On the Mechanism of 1,3-Prototropic Shifts in Acetylene–Allene Isomerizations†

Suzanne R. Abrams* and Angela C. Shaw

Plant Biotechnology Institute, National Research Council of Canada, Saskatoon, Saskatchewan, Canada S7N 0W9

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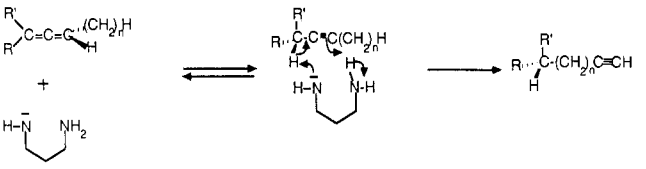
The mechanism of 1,3-proton transfers in allene–acetylene rearrangements mediated by alkali metal amides of 1,3-diaminopropane has been investigated with the object of determining the value of multipositional acetylene isomerizations in syntheses of long chain compounds containing a chiral center with an alkyl branch. The lithium amide of 1,3-diaminopropane-mediated isomerization of two diastereomeric allenes **4** and **5** differing only in the relationship of a methyl group on a cyclohexane ring to the allene afforded identical mixtures containing both terminal acetylenes **8** and **9**. Also with use of a mixed potassium/lithium reagent, rearrangement of an acetylenic alcohol **15** with defined relative stereochemistry gave two products **16** and **18** containing terminal acetylenes. These results demonstrate that 1,3-prototropic shifts effected by alkali metal amides of diamines proceed with some loss of stereochemical integrity, which is most likely caused by discrete anionic intermediates. A cyclic concerted bimolecular mechanism may be operating in part, but cannot be the exclusive mode of proton transfers.

For several years we have been exploring the chemistry of base-mediated acetylene isomerizations with emphasis on developing methods of value in synthesis.[1] Our efforts have led to a procedure for preparing 1-alkynes by isomerization of internal triple bonds that is inexpensive, safe, and amenable to large-scale synthesis.[2] As well, we have developed a novel method of perdeuteriation of all or part of a methylene chain employing deuteriated isomerization reagents.[3] Continuing our method development work, we have undertaken to study the mechanism of the rearrangement process with the idea that, if prototropic shifts take place in a concerted, cyclic fashion (Scheme I), then allene–acetylene isomerizations could be useful in syntheses of chiral alkyl branched molecules.

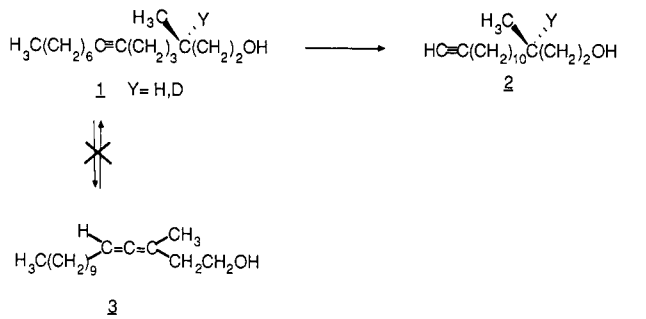
The migration of a triple bond from an internal position in a long methylene chain to the terminus is known to involve a random and reversible sequence of 1,3-proton transfers between acetylenes and allenes.[4] Rates of isomerization and product distributions are observed to vary greatly, depending upon the strength of the base, the reaction conditions, and the presence of other functional groups in the molecule. With exceedingly strong bases such as alkali metal amides of diamines, isomerizations proceed rapidly, and to a useful conclusion, because the terminal acetylene, as it is formed, is trapped as its acetylide salt. Typically, rearrangement of an internal acetylene of a hydrocarbon or acetylenic alcohol mediated by a mixed reagent of lithium 1,3-diaminopropylamide and potassium *tert*-butoxide at room temperature in less than an hour affords exclusively the terminal alkyne on workup.[2] In an early study[1b] on the rearrangement of isomeric linear decyn-1-ols employing the less strong base, the sodium salt of 1,3-diaminopropane, the reversibility of the isomerization reaction was demonstrated. Analysis of the products observed on rearrangement of 5-decyn-1-ol at low temperature showed that the triple bond migrated to all positions on the ten-carbon chain before being trapped at the free terminus.

The mechanism of such 1,3-proton transfers has been studied by a number of workers[4] using different substrates and base systems. The intermediacy of discrete carbanions has been implicated in the rearrangement of acetylenic acids with potassium hydroxide,[5] suggesting intermolecular 1,3-proton transfers. In other work by Cram et al.[6] on the rearrangement of 1,3,3-triphenylprop-1-yne with trimethylenediamine, intramolecularity in the process was

Scheme I



Scheme II



demonstrated. Wotiz et al.[7] observed that isomerization of the triple bond of hexyne proceeded much more rapidly with amides of diamines such as ethylenediamine than with amides of monoamines. Although their results were consistent with a cyclic, concerted mechanism, a proton abstraction–reprotonation sequence could not be ruled out. It has been suggested that the extremely rapid reaction rates observed for acetylene isomerizations using the potassium salt of 1,3-diaminopropane[8] may be the result of facile concerted 1,3-proton transfers.

Acetylene isomerizations may, or may not, be of value in syntheses of chiral alkyl branched molecules, depending upon the mode of proton transfer. If a cyclic concerted process (Scheme I) is the pathway taken, then chirality could be transferred from an allene to a position adjacent to the triple bond, and the reverse process would also hold.

† NRCC No. 27511.

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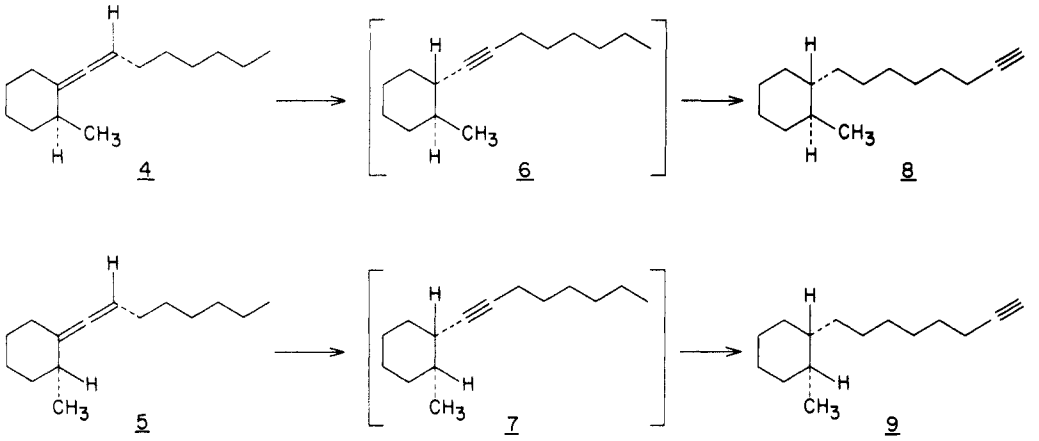
Scheme III



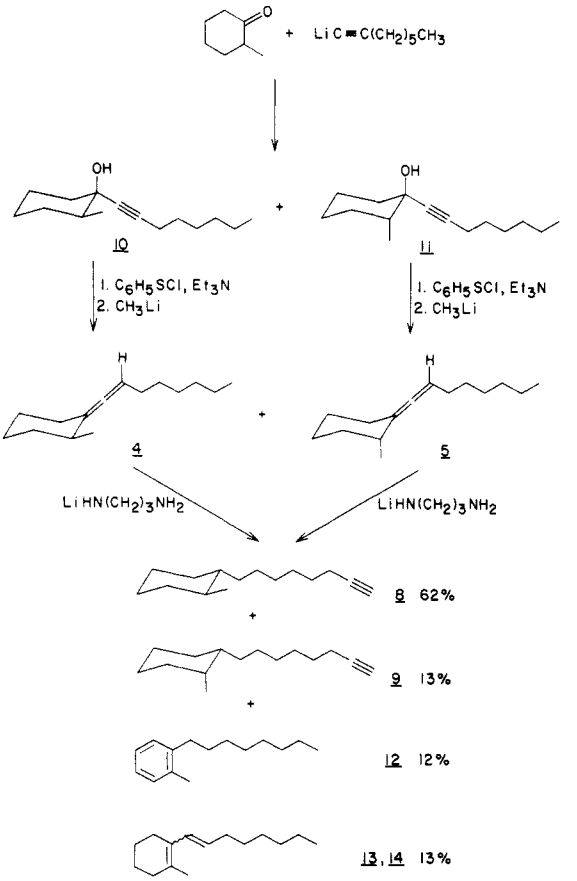
The eventual product of the reaction would be the terminal alkyne having a remote chiral center. If, however, discrete anions are intermediates in the rearrangement reactions, or if the process is trimolecular, then chirality could be lost, and acetylene isomerizations would be of little value for synthetic purposes.

Utimoto et al.[9] reported that isomerization with the potassium salt of 1,3-diaminopropane of an acetylenic alcohol (**1**) containing a chiral center distant from the triple bond proceeded to the terminal alkyne **2** without loss of chirality (Scheme II). Repetition of the isomerization employing a racemic starting material deuteriated at the methyl branch gave the terminal acetylene with no loss of deuterium, indicating that the allene **3** was not an intermediate in the reaction. This observation is interesting but does not address the question of how the rearrangement reaction proceeds, nor does it allow prediction of the fate of chiral allenes or of chiral centers close to acetylenes and allenes. Chiral propargylic alcohols have been employed in isomerization reactions, with the chirality of the carbon bearing the oxygen maintained.[10] This is a special case, however, as it is thought that the carbon bearing the alcohol does not suffer loss of its proton.

Results and Discussion

Two stereochemically defined systems, one employing an allene and one an acetylene, have been devised to establish the mechanism of triple-bond migrations and to evaluate the potential of such rearrangements in syntheses involving chiral intermediates. In the first instance (Scheme III), a pair of diastereomeric trisubstituted allenes **4** and **5** has been chosen to be substrates for rearrangement with a bidentate isomerization system. The allenes differ only in the stereochemical relationship of the methyl group on the cyclohexane ring and the allene. If the prototropic shifts occur by a concerted mechanism, rearrangement of each allene with the isomerization reagent should afford initially the acetylenes **6** (substituents on the ring trans) and **7** (substituents cis). The products isolated from the reactions would be **8** and **9**, which would have the same stereochemical relationship between the substituents on the ring as **6** and **7**. If, however, the rearrangements occur through discrete propargylic and allenic anions, and configurational stability is lost,[11] then the end result of the process should be the observation of a mixture of **8** and **9**, regardless of the stereochemistry of the starting allene.

Scheme IV



The allenes **4** and **5** were prepared in a straightforward manner (Scheme IV). Alkylation of 2-methylcyclohexanone with the lithium salt of octyne afforded two propargylic alcohols **10** and **11** which were readily separated by chromatography. The stereochemistry of the isolated products could be assigned by comparison of ^{13}C NMR data with that of *cis*- and *trans*-2-methyl-1-ethynylcyclohexanol[12] (see Experimental Section for data). Reduction of the propargylic alcohols to the allenes was effected by a two-step procedure known to give overall syn reduction.[13] The process involved reaction of a propargylic alcohol with phenylsulfenyl chloride in the presence of excess base at low temperature, affording initially the

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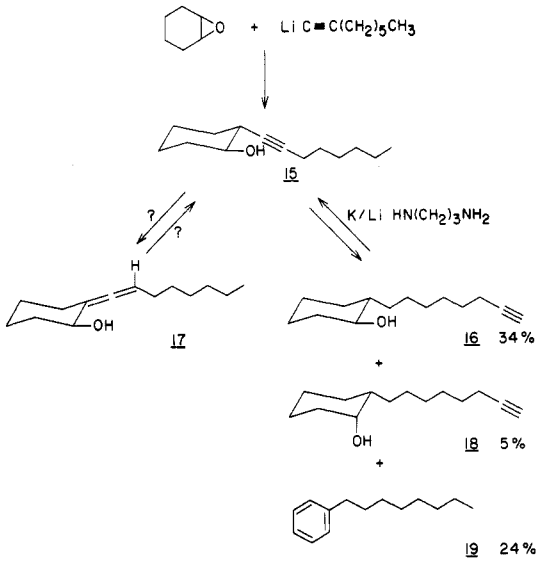
Scheme V



sulfenyl ester. In the course of warming the reaction mixture, a [2,3]-sigmatropic rearrangement to the corresponding allenyl sulfoxide occurred. This product, when treated with methyllithium, was converted to the desulfurized allene in which the allenic proton is attached to the same face of the molecule as the hydroxyl group of the initial propargylic alcohol. Treatment of **10** under these conditions afforded the allene **4** contaminated with 4% of the diastereomer **5** in 33% yield over two steps. Analogous reduction of **11** gave the allene **5** containing 1% **4**, in 29% yield overall.

Reduction of propargylic alcohols to allenes with $LiAlH_4$ is now thought to occur by anti attack of hydride.[14] Treatment of the cis propargylic alcohol **10** with this reagent did give the product of trans attack **5** with 5% of the diastereomer **4**. Reduction of the isomeric species **11** gave, however, a 1:1 mixture of the two allenes. In both reductions employing $LiAlH_4$, reduction of the triple bond of the propargylic system to the trans allylic alcohols also occurred.

The individual allenes **4** and **5** were subjected to the mildest of the 1,3-diaminopropane-based isomerization reagents, the lithium amide. Both compounds, on reaction at room temperature for 24 h, yielded a mixture of five volatile products that had identical retention times and relative proportions on GLC. Three minor components of the reactions were identified as the aromatic dehydrogenation product, 1-methyl-2-octylbenzene[15] (**12**), and a pair of isomeric conjugated dienes **13** and **14**, which were not investigated further. The two terminal acetylenes **8** and **9** were isolated as a mixture in a ratio of 3:1. In the 360-MHz NMR spectrum of the mixture of isomeric terminal alkynes, the larger methyl signal was further downfield (0.06 ppm) as would be expected for the trans compound.[16] This product ratio probably reflects the relative thermodynamic stabilities of the isomeric disubstituted cyclohexyl compounds.[17] Of prime importance to the argument is that both are observed, and thus, that the rearrangement of the allenes **4** and **5** does not involve exclusively a cyclic, intramolecular reaction process, but may involve allenic anions that suffer loss of configuration.

The second system investigated differed in that the isomerization substrate **15** contained a triple bond with a stereochemically defined centre adjacent to it (Scheme V). Isomerization would afford a single alkynol (**16**) if the reaction were concerted. If the process is nonconcerted and if the propargylic anion derived from **15** or the anion derived from the allene **17** is protonated from either face of the ring, then a mixture of two terminal acetylenes **16** and **18** reflecting their relative thermodynamic stabilities would result.

The trans homopropargylic alcohol **15** was prepared by opening of the epoxide ring of cyclohexene oxide with the lithium salt of octyne.[18] Rearrangement with an isomerization reagent prepared by addition of potassium *tert*-butoxide to the lithium amide of 1,3-diaminopropane afforded, after chromatography, three products, phenyloctane (**19**), 24%, and the two isomeric terminal acetylenes **16** (34%) and **18** (5%). The stereochemistry of the products was assigned from examination of the NMR spectra of the isolated components, compared with those reported for *cis*- and *trans*-2-methylcyclohexanol.[19] The chemical shift of the proton of the carbon bearing the hydroxyl group is found at higher field (difference of 0.7 ppm) for the more prominent component, the trans isomer **16**.

This result demonstrates further that the isomerization process is not occurring exclusively through a cyclic concerted route. The propargylic methine proton of **15** suffers abstraction to some extent, and the resultant carbanion is protonated from both faces of the ring scrambling the stereochemistry.

In the light of these results, those reported by Utimoto et al.[9] are somewhat surprising. Due to the random nature of the isomerization process, some loss of deuterium, or loss of optical activity, would be expected in the rearrangement of an internal acetylene with the triple bond three positions away from the chiral center. The experiments described in the present work demonstrate definitevely that alkali metal amides of diamines effect isomerization of triple bonds to some extent through nonconcerted 1,3-proton transfers.

Experimental Section

All reactions required dry conditions and were performed in oven-dried (110 °C for more than 2 h) glassware, under a positive pressure of argon. Solvents were distilled just before use as follows: tetrahydrofuran (THF) from benzophenone ketyl; diglyme and dichloromethane (CH_2Cl_2) from calcium hydride. Triethylamine and 1,3-diaminopropane were distilled from barium oxide and stored over activated 4A sieves.

^1H NMR spectra were recorded on a Bruker AM-360-WB (360 MHz) spectrometer, employing $CDCl_3$ as solvent with $CHCl_3$ as reference. ^{13}C NMR spectra were recorded on the Bruker instrument in the Fourier transform mode at 90.6 MHz with proton noise decoupling, with $CDCl_3$ as solvent and lock. IR spectra were obtained with a Perkin-Elmer 237B instrument. Gas chromatographic separations were carried out with a Varian 3700 instrument equipped with a DB-5 capillary column (J and W Scientific, 30 m) and a flame ionization detector. GC/MS were obtained by using a DB-5 column (60 m) in a Finnigan 4000 E instrument in the electron impact mode with an Incos 2300 data system. Mass spectra are reported in mass to charge units (m/z) with the relative intensities as percentages of the base peak given in parentheses. Exact mass measurements were provided by the

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(19) Pouchert, C. J.; Campbell, J. R. *The Aldrich Library of NMR Spectra.* Vol. IV 3A, Aldrich Chemical Co.; Pouchert, C. J.; *The Aldrich Library of Infrared Spectra.*, Ed. III, Aldrich Chemical Co., 562 g.

Mass Spectrometry Laboratory, Psychiatric Research Unit, University of Saskatchewan, with an MS902S instrument with VG console update. Accurate masses were obtained at 1500 resolution and 3 s/decade by using accurate mass low resolution software with PFTBA internal standard. Elemental analyses were performed by Spang Microanalytical Laboratory, Eagle Harbor, MI.

***cis*- and *trans*-1-(1-Octynyl)-2-methylcyclohexanol (10 and 11).** To octyne (12.1 g, 110 mmol) in THF (200 mL) at −78 °C was added first *n*-BuLi (1.5 M in hexane, 70 mL, 110 mmol) followed by 2-methylcyclohexanone (11.2 g, 100 mmol) in THF (50 mL). The solution was allowed to warm to room temperature, and after 2.0 h, the reaction mixture was poured onto ice water and extracted with ether (3×). The combined ethereal extracts were washed with water (2×) and NaCl solution (2×), then dried over Na_2SO_4, and filtered, and the solvent was evaporated to afford 20.4 g of crude product. Separation of four batches of 2.0 g of mixture over a column of 100 g of silica gel made up in and eluted with 10% ether 90% hexane afforded **10** (2.74 g) [^{1}H NMR δ 2.15 (t, J = 7.0 Hz, $H_2CC{\equiv}C$, 2 H), 1.89–1.95 (m, H-6$_{eq}$, 1 H), 1.2–1.65 (m, CH, CH_2, 16 H), 1.00 (d, J = 6.8 Hz, H_3CCH, 3 H), and 0.85 (t, J = 6.8 Hz, H_3CCH_2, 3 H); ^{13}C NMR (data given in parentheses are those reported[12] for *cis*-2-methyl-1-ethynylcyclohexanol) 69.63 (C1, 69.55), 40.86 (C2, 40.49), 29.37 (C3, 29.32), 25.12 (C4, 25.05), 21.30 (C5, 21.03), 39.70 (C6, 39.32), 16.05 (C7, 15.96), 85.06, 83.52 (C8, C9), 18.63 (C10), 28.77, 28.47 (C11, C12), 31.31 (C13), 22.52 (C14), and 13.97 (C15) ppm; IR (film) ν_{max} 3630, 3480, 2220, and 950 cm^{-1}; MS, 222 (M$^+$, 13), 207 (2), 193 (23), 179 (35), 165 (73), 152 (25), 137 (37), 124 (27), and 55 (100); exact mass calcd for $C_{15}H_{26}O$ 222.1892, found 222.1993] and **11** (2.37 g) [^{1}H NMR δ 2.18 (t, J = 7.0 Hz, $H_2CC{\equiv}C$, 2 H), 1.89–2.15 (m, H-6$_{eq}$, 1 H), 1.12–1.65 (m, CH, CH_2, 16 H), 0.98 (d, J = 6.4 Hz, H_3CCH, 3 H), and 0.85 (t, J = 7.0 Hz, H_3CCH_2, 3 H); ^{13}C NMR (data given in parentheses are those reported[12] for *trans*-2-methyl-1-ethynylcyclohexanol) 73.32 (C1, 73.21), 42.81 (C2, 42.46), 32.42 (C3, 32.22), 25.68 (C4, 25.55), 24.43 (C5, 24.22), 41.15 (C6, 40.77), 16.10 (C7, 16.03), 86.79 (C8), 81.00 (C9), 18.68 (C10), 28.87, 28.48 (C11, C12), 31.29 (C13), 22.53 (C14), and 13.96 (C15) ppm; IR (film) ν_{max} 3620, 3420, 2230, and 1040 cm^{-1}; MS, 222 (M$^+$, 32), 207 (8), 193 (48), 179 (55), 165 (65), 152 (44), 137 (59), 124 (47), and 67 (100); exact mass calcd for $C_{15}H_{26}O$ 222.1892, found 222.1844]. The yield obtained of the two isolated products, after chromatography, was 70%.

Reduction of 10 to Allene 4. To a solution of propargylic alcohol **10** (840 mg, 3.8 mmol) and triethylamine (1.1 mL, 7.6 mmol) in CH_2Cl_2 (10 mL) at −78 °C was added a solution of benzenesulfenyl chloride[20] (580 mg, 4.0 mmol) in CH_2Cl_2 (5 mL). Half way through the addition, the mixture became gelatinous and was warmed to −10 °C for the rest of the addition. The mixture was allowed to stir at room temperature for 2 h, then was added to water, and extracted with CH_2Cl_2 (3×). The combined organic phases were washed successively with water (2×), HCl solution (1×), and potassium carbonate (K_2CO_3) solution (1×) and then dried over anhydrous K_2CO_3. The solvent was evaporated to afford 1.12 g of crude product which was employed directly in the next step. The crude allene sulfoxide was dissolved in ether (anhydrous) and cooled to −78 °C, and a solution of methyllithium (9.1 mL, 1.5 M in hexane, 13 mmol) was added over 5 min. After a further 5 min at −78 °C, the reaction mixture was poured into water, the ether phase separated, and the aqueous phase extracted twice with ether. The combined organic phases were washed with NaCl solution, then dried over Na_2SO_4, and filtered, and the solvent was removed at reduced pressure to afford 780 mg of crude product that was chromatographed over a column of Florisil (75 g), eluting with hexane, yielding 258 mg (33%) of a mixture as estimated by GC (140 °C) of allenes **4** (11.6 min, 96%) and allene **5**) (11.2 min, 4%): ^{1}H NMR δ 5.04 (m, apparent septet, C=C=CH, 1 H), 2.25 (m, H-6$_{eq}$, 1 H), 1.90–1.98 (m, allylic H, 4 H), 1.68–1.78 (m, eq ring H, 3 H), 1.2–1.4 (m, CH_2, 10 H), 1.0–1.1 (m, H-3$_{ax}$, 1 H), 0.93 (d, J = 6.6 Hz, H-7, 3 H), and 0.86 (t, J = 7.1 Hz, H-15, 3 H); ^{13}C NMR 198.0 (C8), 107.9 (C1), 91.1 (C9), 36.2 (C3), 34.5 (C2), 32.3 (C6), 31.8 (C13), 29.6 (C10), 29.4 (C11), 28.8 (C12), 27.5 (C5), 26.2 (C4), 22.7 (C14), 19.7 (C7), and 14.0 (C15) ppm; IR (film) ν_{max} 1960, 960 cm^{-1}; MS (25 eV) (major product), 206 (M$^+$, 0.3), 136 (100), 121 (58), 107 (35), and 95 (27). Anal. Calcd for $C_{15}H_{26}$: C, 87.30; H, 12.70. Found: C, 86.92; H, 13.04.

Reduction of 10 to Allene 5 with $LiAlH_4$. To a suspension of $LiAlH_4$ (420 mg, 10.6 mmol) in diglyme (10 mL) was added a solution of **10** (2.2 g, 10.6 mmol) in diglyme (20 mL). The mixture was refluxed for 3 h. The mixture was cooled and then ice water was added slowly, and the solution was extracted with hexane (3×). The combined organic extracts were washed with water and NaCl solution, then dried over Na_2SO_4, and filtered, and the solvent was evaporated and the product chromatographed over silica gel, eluting with 10% ether 90% hexane to yield a nonpolar (1.2 g, 56%) and a polar fraction (430 mg, 18%). The more polar fraction was a single component by GLC and was assigned the structure of the corresponding allylic alcohol: ^{1}H NMR δ 5.53 (dt, J = 15.6, 6.8, C=C*H*CH_2, 1 H), 5.35 (dt, J = 15.6, 1.2, OCC*H*=C, 1 H), 1.96 (m, H_2CC=C, 2 H), 1.60 (m, H-6$_{eq}$, 1 H), 1.10–1.55 (m, 16 H), 0.80 (t, J = 6.8 Hz, H_3CCH_2, 3 H), and 0.73 (d, J = 6.2 Hz, H_3CCH, 3 H); IR (film) ν_{max} 3600, 3500, 960 cm^{-1}; MS, 224 (13), 206 (2), 195 (13), 181 (15), 167 (45), 139 (62), and 55 (100); exact mass calcd for $C_{15}H_{28}O$ 224.2138, found 224.2068. The nonpolar fraction gave two peaks on GC, **5** (95) and **4** (5): ^{1}H NMR δ 5.02 (apparent septet, H-9, 1 H), 2.26 (m, H-6$_{eq}$, 1 H), 1.9–2.0 (m, allylic H, 4 H), 1.7–1.8 (m, eq ring H, 3 H), 1.2–1.4 (m, CH_2, 10 H), 1.05 (m, H-3$_{ax}$, 1 H), 0.94 (d, J = 6.6 Hz, H-7, 3 H), and 0.88 (t, J = 6.9 Hz, H-15, 3 H); ^{13}C NMR 197.9 (C8), 108.2 (C1), 91.2 (C9), 36.5 (C3), 34.6 (C2), 32.3 (C6), 31.8 (C13), 29.5 (C10), 29.1 (C11), 28.9 (C12), 27.7 (C5), 26.3 (C4), 22.7 (C14), 19.7 (C7), and 14.1 (C15) ppm; IR (film) ν_{max} 1920, 760 cm^{-1}; MS (25 eV) (major product) 206 (M$^+$, 0.5), 136 (100), 121 (79), 107 (64), and 95 (53). Anal. Calcd for $C_{15}H_{26}$: C, 87.30; H, 12.70. Found: C, 86.81; H, 13.14.

Reduction of 11 to Allene 5. The propargylic alcohol **11** (890 mg, 4.0 mmol) was treated first with phenylsulfenyl chloride and triethylamine and subsequently with methyllithium exactly as for the reduction of **10**, affording after chromatography 238 mg (29%) of allene **5** (98%) and allene **4** (2%), as estimated by GC. The ^{1}H NMR and IR data were identical with those obtained above.

Isomerization of Allene 5 Derived from 10. To the isomerization reagent[1] prepared from lithium (210 mg, 30 mmol) and 1,3-diaminopropane (20 mL, corrosive) was added at room temperature a solution of allene **5** (containing 5% **4**, 995 mg, 4.8 mmol) in 1,3-diaminopropane (4 mL). The brown mixture was stirred overnight and then worked up by being poured into ice water and extracted with hexane (3×). The combined organic phases were washed successively with water, 10% HCl solution, and saturated NaCl solution and then was dried over Na_2SO_4, affording a mixture of hydrocarbons (344 mg). Extraction of the aqueous phase with $CHCl_3$ (3×) yielded a further 146 mg of crude product. Five main products were observed on GC analysis (140 °C): **8** (62%), **9** (13%), **12** (12%), **13** (8%), and **14** (5%). The hexane-extracted product was chromatographed over silica gel, eluting with hexane. The first fraction (5 mg) consisted of components **13** and **14** in a ratio of 8 to 5: ^{1}H NMR δ 5.3–6.5 [6.45 (d, J = 15.5 Hz), 5.55 (m), 5.38 (t, J = 7.0 Hz) olefinic signals in a ratio of 1:3:2], 1.1–2.3 (m, allylic and methylene H) and 0.86 (t, J = 7 Hz); IR ν_{max} 960 cm^{-1}; GC/MS of **13** 206 (M$^+$, 19), 121 (79), 108 (100), and 93 (97); GC/MS of **14** 206 (M$^+$, 40), 135 (81), 121 (44), 107 (44), and 93 (100). Compound **12**[15] was obtained in greater than 90% purity: ^{1}H NMR δ 7.1–7.3 (m, ArH, 4 H), 2.57 (m, $ArCH_2$, 2 H), 2.29 (s, $ArCH_3$, 3 H), 1.2–1.7 (m, CH_2, 12 H), and 0.87 (t, J = 7 Hz, CH_3, 3 H); IR ν_{max} 3050 (w), 740 (s) cm^{-1}; MS, 204 (M$^+$, 11) and 105 (100). A mixture of **8** and **9** was obtained in the ratio of 3:1: ^{1}H NMR δ 2.16 (dt, J = 2.6, 7.0 Hz, $H_2CC{\equiv}C$, 2 H), 1.91 (t, J = 2.6 Hz, 1 H), 1.1–1.8 (m, CH_2, CH, 20 H), and two methyl signals in a ratio of 3:1 0.85 (d, J = 6.3 Hz), and 0.79 (d, J = 7.2 Hz). The mixture gave the following: IR ν_{max} 3320 and 2120 cm^{-1}; GC/MS of the major product 206 (M$^+$, 0.03), 97 (76), 96 (74), 95 (76) and 55 (100), and of the minor product 206 (M$^+$ missing), 97 (60), 96 (32), 95 (34) and 55 (100).

Isomerization of Allene 4. When exactly the same isomerization reaction conditions were employed, allene **4** (206 mg, 1.0 mmol) afforded a mixture of hydrocarbons (57 gm) consisting of **8** (63%), **9** (15%), **12** (12%), **13** (8%), and **14** (5%).

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***trans*-2-(1-Octynyl)cyclohexanol (15).** According to the method of Yamaguchi and Hirao,[18] the lithium salt of octyne was allowed to react with cyclohexene oxide, affording **15**: ^{1}H NMR δ 3.31 (6 line m, $w_{1/2}$ = 25 Hz, $J_{apparent}$ = 10, 4 Hz, HCO, 1 H), 2.05–2.15 (m, 3 H), 1.05–2.00 (m, 16 H), and 0.83 (t, J = 7.0 Hz, CH_3, 3 H); IR (film) ν_{max} 3400 cm^{-1}; GC/MS of Me_3Si ether 280 (M^+, 5), 251 (2), 209 (16), 195 (20), and 73 (100); exact mass calcd for $C_{17}H_{32}OSi$ 280.2153, found 280.2186.

Isomerization of *trans*-2-(1-Octynyl)cyclohexanol. To the isomerization reagent (prepared from lithium (84 mg, 12 mmol), 1,3-diaminopropane (8.0 mL), and potassium *tert*-butoxide (900 mg, 8.0 mmol) was added at room temperature a solution of **15** (416 mg, 1.0 mmol) in 1,3-diaminopropane (4 mL). After being stirred for 1.0 h, the mixture was poured into ice/water and extracted with $CHCl_3$ (3×). The combined organic extracts were washed successively with 10% HCl (1×) and saturated NaCl solution (1×), and then dried over Na_2SO_4, and the solvent was evaporated to afford 410 mg of an oil which was chromatographed over silica gel, eluting with 40% ether 60% hexane. First to elute was phenyloctane (**19**) (85 mg, 24%) which gave IR and NMR spectra identical with published data[19] and GC/MS 190 (M^+, 17), 92 (98), and 91 (100). The second product obtained was *cis*-2-(7-octynyl)cyclohexanol (**18**): 20 mg (5%); ^{1}H NMR δ 3.84 (m, $w_{1/2}$ = 10 Hz, $H_{eq}CO$, 1 H), 2.15 (dt, J = 7.0, 2.6 Hz, $H_2CC{\equiv}C$, 2 H), 1.91 (t, J = 2.6 Hz, $HC{\equiv}C$, 1 H), 1.1–1.8 (m, 19 H); IR (film) ν_{max} 3400, 3300, 2100, 1450, and 960 cm^{-1}; GC/MS, 280 (M^+, 2), 129 (47), 75 (100), and 73 (98); exact mass calcd for $C_{17}H_{32}OSi$ 280.2153, found 280.2213. Third to elute was *trans*-2-(7-octynyl)cyclohexanol (**16**): 140 mg (34%); ^{1}H NMR δ 3.14 (6 line m, $J_{apparent}$ = 9.6, 4.4 Hz, $H_{ax}CO$, 1 H), 2.12 (dt, J = 7.0, 2.6 Hz, $H_2CC{\equiv}C$, 2 H), 1.88 (t, J = 2.6 Hz, $HC{\equiv}C$, 1 H), and 0.8–1.8 (m, 19 H); IR (film) ν_{max} 3400, 3300, 2100, 1450, and 1050 cm^{-1}; GC/MS, 280 (M^+, 3), 129 (58), 75 (99), and 73 (100); exact mass calcd for $C_{17}H_{32}OSi$ 280.2153, found 280.2064.

The Kinetics of the Hydroxymercuration of Substituted Atropic Acids

Adolphus Lewis* and Antoine Carty

Department of Chemistry, Howard University, Washington, D.C. 20059

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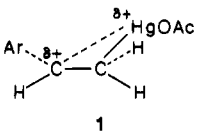
Kinetic studies on the hydroxymercuration of a series of meta- and para-substituted atropic acids in aqueous acetate buffer have been carried out. In the pH 3.7–5.0 range investigated, while the rates of reaction are essentially independent of the pH of the medium, they vary linearly with 1/[NaOAc]. At pH 4.40 and 0.050 M NaOAc, the reaction is first order in the concentrations of the atropic acids and the $Hg(OAc)_2$. In contrast to the results found for the methoxymercuration of the corresponding styrenes, log k(X) gives better correlations with σ^+ than with σ. At 25 °C, ρ^+ (−2.14) is smaller than that (−2.78) found for the methoxymercuration of the styrenes. For each of the atropic acids, the values of its activation parameters are larger, by essentially the same amount, than those for the corresponding styrene and, in contrast to the results obtained for the styrenes, $\Delta H^* > -T\Delta S^*$. Product studies on the hydroxymercuration–demercuration of several of the atropic acids (p-MeO, H, m-Cl, and p-NO_2) showed that the only products formed were the corresponding atrolactic acids. Thus the hydroxymercuration occurs regiospecifically giving the Markovnikov hydroxymercurial. These results are consistent with the formation of an open α-mercuriocarbocation in the rate-determining step, which consequently suggests that the polarity of the solvent is more important than the structure of the alkene in determining the structure of the intermediate cation formed in the rate-determining step of this reaction.

Introduction

As a part of our[1,2] continuing investigations into the relative importance of the factors[3–7]—namely, the structure of the alkene, the electronic nature of the electrophilic atom, and the polarity of the solvent—which determine the structure of the intermediate cation formed in the rate-determining step of an electrophilic addition reaction, we have carried out kinetic studies on the hydroxymercuration of a series of meta- and para-substituted atropic acids in aqueous acetate buffer. Initially we planned to investigate the methoxymercuration of a series of methyl atropates. However, preliminary studies revealed that under our neutral kinetic conditions,[8] methoxymercuration of these compounds occurs too slowly to follow spectrophotometrically. They also showed that it would be impossible for us to determine the rates of methoxymercuration of the atropic acids spectrophotometrically, as planned, since the reaction mixtures became turbid soon after mixing methanolic solutions of the two reactants. The atropic acids were chosen for this study because they contain cross conjugated aryl and carboxyl groups. Thus a study of this type should afford one the opportunity to assess the relative importance of resonance-stabilization of a developing positive charge by an electron-donating aryl group vs. that of the simultaneous destabilization of that same charge by an electron-withdrawing carboxyl group.

The results of our[1,2] studies on the methoxymercuration of substituted styrenes suggested that when stabilization of the intermediate cation formed in the rate-determining step via, both, resonance involving the aryl substituent and bridging of the mercury atom are possible and the solvent in neither extremely polar nor nonpolar—thus, when neither the structure of the alkene nor the polarity of the solvent is clearly dominant—the structure of this cation should be that of an unsymmetric bridged ion, **1**. Thus



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the primary aim of this study was to test the validity of this conclusion. Specifically, since water is much more polar than methanol and the atropic acids may be considered as α-substituted styrenes, we were interested in

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