **7a–d** was examined, using methanol, ethanol, and 2-propanol and carrying out the reductions in several ways: (A) reduction by finely dispersed mercury in the neat alcohol as solvent; (B) same as method A but in a dimethylformamide (DMF) solution of the alcohol; (C) electrochemical reduction in DMF, using the same solvent system as in method B. The results of a series of



7a, R = H
b, R = Me
c, R = Et
d, R = *i*-Pr

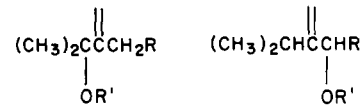
such experiments, somewhat condensed from a longer list, are presented in Table I.

A number of conclusions may be drawn from the data. (a) Reduction method A (finely dispersed mercury, neat alcohol) emerges as the method of choice for carrying out the reductions. The yields in mixed DMF–alcohol solvents are sometimes lower because the alkoxy ketones are slightly soluble in water and are partly lost during the several water washes required to remove DMF.[6] This problem is especially marked with the lower molecular weight products; see runs 12, 13, 15, and 17 for the effects on yield of successively increasing the size of either the alkoxy group or the ketone carbon skeleton. (b) The regioselectivity of attack by alcohol upon intermediate **8** is



8

relatively independent of experimental conditions and the structure of substrates. Almost all of the reactions involve a heavy preponderance of the tertiary ether **9** over its less substituted isomer **10**. This effect, which is undoubtedly



9 **10**

electronic (there is a higher charge density at the tertiary site in cation **8**), is opposed, however, by a smaller steric component, favoring substitution at the less hindered site as the size of the entering alcohol increases; see runs 4–7. It did not prove possible to capitalize upon the interesting reversal of regioselectivity embodied in run 7, inasmuch as **7c** and **7d** afforded little or no α-*tert*-butoxy ketone under the same conditions, presumably again for steric reasons. A few reactions, notably a few electrochemical reductions, afforded α,β-unsaturated ketones (loss of a β-proton from **6**) in addition to **3**, **9**, and **10**). We have insufficient data to draw any inferences about this, e.g., whether it is a special problem with method C.[8]

Conclusion. It is possible to effect regioselective conversion of an unsymmetrical dibromo ketone to the more highly substituted isomer **9** in good yields by finely dispersed mercury. We should point out again[5] the ease with which these reactions are carried out: the dibromo ketone, dissolved in the appropriate solvent, is simply placed in a laboratory ultrasonic cleaner with a small amount of mercury and monitored by TLC until reaction is complete.

Experimental Section

The synthesis of dibromo ketones **a–d** and reduction methods A–C (see text) have both been described previously.[6] Reaction mixtures were analyzed both by VPC and NMR spectroscopy at

(8) At the Editor's suggestion, we have not included data on the electrochemical reductions of **7a–b**. They exhibit similar trends to the mercury reductions, but the yields are somewhat lower.

60 and 200 MHz. As previously, when isomers **9** and **10** were inseparable by VPC, the ratio of **9** to **10** was determined by preparative VPC collection and integration of appropriate segments in the NMR spectrum of the mixture.[9]

Acknowledgment. Financial support was provided by the National Science Foundation, which also, with the Dreyfus Foundation and Wesleyan University, partly funded the Varian XL-200 NMR spectrometer used in this work.

(9) Satisfactory microanalytical data for alkoxy ketones **9** (from runs 3, 5, 6, 8, and 9) and **10** (from run 7) of Table I were provided.

Registry No. **3** ($R_1 = R_2 = Me$; $R_3 = R_4 = H$), 563-80-4; **3** ($R_1 = R_2 = R_3 = Me$; $R_4 = H$), 565-69-5; **3** ($R_1 = R_2 = Me$; $R_3 = Et$; $R_4 = H$), 7379-12-6; **3** ($R_1 = R_2 = Me$; $R_3 = i$-Pr; $R_4 = H$), 1888-57-9; **7a**, 1518-06-5; **7b**, 37010-00-7; **7c**, 69204-79-1; **7d**, 56829-66-4; **9** (R = H; R′ = Me), 36687-98-6; **9** (R = H; R′ = Et), 36687-99-7; **9** (R = H; R′ = *i*-Pr), 76916-70-6; **9** (R = R′ = Me), 10097-21-9; **9** (R = Me; R′ = Et), 76916-71-7; **9** (R = Me; R′ = *i*-Pr), 76916-72-8; **9** (R = Me; R′ = *t*-Bu), 76916-73-9; **9** (R = Et; R′ = Me), 76916-74-0; **9** (R = Et; R′ = *i*-Pr), 76916-75-1; **9** (R = *i*-Pr; R′ = Me), 76916-76-2; **9** (R = R′ = *i*-Pr), 76916-77-3; **10** (R = H; R′ = Me), 65857-35-4; **10** (R = H; R′ = Et), 76916-78-4; **10** (R = H; R′ = *i*-Pr), 76916-79-5; **10** (R = R′ = Me), 66508-06-3; **10** (R = Me; R′ = Et), 76916-80-8; **10** (R = Me; R′ = *i*-Pr), 76916-81-9; **10** (R = Me; R′ = *t*-Bu), 76916-82-0; **10** (R = Et; R′ = *i*-Pr), 76916-83-1; **10** (R = *i*-Pr; R′ = Me), 76916-84-2; **10** (R = R′ = *i*-Pr), 76916-85-3.

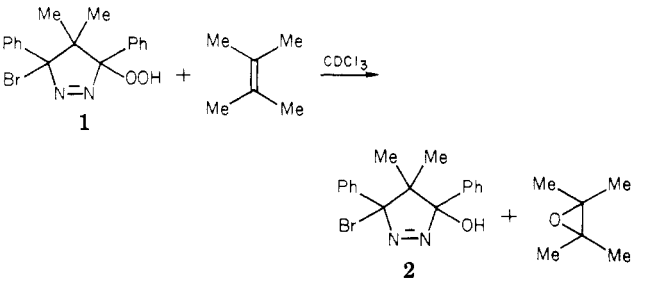
Communications

Epoxidation of 2,3-Dimethyl-2-butene by 3-Bromo-4,5-dihydro-5-hydroperoxy-4,4-dimethyl-3,5-diphenyl-3*H*-pyrazole

Summary: The uncatalyzed reaction of 2,3-dimethyl-2-butene and 3-bromo-4,5-dihydro-5-hydroperoxy-4,4-dimethyl-3,5-diphenyl-3*H*-pyrazole produced tetramethylethylene oxide and 3-bromo-4,5-dihydro-5-hydroxy-4,4-dimethyl-3,5-diphenyl-3*H*-pyrazole in moderate yield.

Sir: The epoxidation of alkenes by hydroperoxides generally[1,2] requires the presence of a catalyst. For example, alkyl hydroperoxides, in the presence of Mo or V catalyst[1-3] or in contact with basic alumina,[4] will epoxidize alkenes. Recent reports indicate that certain olefins undergo direct epoxidation with such unusual hydroperoxides as triphenylsilyl hydroperoxide[4] and 2-hydroperoxyhexafluoro-2-propanol.[5] α-Substituted hydroperoxides,[6] furan endoperoxides,[7] and an intermediate in the metal ion catalyzed oxygenation of azibenzil[8] have also been reported to convert alkenes to oxiranes. The recent synthesis[9] of 3-bromo-4,5-dihydro-5-hydroperoxy-4,4-dimethyl-3,5-diphenyl-3*H*-pyrazole (**1**) prompted us to investigate oxygen atom transfer reactions of this unstable[9] peroxide. We report the uncatalyzed reaction of 2,3-dimethyl-2-butene and **1** to produce tetramethylethylene oxide and 3-bromo-4,5-dihydro-5-hydroxy-4,4-dimethyl-3,5-diphenyl-3*H*-pyrazole (**2**).

2,3-Dimethyl-2-butene (3.4 mg, 0.040 mmol) was added (via syringe) to a cold solution of **1** (14.7 mg, 0.041 mmol) in 0.6 mL of $CDCl_3$ (Merck, no Me_4Si) in a 5-mm NMR tube. Reaction progress was determined by ^1H NMR spectroscopy. After complete disappearance of **1** ($t_{1/2} \simeq$ 45 min), monitored by the disappearance of the upfield methyl signal of **1** [δ −0.10 (s)], 54 ± 6% (average of two experiments) of 2,3-dimethyl-2-butene had been converted to tetramethylethylene oxide [δ 1.3 (s)]. Fifty percent of **1** had undergone reaction to produce **2** as evidenced by a new upfield signal at δ −0.05, while the remainder of **1** underwent decomposition via the reported thermal route.[9] Doubling the amounts of both reactants increased the yield of epoxidation to 67% (70% formation of **2**) with a half-reaction time of ca. 10–20 min. Tetramethylethylene oxide was collected by preparative VPC and shown to be identical with an authentic sample by comparison of spectral data as well as its acid-catalyzed conversion to pinacolone.



1 **2**

The pyrazoline, **2**, was isolated and characterized as follows. **1** (150 mg, 0.42 mmol) was added to 0.5 mL of 2,3-dimethyl-2-butene in 1.5 mL of cold $CDCl_3$. The mixture was agitated for several minutes to dissolve **1** and allowed to sit for 5 min. The solution was transfered to a clean, dry flask and the volatile components were removed under reduced pressure. The residue, recrystallized from $CDCl_3$/pentane, gave 55 mg (38% isolated yield) of pale yellow crystals of **2**: mp 93–94 °C dec; ^1H NMR ($CDCl_3$) δ −0.05 (s, 3 H), 1.7 (s, 3 H), 3.6 (s, 1 H), 7.3–7.8 (m, 10 H); IR (KBr) 3260 (br, OH), 3020, 2930 (w), 1520 (N=N, m), 1480 (m), 2382 (m), 1365 (m), 1220 (m), 1095 (m), 1070 (m), 1010 (m) cm^{-1}; peroxide test negative. Anal. Calcd: C, 59.14; H, 4.96; N, 8.11; Br, 23.15. Found: C, 59.27; H, 5.06; N, 8.11; Br, 23.02. Pure **2**, although considerably more thermally stable in $CDCl_3$ than **1**, underwent decomposition in 1 h at 22 °C with gas evolution. Products of this decomposition have not yet been characterized. **2** was stored at −20 °C as a solid with no decomposition noted after several weeks.

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