Nucleophilic Step of Ring-Opening Reactions of Cyclopropanes with Electrophiles. Electronic Substituent Effects on Stereoselectivity of Reactions of Some 1-Arylbicyclo[4.1.0]heptanes with Mercuric Salts

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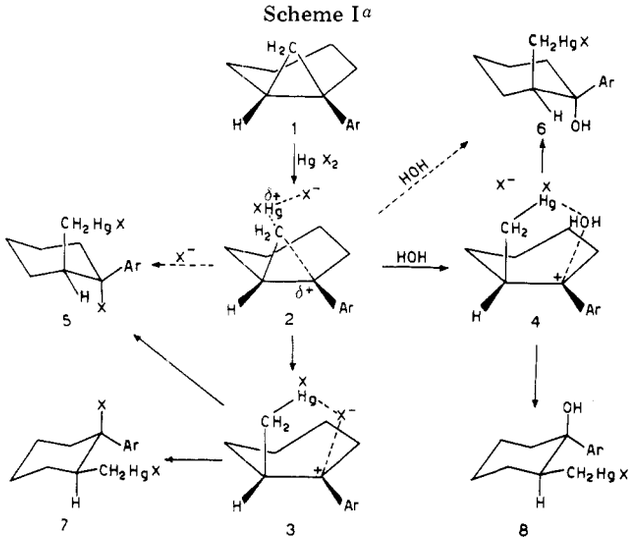
The stereochemistry of the nucleophilic step of the ring-opening reactions of 1-(*p*-tolyl)- (**1b**) and 1-(*m*-chlorophenyl)bicyclo[4.1.0]heptane (**1c**) with mercuric salts has been investigated and compared with that of the corresponding phenylcyclopropane (**1a**) in order to verify how a substituent on the phenyl of **1a**, modifying the conjugative ability of the aromatic system, could influence the stereochemical results. The mercuration reactions of **1b** and **1c** have a behavior parallel to that of **1a**: the stereoselectivity changes markedly with the salt and with the reaction conditions; however, all the percentages of syn products arising from the reactions of **1c** and most of those obtained in the ring opening of **1b** are slightly lower than the corresponding values obtained for the unsubstituted cyclopropane **1a**. Possible explanations of the observed stereochemical results have been given on the basis of a mechanism, modified from that previously suggested for **1a**, implying intermediate structures with a high degree of carbocationic character.

The ring opening of cyclopropanes by electrophiles occurs in the direction of the more stable carbocation with either retention or inversion of configuration at the site of the electrophilic attack, depending on the nature and configuration of the ring substituents, whereas the stereochemistry of the nucleophilic step takes place with complete or strongly predominant inversion of configuration.[1-4]

Recently it has been shown[5] that the ring opening of phenylcyclopropane **1a** with mercuric salts occurs, according to expectation,[1,2,4,6] by attack of the electrophile on the least-substituted carbon, in the direction of the benzylic carbon. However, the stereochemistry of the nucleophilic step was highly variable, ranging from almost complete inversion to markedly predominant retention of configuration depending on the type of mercuric salt and on the solvent.[5] The results obtained,[5] in agreement with kinetic results of the mercuration of arylcyclopropanes,[6] pointed to transition states or intermediates with a high degree of positive charge on the benzylic carbon. In order to justify the results a mechanism was suggested (see Scheme I)[5] analogous to the one previously postulated to rationalize the similar stereochemical behavior of the acid-catalyzed ring opening of 1-aryloxiranes.[7] Attack of the mercury (as HgX_2)[6] on the least-hindered carbon[1,2,4] of **1a** leads to a corner-mercurated intermediate which can evolve through an incipient carbenium ion (like **2**) to selectively interacting ion–nucleophile pairs (**3** for reaction in nonnucleophilic solvents and **4** for reactions in nucleophilic solvents). According to the mechanistic scheme proposed,[5] the anti adducts **5** or **6** should have arisen by attack of the nucleophile (X^- or SOH) at the stage of the incipient carbenium ion **2**, whereas collapse of the ion–nucleophile pairs should have afforded the syn compounds **7** or **8**. Evidently in such a mechanism every factor affecting the relative stability of structures **2**, **3**, or **4** and their reactivity should also modify the syn/anti ratio; factors favoring the development of the positive charge on the benzylic carbon should increase this ratio.

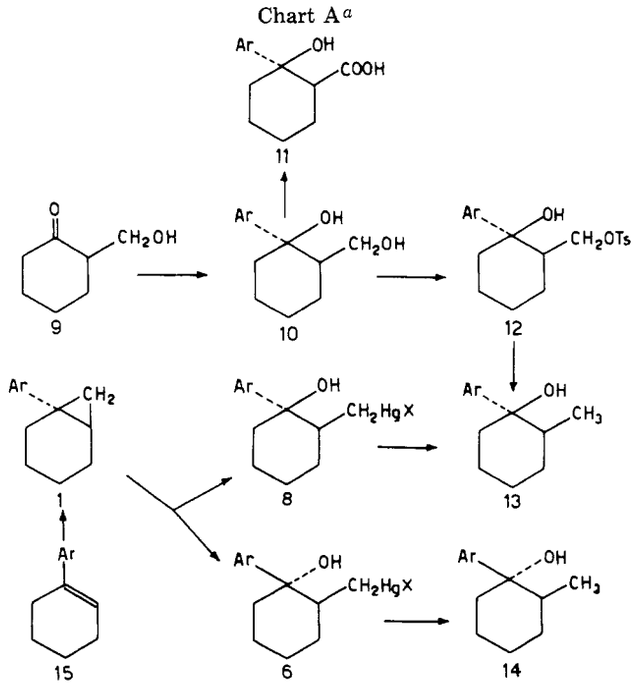
It was therefore of interest to study how a substituent on

Scheme I[a]



[a] a, Ar = C_6H_5; b, Ar = *p*-$CH_3C_6H_4$; c, Ar = *m*-ClC_6H_4.

Chart A[a]



[a] b, Ar = *p*-$CH_3C_6H_4$; c, Ar = *m*-ClC_6H_4; X = CH_3COO, CF_3COO, NO_3, ClO_4.

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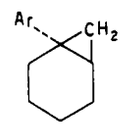
Table I. Stereochemistry of the Nucleophilic Step of the Mercuration of Cyclopropane 1

Cyclopropane	Registry no.	Mercuric salt	Registry no.	Solvent	Cis (13)/trans (14) ratio
1a	2415-82-9	$Hg(OOCCH_3)_2$	1600-27-7	H_2O	13.5:86.5[a]
b	64705-88-0				11.2:88.8
c	64705-89-1				9.2:90.8
a		$Hg(OOCCF_3)_2$	13257-51-7	H_2O	19.5:80.5[a]
b					22.5:77.5
c					15.3:84.7
a		$Hg(NO_3)_2$	10045-94-0	H_2O	22.5:77.5[a]
b					21.4:78.6
c					16.3:83.7
a		$Hg(ClO_4)_2$	7616-83-3	H_2O	23.0:77.0[a]
b					22.3:77.7
c					18.8:81.2
a		$Hg(OOCCH_3)_2$		THF–H_2O (1:1)	25.5:74.5[a]
b					18.1:81.9
c					23.4:76.6
a		$Hg(OOCCF_3)_2$		THF–H_2O (1:1)	28.5:71.5[a]
b					22.9:77.1
c					28.3:71.7
a		$Hg(OOCCH_3)_2$		CH_2Cl_2	58.0:42.0[a]
b					59.1:40.9
c					52.3:47.7
a		$Hg(OOCCF_3)_2$		CH_2Cl_2	75.0:25.0[a]
b					67.3:32.7
c					74.0:26.0

[a] Reference 5.

the phenyl of **1a,** modifying the conjugative ability of the aromatic system, could influence the stereochemistry of the nucleophilic step of the cyclopropane ring opening with mercuric salts. The present investigation deals with the synthesis and the study of the mercuration reactions of cyclopropanes **1b** and **1c.** The *p*-methyl in **1b,** because of its electron-donating properties, should stabilize a benzylic electron-deficient center,[7c,8] whereas the overall electron-withdrawing effect of the *m*-chloro group in **1c** should have an opposite result.[7c,9]

Cyclopropanes **1b** and **1c** have been obtained by the Simmons–Smith reaction of the corresponding olefins **15b** and **15c** and have been purified by treatment with ozone followed by chromatography. Analogously to the unsubstituted cyclopropane **1a,**[5] the hydroxymercuration of **1b** and **1c** with mercuric acetate and mercuric trifluoroacetate in water yielded mixtures of the two corresponding organomercurials *cis*-**8** and *trans*-**6,** in which the latter predominated (see below) and was obtained in a pure state by crystallization. Reductive demercuriation of the trans organomercurials **6b** and **6c** (X = $OOCCH_3$ and $OOCCF_3$) gave the corresponding practically pure trans alcohols **14b** and **14c.** The diastereoisomeric cis alcohols **13b** and **13c** have been prepared in a pure form through unequivocal stereospecific syntheses. The reaction of 2-hydroxymethylcyclohexanone (**9**) with an excess of the suitable arylmagnesium bromide afforded mixtures consisting mainly of the cis diols **10b** and **10c**[10] accompanied by small amounts of their corresponding trans isomers, from which the former were obtained by crystallization. The diols **10b** and **10c** were transformed into their corresponding primary monotosylates **12b** and **12c,** which on reduction with $LiAlH_4$ afforded the alcohols **13b** and **13c** having the same relative configuration as the starting diols **12b** and **12c.** Pure alcohol **13b** has been also obtained by the reaction of 2-methylcyclohexanone with *p*-tolylmagnesium bromide, followed by column chromatography; in this reaction the trans isomer **14b** is practically absent (<2%). The configuration of the *p*-methyl-substituted cis diol **10b** has been proven, as has also that of the *m*-chloro analogue **10c,**[10] by its IR spectrum in the 3-μm range in a dilute solution of CCl_4, which showed



1

a, Ar = C_6H_5
b, Ar = p-CH_3 C_6H_4
c, Ar = m-Cl C_6H_4

Figure 1. Structure of cyclopropanes (1).

a strong band at 3507 cm^{-1}, indicative of a strong intramolecular OH···O bond[10,11] possible in both chair conformers of **10b.** Further confirmation of the configuration of **10b** has been given by the ^1H NMR spectrum of the acid **11b** obtained by Jones oxidation of **10b.** Keeping in mind that the aryl group, due to its larger steric hindrance, should occupy an equatorial position in the preferred conformation of **11b,** the relatively high half-band width (18 Hz)[10,12] of the signal of the proton α to the carboxy group allows one to infer the relative configuration of **11b** and consequently of **10b.** The structures of alcohols **13** and **14** have been confirmed on the basis of their ^1H NMR spectra.

The hydroxymercuration reactions of **1b** and **1c** have been carried out in H_2O and H_2O–THF with several salts, and the crude mixtures of the hydroxymercurials **8b, 6b** and **8c, 6c** have been analyzed, as was previously done for the mercuration reactions of **1a,**[5] through reductive demercuriation of the crude reaction mixtures with $NaBH_4$,[13] followed by GLC of the corresponding alcohols **13** and **14** (see Table I). Mercuration of **1b** and **1c** with $Hg(OOCCH_3)_2$ and $Hg(OOCCF_3)_2$ in CH_2Cl_2 yielded mixtures of the corresponding acyloxyorganomercurials *cis*-**7** and *trans*-**5** (X = $OOCCH_3$ or $OOCCF_3$),[5] whose ratios were determined by their reduction with $LiAlH_4$ to the alcohols **13b, 14b** and **13c, 14c,** respectively, followed by GLC analysis. The results of the nucleophilic step of the mercuration reactions of cyclopropanes **1b** and **1c** are summarized in Table I. Furthermore, the corresponding data for the unsubstituted cyclopropane **1a** have also been reported in the same table for the sake of comparison.

A first inspection of the results obtained (see Table I) shows that, as for the stereochemistry of the nucleophilic step, the mercuration reactions of cyclopropanes **1b** and **1c** have a behavior parallel to that of the phenylcyclopropane **1a** previously studied.[5] It can be observed that the stereoselectivity of the nucleophilic step of the mercuration of all the cyclopropanes **1a–c** changes markedly with the nature of the salt and with the reaction conditions. Higher percentages of syn adducts are formed when the reactions are carried out in the aprotic solvent (CH_2Cl_2), whereas the lower syn percentages are obtained in the reactions in H_2O when less ionic mercuric salt (mercuric acetate) is used. Furthermore, it may be pointed out that all the percentages of syn products arising from the reactions of *m*-chloro-substituted cyclopropane **1c** and most of those obtained in the ring opening of the *p*-methyl-substituted cyclopropane **1b** are slightly lower than the corresponding values obtained in the reactions of the unsubstituted cyclopropane **1a**,[5] even if the differences observed are relatively small.

In connection with the previously proposed mechanism[5] (see above), on the basis of the well-known electronic effects of the substituents (*p*-methyl and *m*-chloro)[9,10] and the known effect of such substituents on the stereochemistry of the acid-catalyzed ring opening of 1-aryloxiranes,[7c] it would be anticipated that in the case of cyclopropane **1c** the *m*-chloro substituent, which reduces the stability of the benzylic electron-deficient center, compared with the unsubstituted compound **1a**, should have favored (see Scheme I; no conformational implication is given to formulas) structures of type **2** more than those of type **3** or **4**, facilitating the formation of the anti adducts **5** and **6** in agreement with the experimental results. On the contrary, in the case of the cyclopropane **1b**, the *p*-methyl group should cause an opposite effect, thus favoring intermediates **3** and **4** and therefore the formation of the syn adducts **7** and **8** in contrast with the experimental results observed. Evidently the mechanism previously suggested in order to rationalize the results of the mercuration of **1a**[5] has to be modified. It must be pointed out, however, that the aryl group has to be important in determining the course of the mercuration of these compounds. As a matter of fact, apart from the clear directive effect of the aryl group in the regioselectivity of these reactions, the stereochemistry of the nucleophilic step of the mercuration of cyclopropanes carrying no aryl group on the ring is completely anti.[1,2,4] Furthermore, it must be kept in mind that the lack of complete anti stereoselectivity in the reactions under consideration clearly implies intermediate structures with high degrees of carbocationic character; the intervention of structures of this type in the mercuration of arylcyclopropanes was supported by a Hammett-type plot of the mercuration rates of arylcyclopropanes.[6] It could be that in the mercuration of cyclopropanes **1**, unlike the acid-catalyzed ring opening of oxiranes,[7] the attack of the nucleophile on the more carbocationic structures **3** and **4** is not completely syn stereoselective and therefore that the formation of both the syn as well as the anti products and consequently the different stereoselectivity of the reactions of each cyclopropane should be mainly due to differences in solvation of the intermediates and to differences in the stability of the selectively interacting ions **3** and **4**. For example, the increase of syn adduct in the mercuration of cyclopropanes **1** in aqueous solvent when the mercuric salt is changed from mercuric acetate to more highly ionic salts could be due to a strong interaction between mercury and the water molecule of **4**. Structures of type **2** in which the C–C bond is not completely broken should be no longer the solely responsible structures for determining the amount of anti adducts (**5** and **6**); perhaps in the present case structures of type **2** could rapidly evolve to the more carbocationic ones, **3** and **4**, before the attack of the nucleophile. However, the steps **2** → **5** or **2** → **6** cannot be completely ruled out. In conclusion, notwithstanding some analogies found between the stereoselectivity of the acid-catalyzed ring opening of aryloxiranes and the mercuration of arylcyclopropanes, the results obtained indicate sensible differences in the mechanisms responsible for the stereochemistry of these reactions.

Experimental Section

All melting points were taken on a Kofler micro hot stage and are uncorrected. Infrared spectra were measured with a Perkin-Elmer Infracord Model 137 on paraffin oil mulls, and the determination of OH stretching bands of **10b** was made with a Perkin-Elmer Model 257 double-beam grating spectrophotometer in dried (P_2O_5) CCl_4 using the indene band at 3110 cm^{-1} as a calibration standard; a quartz cell of 2-cm optical length was employed, and the concentration of the solution was lower then 5×10^{-3} M to prevent intermolecular association. The NMR spectra were determined in ca. 10% $CDCl_3$ solutions with a Jeol C 60 HL spectrometer using tetramethylsilane as an internal standard. All GLC analyses were performed on a Carlo Erba Fractovap GV apparatus with a flame ionization detector using a dual column system with glass columns (1.5 mm × 2.5 m) packed with 10% Carbowax 20M on 80–100 mesh silanized Chromosorb W: column, 160 °C; evaporator, 200 °C; detector, 200 °C; nitrogen flow, 30 mL/min. The order of increasing retention times was **13b, 14b, 13c,** and **14c**. The relative percentages of compounds **13** and **14** were obtained from two or more separate runs on each experiment. Preparative TLC was performed on 2-mm silica gel plates (Merck F_{254}) containing a fluorescent indicator; spots were detected under UV light (245 nm). All comparisons between compounds were made on the basis of IR and NMR spectra and GLC. $MgSO_4$ was always used as a drying agent. Evaporations were made in vacuo (rotating evaporator). Petroleum ether refers to the fraction boiling at 40–70 °C. CH_2Cl_2 was dried over P_2O_5.

1-(*p*-Tolyl)cyclohexene (15b),[14] 1-(*m*-chlorophenyl)cyclohexene (15c),[14] 2-hydroxymethylcyclohexanone (9),[15] and 1-(*m*-chlorophenyl)-*c*-2-tosyloxymethyl-*r*-1-cyclohexanol (12c)[10] were prepared as previously described.

1-(*p*-Tolyl)bicyclo[4.1.0]heptane (1b). A mixture of zinc dust (34.6 g, 0.53 g-atom) and cuprous chloride (5.24 g, 0.053 mol) in anhydrous ether (60 mL) was stirred rapidly and refluxed vigorously for 1 h.[16] After cooling, a few crystals of iodine and then 1-(*p*-tolyl)cyclohexene (**15b**, 20.0 g, 0.116 mol) were added to the zinc–copper couple. The well-stirred mixture was then treated dropwise with methylene iodide (94.8 g, 0.353 mol) to maintain spontaneous refluxing. When the addition was complete the mixture was stirred and refluxed for an additional 24 h. After cooling, the reaction mixture was treated with saturated aqueous NH_4Cl and the ether layer was separated. The aqueous mixture was extracted with ether, and then the organic extracts were washed with water, saturated aqueous $NaHCO_3$, and water, dried, and evaporated to yield crude **1b** (19.5 g), which was ozonized in $CHCl_3$ at 0 °C for 1 h in order to eliminate traces of olefinic products. The chloroformic solution was washed with 2 N Na_2CO_3 and water and evaporated to dryness, and the residue was chromatographed on a 3 × 70 cm column of Al_2O_3 (activity I) using petroleum ether as the eluent and collecting 50-mL fractions. The 5th and the 6th fractions yielded pure **1b** (GLC): 6.5 g; NMR δ 2.25 (s, 3, CH_3), 1.05–0.42 (m, 2, cyclopropane protons); the signal of the third cyclopropane proton is overlapped with the methylenic envelope. Anal. Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.73. Found: C, 90.16; H, 9.75.

1-(*m*-Chlorophenyl)bicyclo[4.1.0]heptane (1c). Reaction of 1-(*m*-chlorophenyl)cyclohexene (**15c**, 10.0 g, 0.052 mol) with a zinc–copper couple,[16] prepared from zinc dust (17.3 g, 0.26 g-atom) and cuprous chloride (2.61 g, 0.026 mol) in anhydrous ether (30 mL) with methylene iodide (47.4 g, 0.17 mol) as described above for the preparation of **1b**, yielded a crude mixture which was ozonized in $CHCl_3$ according to the procedure described for **1b**. Evaporation of the washed (saturated aqueous $NaHCO_3$ and water) $CHCl_3$ solution yielded crude **1c** (8.9 g), which was purified by chromatography on a 2 × 40 cm column of Al_2O_3 (activity I) using petroleum ether as the eluent and collecting 50-mL fractions. Fractions 2–10 yielded pure **1c** (GLC): 5.2 g; NMR δ 1.05–0.54 (m, 2, cyclopropane protons); the signal of the third cyclopropane proton is overlapped with the methylenic envelope. Anal. Calcd for $C_{13}H_{15}Cl$: C, 75.53; H, 7.31. Found: C, 75.45; H, 7.59.

1-(*p*-Tolyl)-*c*-2-hydroxymethyl-*r*-1-cyclohexanol (10b). A solution of **9** (10.0 g, 0.078 mol) in anhydrous ether (20 mL) was added dropwise to a Grignard reagent prepared from *p*-bromotoluene (29.7

g, 0.17 mol) and magnesium (4.15 g, 0.17 g-atom) in anhydrous ether (65 mL). When the addition was complete the reaction mixture was refluxed for 3 h and then hydrolyzed with crushed ice, saturated aqueous NH_4Cl, and then diluted aqueous HCl. The organic layer was separated, and the aqueous portion was extracted with ether. Evaporation of the washed (H_2O, 10% aqueous Na_2CO_3, and H_2O) and dried ether extracts yielded an oily product (11.0 g) from which pure **10b** (2.1 g) was obtained by crystallization from petroleum ether at −5 °C, mp 48–49 °C; IR (CCl_4) ν(OH) 3638 (s, free OH), 3500 cm^{-1} (s, OH···O); NMR δ 3.48 (m, 2, CH_2OH), 2.36 (s, 3, $C_6H_4CH_3$). Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.14. Found: C, 76.21; H, 9.27.

2-(*p*-Tolyl)-*c*-2-hydroxy-*r*-1-cyclohexanecarboxylic Acid (11b). A solution of **10b** (0.185 g, 0.84 mmol) in acetone (20 mL) was treated dropwise with Jones reagent[17] (0.44 mL) and left 10 min at room temperature. The mixture was diluted with water and extracted with ether, and the ether portion was extracted with 10% aqueous Na_2CO_3. Acidification of the alkaline solution with 10% aqueous HCl, extraction with ether, and evaporation of the washed ether extracts yielded crude **11b** (0.130 g) as a solid, which was recrystallized from petroleum ether (bp 60–80 °C) to give pure **11b** (0.080 g), mp 163–164 °C; IR λ 5.97 μm; NMR δ 2.95 (m, 1, W = 18 Hz, CHCOOH), 2.30 (s, 3, $C_6H_4CH_3$). Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 72.00; H, 7.77.

1-(*p*-Tolyl)-*c*-tosyloxymethyl-*r*-1-cyclohexanol (12b). Tosyl chloride (1.85 g, 9.70 mmol) was slowly added to a solution of **10b** (0.46 g, 2.08 mmol) in dry pyridine (6 mL) while keeping the temperature at about 5 °C. After 4 days at room temperature the reaction mixture was treated with crushed ice and extracted with $CHCl_3$. The organic extracts were washed with dilute H_2SO_4 and water and evaporated to give a crude product (0.56 g) which crystallized from CCl_4 to yield pure **12b** (0.41 g), mp 131–133 °C; IR λ (OH) 2.86 μm; NMR δ 3.82 (d, 2, J = 5.3 Hz, CH_2O), 2.47 (s, 3, $OSO_2C_6H_4CH_3$), 2.36 (s, 3, $C_6H_4CH_3$). Anal. Calcd for $C_{21}H_{26}O_4S$: C, 67.35; H, 6.99. Found: C, 67.23; H, 6.75.

1-(*p*-Tolyl)-*c*-2-methyl-*r*-1-cyclohexanol (13b). (A) A solution of 2-methylcyclohexanone (24.7 g, 0.22 mol) in anhydrous ether (50 mL) was added dropwise to the Grignard reagent prepared from *p*-bromotoluene (48.7 g, 0.28 mol) and magnesium (6.8 g, 0.28 g-atom) in anhydrous ether (75 mL). When the addition was complete the resulting mixture was refluxed for 2 h and then left for 12 h at room temperature. After cooling, the mixture was treated with crushed ice, saturated aqueous NH_4Cl, and diluted aqueous HCl. The organic layer was separated, and the aqueous portion was extracted with ether. The combined ether extracts were washed (H_2O, 10% aqueous Na_2CO_3, and H_2O), dried, and evaporated to yield an oily residue (38.7 g) which was distilled to give an oil (34.0 g), bp 154–157 °C (10 mm), consisting essentially of **13b;** the trans isomer **14b** was practically absent (<2%). The distilled oil (3.0 g) was purified by chromatography through a 2 × 50 cm column of silica gel prepared in petroleum ether. On eluting in succession with petroleum ether (4 L), 98:2 petroleum ether–ether (3 L), and 97:3 petroleum ether–ether (2 L), pure **13b** was obtained (1.1 g, eluted with 98:2 petroleum ether–ether) as an oil: IR λ (OH) 2.87 μm; NMR δ 2.32 (s, 3, $C_6H_4CH_3$), 0.62 (d, 3, J = 6.0 Hz, $CHCH_3$). Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.86. Found: C, 82.17; H, 9.72.

(B) A solution of **12b** (0.35 g, 0.93 mmol) in anhydrous ether was added dropwise to a stirred suspension of $LiAlH_4$ (0.70 g, 18.4 mmol) in anhydrous ether (20 mL). When the addition was complete the reaction mixture was refluxed for 15 h, the excess hydride was decomposed with a minimum amount of water and 2 N NaOH, and the dried ether layer was evaporated to dryness to yield pure **13b** (GLC).

1-(*m*-Chlorophenyl)-*c*-2-methyl-*r*-1-cyclohexanol (13c). A solution of **12c** (0.80 g, 2.02 mmol) in anhydrous ether (30 mL) was added to a stirred suspension of $LiAlH_4$ (1.52 g, 40.0 mmol) in anhydrous ether (50 mL). When the addition was complete the reaction mixture was refluxed for 1 hr, the excess hydride was decomposed with a minimum amount of water and 2 N NaOH, and the organic layer was separated and dried. Evaporation of the organic phase yielded an oily residue (0.38 g) consisting of **13c,** which was purified by preparative TLC; a 95:5 mixture of petroleum ether and ether was used as the eluent, yielding pure **13c** (0.21 g) (GLC) as an oil: IR λ (OH) 2.90 μm; NMR δ 0.62 (d, 3, J = 6.0 Hz, CH_3). Anal. Calcd for $C_{13}H_{17}ClO$: C, 69.47; H, 7.62. Found: C, 69.78; H, 7.56.

1-(*p*-Tolyl)-*t*-2-acetoxymercurimethyl-*r*-1-cyclohexanol (6b, X = CH_3COO). A stirred suspension of **1b** (0.72 g, 3.86 mmol) in water (70 mL) was treated with mercuric acetate (1.27 g, 3.98 mmol) and then stirred at room temperature for 3 days. After this time the reaction mixture was extracted with CH_2Cl_2, and the washed (H_2O) extracts were evaporated to give an oily residue (1.20 g) which on crystallization from benzene yielded pure **6b** (X = CH_3COO) (0.97 g), mp 142.5–143 °C; IR λ (OH) 2.93, (CO) 6.30 μm; NMR δ 2.37 (s, 3, $C_6H_4CH_3$), 1.90 (s, 3, $OCOCH_3$). Anal. Calcd for $C_{16}H_{22}O_3Hg$: C, 41.51; H, 4.79. Found: C, 41.86; H, 4.93.

1-(*p*-Tolyl)-*t*-2-trifluoroacetoxymercurimethyl-*r*-1-cyclohexanol (6b, X = CF_3COO). Mercuric trifluoroacetate[18] (0.85 g, 1.99 mmol) was added to a stirred suspension of **1b** (0.36 g, 1.93 mmol) in water (30 mL). After stirring for 3 days at room temperature, the reaction mixture was extracted with CH_2Cl_2 and the washed (H_2O) organic extracts yielded on evaporation a crude product (0.80 g) from which pure **6b** (X = CF_3COO) (0.34 g) was obtained by crstyallization from benzene–petroleum ether (bp 80–100 °C): mp 132–133 °C; IR λ (OH) 2.91, (CO) 5.95 μm; NMR δ 2.35 (s, 3, $C_6H_4CH_3$). Anal. Calcd for $C_{16}H_{19}O_3F_3Hg$: C, 37.17; H, 3.70. Found: C, 37.53; H, 3.69.

1-(*m*-Chlorophenyl)-*t*-2-acetoxymercurimethyl-*r*-1-cyclohexanol (6c, X = CH_3COO). Reaction of **1c** (0.50 g, 2.4 mmol) with mercuric acetate in water as described above for the analogous reaction of **1b** (in the present case the reaction time was 5 days) yielded an oily residue (0.81 g) which crystallized from benzene, affording pure **6c** (X = CH_3COO) (0.22 g), mp 132–133 °C; IR λ (OH) 2.95, (CO) 6.35 μm; NMR δ 1.95 (s, 3, CH_3). Anal. Calcd for $C_{15}H_{19}O_3ClHg$: C, 37.27; H, 3.96. Found: C, 37.60; H, 4.00.

1-(*m*-Chlorophenyl)-*t*-2-trifluoroacetoxymercurimethyl-*r*-1-cyclohexanol (6c, X = CF_3COO). Treatment of **1c** (0.50 g, 2.41 mmol) with mercuric trifluoroacetate[18] in water as described for the analogous reaction of **1b** (in the present case the reaction time was 5 days) yielded a crude product (0.95 g) which on crystallization from benzene–light petroleum (bp 60–80 °C) gave pure **6c** (X = CF_3COO)(0.43 g): mp 122–124 °C; IR λ (OH) 2.94, (CO) 5.97 μm. Anal. Calcd for $C_{15}H_{16}O_3ClF_3Hg$: C, 33.52; H, 3.00. Found: C, 34.07; H, 3.12.

1-(*p*-Tolyl)-*t*-2-methyl-*r*-1-cyclohexanol (14b). (A) A stirred suspension of **6b** (X = CH_3COO) (0.80 g, 1.72 mmol) in water (30 mL) was treated in succession with tetrahydrofuran (30 mL), 4 N NaOH (3.5 mL), and sodium borohydride (0.200 g, 5.28 mmol) and then stirred for 10 min. The reaction mixture was diluted with water and extracted with ether. Evaporation of the washed (H_2O) ether extracts yielded an oily residue (0.37 g) which was purified by preparative TLC (a 95:5 mixture of petroleum ether and ether was used as the eluent and elution was repeated twice). Pure **14b** was obtained (0.155 g) as a solid: mp 48–49 °C; IR λ (OH) 2.88 μm; NMR δ 2.36 (s, 3, $C_6H_4CH_3$), 0.65 (d, 3, J = 7.5 Hz, $CHCH_3$). Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.86. Found: C, 82.20; H, 10.09.

(B) Compound **6b** (X = CH_3COO) (0.30 g, 0.65 mmol) was added to a stirred suspension of $LiAlH_4$ (0.150 g, 3.9 mmol) in anhydrous tetrahydrofuran, and then the reaction mixture was stirred for 15 min. The excess hydride was decomposed with a minimum amount of water and 2 N NaOH, and the organic layer was separated. Evaporation of the dried organic phase yielded a residue (0.126 g) which consisted essentially of **14b.**

(C) Reduction of **6b** (X = CF_3COO) (0.25 g, 0.48 mmol) as described above in A for **6b** (X = CH_3COO) yielded a solid residue of **14b** (0.050 g).

1-(*m*-Chlorophenyl)-*t*-2-methyl-*r*-1-cyclohexanol (14c). (A) Reduction of **6c** (X = CH_3COO) (0.35 g, 0.72 mmol), as described above for the preparation of **14b** in A, gave crude **14c** (0.165 g), which was purified by preparative TLC (a 9:1 mixture of petroleum ether and ether was used as the eluent and elution was repeated twice), yielding pure **14c** (0.080 g) as an oil: IR λ (OH) 2.94 μm; NMR δ 0.66 (d, 3, J = 7.2 Hz, CH_3). Anal. Calcd for $C_{13}H_{16}OCl$: C, 69.47; H, 7.62. Found: C, 69.82; H, 7.70.

(B) Compound **6c** (X = CF_3COO) (0.20 g, 0.37 mmol) was reduced as described above for the preparation of **14b** in A to yield crude oily **14c** (0.057 g).

Reaction of 1b and 1c with Several Mercuric Salts in Water. A suspension of the cyclopropane (**1b** or **1c**) (0.26 mmol) in water (5 mL) was treated with the appropriate mercuric salt (0.24 mmol) and then stirred at room temperature (3 h for the reactions of **1b** and 15 h for the reactions of **1c**). Then the reaction mixture was treated with tetrahydrofuran (4 mL), 4 N NaOH (0.5 mL), and sodium borohydride (0.027 g, 0.73 mmol), stirred for 10 min, diluted with water, and extracted with ether. Evaporation of the washed (water) and dried ether extracts yielded a residue which was analyzed by GLC. The ratios of **13** and **14** are shown in Table I. Reactions of **1b** and **1c,** carried out under the same conditions but reducing the mixtures after shorter reaction times (30 min and 1 h for **1b** and 5 h for **1c**), yielded the same product ratio within experimental error.

Reaction of 1b and 1c with Mercuric Acetate and Mercuric Trifluoroacetate in Tetrahydrofuran–Water. A solution of the cyclopropane (**1b** or **1c**) (0.26 mmol) in a 1:1 (v/v) tetrahydrofuran–

water mixture (5 mL) was treated with mercuric acetate or mercuric trifluoroacetate (0.24 mmol) and stirred at room temperature (3 and 6 h for the reaction of **1b** with mercuric acetate and mercuric trifluoroacetate, respectively, and 15 h for the reactions of **1c**). Then 4 N NaOH (0.5 mL) and sodium borohydride (0.027 g, 0.73 mmol) were added and stirring was continued for 10 min. The workup was carried out as described above for the reactions in water, and the residue obtained was analyzed by GLC. Reactions of **1** carried out under the same conditions but stopping after relatively longer contact times (24 h for both **1b** and **1c**) yielded the same product ratio within experimental error.

Reaction of 1b and 1c with Mercuric Acetate and Mercuric Trifluoroacetate in Anhydrous CH_2Cl_2. A solution of the cyclopropane (**1b** or **1c**) (0.26 mmol) in anhydrous CH_2Cl_2 (5 mL) was treated with the mercuric salt (0.24 mmol), stirred at room temperature (30 min for the reactions of **1b** and 24 h and 15 min for the reactions of **1c** with mercuric acetate and mercuric trifluoroacetate, respectively), then diluted with CH_2Cl_2, washed immediately with water, and evaporated. The residue (in the reactions with $Hg(OOCCF_3)_2$, λ (CO) 5.76, 6.20 μm for **1b** and 5.77 and 6.19 μm for **1c**; in the reactions with $Hg(OOCCH_3)_2$, λ (CO) 5.62, 5.95 μm for **1b** and 5.62 and 5.92 μm for **1c**) was taken up in anhydrous ether (10 mL), treated with $LiAlH_4$ (0.050 g, 1.31 mmol), stirred for 10 min at room temperature, and then refluxed for 10 min. The excess hydride was decomposed with a minimum amount of water and 2 N NaOH, and the dried ether layer was evaporated to dryness to yield a residue which was analyzed by GLC. The ratios between **13** and **14** are shown in Table I. Reactions of **1b** and **1c** with each salt carried out under the same conditions but stopping after relatively different contact times (1, 3, and 6 h for the reaction of **1b** with mercuric acetate, 15 min and 1 h for the reaction of **1b** with mercuric trifluoroacetate, 48 h for the reaction of **1c** with mercuric acetate, and 8 min and 3 h for the reaction of **1c** with mercuric trifluoroacetate) yielded the same product composition within experimental error. However, in the case of the reaction of **1b** with mercuric trifluoroacetate, much longer contact times (3 and 6 h) showed an increase of the percentage of the syn adduct due to a slow epimerization at the benzylic carbon.

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Registry No.—**6b** (X = CH_3COO), 64705-90-4; **6b** (X = CF_3COO), 64705-91-5; **6c** (X = CH_3COO), 64705-92-6; **6c** (X = CF_3COO), 64705-93-7; **9**, 5331-08-8; **10b**, 64705-94-8; **11b**, 64705-95-9; **17b**, 64705-96-0; **12c**, 64705-97-1; **13b**, 64705-98-2; **13c**, 64705-99-3; **14b**, 64706-00-9; **4a**, 64706-01-0; **15b**, 1821-23-4; **15c**, 27163-65-1; methylene iodide, 75-11-6; *p*-bromotoluene, 106-38-7; tosyl chloride, 98-59-9; 2-methylcyclohexanone, 583-60-8.

References and Notes

(1) For a recent review see C. H. DePuy, *Fortschr. Chem. Forsch.*, **40**, 74 (1973), and references cited therein.
(2) C. H. DePuy and R. M. McGirk, *J. Am. Chem. Soc.*, **96**, 1121 (1974).
(3) C. H. DePuy, A. H. Andrist, and P. C. Fünfschilling, *J. Am. Chem. Soc.*, **96** 948 (1974).
(4) F. R. Jensen, D. B. Patterson, and S. E. Dinizo, *Tetrahedron Lett.*, 1315 (1974).
(5) A. Balsamo, C. Battistini, P. Crotti, B. Macchia, and F. Macchia, *J. Org. Chem.*, **40**, 3233 (1975).
(6) R. J. Ouellette, R. D. Robin, and A. South, Jr., *J. Am. Chem. Soc.*, **90**, 1619 (1968).
(7) (a) A. Balsamo, P. Crotti, B. Macchia, and F. Macchia, *Tetrahedron*, **29**, 199 (1973); (b) A. Balsamo, P. Crotti, B. Macchia, and F. Macchia, *J. Org. Chem.*, **39**, 874 (1974); (c) C. Battistini, A. Balsamo, G. Berti, P. Crotti, B. Macchia, and F. Macchia, *J. Chem. Soc., Chem. Commun.*, 712 (1974); (d) C. Battistini, P. Crotti, and F. Macchia, *Tetrahedron Lett.*, 2091 (1975), and references cited therein.
(8) H. C. Brown, J. D. Brady, M. Grayson, and W. H. Bonner, *J. Am. Chem. Soc.*, **79**, 1897 (1957).
(9) H. C. Brown, Y. Okamoto, and G. Ham, *J. Am. Chem. Soc.*, **79**, 1906 (1957).
(10) A. Balsamo, C. Battistini, P. Crotti, and F. Macchia, submitted for publication.
(11) M. Tichý, *Adv. Org. Chem.*, **5**, 115 (1965).
(12) N. S. Bhacca and D. H. Williams, "Application of NMR Spectroscopy in Organic Chemistry. Illustration from the Steroid Field", Holden-Day, San Francisco, Calif., 1964, pp 79, 135.
(13) H. C. Brown and P. J. Geoghegan, *J. Org. Chem.*, **35**, 1844 (1970).
(14) A. Balsamo, C. Battistini, P. Crotti, B. Macchia, and F. Macchia, *Gazz. Chim. Ital.*, **106**, 77 (1976).
(15) H. E. Zimmerman and J. English, Jr., *J. Am. Chem. Soc.*, **76**, 2285 (1954).
(16) R. J. Rawson and I. T. Harrison, *J. Org. Chem.*, **35**, 2057 (1970).
(17) R. G. Curtis, I. Heilbron, E. R. H. Jones, and G. F. Woods, *J. Chem. Soc.*, 461 (1953).
(18) H. C. Brown and M. H. Rei, *J. Am. Chem. Soc.*, **91**, 5646 (1969).

Elimination of Tertiary α Hydrogens from Tosylhydrazones with Lithium Diisopropylamide: Preparation of Trisubstituted Alkenes

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Tosylhydrazones containing only tertiary α hydrogens react with lithium diisopropylamide (LDA) to yield trisubstituted alkenes. The reaction of these and other tosylhydrazones with LDA shows a high degree of regiospecificity which is controlled by the stereochemistry of the imino bond. The stereochemistry of the reaction is manifested by the dominance of the cis alkene except in cases where isomerization to the trans alkene has a low activation barrier. The reaction of LDA with tosylhydrazones of β-keto esters is also successful.

The reaction of tosylhydrazones with alkyllithium reagents is a convenient method of preparing terminal or disubstituted alkenes.[1] This reaction has not, however, proved to be useful for the preparation of trisubstituted alkenes. Although a few isolated examples of tertiary α-hydrogen elimination have been reported,[2,3] no yield or product distribution was given. We recently reported that isobutyrophenone tosylhydrazone does not undergo elimination with methyllithium in ether at 0 °,[1] but at room temperature substitution at the imino carbon competes effectively with elimination.[4] Although substitution can be inhibited by the use of tetramethylethylenediame (TMEDA) as a co-solvent, the yield of isobutenylbenzene is quite poor.

We now wish to report that trisubstituted alkenes are conveniently prepared from tosylhydrazones which contain only tertiary α hydrogens by the use of lithium diisopropylamide (LDA) instead of methyllithium.[5-7] The moderate product yields (38–66%) are compensated by the convenience and by the mild reaction conditions.[8] Table I shows the data for the production of five trisubstituted alkenes.

The data in Table I show that for products which do not tend to undergo isomerization, TMEDA is the solvent of choice. However, in systems which do tend to isomerize, TMEDA appears to facilitate the rearrangement. For example, 2-methyl-2-norbornene isomerizes to 2-methylenenorbornane,[9] and the tricyclic system behaves similarly. The low

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