Table I. Species of Mo(III) in Aqueous Solutions

species	Mo–Mo distance, Å	reduction with Jones reductor
monomeric Mo(III)		no reduction
$[Mo_2(OH)_2]^{4+}$ [a]	2.43[b]	no reduction
$Mo_2Cl_9^{3-}$	2.65[c]	produces Mo_2^{4+} [d]
$Mo_2Br_9^{3-}$	2.82[c]	produces Mo_2^{4+} [d]
$Mo_2Cl_8H^{3-}$	2.37[e]	produces Mo_2^{4+} [d]
$Mo_2Br_8H^{3-}$	2.39[e]	produces Mo_2^{4+} [d]
$Mo_2(HPO_4)_4^{2-}$	2.23[f]	produces Mo_2^{4+} [g]

[a] Ardon, M.; Pernick, A. *Inorg. Chem.* **1974,** *13,* 2275. [b] As found in the crystals of $K[Mo_2(OH)_2(O_2CCH_3)EDTA]$: Kneale, G. K.; Geddes, A. J.; Sasaki, Y.; Shibahara, T.; Sykes, G. *J. Chem. Soc., Chem. Commun.* **1975,** 356. [c] Saillant, R.; Jackson, R. B.; Streib, W. E.; Folting, K.; Wentworth, R. A. D. *Inorg. Chem.* **1971,** *10,* 1453. [d] This work. [e] Reference 2. [f] Reference 13. [g] Reference 14.

distance is *not* a major factor in this process. In $Mo_2Br_9^{3-}$ this distance is 2.82 Å compared with 2.43 Å in $[Mo_2(OH)_2]^{4+}$; yet it is only the former that is reduced. The molybdenum to molybdenum distance is not by itself a sufficient criterion for reducibility, which is probably a combination of this distance, the geometry of the ion and the nature of the bridging ligands.

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(3) (a) Some organometallic dimolybdenum(II) compounds were prepared from $MoCl_4$[3b] or $MoCl_5$.[3c] Molybdenum hexacarbonyl and the halides were prepared either from the metal itself or from MoO_3 by tedious procedures.[4] (b) Cotton, F. A.; Koch, S. A.; Schultz, A. J.; Williams, J. M. *Inorg. Chem.* **1978,** *17,* 2093. (c) Cotton, F. A.; Pipal, J. R. *J. Am. Chem. Soc.* **1971,** *93,* 5441.
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(12) Solutions of $Mo_2X_8H^{3-}$ (X = Cl, Br) were reduced immediately after the dissolution of the Cs salts in H_2SO_4, 1 M, by Jones reductor to Mo_2^{4+}.
(13) Bino, A.; Cotton, F. A. *Inorg. Chem.* **1979,** *18,* 3562.
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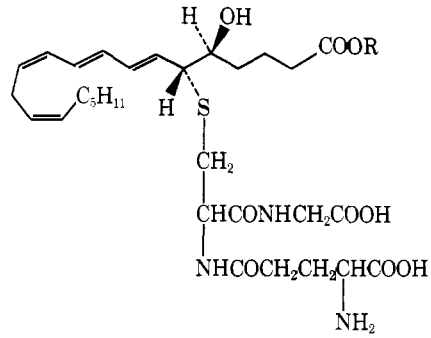
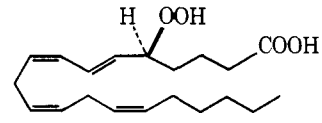
Synthesis of the Slow Reacting Substance of Anaphylaxis Leukotriene C-1 from Arachidonic Acid

Sir:

Mounting evidence implicates the class of "slow reacting substances" (SRS's) as important agonists in asthma and various forms of hypersensitivity.[1-3] A major obstacle to progress in understanding the exact role of SRS's in disease has been the lack of pure, well-defined SRS.[2] Recently this situation has been corrected by the development of an efficient total synthesis of the SRS leukotriene C-1[4] (LTC-1, **1**) and the biologically important Cys,Gly analogue of **1** (LTD) which also served to allow the assignment of chemical structure in all detail.[5] The biosynthesis of **1** is considered[5a-c] to proceed from arachidonic acid via (*S*)-5-hydroperoxy-6-*trans*,8,11,14-*cis*-eicosatetraenoic acid [(*S*)-5-HPETE] (**2**)



1 R = H
5 R = CH_3



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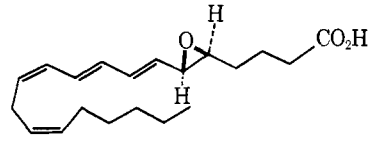

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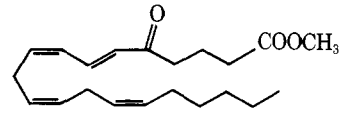

4

and *trans*-5-(*S*),6-(*S*)-oxido-7,9-*trans*-11,14-*cis*-eicosatetraenoic acid (leukotriene A, **3**) as successive intermediates. In this communication we report a simple synthesis of LTC-1 (**1**) which follows the pathway of biosynthesis from arachidonic acid.

Recently an efficient chemical synthesis of (±)-5-HPETE and an enzymic synthesis of (*S*)-5-HPETE (**2**) from arachidonic acid have been reported.[6] Both (±)-5-HPETE and (*S*)-5-HPETE can be utilized for the synthesis of LTC-1 (**1**) by conversion into **3** and subsequent combination with glutathione (natural form). The former has the advantage of being readily available in quantity, but the disadvantage of requiring separation of diastereoisomers of **1** in the final step. A description of the synthesis of **1** from (*S*)-5-HPETE is given here.

The chemical conversion of **2** into **3** (as methyl esters) requires activation of the hydroperoxy group to generate electrophilic oxygen at C-5 under *nonacidic* and mild conditions since the epoxy tetraene **3** is known to be an exceedingly labile substance, e.g., to water and other protic media, mild acids, oxygen, or free radicals. Considerable experimentation was required to achieve the desired results. Not unexpectedly, one troublesome side reaction was formation of dienone **4** by a carbonyl-forming 1,2-elimination process, and another was formation of relatively polar materials, some of which probably originate from the desired product, **3** methyl ester. Methylene chloride (or mixtures with some ether) was found to be the most satisfactory solvent (superior to chloroform, ether, tetrahydrofuran, or acetonitrile, for example). Both the degree of stabilization of the leaving group and low temperature seemed to favor the generation of desired product over the dienone **4.** Finally, it was critical not only that a proton acceptor be present to minimize the destruction of **3** methyl ester, but also that the acceptor be highly hindered to disfavor carbonyl-forming 1,2 elimination. All of these factors had to be

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recognized, explored experimentally, and utilized in the experimental design before a satisfactory result could be obtained.

To a solution of the methyl ester of (*S*)-5-HPETE [prepared by reaction of (*S*)-5-HPETE with diazomethane] in 1:1 methylene chloride–ether (75 mg/mL) and 1,2,2,6,6-pentamethylpiperidine[7] (6 equiv), maintained at −110 °C by means of a liquid nitrogen–ethanol bath, was added 2 equiv of trifluoromethanesulfonic anhydride. After 40 min a large volume of pentane containing 1% triethylamine was added and the crude product was isolated by washing with water, drying with sodium sulfate, and removal of solvent in vacuo. The crude product which consisted of a mixture of the desired methyl ester of **3** and the conjugated dienone **4** could not be separated chromatographically and so it was treated with an excess of sodium borohydride in dimethoxyethane at 0 °C to reduce **4** to the corresponding hydroxy ester. Chromatography of the resulting mixture (preparative layer plate of silica gel impregnated with triethylamine using 1:4 ether–pentane containing 1% triethylamine for elution) afforded pure **3** methyl ester, R_f 0.45 (yield ~25%), chromatographically and spectroscopically identical[9] with pure leukotriene A methyl ester prepared by the previously described[4] synthetic route.[9]

Treatment of **3** methyl ester in methanol containing triethylamine with excess glutathione at 23 °C for 5 h, removal of methanol, and isolation as previously described[4] gave the monoester of LTC-1 (**5**) in essentially homogeneous form as determined by reverse-phase high-performance liquid chromatography (Waters Associates C-18 μ-Porasil column using 65% methanol, 35% water containing 0.1% acetic acid buffered to pH 5.6 with ammonium hydroxide). Cochromatography of this product with methyl ester **5** prepared as previously described[4] resulted in one peak, and identity was also indicated by ultraviolet absorption (maximum in CH_3OH at 280 nm (ε 40 000) with shoulders at 270 and 290 nm).[4] Finally hydrolysis of **5** as described previously[4] led cleanly to **1**, identical with authentic LTC-1 by ultraviolet and chromatographic measurements and by bioassay.[5e,10]

The experimental work outlined herein demonstrates a short (five step) and simple route to the primary SRS LTC-1 (**1**) and also the related LTD. It represents a convenient method for the synthesis of small amounts of these SRS's as well as a chemical mimic of the proposed biosynthetic pathway. It is noteworthy, but hardly surprising, that the chemical conversion of 5-HPETE methyl ester into leukotriene A methyl ester is stereospecific and that the newly generated double bonds and oxirane ring are formed in the more stable trans arrangement.[11]

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(8) Found for synthetic **3** methyl ester: UV max (CH_3OH) 278 nm (ε 40 000) with shoulders at 269 and 289 nm; mass spectrum (*m/e*) 332 (M^+), 301 ($M - OCH_3$), 279, 203, 189, 149, 129, 101, 91; ^1H NMR (in C_6D_6, δ) 1.13 (t, J = 7 Hz, 3 H, $-CH_2CH_3$), 1.40–1.70 (br, 12 H, CH_2), 2.34 (m, 2 H, CH_2–COO), 2.75 (t × d, J = 7, 2 Hz, 1 H, =CHHC(O)C*H*), 3.20 (m, 3 H, C=CCH_2C=C, HC(O)C); 3.60 (s, 3 H, $COOCH_3$), 5.5–5.75 (m, 4 H, olefinic at C(7), C(12), C(14), C(15)), 6.15 –7.0 (m, 4 H, olefinic at C(8)–C(11)).
(9) The dienone **4** was also isolated from the reaction mixture by chromatography on untreated silica gel. The product so obtained was identical with conjugated dienone **4** prepared by oxidation of 5-HETE using manganese dioxide in methylene chloride at 23 °C. Found for **4**: IR max (CCl_4) 1580, 1680, 1735 cm^{-1}; UV max (CH_3OH) 276 nm; mass spectrum (*m/e*) 332 (M^+), 301, 231, 129, 101, 79; partial ^1H NMR (in $CDCl_3$, δ) 1.80 (m, 2 H, C(16) H_2), 2.33 (q, 2 H, J = 6 Hz, CH_2COOCH_3), 2.58 (q, 2 H, $COCH_2$), 2.80 (m, 2 H, C(13) H_2), 3.05 (m, 2 H, C(10) H_2), 3.67 (s, 3 H, $COOCH_3$), 5.40 (m, 4 H, olefinic at C(11), C(12), C(14), C(15)), 5.9 –6.25 (m, 3 H, olefinic at C(6), C(8), C(9)), 7.50 (q, J = 16.9 Hz, 1 H, olefinic at C(7)).

(10) We are indebted to Professor Bengt Samuelsson and associates of the Karolinska Institutet, Stockholm, for the biological comparison.
(11) We are grateful to Dr. Shun-ichi Hashimoto for providing (±)-5-HPETE. This study was assisted financially by the National Science Foundation and the National Institutes of Health.

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Electronic Structure of 2-Fe Ferredoxin Models by Xα Valence Bond Theory

Sir:

We report here calculations of $Fe_2S_2(SH)_4^{2-,3-}$, models for the active sites of oxidized and reduced 2-Fe ferredoxin proteins, by the recently developed Xα valence bond (Xα-VB) theory.[1] We believe that these calculations provide the first accurate theoretical description of the much-studied[2-4] antiferromagnetic coupling between the two iron centers. By including the physically most important aspects of electron correlation in our theoretical model, we find much greater similarity between the 2-Fe and 1-Fe[5,6] active sites than was evident from our previous Xα molecular orbital (Xα-MO) calculations on $Fe_2S_2(SH)_4^{2-,3-}$.[7]

Figure 1 shows SCF-Xα-SW-VB energy levels for

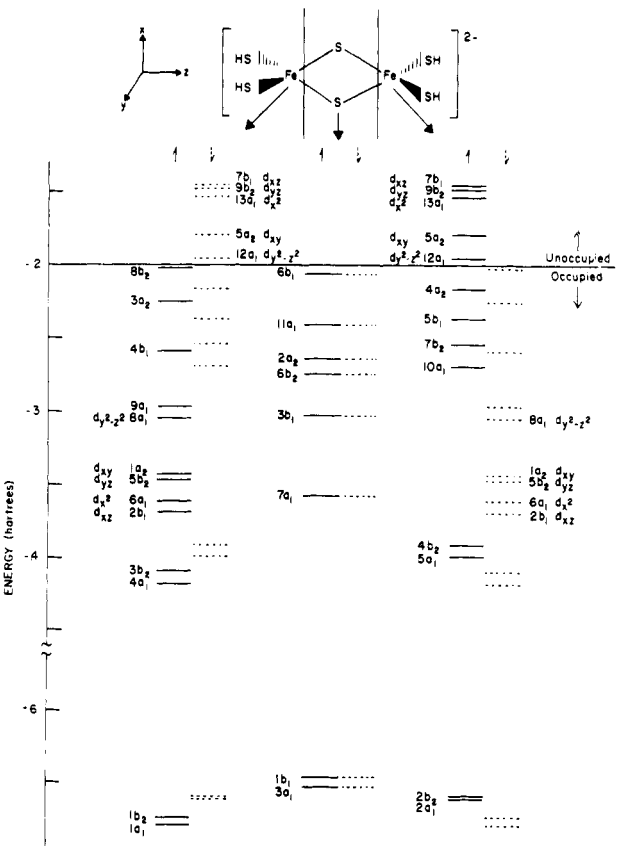

Figure 1. Xα-SW-VB valence levels of $Fe_2S_2(SH)_4^{2-}$. The orbitals are separated according to their localization on the left, center, or right of the molecule. Spin-up levels are depicted with solid lines, spin-down levels with dashed lines. The ten pairs of Fe 3d-like orbitals are indicated.

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