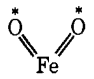
Although ferrate ion (3) was first prepared in 1702, there is little known concerning its reactivity with organic substrates.[8] Like its isostructural relative manganate (MnO_4^{2-}), ferrate is only stable in strongly alkaline solution. Unlike manganate,[9] we find that it reacts very slowly with oleic acid to produce complex product mixtures in low yield. The only products identified were *erythro*- and *threo*-9,10-dihydroxystearic acid, formed in the ratio 7:3. All ferrate salts are instantaneously decomposed by mineral acids, but barium ferrate is unique in exhibiting stability toward acetic acid, in which it is reported to give a red solution.[8] When a slight excess of squalene was treated with a suspension of barium ferrate in glacial acetic acid, epoxidation was the only detectable mode of oxidative attack. Monoepoxysqualenes were formed in 10% yield, based on ferrate.[10] The internal oxides were found by nmr analysis to be a mixture of isomers (90% trans and 10% cis). Thus, the ferrate epoxidation is not completely stereospecific. Chromyl acetate was found to produce only epoxides with squalene in carbon disulfide, and nmr analysis of the internal monoepoxides in this case showed that only trans epoxides had formed. Whatever the mechanism of epoxidation by chromyl acetate might be, it cannot involve the development of significant positive charge on the olefinic carbon atoms since cationic cyclizations are very favorable for such 1,5-dienes.

The above results suggest that some kind of oxoiron (Fe=O) species may play the role of active oxidant in mixed function oxygenase reactions. We feel that partial structures 9, 10, and 11 are possible candidates for the natural oxidant.[12] Formulae 9, 10, and 11 represent monooxo, cis dioxo, and trans dioxo structural types, respectively (* = derived from molecular oxygen). All three types could in principal epoxidize olefins by direct atom transfer, but epoxidation *via* a cyclic ester (*i.e.*, 12) is only possible for cis dioxo formulations such as 10.[13] The recent observations of cis hydroxylation of aromatic nuclei by oxygenases in several[14a,b] microorganisms are not inconsistent with an intermediate such as 12. Our work on oxotransition metal compounds is continuing with special emphasis on distinguishing between monooxo (9) and dioxo (10 and 11) structures for the natural iron oxidant.

9



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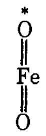

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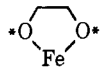

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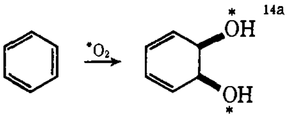

Acknowledgments. One of us (K. B. S.) gratefully acknowledges Professor James P. Collman for many stimulating discussions of oxygenase chemistry. We thank a Du Pont Fundamental Research Grant for providing financial support.

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[8] J. T. Riley, Ph.D. Thesis, University of Kentucky, 1968.

[9] W. Rigby (*J. Chem. Soc.*, 2452 (1956)) reports a 32% yield of *erythro*-9,10-dihydroxystearic acid from the action of manganate on oleic acid.

[10] Since under the conditions of the oxidation the epoxide products were partially opened to the corresponding hydroxyacetates, the reaction mixture was stirred until tlc revealed complete acetolysis of the oxides. Following lithium aluminum hydride reduction of the crude hydroxyacetate mixture, the monointernal diols were isolated by preparative tlc. The diols were transformed to the corresponding oxides using our published procedure.[11] A control experiment established that authentic *trans*-monointernal squalene oxides proceeded through the above sequence (acetolysis and reclosure) with complete retention of the original geometry.

[11] K. B. Sharpless, *Chem. Commun.*, 1450 (1970).

[12] It is generally argued that the active oxidant derives from reduction of a ferroporphyrin oxygen complex. However, since either one- or two-electron reduction is possible, we have avoided specifying oxidation states for 9, 10, and 11. There are other more subtle problems related to assigning the oxidation state of the metal. For example, even if one knew that 10 was a dianion resulting from two-electron reduction, the oxidation state of the iron would not be apparent; it would be somewhere between IV and VI depending on whether the negative changes resided principally on the metal or on the ligands (porphyrin and oxygens). *A priori* there is no reason to doubt that any iron IV, V, or VI oxidant would be potent enough to effect all known oxygenase reactions.

[13] We have recently found that thermolysis of the esters formed by reaction of osmium tetroxide with olefins leads in part to epoxides.

[14] (a) D. T. Gibson, G. E. Cardin, F. C. Maseles, and R. E. Kallio, *Biochemistry*, **9**, 1631 (1970), and references contained therein; (b) D. M. Jerina, T. W. Daly, A. M. Jeffrey, and D. T. Gibson, *Arch. Biochem. Biophys.*, **142**, 394 (1971).

[15] Fannie and John Hertz Foundation Fellow, 1969–1971.

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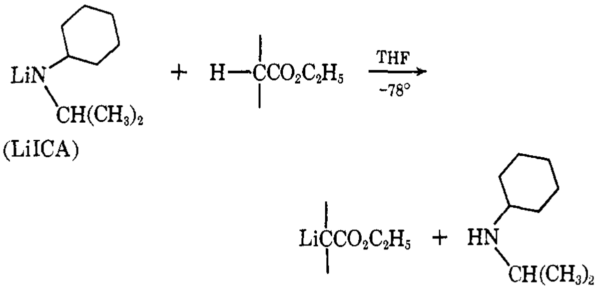
The Reaction of Lithium *N*-Isopropylcyclohexylamide with Esters. A Method for the Formation and Alkylation of Ester Enolates

Sir:

Lithium *N*-isopropylcyclohexylamide (LiICA) reacts with a wide variety of esters at low temperatures in tetrahydrofuran to produce solutions of the corresponding lithium ester enolates (eq 1). Self-condensation of the ester does not occur, even when such solutions are allowed to reach room temperature. This represents the first general method for the preparation of stable solutions of ester enolates.[1] At room tem-



(1)

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[1] Ester enolates have previously been generated by the reaction of esters with 1 and 2 equiv of lithium amide in liquid ammonia[2] and with the alkali metal salts of triphenylmethane.[3] These bases are most successful with relatively unreactive esters such as ethyl isobutyrate or *tert*-butyl esters. Even in these cases the enolate solutions must be utilized soon after their formation to prevent appreciable self-condensation.

[2] W. R. Dunnavant and C. R. Hauser, *J. Org. Chem.*, **25**, 503 (1960); C. R. Hauser and J. K. Lindsay, *J. Amer. Chem. Soc.*, **77**, 1050 (1955); C. R. Hauser and W. H. Puterbaugh, *ibid.*, **75**, 1068 (1953).

[3] W. Schlenk, H. Hilleman, and I. Rodloff, *Justus Liebigs Ann. Chem.*, **487**, 135 (1931); D. F. Thomas, P. L. Bayless, and C. R. Hauser, *J. Org. Chem.*, **19**, 1490 (1954); B. E. Hudson, Jr., and C. R. Hauser, *J. Amer. Chem. Soc.*, **63**, 3156 (1941).

Table I. Results of Deuterium Oxide Quenching Experiments of Ester Enolate Solutions Generated with LiICA[a]

Ester	Recovered ester, %[b]	Deuterium incorp, %[c]
Ethyl propionate	90	50
	60[d]	50
Ethyl hexanoate	100	55
	70[d]	50
tert-Butyl hexanoate	97	45
Ethyl nonanoate	100	50
Ethyl isobutyrate	97	75
	92[d]	70
Ethyl isovalerate	97	60
Ethyl cyclohexanecarboxylate	95	70
Ethyl phenylacetate	98	60

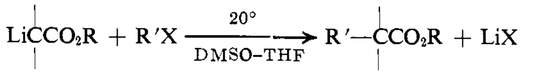
[a] The ester (10 mmol) was added to a 1.0 *M* solution of LiICA (10 mmol) in tetrahydrofuran at a temperature of −78°, except where noted. [b] Determined by glpc analysis of aliquots quenched with deuterium oxide. [c] Determined by proton nmr examination of ester recovered by preparative glpc from the quenched solutions (in a number of cases, the ester was examined in a crude state by simple evaporation of the solvent with identical results). [d] Ester added to base solution maintained at 0°.

Table II. Alkylation of Esters with Lithium *N*-Isopropylcyclohexylamide and Organic Halides

Ester	Alkylating agent[a]	Product[b]	Yield, %[c]
tert-Butyl acetate	*n*-Butyl iodide	$CH_3(CH_2)_4CO_2C(CH_3)_3$	85
tert-Butyl acetate	*n*-Butyl bromide	$CH_3(CH_2)_4CO_2C(CH_3)_3$	75
tert-Butyl acetate	*n*-Octyl iodide	$CH_3(CH_2)_8CO_2C(CH_3)_3$	96
tert-Butyl acetate	Isobutyl iodide	$(CH_3)_2CH(CH_2)_2CO_2C(CH_3)_3$	42
tert-Butyl acetate	Isoamyl iodide	$(CH_3)_2CH(CH_2)_3CO_2C(CH_3)_3$	75
tert-Butyl acetate	Allyl bromide	$CH_2{=}CH(CH_2)_2CO_2C(CH_3)_3$	80
tert-Butyl acetate	Benzyl bromide	$C_6H_5(CH_2)_2CO_2C(CH_3)_3$	96
tert-Butyl acetate	Isopropyl iodide	$(CH_3)_2CHCH_2CO_2C(CH_3)_3$	50
tert-Butyl hexanoate	Methyl iodide	$CH_3(CH_2)_3CHCH_3CO_2C(CH_3)_3$	82
Ethyl hexanoate	Methyl iodide	$CH_3(CH_2)_3CHCH_3CO_2C_2H_5$	83
Ethyl hexanoate	Isopropyl iodide	$CH_3(CH_2)_3CHCH(CH_3)_2CO_2C_2H_5$[d]	50
Ethyl isobutyrate	Methyl iodide	$(CH_3)_3CO_2C_2H_5$	87

[a] Utilized in 50% excess of ester. [b] All products exhibited spectral and physical properties in accordance with the assigned structures or with reported literature values. [c] Isolated yields based on ester. [d] Saponification gave the known 2-isopropylhexanoic acid, $n^{20}D$ 1.4260 (lit.[e] $n^{20}D$ 1.4266). [e] K. L. Rinehart, *et al.*, *J. Org. Chem.*, **22**, 13 (1957).

perature in the presence of dimethyl sulfoxide, the enolate solutions react with a variety of organic halides to provide good yields of the corresponding alkylated esters (eq 2).[4] The procedure is simpler and potentially more versatile than the usual malonic ester synthesis, and in many cases the yield of alkylation product is superior.[8]



$$\mathrm{LiCCO_2R} + \mathrm{R'X} \xrightarrow[\text{DMSO-THF}]{20^\circ} \mathrm{R'{-}CCO_2R} + \mathrm{LiX} \qquad (2)$$

We recently reported that solutions of lithio ethyl acetate may be prepared by the addition of ethyl acetate to a solution of lithium bis(trimethylsilyl)amide (I) at −78°.[10] Unfortunately, attempts to extend this simple procedure to the preparation of other ester enolates were unsuccessful. For example, addition of ethyl hexanoate to a tetrahydrofuran solution of I at −78° results only in a slow condensation of the ester which is complete over a period of 1 hr. Use of the more hindered ester, *tert*-butyl hexanoate, gives similar results except that condensation occurs at a much slower rate.

In an attempt to find a more suitable base, we studied the reaction of ethyl hexanoate with a wide variety of alkyl-substituted lithium amides, prepared in each case by the addition of *n*-butyllithium to the appropriate primary or secondary amine.[11]

In a typical experiment, an equivalent amount of ethyl hexanoate was added to a 1 *M* solution of the base in tetrahydrofuran at −78°. After varying intervals of time, aliquots were removed with a cold syringe and added to deuterium oxide. The yield of recovered ester was determined by glpc and the ester was examined for deuterium content by nmr.

With most of the bases studied, only a more or less rapid disappearance of the ester was observed with no deuterium incorporation in the recovered ester. With LiICA, however, 100% of the ester was recovered and shown to be 50–60% monodeuterated at the α carbon. The yield of recovered ester and the per cent deuterium incorporation remained constant for reaction times varying from less than 5 min to over 2 hr. Furthermore, the solution could be warmed to room temperature prior to quenching with identical results.

The incomplete deuteration of the recovered ethyl hexanoate cannot represent an equilibrium formation of the ester enolate because such a solution would undergo rapid self-condensation. This was demonstrated by the addition of a slight excess of ethyl hexanoate to the enolate solution at −78°. Quenching after 5 min showed almost complete disappearance of all the ester. Consequently the results are consistent only with quantitative formation of the ester enolate and the incomplete deuteration must be attributed to an unusual protonation mechanism during the quenching process.[12]

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(4) The direct alkylation of *tert*-butyl acetate[5] in very low yields and of tertiary esters of dialkylacetic acids[6] in good yields by means of lithium or potassium amide in liquid ammonia has been reported by Hauser. Sisido[7] obtained better results for the alkylation of *tert*-butyl esters with primary organic halides by utilizing a 100% excess of the ester and lithium amide.

(5) C. R. Hauser and W. J. Chambers, *J. Org. Chem.*, **21**, 1524 (1956).

(6) C. R. Hauser, and W. J. Chambers, *J. Amer. Chem. Soc.*, **78**, 3837 (1956).

(7) K. Sisido, *et al.*, *ibid.*, **81**, 5817 (1959).

(8) A useful procedure for the alkylation of metalated carboxylic acids with primary organic bromides was recently described by P. L. Creger, *ibid.*, 92, 1397 (1970). The alkylation of 2-oxazolines with organic halides followed by heating with ethanolic sulfuric acid provides an elegant synthesis of alkylated esters.[9]

(9) A. I. Meyers and D. L. Temple, Jr., *ibid.*, **92**, 6644 (1970).

(10) M. W. Rathke, *ibid.*, **92**, 3222 (1970).

(11) Representative amines utilized in this study include: *n*-butylamine, cyclohexylamine, diisopropylamine, di-*n*-butylamine, and di-*sec*-butylamine.

(12) A more startling lack of deuterium incorporation was recently reported for the deuterium oxide quenching of the dianion of *o*-toluic

The unique success of LiICA may be due in part to its high solubility. A majority of the bases studied appear to be only slightly soluble in tetrahydrofuran at low temperatures, while LiICA readily forms 1 *M* solutions in this solvent at −78°.

LiICA is equally successful in converting other esters to the corresponding enolates as shown by the data in Table I. In each case, quenching experiments indicate formation of the enolate is complete in less than 15 min at −78°. Attempts to generate several of the enolates at 0° resulted in appreciable condensation of the esters (see Table I). However, solutions of the enolates, prepared at −78°, remain stable at room temperature.

Tetrahydrofuran solutions of lithio ethyl acetate prepared according to eq 1 are inert to *n*-butyl iodide at a temperature of −78°. At higher temperatures, only modest yields (20–30%) of the alkylation product, ethyl hexanoate, are obtained. Apparently, condensation of the very reactive ester enolate with the product occurs at a rate which is comparable to that of the alkylation step. Use of the less reactive lithio *tert*-butyl acetate produces a 60% yield of the corresponding alkylation product, *tert*-butylhexanoate. Finally, this yield can be increased to 85% by adding the ester enolate to a solution of *n*-butyl iodide (50% excess) in dimethyl sulfoxide at room temperature. Examination of the crude reaction mixture by glpc demonstrated the complete absence of dialkylated product. Consequently, for the present we are assuming that ester condensation is the major factor limiting the yields.

Enolates derived from esters of substituted acetic acids appear to be less susceptible to condensation and here even the ethyl esters function satisfactorily as shown by the results presented in Table II.

Enolate anions derived from aldehydes or ketones are extremely useful reagents, undergoing a wide variety of synthetically useful reactions. It is possible that the present results will allow a similar versatility for the enolate anions derived from esters. We are actively investigating this possibility.

Acknowledgment. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

acid prepared from lithium diisopropylamide.[13] Recovered *o*-toluic acid showed no detectable deuterium incorporation.

(13) P. L. Creger, *J. Amer. Chem. Soc.*, **92**, 1396 (1970).

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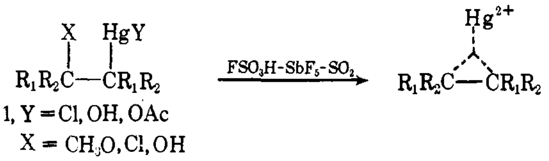
Received March 27, 1971

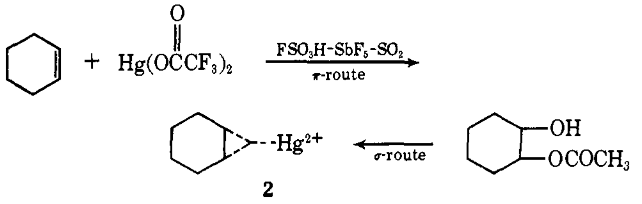
Organometallic Chemistry. II.[1] Direct Mercuration of Olefins to Stable Mercurinium Ions

Sir:

Mercurinium ions have been postulated as intermediates in the mercuration of olefins for many years.[2] Although considerable effort was directed toward direct observation of these ions, it was only recently that we were able to report formation of the first stable, long-lived mercurinium ions.[1] The ions were produced by treating organomercurials of the type **1** with $FSO_3H–SbF_5–SO_2$ solution. We now wish to report the first direct observation of mercurinium ions formed by the mercuration of olefins.



Mercuric trifluoroacetate is soluble in $FSO_3H–SbF_5–SO_2$ solution. When a cyclohexene–sulfur dioxide solution is added to a solution of mercuric trifluoroacetate in a slight excess of $FSO_3H–SbF_5–SO_2$, the cyclohexylenemercurinium ion **2** is formed. The pmr spectrum of this ion at −60° consists of a singlet at δ 8.35 (2 H), an unresolved multiplet at 3.10 (4 H), and a broad, unresolved multiplet at 2.12. The cmr chemical shift of C_1 and C_2 is +35.1 ppm (relative to CS_2). These spectral data are quite analogous to the data previously reported for the ethylene- and norbornylenemercurinium ions. Ion **2** may also be generated directly by addition of cyclohexene in SO_2 to either a solution of mercuric acetate in a slight excess of $FSO_3H–SbF_5–SO_2$ or a mixture of mercuric acetate and $FSO_3H–SO_2$. Alternatively, ion **2** may be formed by ionization of 2-acetoxymercuricyclohexan-1-ol in $FSO_3H–SbF_5–SO_2$ solution (eq 1). On warming to −30°, ion **2** decomposes.



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(1)

The *cis*- (**3**) and *trans*-1,2-dimethylethylenemercurinium ions (**4**) may also be produced by either direct olefin mercuration or by ionization of the appropriately substituted organomercurial. Ion **3** has a pmr spectrum consisting of two broad singlets at δ 7.89 and 2.83 (with $J_{CH_3–H}$ too small to be observed) while ion **4** shows a quartet at 8.23 and a doublet at 2.87 ($J_{CH_3–H}$ = 4 Hz). Somewhat surprisingly, it is *erythro*-3-acetoxymercuributan-2-ol which ionizes to ion **3** in $FSO_3H–SbF_5–SO_2$ while *threo*-3-acetoxymercuributan-2-ol ionizes to **4**. These are the ions obtained by a cis elimination process. Furthermore, it is interesting to note that on warming to +25° for several minutes, ion **3** is converted to ion **4**. Spectral assignments are based on the results of the direct mercuration of *cis*- and *trans*-2-butene as well as comparison with the pmr spectra of the silver complexes of *cis*- and *trans*-2-butene.

Direct mercuration of norbornylene to give the norbornylenemercurinium ion **5** has also been achieved. The pmr spectrum of ion **5** produced in this manner is identical with the previously reported[1] pmr spectrum obtained on treatment of *exo-cis*-3-hydroxy-2-norbornylmercuric acetate with $FSO_3H–SbF_5–SO_2$.

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(1) Part I: G. A. Olah and P. R. Clifford, *J. Amer. Chem. Soc.*, **93**, 1261 (1971).

(2) For a recent review of the role of mercurinium ions in the mercuration of olefins see W. Kitching, *Organometal. Chem. Rev.*, **3**, 61 (1968).