The preparation of VI from IV was similar to the above excepting the separation of the products resulting from the partial reduction of IV. Here fractional crystallization failed but chromatography on alumina gave a clean separation of unreduced IV (28%), V (28%) and 1,10-cycloöctadecanediol (VIII) (20%). Pure V[5] gave VI (66%), upon dehydration, as a waxy solid, m.p. 40–41°, having a musk odor similar to cycloöctadecanone. Both V and VI were characterized as their semicarbazones.

Attempts to effect the partial reduction of I and IV to II and V by using an appropriate quantity of lithium aluminum hydride gave only the diols VII and VIII together with unreduced I and IV.[6]

Experimental[7]

1,9-Cyclohexadecanediol (VII).—A slurry of 0.19 g. (0.005 mole) of lithium aluminum hydride in 50 ml. of dry ether was added to an ether solution of 0.5 g. (0.002 mole) of I.[1] After 5 minutes 25 ml. of water was added, the inorganic salts filtered, and the ether layer separated. Removal of the ether and sublimation of the residual solid gave 0.47 g. (92%) of the white crystalline diol showing m.p. 104.5–106°. This m.p. was not altered by recrystallization from chloroform–hexane.

Anal. Calcd. for $C_{16}H_{32}O_2$: C, 74.94; H, 12.58. Found: C, 74.98, 74.83; H, 12.61, 12.83.

1,10-Cycloöctadecanediol (VIII).—In the manner described above, from 4.83 g. (0.017 mole) of II[1] there was obtained 4.58 g. (94%) of once-sublimed diol as a white crystalline solid, m.p. 125–127°. It showed m.p. 130–131.5° after several recrystallizations from chloroform–pentane.

Anal. Calcd. for $C_{18}H_{36}O_2$: C, 75.99; H, 12.76. Found: C, 75.72; H, 12.80.

9-Hydroxycyclohexadecanone (II).—An acetic acid solution of 0.503 g. (0.002 mole) of I was hydrogenated in a semi-micro apparatus, using 70 mg. of prereduced Adams catalyst, until 104% of one equivalent of hydrogen had been absorbed. After separation of the catalyst and removal of the acetic acid, *in vacuo*, the residual solid was treated with *ca.* 60 ml. of hexane at room temperature. There was obtained 0.07 g. of crude VII, m.p. 102–106°, insoluble in hexane. Cooling the filtered hexane solution to 0–5° gave 0.22 g. of II showing m.p. 75–77°. The remaining hexane solution was then placed on a Magnesol–Celite column. Elution with pentane–benzene gave 0.09 g. of starting diketone I, m.p. 75–80°. Elution with chloroform–benzene gave an additional 0.09 g. of II as fine fluffy needles, m.p. 68–74°. The total yield of II obtained was 0.31 g. (61%). After recrystallization from hexane, II showed m.p. 76–77°.

Anal. Calcd. for $C_{16}H_{30}O_2$: C, 75.53; H, 11.89. Found: C, 75.57; H, 12.01.

The semicarbazone derivative of II was obtained as a white crystalline solid from methanol; m.p. 150–152°.

Anal. Calcd. for $C_{17}H_{33}N_3O_2$: C, 65.55; H, 10.68. Found: C, 65.40; H, 10.30.

10-Hydroxycycloöctadecanone (V).—An acetic acid solution of 0.81 g. (0.0029 mole) of IV was partially hydrogenated using the procedure described for II. After separating the catalyst and removing the acetic acid the residue was dissolved in hexane and placed on a grade 3 alumina column. Elution with hexane–heptane gave 0.23 g. (28.5%) of unreduced IV, m.p. 92–94°. Elution with hexane–benzene gave 0.23 g. (28%) of V showing m.p. 54–55°. Final elution with chloroform gave 0.16 g. (20%) of VIII, m.p. 128–130°.

V, recrystallized from pentane, melted at 54–55°, resolidified immediately and remelted at 80–81°. Another sample of V recrystallized from pentane showed only m.p. 80–81°.

Anal. Calcd. for $C_{18}H_{34}O_2$: C, 76.54; H, 12.13. Found: C, 76.77, 76.73; H, 11.94, 12.06.

The semicarbazone derivative of V, after recrystallization from methanol, showed m.p. 157.5–159°.

Anal. Calcd. for $C_{19}H_{37}N_3O_2$: C, 67.21; H, 10.99; N, 12.38. Found: C, 66.98; H, 10.63; N, 12.87.

8-Cyclohexadecen-1-one (III).—A mixture of 170 mg. (0.0006 mole) of II and 1.5 g. of potassium hydrogen sulfate contained in a small flask was heated for 5 minutes in a Wood's metal-bath at *ca.* 250°. The cooled mixture was extracted with pentane. Evaporation of the pentane solution gave a residual oil having an intense musk odor. Treatment of a methanolic solution of this oil with semicarbazide hydrochloride and sodium acetate gave 145 mg. (80%) of III semicarbazone having m.p. 164–170°. Repeated recrystallization from methanol raised the m.p. to 168–170° (Ruzicka reported m.p. 180–181°[8]).

Anal. Calcd. for $C_{17}H_{32}N_3O$: C, 69.57; H, 10.65. Found: C, 69.49, 69.22; H, 10.52, 10.34.

Treatment of III semicarbazone (90 mg.) with aqueous oxalic acid in the usual way gave 60 mg. (78%) of III as a colorless liquid which solidified on cooling; m.p. 17–22°, using a precooled Nagle block (Ruzicka reported m.p. 23°[8]).

9-Cycloöctadecen-1-one (IV).—A mixture of 155 mg. (0.00055 mole) of V was fused with 2 g. of potassium hydrogen sulfate as described for III. Crude IV was obtained directly from the fused mixture by sublimation. After resublimation 95 mg. (66%) of IV was obtained as a waxy solid, m.p. 40–41° (Ruzicka reported m.p. 37.5–38°[8]).

The semicarbazone derivative of IV was prepared in the usual way. After recrystallization from methanol it showed m.p. 174–175° (Ruzicka reported m.p. 178–180°[8]).

BAKER LABORATORY
CORNELL UNIVERSITY
ITHACA, N. Y.

(5) V was obtained in what appeared to be polymorphic modifications. As first obtained in the chromatographic separation it showed m.p. 54–55°. When recrystallized from pentane it showed m.p. 80–81°.

(6) Quantitative yields of VII and VIII were obtained when compounds I and IV were reduced with excess lithium aluminum hydride. The sharp m.p. of VII, 104.5–106°, suggests that largely one of the two possible stereoisomeric glycols was produced.

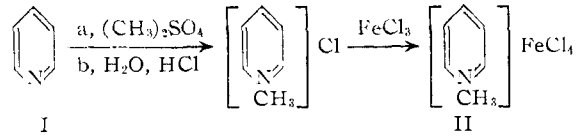
(7) All melting points are uncorrected.

Chloroferrates(III) as Derivatives of Heterocyclic Compounds Containing a C=N Linkage

BY A. H. BLATT AND NORMA GROSS

RECEIVED JUNE 6, 1955

Unsaturated cyclic quaternary ammonium chloroferrates(III) such as II have been known for many years[1] but they have not been used to any extent for the isolation and identification of the heterocyclic compounds such as I from which they are prepared.



I II

On several occasions we have found these chloroferrates so effective for the purposes just indicated that we are using this note to call attention to their advantages as compared with either organic derivatives (picrates, picrolonates, etc.) or salts of other complex inorganic acids (chloroaurates, chloroplatiates, etc.). The chloroferrates are easily and economically prepared, they are conveniently purified and analyzed, and they have sharp melting points and large mixed melting point lowerings.

To prepare an N-methyl chloroferrate(III) the heterocyclic compound is heated on a steam-bath with dimethyl sulfate, hydrochloric acid is added

(1) Examples are 5-phenylphenazinium chloroferrate(III), F. Kehrmann, *Ber.*, **29**, 2316 (1896); and 1-phenylpyridinium chloroferrate(III), W. König, *J. prakt. Chem.*, [2] **69**, 115 (1904).

TABLE I

	Formula	Chlorine, % Calcd.	Found	M.p., °C.
1-Methylpyridinium chloroferrate(III)	$C_6H_8NFeCl_4$	48.6	48.3	148–148.5[2]
1-Benzylpyridinium chloroferrate(III)	$C_{12}H_{12}NFeCl_4$	38.6	38.2	80
1,2-Dimethylpyridinium chloroferrate(III)	$C_7H_{10}NFeCl_4$	46.4	46.5	193–194
1,4-Dimethylpyridinium chloroferrate(III)	$C_7H_{10}NFeCl_4$	46.4	46.3	118–118.5
1-Methyl-2-benzylpyridinium chloroferrate(III)	$C_{13}H_{14}NFeCl_4$	37.2	36.9	70
1,2,6-Trimethylpyridinium chloroferrate(III)	$C_8H_{12}NFeCl_4$	44.4	44.1	204–205[3]
1-Methylquinolinium chloroferrate(III)	$C_{10}H_{10}NFeCl_4$	41.5	41.2	195–196
1,2-Dimethylquinolinium chloroferrate(III)	$C_{11}H_{12}NFeCl_4$	39.9	39.6	165–166
1-Methyl-6-methoxyquinolinium chloroferrate(III)	$C_{11}H_{12}NOFeCl_4$	38.2	37.9	97–98
2-Methyl-3,5-diphenylisoxazolium chloroferrate(III)	$C_{16}H_{14}NOFeCl_4$	32.7	32.4	108.5–109
2-Methyl-3-phenyl-5-*p*-bromophenylisoxazolium chloroferrate(III)				143–144[4]
2-Methyl-3-*p*-bromophenyl-5-phenylisoxazolium chloroferrate(III)				139–140[4]
2-Methyl-3,4,5-triphenylisoxazolium chloroferrate(III)				162[5]

2-Methyl-3-*p*-bromophenyl-5-phenylisoxazolinium chloroferrate(III), m.p. 115–116°, calcd. for $C_{16}H_{15}BrNOFeCl_4$: C, 37.3; H, 2.94. Found: C, 37.4; H, 2.66.

2,5-Dimethyl-3-phenylbenzisoxazolium chloroferrate(III), m.p. 95–96°, calcd. for $C_{15}H_{14}NOFeCl_4$: C, 42.70; H, 3.3 Found: C, 42.85; H, 3.1.

3,5-Dimethyl-2-phenylbenzoxazolium chloroferrate(III), m.p. 142–143°, calcd. for $C_{15}H_{14}NOFeCl_4$: C, 42.7; H, 3.3. Found: C, 42.6; H, 3.2.

to hydrolyze the excess ester, and concentrated aqueous ferric chloride solution is added until precipitation of the salt is complete. The intermediate methosulfate and chloride are not isolated. This procedure works not only for those heterocyclic compounds like pyridine and picoline that react vigorously with dimethyl sulfate, but also for such highly hindered and weakly basic heterocycles as 3,4,5-triphenylisoxazole. If the heterocyclic compound reacts too vigorously with dimethyl sulfate, benzyl chloride can be used instead: 1-benzylpyridinium chloroferrate(III) is an example of a derivative prepared by this variant procedure.

The chloroferrates(III) that we have prepared (Table I) are yellow solids, varying from greenish-yellow to orange-yellow. They are sparingly soluble in glacial acetic acid at room temperature and quite soluble by comparison in the same solvent hot, so that they are readily purified by crystallization from acetic acid. Most of them are conveniently analyzed for ionic chlorine by the Volhard procedure and, since they contain ferric iron, it is not necessary to add an indicator. The chloroferrates(III) from the heterocyclic compounds that contain oxygen as well as nitrogen in the ring develop purple colored solutions on addition of silver nitrate. With these colored solutions the end-point on titration with thiocyanate is not readily determined. Carbon and hydrogen analyses are therefore preferred, although the alternative procedure of ashing and determining iron can be used.

The salts listed in Table I were prepared either because we needed them for identification or because the heterocyclic compounds were available to us. They do not constitute an exhaustive test of the usefulness of the chloroferrates(III). Although such a test will have to wait upon more extended use of these derivatives, we can indicate the limitations we have observed so far. One heterocyclic compound, 3,5-diphenylisoxazoline, yielded an oil rather than a crystalline chloroferrate(III). The chloroferrates(III) from two compounds that contained more than one C=N linkage [2,3-diphenylquinoxaline and 1,4-bis-(6,7-dimethoxy-1-isoquinolyl)-butane] did not have good physical properties. Otherwise we have encountered no complications in the preparation and use of the chloroferrates(III).

(2) M. Scholtz, *Arch. Pharm.*, **247**, 5 (1904), prepared this chloroferrate(III) but did not report a melting point.

(3) R. Lukeš and M. Jureček, *Chem. Listy*, **37**, 177 (1943); *C. A.* **39**, 2505 (1945).

(4) A. H. Blatt, THIS JOURNAL, **71**, 1862 (1949).

(5) E. P. Kohler and A. H. Blatt, *ibid.*, **50**, 1222 (1928).

Experimental

It is convenient to add liquid heterocyclic compounds (*e.g.*, pyridine) dropwise to excess dimethyl sulfate and to add dimethyl sulfate to solid heterocyclic compounds. The usual quantities are 0.5 ml. or g. of the heterocyclic compound and 1.5 ml. of dimethyl sulfate. These reactants are heated on a steam-bath for three hours then left to cool. Five ml. of hydrochloric acid (one part concentrated acid and one part water) is added and, after the excess dimethyl sulfate has been hydrolyzed, 5 ml. of ferric chloride solution (two parts of $FeCl_3 \cdot 6H_2O$ in one part of water) is added.

Usually the salt crystallizes at once. Occasionally it appears as an oil that crystallizes on standing overnight. The crystalline salt is filtered, washed with a little glacial acetic acid, and crystallized from the same solvent.

Reactive heterocyclic compounds add dimethyl sulfate in less than the three hours prescribed above. If the heterocyclic compound is heavily substituted near the C=N linkage, longer heating may be necessary. A convenient test for completeness of reaction is the formation of a clear solution when the excess dimethyl sulfate has been hydrolyzed.

DEPARTMENT OF CHEMISTRY
QUEENS COLLEGE
FLUSHING 67, NEW YORK

3-Substituted Thiophenes. X. Barbituric Acid Derivatives[1]

BY E. CAMPAIGNE AND ROBERT L. PATRICK

RECEIVED APRIL 19, 1955

The 2-thienyl analog of phenobarbital, 5-(2-thienyl)-5-ethylbarbituric acid, was prepared by Blicke and Zienty,[2] and found to have the same order of activity as phenobarbital in the rat, being slightly less hypnotic but also slightly less toxic. 5-(2-Thenyl)-5-ethylbarbituric acid, prepared by Owen and Nord,[3] was found to be qualitatively

(1) Contribution No. 679. Taken from part of a thesis submitted by R. L. Patrick in partial fulfillment of the requirements for the degree Doctor of Philosophy at Indiana University, June, 1950.

(2) F. F. Blicke and M. F. Zienty, THIS JOURNAL, **63**, 2945 (1941).

(3) L. J. Owen and F. F. Nord, *J. Org. Chem.*, **15**, 988 (1950).