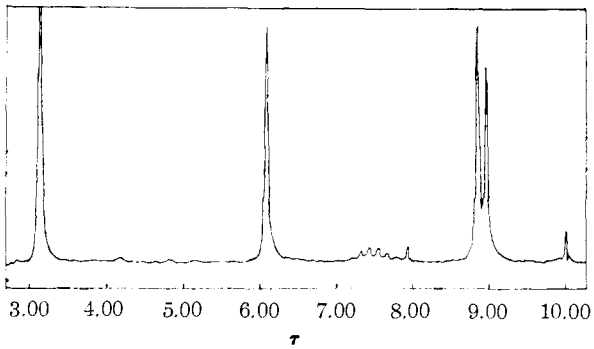
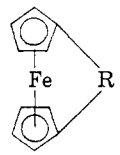



Fig. 2.

Found: C, 75.50; H, 7.16; Fe, 17.54]. In this reaction sodium presumably functions as a base to give the alkenyl cyclopentadienyl anion from the fulvene much as does sodium amide in an alternative preparation of alkenyl ferrocenes.[10,11] The structure II may be assigned on the basis of its infrared spectrum (conjugated C=C stretching band at 1630 cm.$^{-1}$) and ultraviolet absorption ($\lambda_{max}$ 275 m$\mu$, $\epsilon_{max}$ 13,700).[1] Conclusive evidence is derived from the n.m.r. spectrum, which contains an olefinic proton (triplet) at ($\tau$ = 4.33).[4]

While the rings are sufficiently canted when spanned by a two-carbon bridge to cause chemical shift of the ring protons, this is apparently not the case with simple saturated three-atom bridges. Thus, the ring protons appear as a singlet in both 1,1′-(trimethylene)-ferrocene (III)[12] ($\tau$ = 6.05) and 1,1′-(dimethyleneoxy)-ferrocene (IV)[13] ($\tau$ = 5.88), m.p. 148° (sinters 100°) [*Anal.* Found: C, 63.34; H, 5.44; mol. wt. (isothermal distillation), 233].




I, R = $-C(CH_3)_2C(CH_3)_2-$
III, R = $-(CH_2)_3-$
IV, R = $-CH_2OCH_2-$

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DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING
UNIVERSITY OF ILLINOIS
URBANA, ILLINOIS
KENNETH L. RINEHART, JR.
ALMUT K. FRERICHS
PAUL A. KITTLE[14]
LARS F. WESTMAN
DAVID H. GUSTAFSON

UNION CARBIDE CHEMICALS COMPANY
SOUTH CHARLESTON, WEST VIRGINIA
ROY L. PRUETT

THE LINDE COMPANY
TONAWANDA, NEW YORK
JOHN E. McMAHON

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## ACYL- FROM ALKYL-FERROCENES BY MANGANESE DIOXIDE OXIDATION. FERROCOBENZOQUINONE

*Sir:*

Alkyl ferrocenes frequently may be prepared directly from alkyl cyclopentadienes[1] and could provide useful starting materials for the preparation of functionally substituted ferrocenes if the alkyl groups could be oxidized selectively without concomitant or preferential oxidation of the ferrocene nucleus to ferricinium ion. In the present, initial studies toward this end manganese dioxide (which usually selectively oxidizes allylic or benzylic alcohols to the corresponding conjugated carbonyls,[2] and which has been used for conversion of hydroxymethylferrocene to ferrocenecarboxaldehyde)[5b] was selected as a mild, heterogeneous oxidant and shown to oxidize readily alkyl ferrocenes to the corresponding acyl compounds.

Methylferrocene[3] was heated for two days with a large excess of activated manganese dioxide (commercial, Beacon Labs.) in refluxing methylcyclohexane.[4] Chromatography of the product gave 55% of recovered methylferrocene and a 52% yield (based on unrecovered methylferrocene, *i.e.*, a 23% conversion) of ferrocenecarboxaldehyde,

(10) P. L. Pauson, G. R. Knox, J. D. Munro and J. M. Osgerby, XVIIth International Congress of Pure and Applied Chemistry, Munich, August–September, 1959, *cf. Angew. Chem.*, **72**, 37 (1960).

(11) A cyclopentenylferrocene has been prepared previously by reaction of ferrocene with hot hydrogen fluoride under pressure [V. Weinmayr, THIS JOURNAL, **77**, 3009 (1955)]. While this reference does not assign the position of the double bond, its ultraviolet spectrum, ($\lambda_{max}$ 275 m$\mu$, $\epsilon_{max}$ 10,400) allows the double bond to be located in conjugation with the ferrocene ring, as in the di-substituted II.

(12) A. Lüttringhaus and W. Kullick, *Angew. Chem.*, **70**, 438 (1958).

(13) Compound IV was prepared by treatment of 1,1-di-(hydroxymethyl)-ferrocene (V) with *p*-toluenesulfonyl chloride in refluxing benzene. Compound V, m.p. 107–108° [*Anal.* Found: C, 58.85; H, 5.77], in turn, was prepared by lithium aluminum hydride reduction of dimethyl 1,1-ferrocenedicarboxylate, a method employed previously [A. N. Nesmeyanov, E. G. Perevalova and Z. A. Beinoravichute, *Doklady Akad. Nauk S. S. S. R.*, **112**, 439 (1957)] the earlier authors reported m.p. 85–86°.

(1) (a) P. L. Pauson, THIS JOURNAL, **76**, 2187 (1954); (b) K. L. Rinehart, Jr., K. L. Motz and S. Moon, *ibid.*, **79**, 2749 (1957); (c) R. E. Benson and R. V. Lindsey, *ibid.*, **79**, 5471 (1957); (d) K. L. Rinehart, Jr., and K. L. Motz, *Chem. and Ind. (London)*, 1150 (1957); (e) R. C. Koestler and W. F. Little, *ibid.*, 1589 (1958); (f) G. R. Knox and P. L. Pauson, *Proc. Chem. Soc.*, 289 (1958); (g) L. T. Reynolds and G. Wilkinson, *J. Inorg. and Nucl. Chem.*, **9**, 86 (1959); (h) P. L. Pauson, G. R. Knox, J. D. Munro and J. M. Osgerby, *Angew. Chem.*, **72**, 37 (1960).

(2) For recent reviews of manganese dioxide oxidations, *cf.* R. M. Evans, *Quart. Revs. (London)*, **13**, 61 (1959), and C. D. Robeson, *Org. Chem. Bull.*, **32**, No. 2 (1960). Other oxidations by manganese dioxide, though less common, have been reported. For example, toluene and *o*-nitrotoluene gave the corresponding benzaldehydes and/or benzoic acids with manganese dioxide in sulfuric acid [F. Raschig, *Chemiker Ztg.*, **24**, 446 (1900)], while the allylic ring methylene group of vitamin A$_1$ and of reinene was oxidized to the corresponding allylic alcohol or to the $\alpha,\beta$-unsaturated ketone, or unattacked, depending on the manganese dioxide employed [H. B. Henbest, E. R. H. Jones and T. C. Owen, *J. Chem. Soc.*, 4909 (1957)].

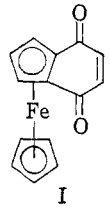
(3) A. N. Nesmeyanov, E. G. Perevalova, L. S. Shilovtseva and Z. A. Beinoravichute, *Doklady Akad. Nauk S.S.S.R.*, **121**, 117 (1958).

(4) The conditions described are not considered optimum, experimeutal results in this direction will be treated in the full paper.

m.p. 119–120°, identical with an authentic sample from an independent route.[5a,b]

Similar oxidation of ethylferrocene[6] gave acetylferrocene[7] in 52% yield (15% conversion), while the only product obtained (as judged by paper chromatographic analysis)[8] from 1,1′-dimethylferrocene[1d] was 1′-methyl-1-ferrocenecarboxaldehyde, (15% yield, 7% conversion) m.p. 79.5–80.5° [*Anal.* Found: C, 63.07; H, 5.22]. More easily oxidizable alkylferrocenes gave better yields under milder conditions (chloroform solution, room temperature four to six hours). Thus, diferrocenylmethane (prepared in 83% yield by lithium aluminum hydride–aluminum chloride reduction[9] of diferrocenylketone[10]), m.p. 124–125° [*Anal.* Found: C, 65.27; H, 5.36] was reoxidized by manganese dioxide to the ketone in 72% yield (and conversion). Deoxyferrocoin[11] similarly gave in 86% yield (66% conversion) the purple ferrocil, m.p. 193.5–195.5° [*Anal.* Found: C, 61.84; H, 4.19].

A novel use of the reagent is in the preparation (11% yield) of a ferroçobenzoquinone (I) from 1,2-(α-ketotetramethylene)-ferrocene.[12] The deep violet quinone (I), purified by sublimation at 135–145° (atm.), m.p. 146–147° (*Anal.* Found: C, 62.96; H, 4.14], has an infrared carbonyl band




I

at 1653 cm.$^{-1}$ and electronic absorption maxima at 520 mμ ($\epsilon_{max}$ 2260), 320 mμ ($\epsilon_{max}$ 3200) and 248 mμ (shoulder, ε 8400). For comparison, naphthoquinone is reported to have a carbonyl band at 1682 cm.$^{-1}$,[13] and electronic absorption maxima at 338 mμ ($\epsilon_{max}$ 3160) and 246–251 mμ ($\epsilon_{max}$ 21,900).[14] I may be reduced either chemically (sodium hydrosulfite) or polarographically to the unstable pale yellow hydroquinone ($\lambda_{max}$ 320 mμ, $\epsilon_{max}$ 5000; naphthalenediol[14] $\lambda_{max}$ 327–334, $\epsilon_{max}$ 5240, $\lambda_{max}$ 244 mμ, $\epsilon_{max}$ 15,100), which is reoxidized rapidly to the quinone.

**Acknowledgment.**—Financial assistance was provided in part by the Materials Laboratory, Wright Air Development Division, Wright-Patterson Air Force Base, Ohio.

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(7) R. B. Woodward, M. Rosenblum and M. C. Whiting, *ibid.*, **74**, 3458 (1952).

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(9) R. F. Nystrom and C. R. A. Berger, THIS JOURNAL, **80**, 2896 (1958); B. R. Brown and A. M. S. White, *J. Chem. Soc.*, 3755 (1957).

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(11) K. L. Rinehart, Jr., C. J. Michejda and P. A. Kittle, *ibid.*, **81**, 3162 (1959).

(12) K. L. Rinehart, Jr., and A. J. Cury, Jr., *ibid.*, **79**, 3290 (1957).

(13) R. T. O'Connor, P. von der Haar, E. F. DuPre, L. E. Brown and C. H. Pominski, *ibid.*, **76**, 2368 (1954).

(14) C. Daglish, *ibid.*, **72**, 4859 (1950).

(15) Alfred P. Sloan Foundation Fellow.

(16) Undergraduate Research Participant, supported by a grant (NSF G-8521) from the National Science Foundation.

KENNETH L. RINEHART, JR.[15]
DEPARTMENT OF CHEMISTRY
AND CHEMICAL ENGINEERING ALAN F. ELLIS
UNIVERSITY OF ILLINOIS CHRISTOPHER J. MICHEJDA
URBANA, ILLINOIS PAUL A. KITTLE[16]

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## PROPERTIES OF A PURIFIED SIALIDASE AND ITS ACTION ON BRAIN MUCOLIPID

*Sir:*

The various biological high polymers containing sialic acid, *e.g.*, the mucoproteins and mucolipids, command increasing interest. Our original observations[1] on the enzymic release of sialic acid from normal brain mucolipid,[2] but not from ganglioside[1,3,4] prompted the use of sialidase for the elucidation of the mode of linkage of glycolipid-bound sialic acid. As crude filtrates of cultures of *Vibrio cholerae* were inadequate for this purpose, a relatively simple procedure for the isolation from such filtrates of highly purified enzyme preparations in satisfactory yield was elaborated. It differs from recent adaptations,[5,6] published while this work was in progress, of the ingenious method employing adsorption on erythrocytes as proposed by the discoverers of the enzyme.[7] Since the properties of sialidase are largely unknown, we present preliminary information on this enzyme and its action on mucolipids.

The essential features of the isolation of sialidase are listed in the table.

TABLE I

ISOLATION OF *V. Cholerae* SIALIDASE

| Stage | Procedure | Activity Recovery of total (%)[a] | Specific[b] |
|---|---|---|---|
| 1 | Original culture filtrate | 100 | 10 |
| 2 | Pptd. 26% ammonium sulfate, *p*H 6.2 | 95 | |
| 3 | Pptd. 30% ammonium sulfate, *p*H 6.6 | 105 | 100 |
| 4 | Pptd. 26% ammonium sulfate, *p*H 5.3 | 100 | |
| 5 | $H_2O$ extraction and lyophilization | 22 | 1,300 |
| 6 | DEAE cellulose, 0 to 0.6 *M* NaCl, *p*H 6.65 | 22 | 12,600 |
| 7 | Pptd. 15–25% ammonium sulfate, *p*H 5.3 | 22 | 303,000 |

[a] The original culture filtrate contained 180,000 units per liter. [b] Units per μg. of protein.

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