612-22-6; 1-ethyl-3-nitrobenzene, 7369-50-8; 1-ethyl-4-nitrobenzene, 100-12-9; 1-nitro-2-propylbenzene, 7137-54-4; 1-nitro-3-propylbenzene, 73585-59-8; 1-nitro-4-propylbenzene, 10342-59-3; 1-nitro-2-isopropylbenzene, 6526-72-3; 1-nitro-3-(isopropyl)benzene, 6526-74-5; 1-nitro-4-isopropylbenzene, 1817-47-6; 1-(*tert*-butyl)-3-nitrobenzene, 23132-52-7; 1-(*tert*-butyl)-4-nitrobenzene, 3282-56-2; 1,2-dimethyl-3-nitrobenzene, 83-41-0; 1,2-dimethyl-4-nitrobenzene, 99-51-4; 1,3-dimethyl-2-nitrobenzene, 81-20-9; 1,3-dimethyl-4-nitrobenzene, 89-87-2; 3-nitro-1,2,4-trimethylbenzene, 52414-96-7; 5-nitro-1,2,4-trimethylbenzene, 610-91-3; 6-nitro-1,2,4-trimethylbenzene, 609-88-1.

Highly Stereoselective Friedel–Crafts Alkylations via Epoxide Transannular Reactions[1]

Stephen K. Taylor,* Gay L. Lilley, Kevin J. Lilley, and Patricia A. McCoy

Department of Chemistry, Olivet Nazarene College, Kankakee, Illinois 60901

Received February 5, 1981

Under catalytic conditions, *trans*-5,6-epoxy-*cis*-cyclodecene (1) undergoes a Friedel–Crafts (FC) reaction with various aromatic molecules. Four chiral centers are formed via transannular ring closure in this remarkably stereoselective FC reaction (Scheme I). The side products are all consistent with the proposed reaction intermediate, for which oxygen bridging is proposed to account for experimental observations. Geraniolene monoepoxide (14) was also investigated for transannular FC reactions. In this case, FC alkylation was observed (in low yield) only when anisole was the aromatic solvent.

Typically, Friedel–Crafts (FC) alkylation reactions are accompanied by isomerization and disproportionation processes[2] and hence are not considered highly selective. Quite generally, this lack of selectivity has proved true for what few epoxides that have been studied.[2b,3-8] For example, seven products are formed in an alkylation of benzene by the simple compound propylene oxide, and for the most part very little work has been done on FC reactions of the more complex epoxides[8] (possibly because very complex product mixtures would be expected). However, recently the FC products of the latter reaction were shown to result from a stereospecific inversion reaction[5] despite the multiplicity of products. We further demonstrate the novelty of epoxide FC reactions and hope to encourage further interest in this area by reporting a highly stereoselective reaction that minimizes skeletal rearrangements and gives predominantly one product. In this reaction, four chiral centers are generated. Also, in contrast to other epoxides FC reactions,[3-8] our reaction requires only catalytic quantities of Lewis acid promoter.

Although exceptionally selective biomimetic epoxide cyclizations have been reported,[9-12] they differ from our intermolecular FC reactions in that they are strictly intramolecular and involve large amounts of acid promoter.[9-12]

The reaction was discovered while trying to isomerize *trans*-5,6-epoxy-*cis*-cyclodecene[13] (1) with $SnCl_4$ by a

Scheme I

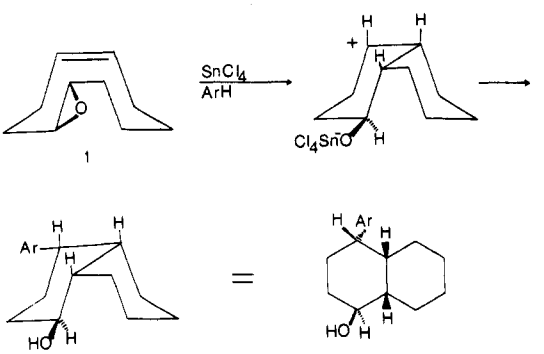


Table I. Products Obtained from Friedel–Crafts Reactions of *trans*-5,6-Epoxy-*cis*-cyclodecene

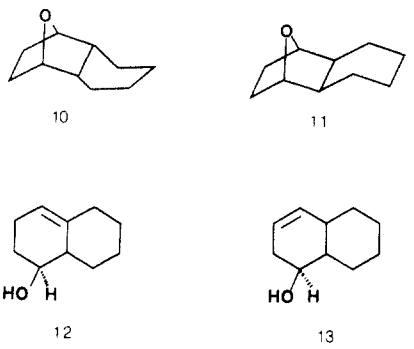
aromatic	Ar = (product no.)	isolated % yield (ratio of products)	mp, °C
toluene	*p*-methylphenyl (2)[a,b]	64 (75% GC)	156–158
	o-methylphenyl (3)[b]	(2:3 = 75:25)	
o-xylene	3,4-xylyl[a,b] (4)	76	144–146
methoxybenzene	*p*-methoxyphenyl (5)[b]	55	138.5–139
	o-methoxyphenyl (6)[b]	(5:6 = 53:47)	168–170
furan	2-furyl (7)[a]	48	97.5–99.5
ethylbenzene	*p*-ethylphenyl (8)[a,c]	50	128–129
thiophene	2-thienyl (9)[b]	30[d]	102–105

[a] Satisfactory C, H, combustion analytical data (±0.3%) were obtained for these compounds. [b] Satisfactory high-resolution mass spectral data (±0.002 amu) were obtained for these compounds. [c] The ortho isomer was not separated on Carbowax 20M, OV17, or OV1 columns, but a weak IR band was present at 750 cm^{-1}, suggesting some ortho compound was present. [d] Estimated yield (by NMR).

(1) Presented in part at the 179th American Chemical Society National Meeting, Houston, Tx, Mar 1980.
(2) (a) Olah, G. A. *Aldrichimica Acta* **1979**, *12*, 45. (b) Olah, G. A. "Friedel-Crafts Chemistry"; Wiley-Interscience Publishers: New York, 1973.
(3) Colonge, J.; Rochas, P. *Bull. Soc. Chim. Fr.* **1948**, 818 and the following articles.
(4) Inoue, M.; Sugita, T.; Ichikawa, K. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 174.
(5) Nakajima, T.; Suga, S.; Sugita, T.; Ichikawa, K. *Tetrahedron* **1969**, *25*, 1807.
(6) Inoue, M.; Sugita, T.; Kiso, Y.; Ichikawa, K. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1063.
(7) Inoue, M.; Chano, K.; Itoh, O.; Sugita, T.; Ichikawa, K. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 458.
(8) Nakamoto, Y.; Nakajima, T.; Suga, S. *Kogyo Kagoku Zasshi* **1969**, *72*, 2594; *Chem. Abstr.* **1970**, *72*, 100192.
(9) van Tamelen, E. E. *Acc. Chem. Res.* **1975**, *8*, 152 and references therein.
(10) Johnson, W. S. *Bioorg. Chem.* **1976**, *5*, 51.
(11) (a) van Tamelen, E. E.; Loughhead, D. G. *J. Am. Chem. Soc.* **1980**, *102*, 869. (b) van Tamelen, E. E.; Freed, J. H. *Ibid.* **1970**, *92*, 7202, 7206.
(12) (a) Goldsmith, D. J. *J. Am. Chem. Soc.* **1962**, *84*, 3913. (b) Goldsmith, D. J.; Cheer, C. J. *J. Org. Chem.* **1965**, *30*, 2264.

0022-3263/81/1946-2709$01.25/0

Scheme II



conventional technique.[12] A sodium-dried toluene solution of 1 was treated with a catalytic quantity of $SnCl_4$ (instead of the usual solvent benzene, toluene was used in the interest of safety). After suitable workup, we expected to isolate a mixture of C_{10} rearrangement products.[13] Instead, evaporation of the solvent left a white high-melting soild. NMR and mass spectral data (vide infra) showed that the compound had a tolyl group bonded to a C_{10} bicyclic alcohol. By analogy with the reported ring-opening reactions of 1,[13,14] we suspected that such a compound could arise by the pathway shown in Scheme I.

The proposed product's identity was confirmed by NMR comparison with decalins of the same stereochemistry and substitution pattern. The proton NMR spectrum of these (1*R**, 4*R*, 4a*R*, 8a*R*)-decahydro-4-aryl-1-naphthols agreed with the strong evidence of two independent investigators[15-17] that suggested the CH—O should give a triplet of doublets and the proton attached to the same carbon as the aromatic substituent should give an overlapping doublet of triplets. Table I lists the FC alkylation products of several aromatic compounds.

The mild conditions required for this reaction are surprising. In a typical experiment, 1.0 g of 1 in 22 mL of aromatic solvent was treated with 22 μL of $SnCl_4$ at room temperature or 0 °C. The reaction was essentially complete after 1.5 h. By comparison, phenyloxirane, a conjugated epoxide, failed to undergo significant ring opening under the same conditions. Other epoxide FC reactions have involved at least stoichiometric quantities of Lewis acid promoters,[3-7] We attribute this novel behavior to significant medium-ring strain and through-space interaction in the transition state, which contribute to the expceptionally facile ring opening[13,14,18] of 1.

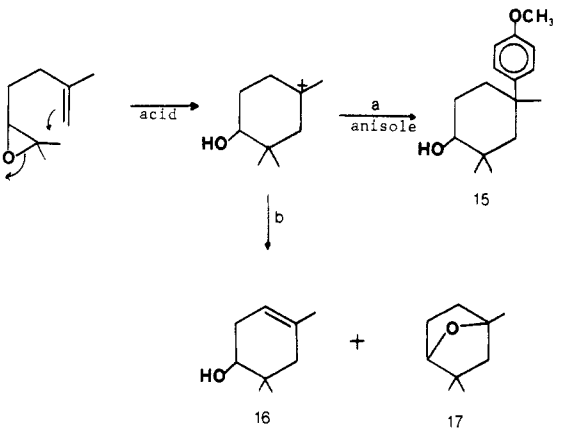
Although toluene gives a high-yield reaction, benzene failed to undergo a FC reaction with *trans*-5,6-epoxy-*cis*-cyclodecene under typical conditions.[19] A similar threshold has been observed for phenyloxirane (styrene oxide)[20] and propylene oxide[4] under certain conditions. Thus, epoxides apparently require a more reactive aromatic compound for FC alkylation to occur than do alkyl halides under similar conditions.[2b] This behavior has been attributed to a large amount of covalent character remaining in the C–O bond broken during the transition state of the alkylation process[7] (thereby reducing the positive character of the reactive species).

Table II. Comparison of Catalysts at Ambient Temperature. Friedel-Crafts Reactions of *trans*-5,6-Epoxy-*cis*-cyclodecene

	distribution (±2%)	
catalyst[a]	% para	% ortho
toluene		
SnCl	75	25
$BF_3 \cdot Et_2O$	73	27
$AlCl_3$	83	17
anisole		
$SnCl_4$	53	47
$BF_3 \cdot Et_2O$	53	47
$AlCl_3$	51	49

[a] Molar quantities of Lewis acids used were equal to that of $SnCl_4$ as described in the Experimental Section.

Scheme III



The FC reaction of 1 and thiophene gave the lowest yield and the largest number of side products and therefore we investigated the identity of these comdpounds. The product distribution (see Scheme II) of this reaction was 62% 7, 10% *endo*-1,4-epoxydecahydronaphthalene[21] (10), 3% *exo*-1,4-epoxydecahydronaphthalene[21] (11), and 25% of an equal mixture of 12 and 13 ($\Delta^{1(2)}$- and $\Delta^{3(4)}$-octalols).[22]

The influence of catalyst on ortho/para ratios was investigated for the FC reactions of 1 with toluene and anisole. Results are shown in Table II. Results with other Lewis acid promoters were similar to those of $SnCl_4$ except for $AlCl_3$. This has been noted before[2b,3-8] and has been attributed to the fact that $AlCl_3$ is insoluble in the reaction medium.

The side products 10–13 can all be formed from the intermediate shown in Scheme I. However, we also suggest the possibility that there is oxygen bridging to the cationic center. The reduced electrophilicity of the reaction intemediate (vide supra) can be explained by the reduced positive character resulting from this bridging. Also, the minimization of skeletal rearrangements (e.g., to the *trans*-fused ring system, which is more stable) may also be a consequence of this bridging. Compound 10 also suggests this conformation is probable and the instability of a secondary carbocation in the nonpolar medium requires stabilization of this sort. Thus the oxygen in epoxide FC reactions can assist selectivity.

(13) Taylor, S. K.; Rose, C. B. *J. Org. Chem.* **1977**, *42*, 2175.
(14) Dittman, W.; Sturzenhofecker, F. *Justus Liebigs Ann. Chem.* **1965**, *688*, 57.
(15) Traynham, J. G.; Hsieh, H. H. *J. Org. Chem.* **1973**, *38*, 868.
(16) Haufe, G.; Muhlstadt, M. *Monatsh. Chem.* **1977**, *108*, 199.
(17) The same ring system and substitution pattern were reported, but the positions occupied by Ar and OH are occupied by other groups in the NMR studies of ref 15 and 16.
(18) Bishoff, P.; Heilbronner, E. *Helv. Chem. Acta* **1970**, *53*, 1677.
(19) Sodium-dried solvent, freshly distilled epoxide, and freshly opened $SnCl_4$ or $BF_3 \cdot Et_2O$ (or fairly anhydrous conditions).
(20) Summerbell, R. K.; Kland-English, M. J. *J. Am. Chem. Soc.* **1955**, *77*, 5095. Under Friedel–Crafts conditions, the authors treated styrene oxide with $SnCl_4$ in benzene and did not observe an alkylation reaction.
(21) Rose, C. B.; Taylor, S. K. *J. Heterocycl. Chem.* **1979**, *16*, 705.
(22) A small amount of carbonyl compound was also present, as indicated by IR spectroscopy.

Potentially, even more selective FC reactions could be accomplished on epoxides such as those studied for biomimetic cyclization.[9-12] We therefore investigated Lewis acid promoted reactions of one such system, geraniolene monoepoxide (14), whose cyclization has been investigated.[12] The reaction is represented in Scheme III, pathway b. In benzene, no FC alkylation was reported.[12] However, we had reason to suspect that toluene or anisole might be alkylated by this epoxide. Despite these expectations, in this case, very little FC alkylation was observed under any conditions. Various concentrations (up to 0.2 equiv relative to epoxide) of Lewis acids ($SnCl_4$, $BF_3{\cdot}Et_2O$, $AlCl_3$, and SbF_5) were combined with freshly distilled geraniolene monoepoxide in sodium-dried toluene or anisole. Also, the reaction was investigated where 50 vol % of the aromatic solvent was replaced by nitromethane acetonitrile, or carbon disulfide. Under these conditions, toluene was never alkylated by geraniolene monoepoxide.[23] Anisole gave only a 5% yield of the product 15, shown in pathway a (Scheme III). Product indentification was based on the absence of vinyl peaks in the NMR spectrum of 15, the presence of a CHOH multiplet that matches that of 16, and mass spectral data (including $M^+ = 248$ for $C_{16}H_{24}O_2$).

Thus we have demonstrated a highly selective catalytic FC alkylation which generates four chiral centers and suggested rationale[24] as to why epoxides may be more selective as Friedel–Crafts alkylating agents than some other compounds. We are continuing studies in this area, particularly with unsaturated epoxides, where not much work has been done and where electronic effects can facilitate selective reactions.

Experimental Section

Infrared spectra were obtained with Perkin-Elmer 137 and Beckman IR 10 spectrophotometers. Gas chromatographic analyses were performed on a Varian A90-P3, F&M 700, Nester/Faust Anakro, or Hewlett-Packard 5712 TC detector instrument, using a 10 ft × 0.25 in. Carbowax 20 M or 7 ft. × 0.25 OV 101 (on Chromosorb W-HP) column. Integration of peak areas was done by cut and weigh techniques or on a Hewlett-Packard 3380 A integrator–recorder. NMR spectra were recorded on Varian A-60 and EM-360 spectrometers. Low-resolution mass spectra were obtained on a Varian MAT A GC/MS, and high-resolution spectra on a Du Pont 21-110 B double-focusing spectrometer. Melting points are uncorrected and were obtained on a Mel-Temp apparatus. Elemental analyses were determined by Galbraith Laboratories, Inc. Epoxides 1[14] and 14[12] were made by previously reported methods. All other chemicals were commercially obtained in reagent purity unless otherwise noted.

General Procedure for the Friedel–Crafts Reaction of *trans*-5,6-Epoxy-*cis*-cyclodecene (1). A 22-μL sample of $SnCl_4$ was injected into a dry flask filled with a stirred mixture of 1.0 g of 1 and 22 mL of sodium-dried aromatic solvent at 25 °C (or 0 °C for thiophene, furan, and anisole). The mixture was stirred for 1.5–3 h and then the organic layer was washed with 5% $NaHCO_3$ and water and dried ($MgSO_4$). Evaporation of the solvent normally left a crystalline solid. If not, the sample was triturated with ether/pentane. The triturated sample was then sublimed [normally at 90 °C (10 mmHg)]. (Product 9 was not sublimed, but was triturated with ether/pentane six times.) Melting points of the sublimed products are given in Table I. The NMR of the C_1HO multiplet was characteristic of compounds 2–9 and is described for compound 2 below.

(1*R,4*R*,4a*R*,8a*R*)-Decahydro-4-(*p*-toluyl)-1-naphthol (2):** mp 156–158 °C IR (KBr) 3100–3650 (OH), 1018 and 809 (para-disubstituted benzene) cm^{-1}; NMR ($CDCl_3$) δ 7.07 (s, 4 H), 3.96 (m, 1 H, HCO, $J_1 = J_2 = 9.5$, $J_3 = 4$ Hz), 2.84 (m, 1 H, Ar CH, $J_1 = 10$, $J_2 = J_3 = 5.3$ Hz), 2.31 (s, 3 H, Ar CH_3), 0.85–2.3 (m, 15 H, remaining hydrogens); mass spectrum *m/z* (relative intensity) 244 (22), 226 (100), 184 (30), 183 (31), 118 (96). The CHO and ArCH multiplets are a triplet of doublets and an overlapping doublet of triplets, respectively. This splitting is discussed in detail in ref 16. GC retention time (oven 210 °C, flow 43 mL/min, Carbowax column) was 37 min.

(1*R,4*R*,4a*R*,8a*R*)-Decahydro-4-(*o*-toluyl)-1-naphthol (3):** IR (NaCl disks) 3100–3650 (OH), 1018 and 755 (ortho-disubstituted benzene) cm^{-1}. GC retention time (oven 210 °C, flow 43 mL/min, Carbowax column) was 33 min (peak slightly overlapped with that of 2). Preparative GC collection of this compound gave contaminated sample due to column bleed at the high temperatures used.

(1*R,4*R*,4a*R*,8a*R*)-Decahydro-4-(3,4-xylyl)-1-naphthol (4).** After the above procedure, evaporation of the *o*-xylene solvent gave 1.29 g (76%) of 4 as white crystals. Sublimation as described yielded crystals: mp 144–146 °C; IR (KBr) 815 (1,2,4-trisubstituted benzene), 1015 (br, OH), 3100–3650 (OH) cm^{-1}; NMR ($CDCl_3$) δ 6.90 (m, 3), 3.94 (td, 1 H, see above), 2.8 (dt, 1 H, see above), 2.21 (s, 6 H, Ar CH_3), 0.8–2.3 (m, 15 H); mass spectrum, *m/z* (relative intensity) 258 (13), 240 (42), 198 (20), 197 (19), 132 (100).

(1*R,4*R*,4a*R*,8a*R*)-Decahydro-4-(*p*-methoxyphenyl)-1-naphthol (5).** After evaporation of the anisole solvent, the concentrate was analyzed by VPC (OV 101 column, column temperature 230 °C) which showed two peaks, 5 and 6, in a 53:47 ratio (5 and 6.6 min, respectively). Preparative VPC collection of the para isomer gave a solid which was triturated with ether/pentane: mp 138.5–139 °C; IR (KBr) 830 (para-disubstituted benzene), 1015 (d, br, OH), 1230 (ether), 3100–3600 (OH) cm^{-1}; NMR ($CDCl_3$) δ 6.9 (AB, $J_{AB} = 9$ Hz, 4 H), 7.78 (s, Ar OCH_3), 3.94 (td, 1 H), 2.8 (dt, 1 H), 0.85–2.4 (remaining 15 H); mass spectrum, *m/z* (relative intensity) 91 (52), 119 (62), 134 (100), 242 (12), 260 (3).

(1*R,4*R*,4a*R*,8a*R*)-Decahydro-4-(*o*-methoxyphenyl)-1-naphthol (6).** After evaporation of the anisole solvent, trituration with ether/pentane enriched the ortho isomer. Sublimation of the solid gave white needles: mp 168–170 °C; IR (KBr) 755 (ortho-disubstituted benzene), 1035 (d, br, OH), 1240 (ether), 3100–3600 (br, OH) cm^{-1}; NMR ($CDCl_3$) δ 6.8–7.2 (m, 4 H, ArH), 3.82 (s, CH_3O), 3.94 (td, 1 H), 3.2 (dt, CHAr, see above for *J*'s), 0.85–2.3 (remaining 15 H); mass spectrum, *m/z* (relative intensity) 91 (26), 119 (15), 121 (16), 134 (100), 242 (11), 260 (5).

(1*R,4*R*,4a*R*,8a*R*)-Decahydro-4-(2-furyl)-1-naphthol (7).** (Reaction temperature −5–0 °C) After evaporation of the furan solvent, the resulting oil was triturated by dissolving in methylene chloride and adding petroleum ether. Repeated trituration and then sublimation [85 °C (30 mmHg)] gave pure crystals: mp 97.5–99.5 °C; NMR of the crude product (aromatic region) showed good evidence for a 2-substituted furan; IR (NaCl disks) 725 (s), 950 (s), 3100–3600 (br, OH) cm^{-1}; NMR ($CDCl_3$) δ 7.3 (m, 1 H), 6.25 (m, 1 H), 5.9 (m, 1 H), 3.94 (t d, 1 H), 2.93 (dt, 1 H), 0.8–2.4 (m, 15 H).

(1*R,4*R*,4a*R*,8a*R*)-Decahydro-4-(*p*-ethylphenyl)-1-naphthol (8).** After the reaction procedure, the oil obtained was triturated with petroleum ether (bp 40–60 °C). The product was recrystalized slowly from ether/pentane at −10 °C, giving crystals: mp 128–129 °C; IR (melted onto NaCl disks) 830 (para-disubstituted benzene), 1040 (br, OH), 3100–3600 (br, OH) cm^{-1}; NMR ($CDCl_3$) δ 7.1 (s, 4 H, Ar H), 3.94 (td, 1 H), 2.84 (dt, 1 H), 3.6 (q, 2 H, $J = 7.5$ Hz), 1.2 (t, 3, $J = 7.5$ Hz), 0.8–2.3 (m, 15 H).

(1*R,4*R*,4a*R*,8a*R*)-Decahydro-4-(2-thienyl)-1-naphthol (9).** The reaction (conducted at 0 °C) product was an oil, which when analyzed by VPC (20% SE-30 column, 6 ft × 0.25 in., 180 °C column temperature) showed five compounds as described in the discussion. NMR, IR, and GC of the side products is describeed in ref. 13 and 21: IR (NaCl disks) 690 (s), 1040 (d, br, OH), 1440 (s), 3100–3600 (br, OH) cm^{-1}; NMR ($CDCl_3$) δ 6.9–7.3 (m, 3 H), 3.94 (td), 2.8 (m, 1 H), 0.8–2.3 (m, 15 H); mass spectrum, *m/z* (relative intensity) 110 (60), 134 (47), 218 (100), 236 (47).

(23) The intermediate represented in Scheme III is tertiary and therefore steric hindrance may inhibit FC alkylation. This has been suggested as a reason for the lack of FC alkylation with isobutylene oxide (see ref 7).

(24) A reviewer has pointed out that the reduced reactivity of epoxide 1 may result from some steric hindrance to alkylation. He also suggested that the stereoselectivity of the FC alkylation could be a result of a near concerted reaction. The latter suggestion is quite plausible since other epoxides have been shown to undergo S_N2-like reactions (see ref 4–7). We appreciate the reviewer for his suggestions.

2,2,4-Trimethyl-4-(*p*-methoxyphenyl)cyclohexanol (15). To freshly distilled geraniolene monoepoxide (0.85 g, 6 mmol) in 15 mL of sodium-dried anisole was added slowly 0.4 g (1.5 mmol) of $SnCl_4$ at 0 °C. The resulting mixture was stirred at room temperature for 3 h. The organic layer was diluted with 25 mL of ether, then washed with 10% HCl, 5% $NaHCO_3$, and H_2O, and dried ($MgSO_4$). The in vacuo evaporated organic layer (0.12 g) was analyzed by VPC (Carbowax column, 192 °C) and found to give the same compounds as reported by Goldsmith for the previous reaction in benzene[12a] and also a late peak at 30.5 min (which was 67% of the product distribution, or 5% yield) identified as **15** as follows. The compound was isolated by preparative VPC: IR (AgCl disks) 825 (m, para-disubstituted benzene), 1015 (s, br, OH), 1250 (s, anisole ether), 1510 (s), 3100–3600 (br s, OH) cm^{-1}; NMR (CCl_4) δ 6.9 (AB, 4 H, *p*-anisyl, J_{AB} = 9 Hz), 3.7 (s, 3 H), 3.2 (m, 1 H, CH–O), 0.8–2.3 (m, br, remaining 16 H); mass spectrum, *m/z* (relative intensity) 51 (100), 77 (20), 91 (22), 121 (42), 133 (22), 147 (20), 148 (44), 161 (35), 162 (21), 215 (43), 230 (4), 233 (12), and 248 (6).

Acknowledgment. The support of Research Corporation (C1108), Olivet Research Associates, and the National Science Foundation (CDP-8006131) is gratefully acknowledged. Discussions with Peter Beak, Peter Kovacic, Michael P. Doyle, Frank L. Schadt III, and Thomas E. Dueber were also very helpful. M. Beeny provided valuable mass spectral assistance, and Kurt L. Loening of Chemical Abstracts Service gave nomenclature advice.

Registry No. 1, 24639-32-5; 2, 77461-84-8; 3, 77461-85-9; 4, 77461-86-0; 5, 77461-87-1; 6, 77461-88-2; 7, 77461-89-3; 8, 77461-90-6; 9, 77461-91-7; 14, 62823-51-2; 15, 77461-92-8.

Addition Compounds of Alkali Metal Hydrides. 20. Reaction of Representative Mono- and Dialkylboranes with Saline Hydrides To Form the Corresponding Alkylborohydrides

Herbert C. Brown,* Bakthan Singaram,[1a] and C. Punnoose Mathew[1b]

Richard B. Wetherill Laboratory, Purdue University, West Lafayette, Indiana 47907

Received September 16, 1980

The reaction of lithium, sodium, and potassium hydrides with representative mono- and dialkylboranes in tetrahydrofuran was examined in detail with respect to rate, stoichiometry, and products. With the exception of 9-borabicyclo[3.3.1]nonane and thexylborane, all other organoboranes examined react with lithium hydride sluggishly and incompletely. On the other hand, sodium hydride exhibits a much greater reactivity than lithium hydride in these reactions. The rate of the reaction is strongly influenced by the steric requirements of the alkylboranes. Thus, the rates of reaction of sodium hydride with a series of dialkylboranes at 25 °C follow the order 9-borabicyclo[3.3.1]nonane > dicyclohexylborane > disiamylborane > diisopinocampheylborane. The reactivity of potassium hydride in this reaction greatly exceeds that of sodium hydride. It reacts almost instantaneously and quantitatively. The reaction with mono- and dialkylboranes involves a 1:1 stoichiometry, producing the corresponding alkali metal mono- and dialkylborohydrides, characterized by hydride analysis, IR, and ^{11}B NMR spectral characteristics. These derivatives are very stable and can be stored under nitrogen at 25 °C without any hydride loss, redistribution, or isomerization of the alkyl groups. Methyl iodide readily and quantitatively removes metal hydride from these adducts, regenerating the free mono- and dialkylboranes. The present study also provides a simple method for preparing a wide variety of hitherto unknown lithium, sodium, and potassium mono- and dialkylborohydrides under mild conditions, as well as a procedure for storing mono- and dialkylboranes for extended periods of time.

In recent years a number of alkali metal trialkylborohydrides have emerged as highly attractive reducing agents in organic synthesis, capable of achieving stereo- and regioselective transformations unequaled by other reagents currently available. Numerous applications of these new reducing agents have already been reported.[2]

This paper deals exclusively with the alkali metal alkylborohydrides. Consequently, a short history of these derivatives is in order. Trialkylborohydrides were first prepared by Schlesinger, Brown, and co-workers in the period of 1942 to 1945.[3] A detailed study of these reactions was later carried out using vacuum-line techniques.[4] Köster and co-workers have reported the synthesis of a number of trialkylborohydrides using rather harsh reaction conditions in the absence of ethereal solvents.[5] However, the results reveal that the reaction between trialkylboranes and alkali metal hydrides proceeds far better in tetrahydrofuran (THF)[2a] or ethyl ether (EE) than in hydrocarbon solvents or under neat conditions.[5]

Recently a systematic study of the rates of reaction of lithium and sodium hydrides with trialkylboranes of increasing steric requirements has been described.[6] Most unhindered organoboranes react completely with lithium hydride in a few hours under reflux. The corresponding deuterium derivatives can be conveniently prepared from lithium deuteride. However, the reaction of hindered

(1) (a) Postdoctoral research associate on Grant No. GM-10937 from the National Institutes of Health. (b) Postdoctoral research associate on Grant No. DAAG 29-79-C-0027 from the U.S. Army Research Office.

(2) (a) Krishnamurthy, S. *Aldrichimica Acta* **1974**, *7*, 55. (b) Brown, H. C.; Dickason, W. C. *J. Am. Chem. Soc.* **1970**, *92*, 709. (c) Krishnamurthy, S.; Brown, H. C. *Ibid.* **1976**, *98*, 3383. (d) Krishnamurthy, S.; Brown, H. C. *J. Org. Chem.* **1976**, *41*, 3064. (e) Krishnamurthy, S.; Vogel, F.; Brown, H. C. *Ibid.* **1977**, *42*, 2534.

(3) Brown, H. C.; Schlesinger, H. I.; Sheft, I.; Ritter, D. M. *J. Am. Chem. Soc.* **1953**, *75*, 192.

(4) Khuri, A. Ph.D. Thesis, Purdue University, 1960.

(5) Binger, P.; Benedikt, G.; Rotermund, G. W.; Köster, R. *Justus Liebigs Ann. Chem.* **1968**, *717*, 21.

(6) Brown, H. C.; Krishnamurthy, S.; Hubbard, J. L. *J. Am. Chem. Soc.* **1978**, *100*, 3343.

0022-3263/81/1946-2712$01.25/0