was a mercury-containing material, which, on reduction with alkaline $NaBH_4$, furnished a gray precipitate, which was probably metallic Hg.[6]

Neopine and Isoneopine (Wunderly and Brochmann-Hansen[3]). A suspension of 400 mg (1.3 mmol) of thebaine in 16 mL of CH_3OH was added to a stirred suspension of 616 mg (1.9 mmol) of Hg $(O_2CCH_3)_2$ in 12 mL of CH_3OH and the resultant mixture was heated at reflux under N_2 for 50 min. The hot suspension was filtered and the filter cake was washed with 30 mL of CH_3OH. The combined filtrates were evaporated to dryness, leaving 1.005 g of a glassy residue, which was dissolved in 40 mL of 3 N acetic acid. The solution was stirred at room temperature under N_2 for 90 min before being treated with 28 mL of saturated KBr solution. Stirring at room temperature was continued for 60 min and the mixture was filtered. The cake was washed with H_2O, and the combined filtrates were cooled to 0 °C and made strongly alkaline by cautious, portionwise addition of 8.0 g of KOH pellets. A solution of 1.0 g of $NaBH_4$ in 20 mL of H_2O was added over a period of about 5 min. When the addition was complete, the dark-gray suspension was extracted with several portions of $CHCl_3$. The combined extracts were filtered, and the filtrate was concentrated to dryness to leave a brownish, glassy solid, wt 346 mg. This material was chromatographed on 25 g f neutral alumina, using a 3:1 mixture of benzene:$CHCl_3$ for the first three fractions and a 3:2 mixture of the same solvents for the next 3 fractions. Fraction A (1 mg) was thebaine; fraction B (11 mg) was a mixture of thebaine, neopine, and a minor unidentified product; fraction C (10.5 mg) was TLC pure neopine; fraction D (59.4 mg) consisted mainly of neopine and two minor impurities; fraction E (147 mg) was isoneopine contaminated with two minor impurities; fraction F (109 mg) was isoneopine contaminated by one minor impurity. Thus, there was obtained 81 mg (21%) of slightly impure neopine and 256 mg (67%) slightly impure isoneopine. The reported yield[3] of neopine was 11% and 89% for isoneopine, without comment concerning the purity of these isomers.

(6) Dr. R. Ravichandran, a colleague of Professor A. Schultz of this laboratory, repeated this experiment with essentially the same results.

Acknowledgment. This work was supported by a grant (DA-01674) from the National Institute on Drug Abuse.

Registry No. 1, 115-37-7; 3, 16008-33-6; neopinone, 509-66-0; neopine, 467-14-1.

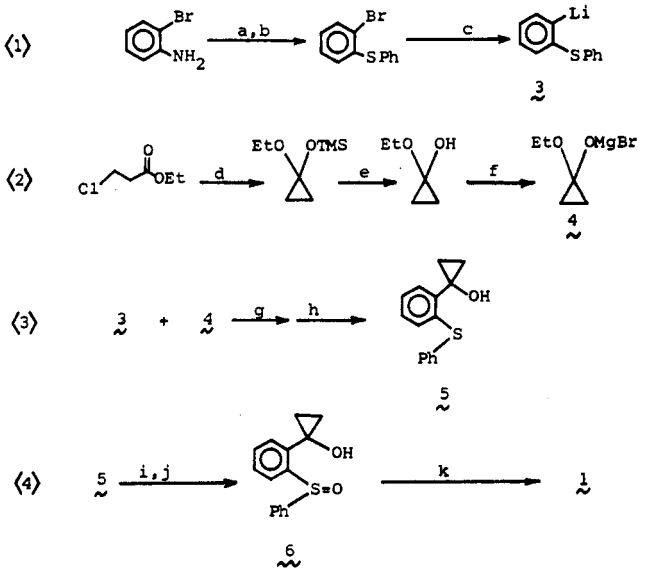
Communications

Synthesis and Reactivity of a Cyclopropyloxy Sulfurane

Summary: We have synthesized cyclopropyloxy sulfurane 1 and report its reactivity relative to *gem*-dimethyl sulfurane 2; the change in reactivity brought about by a minor alteration of the geometry of the five-membered ring is large.

Sir: Westheimer's 1956 observation[1] that barium ethylene phosphate hydrolyzes about 10^7 times faster than barium dimethyl phosphate prompted investigation of the hydrolytic behavior of five-membered cyclic phosphates,[2] phosphonates,[3] phosphonium salts,[4] sulfites,[5] and sulfates[6] vs. their respective acyclic analogues. To one extent or another, it was found that a process that converts a tetrahedral phosphorus or sulfur contained in a five-membered ring to a trigonal-bipyramidal (TBP) phosphorus or sulfur with the five-membered ring spanning axial and equatorial sites is very strongly favored over the same tetrahedral-to-TBP process in a different-sized ring or an acyclic system. The connection between this "five-membered ring effect" and sulfurane chemistry was pointed out by Martin,[7] who realized that sulfurane hydrolysis converts sulfur from TBP to tetrahedral, and therefore this process in a five-membered ring should be, and is,[8] very strongly disfavored relative to acyclic analogues. The exact origin of the five-membered ring effect is subject to various interpretations. In some cases,[9] it may be fairly argued that tetrahedral phosphorus is strained and the facility of hy-

Scheme I[a]



[a] (a) H_2SO_4, $NaNO_2$, 0 °C; (b) NaOH, Cu bronze, PhSH, 5 °C; (c) *n*-BuLi; (d) Na, Et_2O, Me_3SiCl; (e) MeOH, 2 days, room temperature; (f) MeMgBr; (g) Et_2O, reflux 24 h; (h) 0 °C, saturated aqueous NH_4Cl; (i) *t*-BuOCl; (j) 10% aqueous NaOH; (k) CH_3COCl.

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(2) (a) Westheimer, F. H. *Acc. Chem. Res.* **1968**, *1*, 70. (b) Hudson, R. F.; Brown, C. *Ibid.* **1972**, *5*, 204.
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drolysis is a reflection of release of strain on going to the TBP geometry. In other cases,[4a,5b,d,e] mainly involving sulfur, the rate acceleration is clearly not an enthalpy effect. Rather, the differences in $\Delta G^{\ddagger}$ are dominated by the $T\Delta S^{\ddagger}$ term, a phenomenon termed "entropy strain".[10]

We report here the synthesis of sulfurane **1** and a comparison of its hydrolysis with that of the known sulfurane **2**.[11] The angle θ in **1** will probably be significantly larger

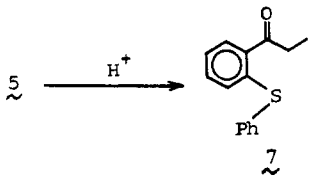
1 **2**

than the corresponding angle in **2**.[12] Thus we hoped to assay the change in reactivity caused by a relatively minor alteration of the geometry of the five-membered ring.

Synthesis of **1** is outlined in Scheme I. A mixture of **3**, obtained by treatment of 2-bromodiphenyl sulfide[17] with *n*-butyllithium, and **4**, from reaction of methylmagnesium bromide with 1-ethoxycyclopropanol,[18] was refluxed in ether for 24 h[19] and afforded sulfide cyclopropanol **5** in 62% yield, after recrystallization from 1:4 CCl_4/hexane. Analytically pure **5** could be obtained by treatment with *n*-butyllithium to give the alkoxide, followed by treatment with wet ether to regenerate **5**. Experimental details appear in the supplementary material.

The stability of **5** deserves comment. When treated with a drop of $CDCl_3$ solution through which HCl had been passed, 1-phenylcyclopropanol rearranged to propiophenone completely in several minutes.[20] Under the same conditions, **5** took 3 days to rearrange to **7**. Nevertheless, all attempts to purify **5** by column chromatography gave substantial amounts of **7**.

The conversion of **5** to **1** could be accomplished directly by treatment with *tert*-butyl hypochlorite, although this method gave side products, noted by NMR but not identified. Conversion of **6** to **1** by either HCl gas or acetyl chloride is well-known sulfurane chemistry,[11] and in our



5 **7**

hands the acetyl chloride method was most satisfactory for **1**. The new sulfurane, mp 126–127 °C, gave satisfactory elemental analysis (C, H, S, Cl) and exhibited the downfield aromatic signal (H ortho to S in fused ring) characteristic of chlorosulfuranes, at 9.25 ppm ($CDCl_3$).[11]

The competitive hydrolysis of **1** and **2** could be followed by ^{13}C NMR. Peaks due to **1** (C_q 71.9 ppm; CH_2 17.3, 11.7 ppm), its hydrolysis product **6** (C_q 55.7 ppm; CH_2 15.8, 14.2 ppm), **2** (C_q 98.5 ppm; CH_3 30.5, 28.6 ppm), and its hydrolysis product 2-(2-hydroxy-2-propyl)-1-(phenylsulfinyl)benzene (C_q 74.7 ppm; CH_3 32.7, 31.5 ppm) do not overlap. When a 1:1 mixture of **1** and **2** in $CDCl_3$ was treated with 1 equiv of D_2O, the resultant spectrum showed that cyclopropyl sulfurane **1** had completely hydrolyzed to form **6** and **2** was unchanged. Conservatively, hydrolysis of **2** to the extent of 10% could have been detected, so **1** is at least 1 order of magnitude more reactive than **2**. In another experiment **1** and **2** separately were treated with a large excess of D_2O and followed by ^1H NMR analysis. Sulfurane **1** had a half-life of 14 min, whereas sulfurane **2** was 52% consumed after 15.8 days. This very crude comparison indicates **1** is roughly 2×10^3 times more reactive than **2**.

The change from *gem*-dimethyl to cyclopropyl, i.e., **2** → **1**, changes not only the geometry of the five-membered ring but also the electronic character of the apical ligand. The cyclopropyl group is known to be an electron-withdrawing group when held "perpendicular" to an adjacent positive center. Adamantyl-1-tosylate having a cyclopropyl ring spiro-fused at C-2, solvolyzes 6.3×10^{-3} times as fast as adamantyl-1-tosylate.[21] In sulfurane **1**, the cyclopropyl group is held perpendicular to the adjacent terminus of the hypervalent bond. Since the termini of three-center four-electron bonds are quite electron rich,[16] the cyclopropyl group in this case would exert a stabilizing effect. In the probable sulfonium ion intermediates, the electron-withdrawing cyclopropyl group would destabilize **8** relative to **9**. Thus, on purely electronic grounds, one predicts **1** to be less reactive than **2** toward hydrolysis, contrary to fact.

8 **9**

A plausible explanation involves the following steric argument. If the angle θ is indeed larger in **1** than in **2**, the S–O bond in **1** is longer than that in **2**. Since the lengthening (and eventual breaking) of the S–Cl bond most likely involves lengthening of the S–O bond, the longer S–O bond of **1** places it further along the reaction coordinate than **2**. This is entropy strain. Such an argument is of course conjectural, albeit reasonable. No crystal structure data exist for either **1** or **2**; however, we are in the process of obtaining suitable crystals of each.

Cyclopropyloxy sulfurane **2** also exhibits some interesting chemistry that we discuss below in a preliminary

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(11) Martin, J. C.; Balthazor, T. M. *J. Am. Chem. Soc.* **1977**, *99*, 152.
(12) Examples from the literature suggest that this will be true only to the extent that the S–O bond is weak and deformable. For example when the effect of the *gem*-dimethyl-to-cyclopropyl change is transmitted to a nonrigid (indeed, acyclic) skelton a[13] vs. b,[14] the change in angle is

a b

dramatic. When the change is transmitted to a rigid skelton, c[15] vs. d[15] (albeit c lacks the *gem*-dimethyl moiety), the change in angle is nil. Since the S–O bond order is low,[8,16] the skeleton absorbing the *gem*-dimethyl-to-cyclopropyl change is not rigid, and we expect a larger C_{Ph}–C–O angle and a longer S–O bond in **1** relative to **2**.

c d

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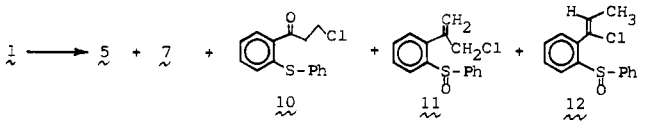
(20) DePuy, C. M.; Mahoney, L. R. *J. Am. Chem. Soc.* **1964**, *86*, 2653.
(21) (a) Martin, J. C.; Ree, B. R. *J. Am. Chem. Soc.* **1970**, *92*, 1660. (b) Schleyer, P. v. R.; Buss, V. *Ibid.* **1969**, *91*, 5880.

fashion. Sulfurane **2** exhibits an ^1H NMR spectrum that is noticeably broad in the cyclopropyl region 0.6–1.7 ppm when $CDCl_3$ purified by passage down a short column of basic alumina is used as the solvent. With a drop of dry HCl-laden $CDCl_3$, the broadening increases, or with a drop of dry pyridine, the broadening is eliminated. This acid-catalyzed process is akin to the racemization observed previously for **2**.[11]

Under strictly anhydrous conditions, **1** decomposes as shown:



Products **10–12** have been identified tentatively. A full description of the chemistry of **1** will be presented in a future publication. At present, the rate enhancement of **1** over **2** is an intriguing result, regardless of the explanation ultimately accepted.

Acknowledgment. We acknowledge an Auburn University Intramural Grant-In-Aid (80-168) and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for financial support of this work.

Registry No. 1, 86064-62-2; **5**, 86046-43-7; **6**, 86046-44-8; 1-ethoxycyclopropanol, 13837-45-1; 2-bromodiphenylsulfide, 15861-48-0.

Supplementary Material Available: Experimental data for **1**, **2**, **5**, and **6** and experimental procedures for preparation of compounds used in this study (3 pages). Ordering information is given on any current masthead page.

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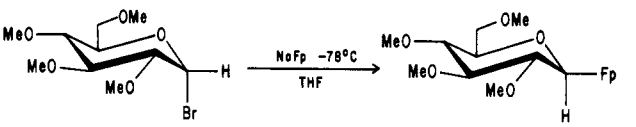
Preparation of a Stable Glucopyranosyliron Compound[1]

Summary: α-D-Glucopyranosyl bromide **1** reacts with sodium (η^5-cyclopentadienyl)dicarbonylferrate at low temperature to afford the stable, stereochemically pure (β-D-glucopyranosyl)iron compound **2**.

Sir: The use of organo-transition-metal chemistry to solve selectivity problems in organic synthesis has been amply demonstrated in recent years.[2] The application of this technology to the carbohydrate field where regioselectivity and stereoselectivity problems are often severe, however, has been rather limited.[3-7] Only a few organo-transition-metal derivatives of carbohydrates have been isolated and characterized.[2a,5b,8] A recent report[9] on the preparation of a series of pyranos-6-yliron compounds and their use in the synthesis of chain-extended sugars prompts us to report our preliminary results on the organoiron chemistry of carbohydrates. We have focused our attention on pyranose derivatives substituted with iron at the anomeric center (C-1). We herein report the preparation and characterization of an unusually stable glucopyranosyliron compound (**2**).



2,3,4,6-Tetra-*O*-methyl-α-D-glucopyranosyl bromide (**1**)[10] in THF reacted immediately when it was added to a solution of sodium (η^5-cyclopentadienyl)dicarbonylferrate (NaFp)[11] (1.2 equiv) in THF at −78 °C.[12] After the THF was removed, the residual crude product was chromatographed on silica gel (ethyl acetate/benzene, 1:2) and then distilled (140 °C (0.2 torr)) to give stereochemically pure (2,6,4,6-tetra-*O*-methyl-β-D-glucopyranosyl)(η^5-cyclopentadienyl)iron dicarbonyl (**2**) as a yellow, crystalline solid (47%). Recrystallization from boiling hexane afforded yellow needles (mp 76–77.5 °C). The structure of **2** was established on the basis of the following spectroscopic and analytical data: NMR ($CDCl_3$) δ 4.80 (s, 5 H), 4.56 (d, 9.3 Hz, 1 H), 3.64 (s, 3 H), 3.57 (s, 3 H), 3.52 (s, 3 H), 3.50 (m, 2 H), 3.39 (s, 3 H), 3.04 (m, 4 H); IR (KBr) cm^{-1} 2008, 1950; high-resolution mass spectrum, *m/z* 340.0948 ($C_{15}H_{24}O_5Fe$, $(M-2CO)^+$, calcd 340.0972). Anal. Calcd C, 51.53; H, 6.11. Found: C, 51.78; H, 6.08. The ^{13}C NMR spectrum exhibited the expected pair of resonances (δ 216.82 and 216.63) for the diastereotopic carbonyls. Pure, crystalline **2** can be handled for short periods of time in air and is stable indefinitely when stored under argon. Solutions of **2** are rapidly attacked by atmospheric oxygen, particularly in the presence of light.

When the glucosylation of NaFp by **1** was carried out at 25 °C and worked up as described above, a comparable yield of product was obtained. The product was shown by NMR to be a 5:1 mixture of **2** and a new, similar compound whose key spectral features (δ 6.54 (d, 5.4 Hz 1 H)

(1) Contribution No. 3158 from E. I. du Pont de Nemours & Co., Inc.
(2) "Transition Metal Organometallics in Organic Synthesis"; Alper, H., Ed.; Academic Press: New York, 1978. Tsuji, J. "Organic Synthesis with Palladium Compounds"; Springer-Verlag: West Berlin, 1980. Rosenblum, M.; et al. *Proc. 3rd IUPAC Symp. Org. Synth. 1980.* Hegedus, L. L. *J. Organomet. Chem.* **1981**, *207*, 185–341.
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(11) Laycock, D. E.; Hartgerink, J.; Baird, M. C. *J. Org. Chem.* **1980**, *45*, 291–299.
(12) All operations were carried out under an argon atmosphere by using standard Schlenk techniques.

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