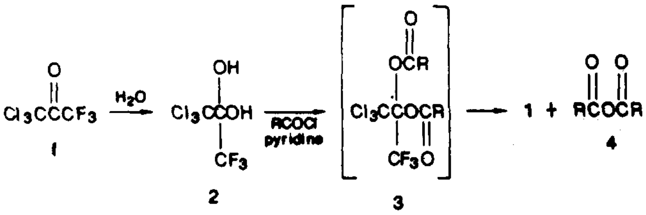
Table I. Preparation of Acid Anhydrides

product [RC(=O)-OC(=O)R],^{a} R	yield, %	mp or bp (torr), °C		crystallization solvent
		this expt	lit.	
C_6H_5	97	41	42–43^{9}	hexane
C_6F_5	97	67	69^{10}	hexane
p-ClC_6H_4	89	196	192–193^{3,11}	benzene
$C_6H_4CH{=}CH$	91	138	138^{1,9}	hexane–acetone
2-naphthyl	89	138	133–134^{12}	hexane–acetone
$CH_2{=}C(CH_3)$	93	197–205 (760)	89 (5)^{4}	
p-$HO_2CC_6H_5$^{b}	80	>360		
succinic	85	118	119–120^{9}	chloroform
pivalic	0			

[a] Known compounds were confirmed by MS and also by comparing their IR's with those found in the literature. [b] New Compound: IR (KBr) 3430 (br, OH), 1785 and 1730 (C=O, ánhydride), 1210 cm^{-1}; MS, *m/z* 314 (M^+), 165 ($HOOCC_6H_4COO$), 149 ($C(=O)C_6H_4COOH$), and 104 ($C(=O)C_6H_4$). Anal. Calcd for $C_{16}H_{10}O_7$: C, 61.15; H, 3.21. Found: C, 61.21; H, 3.18. This compound was a white solid and was insoluble in all solvents tested.

the reaction time is short, and several anhydrides are obtained in high yields as summarized in Table I.

The strategy for this reaction is derived from the work of Newallis and Lombardo[7] who prepared and pyrolyzed hemiketal esters from *sym*-dichlorotetrafluoroacetone. Thus we postulate here that trichlorotrifluoroacetone (1) reacts with water to form hydrate[8] 2, which reacts in turn with a carboxylic acid chloride, giving diacyl intermediate 3, which collapses to the desired anhydride 4.



Attempts to isolate 3 by performing the reaction at 0 °C (for R = C_6H_5) were unsuccessful, but the desired product was obtained as usual. Reaction of pivalyl chloride and trichlorotrifluoroacetone hydrate gave no product; instead starting material and pivalic acid were recovered.

Experimental Section

Infrared spectra were taken on Perkin-Elmer Model X99 spectrophotometer and the absorptions are reported in wave numbers (cm^{-1}). Mass spectra were obtained on a Nuclide 12-90-G instrument. Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Elemental analysis was performed by MultiChem Laboratories. 1,1,1-Trichloro-3,3,3-trifluoroacetone was obtained from Fluka Chemical Co. Toluene, pyridine, and ethyl acetate were obtained from Aldrich Chemical Co.

General Method. Trichlorotrifluoroacetone (10 mmol) and water (10 mmol) were stirred at room temperature for 5 min. Toluene (8 mL) was added followed by a carboxylic acid chloride (20 mmol). Pyridine (20 mmol) was added over 5 min (exothermic reaction). After the reaction mixture was stirred at room temperature under N_2 for 30 min, EtOAc (30 mL) and 5% aqueous HCl (10 mL) were added. The separated organic layer was washed once with 20 mL of water and dried over anhydrous Na_2SO_4. Evaporation of the solvent afforded nearly a pure product, which could be purified by the usual techniques.

Acknowledgment. This work was supported by Grant CR812740 from the Reproductive Effects Assessment Group of the U.S. Environmental Protection Agency and National Cancer Institute Grant CA35843. Contribution 285 from the Barnett Institute of Chemical Analysis.

Registry No. 1, 758-42-9; 4 (R = C_6H_5), 93-97-0; 4 (R = C_6F_5), 15989-99-8; 4 (R = *p*-ClC_6H_4), 790-41-0; 4 (R = $C_6H_4CH{=}CH$), 538-56-7; 4 (R = 2-napthyl), 20176-11-8; 4 (R = methacryl), 760-93-0; 4 (R = *p*-$HO_2CC_6H_4$), 18431-45-3; 4 (R = succtine), 108-30-5; 4 (R = pivalic), 1538-75-6; C_6H_5COCl, 100-44-7; C_6F_5-COCl, 2251-50-5; *p*-ClC_6H_4COCl, 122-01-0; $C_6H_4CH{=}CHCOCl$, 102-92-1; $CH_2 = C(CH_3)COCl$, 920-46-7; *p*-$HO_2CC_6H_4COCl$, 100-20-9; 2-napthoyl chloride, 2243-83-6; succinoyl chloride, 543-20-4; pivaloyl chloride, 3282-30-2.

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(6) Other applications of trichlorotrifluoroacetone are its good solvent properties for polymers (Middleton, W. J.; Lindsey, R. V. *J. Am. Chem. Soc.* **1964**, *86*, 4948) and the trifluoroacetylation of amines and amino acids (Panetta, C. A. *Org. Synth.* **1977**, *56*, 122).

(7) Newallis, P.; Lombardo, P. *J. Org. Chem.* **1965**, *30*, 3834.

(8) Halogenated acetones readily form hydrates such as **2**: Miller, C. B.; Woolf, C. U.S. Patent 2 870 211, 1959.

(9) *Handbook of Chemistry and Physics*, 64th ed.; CRC: Cleveland, OH, 1983.

(10) Schmeisser, M.; Weidenbruch, M. *Chem. Ber.* **1967**, *100*, 2306.

(11) Allen, C. F.; Kibler, C. J.; McLachlin, D. M.; Wilson, C. V. *Organic Syntheses*; Wiley: New York, 1955; Collect. Vol. III, p 28.

(12) *Handbook of Data on Organic Compounds*; CRC: Boca Raton, FL, 1985.

Calcium and Lithium Reductions of Epoxides in Ethylenediamine. A Comparison Study

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Recently we reported[1,2] that calcium dissolved in ethylenediamine (or in mixtures containing ethylenediamine) is very effective in reducing aromatic ring systems to monoalkenes. In this respect, it resembles the chemistry of lithium dissolved in low molecular weight amines.[3] Furthermore, in the presence of a proton source like *tert*-butyl alcohol, calcium reductions (like lithium) can be stopped at the dihydro stage to give Birch-type products.[4] Thus far we have not reported reduction of functional groups with the calcium–ethylenediamine reagent. Herein we report that the calcium reagent is capable of reducing epoxides to alcohols.

Elegant work by Brown[5] and co-workers has shown that lithium in ethylenediamine can effect facile reductions of labile epoxides. It is a particularly useful procedure in those cases where lithium aluminum hydride reductions are slow or result in rearrangements. In Table I are compared the results obtained with both calcium and lithium reductions of six epoxides. The lithium reductions were carried out exactly as those previously described[5a] except that the amount of epoxide used was somewhat larger. The yields reported in all cased are based on material actually in hand after workup.

The 9,10-epoxyoctahydronaphthalene was prepared from $\Delta^{9,10}$-octalin[6] of 96% purity. Likewise, the 8,9-ep-

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(1) Benkeser, R. A.; Kang, J. *J. Org. Chem.* **1979**, *44*, 3737.

(2) (a) Benkeser, R. A.; Belmonte, F. G.; Kang, J. *J. Org. Chem.* **1983**, *48*, 2796. (b) Benkeser, R. A.; Belmonte, F. G.; Yang, M. *Synth. Commun.* **1983**, *13*, 1103.

(3) Benkeser, R. A.; Robinson, R. E.; Sauve, D. M.; Thomas, O. H. *J. Am. Chem. Soc.* **1955**, *77*, 3230.

(4) Benkeser, R. A.; Laugal, J. A.; Rappa, A. *Tetrahedron Lett.* **1984**, *25*, 2089.

(5) (a) Brown, H. C.; Ikegami, S.; Kawakami, J. H. *J. Org. Chem.* **1970**, *35*, 3243. (b) Brown, H. C.; Ikegami, S.; Kawakami, J. H. *J. Am. Chem. Soc.* **1970**, *92*, 6914.

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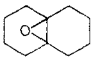
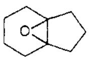
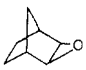
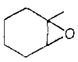
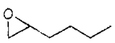
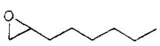
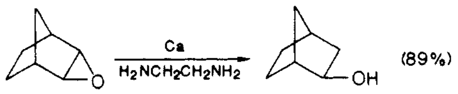
Table I. Comparison of Lithium and Calcium Reduction of Epoxides in Ethylenediamine

entry	starting material[a]	products	product yield,[b,c] %			ref
			1.5 equiv of Li	2 equiv of Ca	5 equiv of Ca	
1		$\Delta^{9,10}$-octalin	3[b]	16	18	
		trans-9-decalol	85 (100)	75 (88)	72 (100)	9, 10
		cis-9-decalol	11	10	10	11
2		4,5,6,7-tetrahydroindan	2	10	10	
		trans-8-hydrindanol	39 (90)	42 (95)	45 (95)	12
		cis-8-hydrindanol	53	47	45	12, 13
3		*exo*-2-norbornanol[d]	99 (93)	99 (90)	100[e] (91)	14, 15
4		1-methylcyclohexene	1	3		
		1-methylcyclohexanol	96 (82)	97 (94)		15
5		2-hexanol	100 (88)	100 (91)		15
6		*n*-octane	1[e]	3		
		2-octanol	98 (88)	97 (89)		15

[a] In every case, 19–25 mmol of epoxide was used. [b] Where percentages do not sum to 100% the remaining material was not identified. [c] Isolated yield or material balance is reported in parentheses. [d] The absence of *endo*-2-norbornanol was confirmed by coinjection of an authentic sample. [e] Analysis was made after solvent removal.

oxytetrahydroindan was prepared from 4,5,6,7-tetrahydroindan of 95% purity. The reduction of *exo*-2,3-epoxynorbornane (Table I, entry 3) with calcium is particularly noteworthy (eq 1). As with lithium, *exo*-2-norbornanol was obtained without any noticeable rearrangement. This epoxide is rather difficult to reduce with lithium aluminum hydride. Because of the stringent conditions[7] needed with this reagent, there was 16% of 7-norbornanol obtained as a rearrangement product in addition to the expected 2-norbornanol.



(1)

The calcium reductions were normally carried out with a 100% excess of the metal (2 equiv) as shown in Table I. When larger amounts of calcium (5 equiv) were used, the yields and product distribution were not improved (Table I). In addition, such reductions were accompanied by excessive foaming, the workups were plagued with emulsion problems, and the crude products were more colored.

An examination of Table I indicates that calcium reductions in most instances give quite similar results to those with lithium. The use of calcium may be the method of choice in large-scale reductions of epoxides where costs and safety become significant factors.

Experimental Section

General. Calcium and lithium were obtained from Alfa Products as 1–3-mm shot and 3.2-mm wire, respectively, and were stored in an argon atmosphere until use. Ethylenediamine (Aldrich) was predried over NaOH pellets for several days, then refluxed over CaH_2 for at least 6 h, and distilled immediately before use. The 1,2-epoxyhexane, 1,2-epoxyoctane, and *exo*-2,3-epoxynorbornane (Aldrich) were used without further purification. The 1-methyl-1,2-epoxycyclohexane, 9,10-epoxyoctahydronaphthalene, and 8,9-epoxytetrahydroindan were prepared from the olefins by standard procedures[5] and distilled before use. The alkenes used in the preparation of the latter two epoxides were prepared in high purity by calcium reduction of the corresponding aromatics.[6] All alcohols were identified by comparison of their melting points, ^1H and/or ^{13}C NMR spectra with published data. Proton spectra were obtained with a Perkin-Elmer Model R-32 operating at 90 MHz. Carbon NMR data were obtained with a Varian Model XL-200 operating at 50.3 MHz. All GLC analyses were performed on a Varian Model 3700 chromatograph containing a 45 m × 0.2 mm (i.d.) capillary column [FFAP; WCOT on vitreous silica (Analabs)]. Product distributions are uncorrected. The presence of alkene and alkane byproducts was confirmed by coinjection of authentic samples. For preparatory GLC work, an Aerograph Model 200 equipped with a 12 ft × $^1/_4$ in. FFAP column (10% on Chromosorb W-HP) was used.

Method A. Lithium Reduction Procedure.[5] To a 300-mL three-necked flask equipped with a septum outlet and a Teflon mechanical stirrer (under argon) were added 25 mmol of epoxide and 25 mL of ethylenediamine. Then 0.52 g (0.075 mol) of lithium (2–5-mm pieces, pentane washed) was added with vigorous stirring. Reaction began immediately and was vigorously exothermic. An ice–water bath was sufficient, when necessary, to control the refluxing. The reaction was considered complete when the deep blue color had faded to off-white and a lavender appeared (10 min–2 h). The mixture was cooled to 0 °C, and 25 mL of ice water was added rapidly. Sufficient water (ca. 50 mL) was added to dissolve the solids, and the solution was extracted twice with 80 mL of diethyl ether. The combined extracts were washed with 40 mL of brine, dried with Na_2SO_4, and analyzed. The ether was removed by rotary evaporation at reduced pressure or by fractional distillation at atmospheric pressure. The isolated crude products were typically colorless or pale yellow.

Method B. Calcium Reduction Procedure. To an oven-dried 500-mL three-necked flask equipped with a septum outlet and a Teflon mechanical stirrer (under argon) were added 2.00 g (0.05 mol) of calcium shot, 20 g of white sand (water washed and dried), 25 mmol of epoxide, and 75 mL of ethylenediamine. Reaction was apparent during the first hour of vigorous stirring, evidenced by foaming and subtle color changes, including the appearance of dissolving calcium as dark blue streaks in an opaque blue-gray mixture. The reactions were at most mildly exothermic. After 24 h the mixture was cooled to 0 °C, and 50 mL of diethyl ether was added, followed by 50 mL of saturated aqueous NH_4Cl over a 15-min period. The mixture was further diluted with 50 mL of water and extracted three times with 50 mL of ether. The combined extracts were washed with two 50-mL portions of water, two 50-mL portions NH_4Cl, and 50 mL of saturated aqueous $NaHCO_3$, then dried with Na_2SO_4, and analyzed. (It had been established that the acid and base washes do not affect the epoxide starting materials.)[8] The solvent was removed as in method A.

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(6) Prepared by reducing tetralin or indan with calcium in ethylenediamine or a mixture of methylamine–ethylenediamine (ref 2) followed by a purification of the crude product by oxymercuration–demercuration.

(7) Kwart, H.; Takeshita, T. *J. Org. Chem.* **1963**, *28*, 670.

(8) Rappa, A., Purdue University, unpublished results, 1984.

(9) Christol, H.; Solladie, G. *Bull. Soc. Chim. Fr.* **1966**, 1299.

(10) Ayer, W. A.; Browne, L. M.; Fung, S.; Stothers, J. B. *Org. Magn. Reson.* **1978**, *11*, 73.

(11) Browne, L. M.; Klinck, R. E.; Stothers, J. B. *Org. Magn. Reson.* **1979**, *12*, 561.

(12) Schneider, H.-J.; Nguyen-Ba, N. *Org. Magn. Reson.* **1982**, *18*, 38.

The crude products were typically light pale yellow or amber.

Acknowledgment. This work was supported by the Department of Energy Office of Basic Energy Sciences under Contract DE-AC02-81ER10989.

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(13) Arnal, C.; Bessiere, J.-M.; Christol, H.; Vanel, R. *Bull. Soc. Chim. Fr.* **1967**, 2479.

(14) Walborsky, H. M.; Loncrini, D. F. *J. Am. Chem. Soc.* **1954**, *76*, 5396.

(15) Aldrich proton NMR library.

Communications

Stereocontrolled Synthesis of American Cockroach Sex Pheromone, Periplanone B

Summary: The stereoselective synthesis of periplanone B, the sex excitant pheromone of the American cockroach, and a discussion of the diastereoselectivity of C(2),C(3)-epoxidation based on MM2 calculations are presented.

Sir: Periplanone B (**9**), the sex excitant pheromone of the American cockroach, is an attractive synthetic target because of its challenging structural features as well as its high level of biological activity.[1] Syntheses of periplanone B have been achieved by Still[2] and Schreiber[3] in which crucial germacranoid intermediates were constructed by anion-induced oxy-Cope rearrangement.[4] Our approach described here is strategically quite different from the existing ones in the construction of the ten-membered ring. It also presents an epoxidation which is highly stereoselective.

Predictions of stereoselectivity in medium ring systems can be quite difficult since they have many conformational options. Molecular mechanics calculations have proven useful in the prediction of the stereoselectivity in macrocyclic systems.[5] As described below, MM2 calculations[6] of the model compound **10** in respect to strain energies and conformational distributions (Figure 1) suggest that changing the C(5) stereochemistry to the silyloxy methyl **6** from the C(5) exocyclic methylene (Still's intermediate) could provide a highly stereoselective C(2,3)-β-epoxidation. Previous workers[2-4] who used the exocyclic methylene reported only 4:1 stereoselectivity. Thus, in our synthetic plan (Scheme I) the enone **6** is the key intermediate and its ten-membered skeleton is constructed by the intramolecular alkylation[7] of the protected cyanohydrin **4** (X = CN, Y = OCHMeOEt). The cis 1,4-relative stereochemistry[8] between C(5) and C(8) in **6** is constructed by a stereoselective Claisen rearrangement of the allylic alcohol **2** in which the syn-1,2-stereochemical relationship at C(5) and C(6) is introduced by the reduction of the carbomethoxy ketone **1** with L-Selectride (Aldrich).

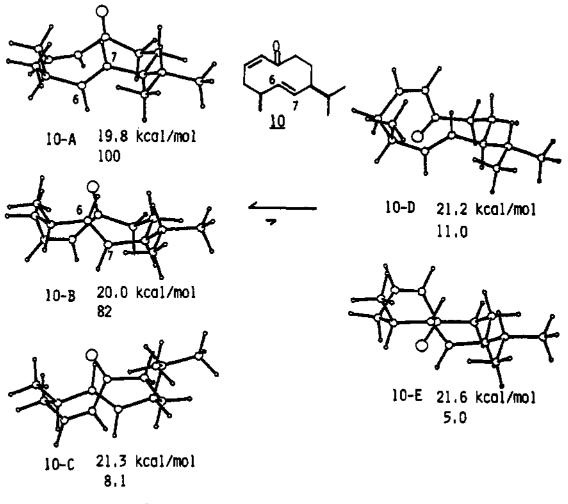
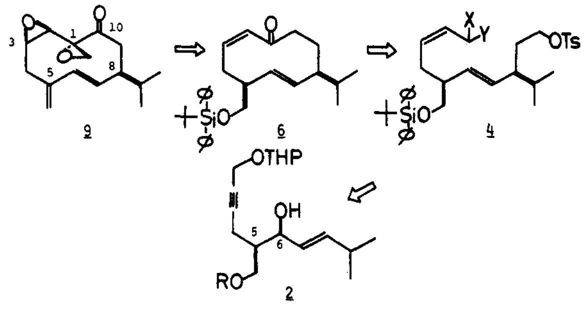


Figure 1. ORTEP drawing of conformers **10A–E** with calculated steric energies and relative ratio (at room temperature).

Scheme I



With use of the ring-making computer program at 30° dihedral angle resolution and the MM2 molecular mechanics program, the lower energy conformations of the enone **10** were constructed (Figure 1). The calculated lowest energy conformations were qualitatively the same as those found from ^{1}H NMR spectra.[9] When an early transition state was assumed in the peripheral attack epoxidation at C(2),C(3), conformations **10-A,B,C** and **10-D,E** should lead to the α- and β-epoxy ketones, respectively. These conformational distributioins of **10** suggest

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[1] (a) Persoons, C. J.; Verwiel, P. E. J.; Talman, E.; Ritter, F. J. *J. Chem. Ecol.* **1979**, *5*, 219. (b) Adams, M. A.; Nakanishi, K.; Still, W. C.; Arnold, E. V.; Clardy, J.; Persoons, C. J. *J. Am. Chem. Soc.* **1979**, *101*, 2495. (c) Kitamura, C.; Takahashi, S. *Appl. Ent. Zool.* **1976**, *11*, 373.

[2] Still, W. C. *J. Am. Chem. Soc.* **1979**, *101*, 2493.

[3] Schreiber, S. L.; Santini, C. *J. Am. Chem. Soc.* **1984**, *106*, 4038.

[4] Recently German and Japanese groups have independently succeeded the synthesis of periplanone B using oxy-Cope rearrangement and internal alkylation, respectively. (a) Hauptmann, H.; Muhlbauer, G.; Walker, N. C. P. *Tetrahedron Lett.* **1986**, *27*, 1315. (b) Kitahara, T.; Mori, M.; Koseki, K.; Mori, K. *Ibid.* **1986**, *27*, 1343.

[5] (a) Still, W. C.; Galynker, I. *Tetrahedron* **1981**, *37*, 3981. (b) Still, W. C.; Macpherson, L. J.; Harada, T.; Callahan, J. F.; Rheingold, A. L. *Tetrahedron* **1984**, *40*, 2275.

[6] Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 3282.; QCPE No. 395. Parameters for the conjugated π-system (enone) were estimated using VESCF-MO calculation of the MMPI method. Allinger, N. L.; Sprague, J. T. *J. Am. Chem. Soc.* **1973**, *95*, 3893; QCPE No. 318.

[7] Takahashi, T.; Kitamura, K.; Tsuji, J. *Tetrahedron Lett.* **1983**, *24*, 4695.

[8] Our epoxidation (**6**–**7**) is analogous to Still's and Schreiber's epoxidations; however, the stereoselective construction of cis stereochemistry at C(5) and C(8) in **6** is difficult by their methods.

[9] Although conformational distributions (5:4) based on calculation are not consistent with those (3:1) observed in NMR spectrum, significant changes of C(6) and C(7) protons at 25 °C and −30 °C suggest that two lower energy conformations of **10** are **10A** and **10B**. Modification of parameters are necessary to obtain more exact calculations. ^{1}H NMR spectra of **10** at −30 °C to +40 °C and preparative procedures of **1** and **10** are available in supplementary material.

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