

solutions from all three compounds, and the isolation of the expected product from III<sup>4</sup> indicate that the coefficients measured represent for the most part the expected displacement of chlorine by the thiophenoxy group.

The data show that *p*-chloronitrobenzene reacts with sodium thiophenoxide, under the conditions of our experiments, 6.4 times as fast as *o*-chloronitrobenzene. The *para* isomer is known to react more rapidly, by about the same margin, with alkoxide reagents.<sup>2</sup> We tentatively conclude that the chlorine atom in *p*-chloronitrobenzene in general is replaced more readily by anion reagents.<sup>5</sup>

The data in Table I for the last two substrates permit a recalculation<sup>4</sup> of the Hammett  $\rho$ -constant for the reactions of 4-substituted-2-nitrochlorobenzenes with sodium thiophenoxide in 60% dioxane. The three points now available (for H, *p*-Cl and *p*-CF<sub>3</sub>) fall neither precisely in line nor so far out of line as to raise doubt about the applicability of the Hammett treatment.  $\rho$ , calculated by the method of least squares, is +4.5. This is somewhat higher than previously estimated, but still of the same order of magnitude as  $\rho$ -constants for other nucleophilic displacements at aromatic carbon atoms.<sup>6</sup>

#### Experimental

**Materials.**—I, II and III were commercial products recrystallized. *o*-Nitrodiphenyl sulfide, m.p. 80°, *p*-nitrodiphenyl sulfide, m.p. 54–55°, and 4-chloro-2-nitrodiphenyl sulfide, m.p. 84–85.5°, were prepared, for use in standardizing the spectrophotometric analytical method, by condensation of the corresponding chloro compounds with sodium thiophenoxide in alcoholic or aqueous dioxane media. 60% Dioxane (by volume) was prepared as previously described.<sup>4</sup> Commercial thiophenol was redistilled and stored in a nitrogen atmosphere. Standard solutions of sodium thiophenoxide in 60% dioxane were prepared by combining weighed amounts of thiophenol with calculated volumes of standard sodium hydroxide. These solutions contained about 0.02 mole of sodium hydroxide per 0.15 mole of sodium thiophenoxide, to ensure complete conversion of thiophenol to thiophenoxide ion, and were used within one day of their date of preparation. The presence of free hydroxide ion can be tolerated because hydroxide ion is such a poor nucleophilic reagent compared to thiophenoxide ion.<sup>4</sup>

**Rate Measurements.**—In the reaction solutions, the concentrations of sodium thiophenoxide and the aryl chloride were equal and about 0.015 *M*. At measured times, samples were quenched by excess sulfuric acid and analyzed by titration<sup>4</sup> or by spectrophotometric measurements<sup>3</sup> as previously described. Reactions were followed to about 50, 30 and 50% of completion, respectively, in the cases of substrates I, II and III. Plots  $1/(a-x)$  vs.  $t$  were strictly linear in the case of I, whereas the rate coefficient decreased slightly (less than 10% from beginning to end) in the case of III, and decreased in a more pronounced fashion (20% in the extreme) in the case of II.

Reactions of all three aryl chlorides were allowed to stand for several days after the completion of kinetics runs, and then samples were removed and diluted in a standard fashion. At the same time, samples were removed from synthetic infinity solutions made from the pure sulfide products, and these samples were diluted in the same fashion. The visible and ultraviolet absorption spectra of the corresponding diluted samples were determined and compared one against the other. The spectra showed that I, II and III had formed, respectively, 69, 42 and 87% of the expected sulfides. The last was a maximum value which did not increase with time. In all three cases, the spectra of the

reaction solutions closely resembled the spectra of the pure products, indicating that the expected products had been formed.

**Acknowledgment.**—We thank the Office of Ordnance Research, U. S. Army, for financial assistance.

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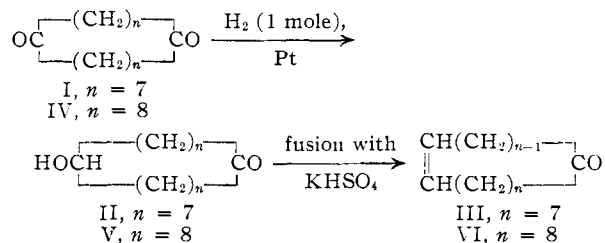
## Many-membered Carbon Rings. XI.<sup>1</sup> Civetone Homologs

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RECEIVED MAY 21, 1955

Although several syntheses for the perfumery fixative civetone have been developed,<sup>2</sup> little attention has been given to the synthesis of civetone homologs possessing the important musk odor. Ruzicka's method for 8-cyclohexadecen-1-one (III) and 9-cyclooctadecen-1-one (VI)<sup>3,4</sup> via the pyrolysis of the appropriate dibasic acids is not particularly attractive as the yields of ketones are quite low and the syntheses of the requisite unsaturated dibasic acids are lengthy.

The successful use of 1,9-cyclohexadecanedione (I) and 1,10-cyclooctadecanedione (IV) as precursors for muscone analogs<sup>1</sup> prompted a study of the utility of I and IV as intermediates for the synthesis of III and VI. The latter were in fact easily obtained by dehydration of the hydroxyketones II and V, prepared by the partial reduction of I and IV.



Using Adams catalyst in acetic acid, partial reduction of I was achieved by allowing one equivalent of hydrogen to be absorbed. The resulting mixture of products then was recrystallized from hexane, 1,9-cyclohexadecanediol (VII) being insoluble at room temperature and nearly pure II separating on cooling to 0–5°. Unreduced I and II, contained in the mother liquor, were separated by chromatography. II, thus obtained in 60% yield and characterized as its semicarbazone derivative, on fusion with potassium hydrogen sulfate gave III, isolated as its semicarbazone derivative (80%). Oxalic acid hydrolysis of III semicarbazone gave pure III, m.p. 17–22°, having an intense musk odor.

(1) For the preceding paper in this series see A. T. Blomquist, J. Prager and J. Wolinsky, *THIS JOURNAL*, **77**, 1804 (1955).

(2) E. H. Rodd, "Chemistry of Carbon Compounds," Elsevier Publishing Co., New York, N. Y., 1933, Vol. 11, Part A, p. 277.

(3) L. Ruzicka, M. Stoll, W. Scherrer, H. Schinz and C. F. Seidel, *Helv. Chim. Acta*, **15**, 1459 (1932).

(4) Soc. anon. M. Naef and Cie, Swiss Patent 135,921 (1928); *C. A.*, **24**, 2761 (1930); L. Ruzicka, U. S. Patent 1,873,154; *C. A.*, **26**, 5065 (1932).

(4) J. F. Bunnett and G. T. Davis, *THIS JOURNAL*, **76**, 3011 (1954).

(5) *o*-Chloronitrobenzene is more reactive toward amines.<sup>2</sup>

(6) J. F. Bunnett, H. Moe and D. Knutson, *THIS JOURNAL*, **76**, 3936 (1954); E. Berliner and L. C. Moadack, *ibid.*, **74**, 1574 (1952).

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-cyclooctadecanediol (VIII) (20%). Pure V<sup>6</sup> gave VI (66%), upon dehydration, as a waxy solid, m.p. 40–41°, having a musk odor similar to cyclooctadecanone. 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.<sup>6</sup>

#### Experimental<sup>7</sup>

**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.<sup>1</sup> 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<sub>16</sub>H<sub>32</sub>O<sub>2</sub>: C, 74.94; H, 12.58. Found: C, 74.98, 74.83; H, 12.61, 12.83.

**1,10-Cyclooctadecanediol (VIII).**—In the manner described above, from 4.83 g. (0.017 mole) of II<sup>1</sup> 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<sub>18</sub>H<sub>36</sub>O<sub>2</sub>: 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 pre-reduced 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<sub>16</sub>H<sub>30</sub>O<sub>2</sub>: 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<sub>17</sub>H<sub>33</sub>N<sub>3</sub>O<sub>2</sub>: C, 65.55; H, 10.68. Found: C, 65.40; H, 10.30.

**10-Hydroxycyclooctadecanone (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°.

(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.

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<sub>18</sub>H<sub>34</sub>O<sub>2</sub>: 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<sub>19</sub>H<sub>37</sub>N<sub>3</sub>O<sub>2</sub>: 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°).

*Anal.* Calcd. for C<sub>17</sub>H<sub>32</sub>N<sub>3</sub>O: 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°).

**9-Cyclooctadecen-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 re-sublimation 95 mg. (66%) of IV was obtained as a waxy solid, m.p. 40–41° (Ruzicka reported m.p. 37.5–38°).

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°).

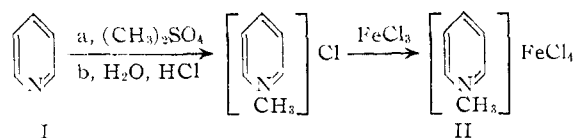
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### Chloroferrates(III) as Derivatives of Heterocyclic Compounds Containing a C=N Linkage

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RECEIVED JUNE 6, 1955

Unsaturated cyclic quaternary ammonium chloroferrates(III) such as II have been known for many years<sup>1</sup> 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.



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, picolonates, etc.) or salts of other complex inorganic acids (chloroaurates, chloroplatates, 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. Kehrman, *Ber.*, **29**, 2318 (1896); and 1-phenylpyridinium chloroferrate(III), W. König, *J. prakt. Chem.*, [2] **69**, 115 (1904).