instrumentation and calculations associated with our work.

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Cation Radicals. I. Chlorination of Carboxylic Acids *via* Oxygen Cation Radicals. The McLafferty Rearrangement in Solution

Sir:

The Hofmann–Löffler reaction is the selective internal chlorination of amines at C-4 *via* a nitrogen cation radical in a six-membered cyclic transition.[1-3] Alkyl hypochlorites, both primary[4] and tertiary,[5-8] also selectively chlorinate C-4. The Barton[9] and Yang[10] reactions also involve selective abstraction of H from C-4. Even in mass spectra, oxygen cation radicals abstract H internally and selectively at C-4 (McLafferty rearrangement).[11] All of these reactions are free-radical processes. By their precedent, selective H abstraction at C-4 is diagnostic for such internal, free-radical H abstractions *via* six-membered cyclic transition states.

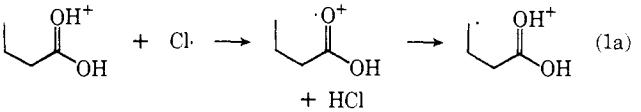
We have now observed selective chlorination at C-4 in butyric, hexanoic, and octanoic acids by conducting the chlorination of these acids in 90% H_2SO_4 (Table I).

Table I. Yields of Monochloro Acids Based on RCOOH Consumed[a]

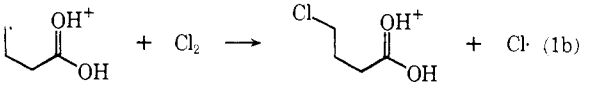
RCOOH[a]	% yields 2-Cl	3-Cl	4-Cl	5-Cl	6-Cl	7-Cl	8-Cl
			Cl_2, 90% H_2SO_4, 25°				
Octanoic acid	5	8	31	10	2	3	41
Octanoic acid[b]	3	6	27	8	2	3	51
Hexanoic acid	4	7	40	7	42		
Butyric acid	0	21	79				
			Cl_2, CCl_4, 25°				
Octanoic acid	1.5	9	15	15	19	24	17
Hexanoic acid	4	13	28	37	18		
Butyric acid	5	53	42				
			Cl_2, C_6H_6, 25°				
Octanoic acid	0	3	14	24	30	26	3
			tert-BuOCl, CCl_4, 25°				
Octanoic acid	6	7	14	17	22	28	6

[a] Twofold excess of RCOOH over Cl_2. [b] Reaction conducted at 60°.

The reasons for interpreting this selectivity as due to an oxygen cation radical process, eq 1, are identical with those used in establishing the nitrogen cation radical mechanism for the Hofmann–Löffler reaction.[1-3] These are: (1) the reaction abstracts H at C-4, (2) the reaction fails with chains shorter than four carbons (in our case, propionic and acetic acids reacted very slowly), (3) the selectivity was not affected by concentration of reactant, (4) the reaction is photochemical with very high quantum yields (in our case, 0.1 mol of RCOOH reacted completely in 1 hr with sunlamp irradiation), and (5) the selectivity is found only in highly acidic systems.



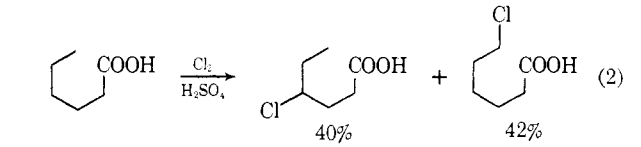
(1a)



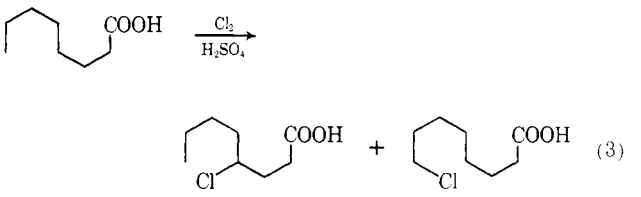
(1b)

Table I includes data on chlorination of butyric, hexanoic, and octanoic acids in CCl_4 to show the near randomness of the chlorinations in CCl_4 and the dramatic contrast with chlorinations conducted in 90% H_2SO_4. Chlorination of octanoic acid by the more selective reagents (*tert*-BuOCl and $C_6H_6Cl\cdot$) are also included in Table I and these are also nearly random except for the marked reduction in the chlorination of the primary hydrogens (terminal methyl) and the usual avoidance of α chlorination at C-2.

In addition to the selective chlorination on C-4, hexanoic acid gives a comparable amount of chlorination on C-6 (eq 2) and octanoic acid gives a comparable amount of chlorination on C-8 (eq 3). Experiments are in progress to see if these patterns are followed in the Hofmann–Löffler, alkyl hypochlorite decomposition, and the Barton and Yang reactions.



(2)



(3)

Regardless of the mechanism, the selective chlorinations illustrated in eq 2 and 3 are most novel and represent the highest yields of ω chlorination that have been achieved.

Several amino and diamino carboxylic acids have been chlorinated in good yield in 90% sulfuric acid.[12] The alkyl chains were generally too short to detect the effects shown in Table I and the presence of one or two NH_3^+ substituents complicated the problem.

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The products in Table I were converted to their methyl esters and analyzed by gc as described.[13]

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Stereospecific Synthesis and Reactions of Optically Active Isopropyl Methylphosphinate

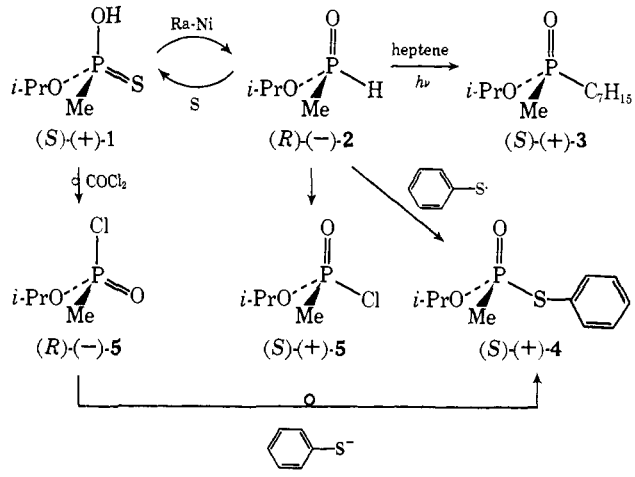
Sir:

The recent publication of the resolution of a diastereoisomeric hydrogen phosphinate[1] and the separation of the geometric isomers of a cyclic hydrogen phosphite[2] prompts us to report our results on the stereospecific synthesis of an optically active acyclic hydrogen phosphinate (**2**), whose chirality is due solely to the presence of an asymmetric phosphorus atom. Hydrogen phosphinates are highly versatile synthetic intermediates that undergo a wide variety of interesting reactions.[3] We include here a preliminary report on the stereochemistry of a number of these reactions.

We find that (*S*)-(+)-isopropyl methylphosphonothioic acid (**1**), α_D +14.0° (neat) (100% optically pure),[4,5] is desulfurized on refluxing with Ra–Ni[6] in ethanol to give (*R*)-(−)-isopropyl methylphosphinate (**2**); similarly, (*S*)-(+)-**2** has been obtained from (*R*)-(−)-**1**. On a 20-mmol scale, after vacuum distillation at room temperature, a 60% yield of **2** (generally containing 5–10% ethanol) was regularly obtained: $[\alpha]_D$ −30° (EtOH), −19° (CCl_4), −14° (benzene). Once separated from nickel salts and acidic material in the reaction mixture, it was redistilled (bp 77° (7 mm)) with little or no racemization. The (−)-**2** is rapidly (if not instantaneously) racemized by traces of sodium methoxide in methanol, presumably *via* the anion (**7**) (see below). In contrast to the reported instability of the Ar(R)P(H)O system,[7] however, it appears stable toward acid-catalyzed racemization. Thus, it did not racemize in the presence of an equal weight of isopropyl methylphosphonic acid in ethanol solution. A slow loss of optical activity (half-life of about 5 days) was noted for (−)-**2** in 95% methanolic 0.05 *N* hydrochloric acid, probably due to hydrolysis of the ester function.

As shown in Chart I, (*R*)-(−)-**2** adds sulfur in dioxane in the presence of dicyclohexylamine, undoubtedly with retention of configuration[2] and apparently by a radical mechanism,[8] to return (*S*)-(+)-**1**, isolated as the dicyclohexylamine salt, $[\alpha]_D$ +6.80° (methanol), 89 ± 1% optically pure.[4] The desulfurization and the sulfur addition reactions are thus shown to be essentially stereospecific. Based on the assigned stereochemistry of the latter, the desulfurization must take place also with retention of configuration.

Chart I



For studies of the stereochemistry of other reactions of **2**, the optically active compound was generally diluted with racemic material, synthesized essentially as described.[9]

In CH_3OD, (−)-**2** exchanged the hydrogen on phosphorus for deuterium, as followed by the decrease of the P–H band in the pmr spectrum. The exchange was accompanied by a slight increase in the specific rotation (from −13.57 to −13.61°), showing that the exchange occurred by a front-sided replacement of the hydrogen in (*R*)-**2**, presumably *via* its (*R*)-**2a** tautomer,[10] with overall retention of configuration.

Photochemically initiated radical reactions of **2**, if run at or near room temperature, proceed stereoselectively (if not stereospecifically) with retention of configuration. Thus, (*S*)-(+)-**2**, $[\alpha]_D$ +18.8° (ethanol) (63% optically pure), with phenyl disulfide in the presence of uv light,[8] gave (*R*)-(−)-*O*-isopropyl *S*-phenyl methylphosphonothiolate (**4**), bp 94° (15 μ), 93% pure (glpc), $[\alpha]_D$ −52.2° (benzene), identical (ir, glpc) with the enantiomorph of the product obtained with predominant inversion of configuration from the reaction of (*R*)-(−)-isopropyl methylphosphonochloridate (**5**) with sodium thiophenoxide, as indicated in Chart I. Also, the radical addition of (−)-**2**, $[\alpha]_D$ −17.4° (eth-

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(10) See, for example, the summary discussion on p 612 in the review by S. G. Warren, *Angew. Chem.*, 7, 606 (1968).