The Reaction of Acylferrocenes with Dimethyloxosulfonium Methylide and Dimethylsulfonium Methylide

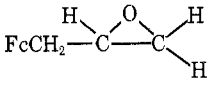
JOHN P. SEVENAIR, DANNY H. LEWIS, AND B. W. PONDER*

Department of Chemistry, University of Alabama, University, Alabama 35486

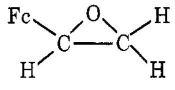
Received June 5, 1972

The reactions of ferrocenecarboxaldehyde, acetylferrocene, and benzoylferrocene with dimethylsulfonium methylide (**4**) give rise, not to the expected epoxides, but to ferrocenylacetaldehydes. Although the epoxides are presumably intermediates in these reactions, ring opening occurs in the direction giving rise to the greatest stabilization of positive charge. The reaction of acylferrocenes with dimethyloxosulfonium methylide (**5**) shows lower reactivity, gives products derived from the attack of both one and two molecules of the ylide, and in the case of ferrocenecarboxaldehyde gives some products not derived from intermediate epoxide formation. The reaction of **4** with acylferrocenes is of synthetic utility.

The synthesis of epoxides containing a ferrocenyl group is not straightforward, since the peroxy reagents often used in such preparations normally oxidize the iron atom to Fe(III). The base-catalyzed formation of epoxides from the corresponding chlorohydrins has been used by Japanese workers[1,2] to prepare 3-ferrocenyl-1,2-epoxypropane (**1**) and some related compounds, but a similar effort by German workers[3] to prepare vinylferrocene oxide (**2**) gave rise to a condensation product of ferrocenylacetaldehyde (**3**). The epoxide **2** was postulated as an intermediate, but no direct evidence for its presence was obtained.



1



2

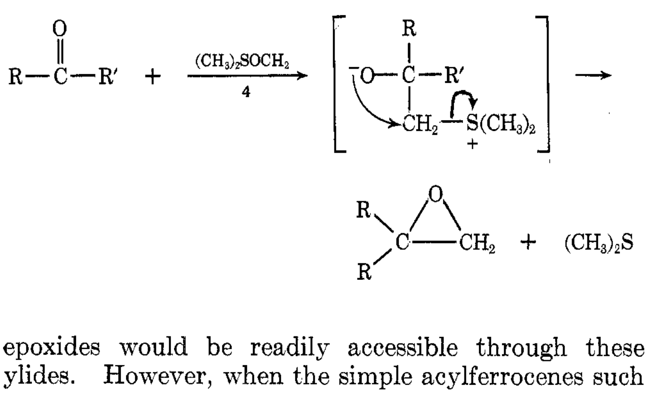
$FcCH_2CHO$

3

Fc = ferrocenyl

The reagents dimethylsulfonium methylide (**4**)[4-6] and dimethyloxosulfonium methylide (**5**),[4,7] introduced by Corey and Chaykovsky, are epoxide-forming reagents but show essentially no oxidizing properties. Both have been found[4] to be of wide application in the preparation of epoxides from aldehydes and ketones; a possible mechanism for their action is given in Scheme I. We originally thought, therefore, that 1-ferrocenyl epoxides would be readily accessible through these ylides. However, when the simple acylferrocenes such as ferrocenecarboxaldehyde, acetylferrocene, and benzoylferrocene were treated with these ylides, the major products were aldehydes, the products of regiospecific epoxide ring opening. These products are shown in Table I.

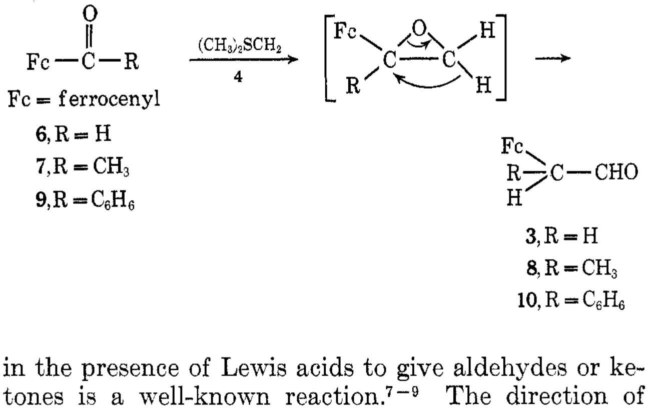
SCHEME I



For example, the reaction of **4** generated under a nitrogen atmosphere at −15° in dimethyl sulfoxide–tetrahydrofuran solution with ferrocenecarboxaldehyde gave ferrocenylacetaldehyde (**3**) and not vinylferrocene oxide (**2**) as the major product. The yield of the aldehyde was 64% and none of the ketone, which would result from the alternate direction of ring opening, was detected. Under the same conditions acetylferrocene (**7**) gave rise to 2-ferrocenylpropionaldehyde (**8**) in 70% yield. Ferrocenylphenylacetaldehyde (**10**) was obtained in 72% yield from benzoylferrocene, but it was observed that the aldehyde was not the initial product in this case. The aldehyde was only isolated after the extremely air- and temperature-sensitive intermediate product, having no aldehyde protons in the nmr, was allowed to stand at room temperature overnight. The latter result suggests that the epoxide in this case is somewhat stable; it seems likely therefore that even more stable 1-ferrocenyl epoxides might be prepared if appropriate substituents were introduced.

These products may be explained by assuming the intermediate formation of the epoxide, followed by regiospecific ring opening and hydride shift to give the aldehyde (Scheme II). The ring opening of epoxides in the presence of Lewis acids to give aldehydes or ketones is a well-known reaction.[7-9] The direction of ring opening in these latter cases is dictated by the

SCHEME II



---

(1) K. Hata, I. Motoyama, and H. Watanabe, *Bull. Chem. Soc. Jap.*, **36**, 1698 (1963).

(2) H. Watanabe, I. Motoyama, and K. Hata, *ibid.*, **39**, 784 (1966).

(3) H. Egger and K. Schlogl, *J. Organometal. Chem.*, **2**, 398 (1964).

(4) E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **87**, 1353 (1965).

(5) E. J. Corey and M. Chaykovsky, *ibid.*, **84**, 3782 (1962).

(6) E. J. Corey and M. Chaykovsky, *Tetrahedron Lett.*, 169 (1963).

(7) E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **84**, 867 (1962).

(8) E. L. Eliel and D. W. Delmonte, *ibid.*, **80**, 1744 (1958).

(9) N. L. Wendler in "Molecular Rearrangements," Part 2, P. de Mayo, Ed., Interscience, New York, N. Y., 1963, p 1035.

TABLE I
PRODUCTS OF THE REACTION OF ACYLFERROCENES WITH SULFONIUM YLIDES

Ylide	Acylferrocene[a]	Product	Yield, %	Scheme
$(CH_3)_2SCH_2$ (**4**)	$FcCHO$ (**6**)	$FcCH_2CHO$ (**3**)	64	II
	$FcCOCH_3$ (**7**)	$FcCH(CH_3)CHO$ (**8**)	70	II
	$FcCOC_6H_5$ (**9**)	$FcCH(C_6H_5)CHO$ (**10**)	72	II
$(CH_3)_2SOCH_2$ (**5**)	$FcCHO$ (**6**)	$FcCH_2COCH_3$ (**11**)	27	II and III
		$FcCH_2CHCH_2O$ (**1**)	18	I and II
		$FcCOCH_3$ (**7**)	1	III
	$FcCOCH_3$ (**7**)	$FcCH(CH_3)CHCH_2O$ (**12**)	40	IV
		$FcCH(CH_3)CHO$ (**8**)	8	IV
	$FcCOC_6H_5$ (**9**)	No reaction		

[a] Fc = ferrocenyl.

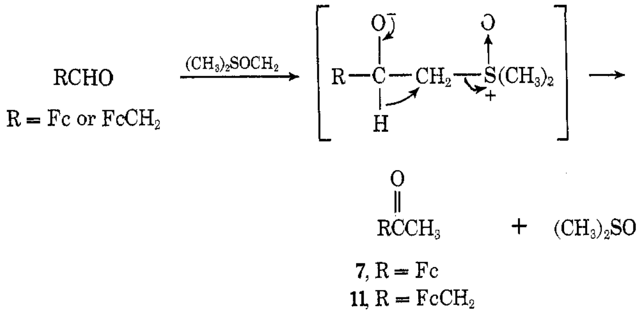
greater stability of an intermediate with positive charge delocalized from a benzyl or other stabilized carbon atom.

The reaction of the acylferrocenes with **4**, however, is conducted under rather basic conditions; the strongest acid employed throughout is water. However, the ability of the ferrocenyl group to stabilize an adjacent positive charge is much greater than that of a phenyl group,[10] and it is not surprising, therefore, that the opening of 1-ferrocenyl epoxides takes place under these very mild conditions.

The yields obtained are such that this method is of considerable utility in the synthesis of ferrocenylacetaldehyde and its derivatives. It should be noted that these products react rather rapidly with atmospheric oxygen; when stored and handled under nitrogen they are stable.

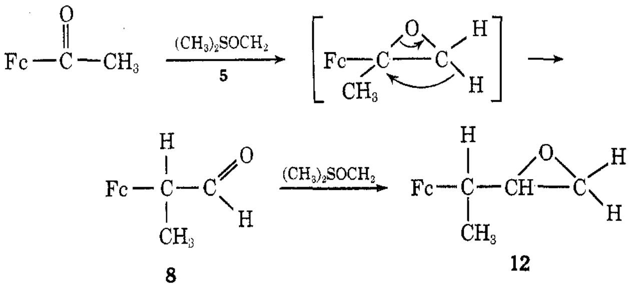
Dimethyloxosulfonium methylide (**5**) is both less reactive and less specific in its reactions with the acylferrocenes than is dimethylsulfonium methylide (**4**). In the reaction of **5** with ferrocenecarboxaldehyde, neither the epoxide **2** nor the aldehyde **3** was detected; however, 3-ferrocenyl-1,2-epoxypropane (**1**), the product resulting from the attack of two molecules of ylide on the original aldehyde, is obtained in 18% yield. The other two products are acetylferrocene (**7**), formed in 1% yield, and ferrocenylacetone (**11**), formed in 27% yield. A reasonable mechanism for the formation of the latter products is shown in Scheme III.

SCHEME III



Addition of the ylide to the aldehyde gives a zwitterionic intermediate similar to that shown in Scheme I, but in this case expulsion of the dimethyl sulfoxide molecule occurs *via* a hydride shift rather than *via* direct displacement by oxygen. The reaction of **5** with acetylferrocene gives products which can be explained by a reaction sequence involving epoxide formation, regiospecific ring opening to the aldehyde, and the formation of a second epoxide as shown in Scheme IV. The products observed from this reaction are the aldehyde **8**, formed in 8% yield, and 3-ferrocenyl-1,2-epoxybutane (**12**), obtained as a mixture of diastereomers in 40% yield. Compound **12** was also synthesized by the reaction of **8** with ylide **4**.

SCHEME IV



The lower reactivity of ylide **5** as compared to ylide **4** is demonstrated by the 41% recovery of acetylferrocene in the previous reaction. Ylide **5** failed to react with benzoylferrocene significantly, even over a 2-day period. The lesser selectivity of **5** in this case may be partially attributed to its greater stability; **4** appears to decompose faster than the intermediate leading to the aldehyde products, while **5** survives long enough under the reaction conditions to react with the initial aldehyde product as it is generated.

This difference in stability of the two ylides might also be a clue as to why the reaction of ylide **5** with ferrocenecarboxaldehyde leads to ketones **7** and **11** (in addition to epoxide **1**) while the reaction of ylide **4** with ferrocenecarboxaldehyde gave only ferrocenylacetaldehyde **3** as the major product. A more complete answer to this question, however, must await further experimental evidence.

Experimental Section

Spectra were recorded using a Perkin-Elmer 337 ir spectrophotometer and a Hitachi Perkin-Elmer R-20B nmr spectrometer; tetramethylsilane was used as internal standard in the nmr work. Microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn., or by Atlantic Microlab, Atlanta, Ga.

---

(10) (a) M. D. Rausch, *Can. J. Chem.*, **41**, 1289 (1963); (b) M. Cais, *Organometal. Chem. Rev.*, **1**, 435 (1966); (c) T. G. Traylor and I. C. Ware, *J. Amer. Chem. Soc.*, **89**, 2304 (1967).

Acylferrocenes were purchased or prepared by standard methods. Trimethyloxosulfonium iodide and trimethylsulfonium iodide were prepared as described by Corey and Chaykovsky.[4] Dimethyl sulfoxide (DMSO) was purified by vacuum distillation from calcium hydride; tetrahydrofuran (THF) was dried by distillation from lithium aluminum hydride under nitrogen.

Reaction of Dimethylsulfonium Methylide with Ferrocenecarboxaldehyde.—A solution of methylsulfinyl carbanion[11] (0.035 mol) in 1:1 DMSO-THF (50 ml) was cooled to −15° under a nitrogen atmosphere. To this solution was added, dropwise over 3 min, 7.0 g (0.035 mol) of trimethylsulfonium iodide dissolved in 30 ml of DMSO. After stirring for 1 min a solution of ferrocenecarboxaldehyde (1.5 g, 0.0069 mol) in THF (20 ml) was added dropwise to this ylide solution over a period of 2–3 min. The mixture was stirred at −15° for 5 min, and then allowed to warm to room temperature over 0.5 hr and poured into 300 ml of water. The resulting solution was extracted three times with 50-ml portions of diethyl ether; the combined ether portions were washed with water and dried ($MgSO_4$). Removal of the solvent gave the crude product, the components of which were separated by chromatography on silica gel with benzene as eluent.

The major product was ferrocenylacetaldehyde, formed in 64% yield: ir (neat) 1705 (C=O), 1100, and 995 cm^{-1}; nmr ($CDCl_3$) δ 3.22 (J = 3 Hz), 4.09 (s, 9), and 9.68 (t, 1, J = 3 Hz). This compound, a liquid, decomposed quantitatively in 2 days in contact with air to a brown powder, in keeping with its known behavior.[3]

A small amount of unreacted ferrocenecarboxaldehyde was recovered.

Reaction of Dimethylsulfonium Methylide with Acetylferrocene.—The reaction was run and the product was purified as described above for ferrocenecarboxaldehyde.

The major product, isolated in 70% crude yield, was 2-ferrocenylpropionaldehyde; ir (neat) 1725, 1101, and 997 cm^{-1}; nmr ($CDCl_3$) δ 1.30 (d, 3, J = 7.5 Hz), 3.19 (quartet of doublets, 1, J = 7.5 and 2.2 Hz), 4.10 (m, 9), 9.71 (d, 1, J = 2.2 Hz). *Anal.* Calcd for $C_{13}H_{14}FeO$: C, 64.49; H, 5.83; Fe, 23.07. Found: C, 64.41; H, 5.71; Fe, 22.92. This compound, a liquid, decomposed slowly in contact with air to a brown powder.

A small amount of acetylferrocene was recovered.

Reaction of Dimethylsulfonium Methylide with Benzoylferrocene.—The reaction was run as described for ferrocenecarboxaldehyde; the work-up was carried out in the absence of oxygen, with benzene used as the extracting solvent instead of ether.

An nmr of the initial product showed multiplets at δ 1.6, 2.2, 4.1, and 7.3, but no absorption in the region δ 9–11. Several attempts to purify this product always led to either complete decomposition or to the isolation of a small amount of the major product described below.

After standing overnight at room temperature, a 72% crude yield of ferrocenylphenylacetaldehyde was obtained. This product was sublimed at 140° (0.25 mm): nmr (CCl_4) δ 4.1 (m, 9), 4.41 (d, 1, J = 4.2 Hz), 7.2 (m, 5), and 9.74 (d, 1, J = 4.2 Hz); ir (neat) 1725 (aldehyde C=O), 1101, and 994 cm^{-1}. *Anal.* Calcd for $C_{18}H_{16}FeO$: C, 71.08; H, 5.30; Fe, 18.36. Found: C, 67.80; H, 5.13; Fe, 17.50. This compound decomposes quickly on exposure to air, which probably accounts for the low elemental analysis.

Reaction of Dimethyloxosulfonium Methylide with Ferrocenecarboxaldehyde.—Sodium hydride (1.4 g, 0.035 mol of 58% mineral oil dispersion) was washed three times with hexane and dried under vacuum. To this was added 7.6 g (0.035 mol) of trimethyloxosulfonium iodide and 50 ml of DMSO. After 30 min, sufficient time to generate the ylide, the temperature was raised to 55° and the dropwise addition of ferrocenecarboxaldehyde was carried out over a period of 1.5 hr. After an additional 30 min of stirring, followed by cooling, the reaction mixture was poured into water (300 ml) and the resulting solution was extracted three times with ether. The combined ether washings were washed with water, dried ($MgSO_4$), and evaporated to give the crude product. Products of the reaction were separated by column chromatography on silica gel, with benzene as the eluent.

The liquid compound 3-ferrocenyl-1,2-epoxypropane was formed in 18% yield, as calculated from the nmr of the crude material: ir (neat) 1257, 1102, and 997 cm^{-1}; nmr ($CDCl_3$) δ 2.55 (m, 4), 3.05 (m, 1), and 4.10 (m, 9). *Anal.* Calcd for $C_{13}H_{14}FeO$: C, 64.49; H, 5.83; Fe, 23.07. Found: C, 64.68; H, 6.00; Fe, 22.92.

The ir spectrum of ferrocenylacetone showed peaks at 1705, 1103, and 998 cm^{-1}; nmr δ 2.04 (s, 3), 3.37 (s, 2), and 4.11 (s, 9). *Anal.* Calcd for $C_{13}H_{14}FeO$: C, 64.49; H, 5.83; Fe, 23.07. Found: C, 61.43; H, 5.46; Fe, 20.84. The yield was 27%; the product, a liquid, decomposed in contact with air in 2 days to a brown solid. This sensitivity to air probably accounts for the low elemental analysis.

Acetylferrocene, obtained in 1% yield, was identified by the comparison of the ir and nmr spectra with those of an authentic sample. Vacuum sublimation gave purified material, mp 83° (lit.[12] mp 85–86°).

No ferrocenecarboxaldehyde was recovered.

Reaction of Dimethyloxosulfonium Methylide and Acetylferrocene.—The reaction was carried out as described for ferrocenecarboxaldehyde, above.

The yield of 2-ferrocenylpropionaldehyde was 8%; the compound was characterized by comparison of its ir and nmr spectra with those of authentic samples.

The ir spectrum of 3-ferrocenyl-1,2-epoxybutane, obtained as a liquid mixture of diastereomers, showed peaks at 1256, 1102, and 995 cm^{-1}; nmr δ 1.30 (overlapping doublets, 3), 2.1–3.1 (m, 4), 4.01 (m, 9). *Anal.* Calcd for $C_{14}H_{16}FeO$: C, 65.64; H, 6.29; Fe, 21.83. Found: C, 65.85; H, 6.39; Fe, 21.66. The spectra of the product thus obtained were identical with those obtained from this product as prepared by another method). The crude yield was 40%.

The recovery of acetylferrocene was 41%.

Attempted Reaction of Benzoylferrocene and Dimethyloxosulfonium Methylide.—When reaction was attempted under the conditions used for ferrocenecarboxaldehyde and acetylferrocene above the recovery of benzoylferrocene was quantitative. If reaction was continued for 2 days a small amount of an apparently polymeric product was obtained.

3-Ferrocenyl-1,2-epoxybutane.—A sample of 2-ferrocenylpropionaldehyde was prepared by the reaction of acetylferrocene and dimethylsulfonium methylide, as above. A second ylide solution was prepared, and the 2-ferrocenylpropionaldehyde was added to it in the usual manner. The product, identified by comparison of its ir and nmr spectra with those of an authentic sample, was 3-ferrocenyl-1,2-epoxybutane, bp 144–154° (3.5 mm). The yield was 30%, based on acetylferrocene.

Registry No.—**1,** 1298-50-6; **3,** 36731-63-2; **4,** 6814-64-8; **5,** 5367-24-8; **6,** 12093-10-6; **7,** 1271-55-2; **8,** 36731-64-3; **9,** 1272-44-2; **10,** 36731-65-4; **11,** 12215-52-0; **12,** 36731-67-6.

Acknowledgment.—The authors wish to thank Professor Robert H. Garner of this department for many helpful discussions relating to this work. The financial support of this work by the National Aeronautics and Space Administration, Grant No. NGL-01-002-064, is gratefully acknowledged.

---

[11] F. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **84**, 866 (1962).

[12] P. J. Graham, R. V. Lindsey, G. W. Parshall, M. L. Patterson, and G. M. Whitman, *ibid.*, **79**, 3416 (1957).