Synthesis of Some Heterocyclic Systems from Nucleophilic Substitution Reactions with η^6-*o*-Dichlorobenzene-η^5-cyclopentadienyliron Hexafluorophosphate

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Received December 7, 1981

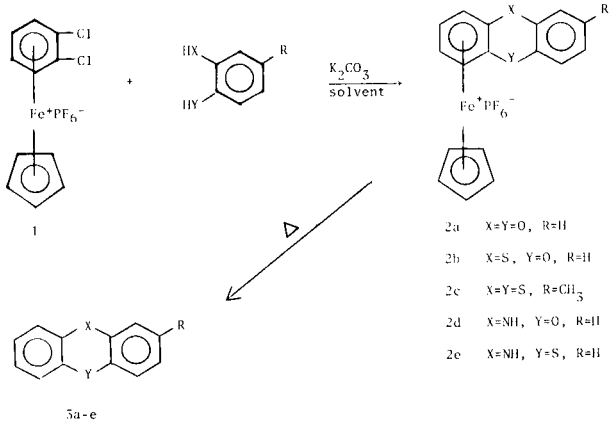
A method for the synthesis of heterocylic systems related to 9,10-dihydroanthracene with two hetero-atoms at the 9,10-positions is described. It involves the nucleophilic substitution reaction of η^6-*o*-dichlorobenzene-η^5-cyclopentadienyliron hexafluorophosphate with two nucleophilic groups (OH, SH and/or NH_2) located in the 1,2-positions of a benzene ring to give a cyclopentadienyliron complexed heterocycle. Upon pyrolytic sublimation of the complex, the free heterocyclic compound is then obtained.

J. Heterocyclic Chem., **19**, 801 (1982).

Nesmeyanov and coworkers (3,4) have shown that the organometallic complex, η^6-chlorobenzene-η^5-cyclopentadienyliron tetrafluoroborate, could readily undergo nucleophilic substitution of the chlorine atom by nucleophiles such as the ethoxy, phenoxy, thiophenoxy, η-butylthio, phathalimido and cyano groups. Similar nucleophilic substitution have also been studied with other metal-complexed halogenobenzenes including chromium or manganese tricarbonyl complexes of aryl halides (5-7). Recently, we have reported the reactions of an number of amines with the cyclopentadienyliron complex of *o*-, *m*- or *p*-chlorotoluene to give rise to a variety of *N*-substituted aminoarene complexes (8). In the present work, we have investigated the utility of such nucleophilic substitution reactions on η^6-*o*-dichlorobenzene-η^5-cyclopentadienyliron hexafluorophosphate (*o*-$Cl_2C_6H_4$-$FeCp^+PF_6^-$, **1**) as an approach to the synthesis of a number of heterocyclic systems.

The reactions given to Scheme I, with X and Y being various combinations of O, S and N, show the syntheses of heterocyclic systems related to 9,10-dihydroanthracene containing two heteroatoms at the 9,10-positions.

Scheme 1



The first step in Scheme I involves substitution of the chlorine atoms with two nucleophiles giving ring closure to a complexed heterocyclic system. With η^6-arene-η^5-cyclopentadienyliron cations, pyrolytic sublimation or photolysis is known to be capable of liberating the free arene ligand (9), presumably *via* a disproportionation type of reaction. An early example of such a photodisproortionation was reported by Nesmeyanov and coworkers (10) who showed that the photolysis of η^6-benzene-η^5-cyclopentadienyliron tetrafluoroborate gave rise to benzene, ferrocene and ferrous tetrafluoroborate. The second step in Scheme I is a pyrolytic sublimation which gave rise to the heterocyclic compound. As an example of this method of synthesis, the reaction of **1** with catechol gave a 78% yield of η^6-dibenzodioxin-η^5-cyclopentadienyliron hexafluorophosphate (**2a**) which upon pyrolytic sublimation gave a 91% yield of dibenzodioxin (9,10-dioxaanthracene, **3a**). The overall yield of 71% (based on **1**) compares favorable with, for example, the synthesis of **3a** from the heating of potassium *o*-bromophenoxide in the presence of copper powder (11), which gave yields of 51-61%.

Given in Table I are the yields of the complexed heterocycles **2a-e** derived from the nucleophilic substitution reactions with **1** and the yields of the heterocyclic compounds **3a-e** obtained from the pyrolytic sublimation of **2a-e**. The analytical data for **2a-d**, which are new com-

Table 1

Yields of η^6-Heterocycle-η^5-cyclopentadienyliron Hexafluorophosphates **2a-e** and the Liberated Heterocycles **3a-e** and Analytical Data for **2a-d**

	Yields (%)		Analysis for **2** (%)			
			C		H	
Ligand (a)	**2**	**3**	Calcd.	Found	Calcd.	Found
a	78	91	45.36	45.66	2.91	2.81
b	76	90	43.80	43.78	2.81	2.81
c	82	94	43.57	43.71	2.84	3.18
d	45	48	45.46	45.70	3.14	3.30
e	23 (b)	24 (c)	—	—	—	—

(a) The designations **a-e** for the complexed heterocyclic ligands in **2a-e** and for the freed ligands **3a-e** are, respectively, dibenzodioxin, phenoxathiin, 2-methylthianthrene, phenoxazine and phenothiazine. (b) Crude product that was difficult to purify. (c) Based on the crude product.

Table II

^{13}C NMR Data for **2a-e** and **3a-e**

Compound	CH_3	Cp	Chemical shift (δ(acetone-d_6) ppm) Complexed (a) aromatic	Uncomplexed (a) aromatic
2a	—	77.2	75.2, 83.3, 117.4*	116.6, 125.6, 138.1*
3a (b)	—	—	—	116.2, 123.6, 142.1*
2b	—	77.4	77.9, 84.3, 84.8, 93.1*, 115.3*	117.9, 126.0, 126.6, 128.9, 123.1*, 148.6*
3b (b)	—	—	—	117.5, 124.3, 126.5, 127.4, 119.9*, 151.9*
2c	19.1	77.5	85.6, 87.6 104.1*, 104.3*	128.6, 129.3, 129.7, 128.1*, 131.5*, 139.7*
3c	19.0	—	—	126.9, 127.3, 127.7, 127.8, 128.1, 130.7*, 134.2*, 134.4*, 134.7*, 137.1*
2d	—	76.0	70.0, 74.0, 79.4, 82.2, 107.5*, 116.1*	114.9, 115.7, 123.2, 125.0, 126.7*, 139.2*
3d (c)	—	—	—	112.8, 114.5, 120.0, 123.0, 131.8*, 142.7*
2e (d)	—	76.6	72.9, 81.7, 82.8, 84.1, 89.5*, 112.7*	116.0, 124.0, 126.0, 128.1, 113.0*, 137.3*
3e (c)	—	—	—	113.8, 121.3, 125.6, 126.7, 116.8*, 141.7*

(a) Absorption marked with an asterisk are due to quarternary carbons. (b) As reported in ref. (12). (c) As reporter in ref (13). (d) As reported in ref (14).

plexes synthesized in the present work, are also given in Table I. The ^{1}H and ^{13}C nmr spectra of these compounds are consistent with their assigned structures, the ^{13}C nmr data being summarized in Table II.

From Table I, it is seen that besides the good overall yield of **3a** already mentioned above, the present method also gave good yields of phenoxathiin (9-oxa-10-thiaanthracene, **3b**) and 2-methylthianthrene (2-methyl-9,10-dithiaanthracene, **3c**). A review on the methods of preparation of thianthrene (15) showed that such preparations generally would lead to the formation of unsubstituted or symmetrically substituted thianthrenes. The present synthesis of **3c** is an approach to the preparation of an unsymmetrically substituted thianthrene, and indeed **3c** is a new compound that has not been prepared previously.

When one of the hetero-atoms in N, as is the synthesis of phenoxazine (10*H*-9-oxa-10-azaanthracene, **3d**) or phenothiazine (10*H*-9-thia-10-azaanthracene, **3e**), the yield was much lower. Moreover, and attempt to prepare 5,10-dihydrophenazine (9*H*, 10*H*-9,10-diazaanthracene) by the present method *via* reaction of **1** with *o*-phenylenediamine failed to give any isolable complexed heterocycle. The reason for these relatively poorer results is not clear, but the possibility that an amino group might act as a nucleophilie in further substitution reactions could be a contributing factor.

From the results obtained in the present work, it may be concluded that the method of sythesis we have described is capable of giving good yields of symmetrically or unsymmetrically substituted heterocycles related to 9,10-dihydroanthracene containing O and/or S as hetero-atoms in the 9,10-positions. While the yields of heterocycles containing N is poorer, phenoxazine (**3d**) and phenothiazine (**3e**) were obtained. Since phenoxazine and phenothiazine derivatives with substituents at C-2 and at the N function may be of pharmacological interest (16,17), the present method possibly could provide a relatively simple approach to the synthesis of such biologically active compounds.

EXPERIMENTAL

Nucleophilic Substitution Reactions.

η^6-*o*-Dichlorobenzene-η^5-cyclopentadienyliron hexafluorophosphate (**1**) was prepared from the aluminum chloride catalyzed ligand exchange reaction between ferrocene and *o*-dichlorobenzene as reported in the literature (18). The general procedure for the nucleophilic substitution reaction with **1** is described below.

A suspension of 1.00 mmole of **1**, 1.05 mmoles of the nucleophile and an excess of potassium carbonate in an appropriate solvent (THF or THF-DMSO) was stirred at room temperature for 48 hours. The resulting material was neutralized with 10% hydrochloric acid and then 1.00 mmole of ammonium hexafluorophosphate was introduced. After stirring for 0.5 hour the product that precipitated was collected by filtration, washed with water and air-dried. It was then redissolved in dichloromethane and dried over magnesium sulfate. After filtration, concentration and addition of ether, the complexed heterocycle **2** reprecipitated.

In the following illustrations of typical experiments, 1.00 mmole of the *o*-dichlorobenzene complex **1** and 1.05 mmoles of the nucleophilic reagent were used as reactants. Some larger scale experiments with 6.0 mmoles of **1** have also been carried out in this laboratory. For synthetic applications, it is anticipated the still larger amounts of reactants could be employed.

Specifically, from 413 mg (1.00 mmole) of **1**, 115 mg (1.05 mmoles) of catechol and 250 mg (1.81 mmoles) of potassium carbonate in 20 ml of THF, the yield of η^6-dibenzodioxin-η^5-cyclopentadienyliron hexafluorophosphate (**2a**) was 351 mg (78%); ^{1}H nmr (acetone-d_6): δ 5.33 (s, 5H, Cp), 6.35, 6.63 (m, 4H, complexed arom), and 7.25 (m, 4H, uncomplexed arom). Similarly, from 1.00 mmole of **1**, 250 mg of potassium carbonate and 132 mg (1.05 mmoles) of *o*-hydroxythiophenol in 20 ml of THF, the yield of η^6-phenoxathiin-η^5-cyclopentadienyliron hexafluorophosphate (**2b**) was 354 mg (76%); ^{1}H nmr (acetone-d_6): δ 5.08 (s, 5H, Cp), 6.33, 6.56

(m, 4H, complexed arom), and 7.26 (m, 4H, uncomplexed arom). The same reaction with 1.00 mmole of **1**, 250 mg of potassium carbonate and 164 mg (1.05 mmoles) of 3,4-dimercaptotoluene in 20 ml of THF gave 407 mg (82%) of η^6-2-methylthianthrene-η^5-cyclopentadienyliron hexafluorophosphate (**2c**); ^{1}H nmr (acetone-d_6): δ 2.40 (s, 3H, CH_3), 4.97 (s, 5H, Cp), 6.52, 7.03 (m, 4H, complexed arom), and 7.51 (m, 3H, uncomplexed arom).

From the reaction of 1.00 mmole of **1**, 250 mg of potassium carbonate and 114 mg (1.05 mmoles) of *o*-aminophenol in 10 ml of a 9:1 mixture of THF-DMSO, the yield of η^6-phenoxazine-η^5-cyclopentadienyliron hexafluorophosphate (**2d**) was 202 mg (45%); ^{1}H nmr (acetone-d_6): δ 5.08 (s, 5H, Cp), 6.08 (m, 4H, complexed arom), 6.92 (m, 4H, uncomplexed arom), and 8.0 (br.s, 1H, NH). Its IR spectrum also showed a strong N-H absorption at 3410 cm^{-1}. From a similar reaction with 1.00 mmoles of **1**, 250 mg of potassium carbonate and 131 mg (1.05 mmoles) of *o*-aminothiophenol (freshly distilled in vacuo) in 10 ml of 9:1 mixture of THF-DMSO, the yield of a crude product was 107 mg (23% asuming that it was the expected η^6-phenothiazine-η^5-cyclopentadienyliron hexafluorophosphate **2e**). The ^{1}H nmr spectrum of this material showed three peaks in the Cp region at 4.9, 5.0 and 5.2 ppm, and the Cp absorption for **2e** at 5.0 ppm (14) constituted about 50% of the product mixture. Attempts to separate **2e** by crystallization or by passage through an alumina column failed.

Pyrolytic Sublimation.

Each sample of the complexed heterocycles **2a-e** was heated for 1 hour at 200-250° and 1 torr in a Büchi GKR-50 Sublimator. The material that collected on the cold finger was removed by dissolution wtih chloroform. The solution was then evaported to dryness and the residue was redissolved in hexane or hexane containing a small amount of chloroform for chromatography through a 25 cm × 2 cm dia alumina column (F20 absorption alumina supplied by Alcoa Chemicals, deactivated by exposure to air for 48 hours). The first orange-yellow fraction containing ferrocene was eluted with hexane. The second colorless fraction, containing the desired heterocylic compound, was eluted with chloroform. After removal of the chlorofrom, the product was further purified by crystallization from ether. The mass spectrum of each product gave a molecular ion with the expected molecular weight.

Specifically, from the pyrolytic sublimation of 250 mg of **2a**, the yield of dibenzodioxin (**3a**) was 93 mg (91%), mp 119° (lit (11) mp 119°). From 372 mg of **2b**, the yield of phenoxathiin (**3b**) was 142 mg (90%), mp 58° (lit (19) mp 59°). Similarly, the pyrolytic sublimation of 230 mg of **2c** gave 102 mg (94%) of 2-methylthianthrene (**3c**), mp 74°; ^{1}H nmr (acetone-d_6): δ 2.26 (s, 3H, CH_3) and 7.26 (m, 7H, arom).

Anal. Calcd. for $C_{13}H_{10}S_2$: C, 67.79; H, 4.38. Found: C, 68.03, H, 4.34.

From 250 mg of **2d**, yield of phenoxazine (**3d**) was 44 mg (48%), mp 156° (lit. (19) mp 156°). Starting with 500 mg of the crude product mixture containing **2e**, pyrolytic sublimation gave 49 mg (24%) of phenothiazine (**3e**, mp 181-182° (lit (19) mp 182°).

Acknowledgment.

The financial support given by the Natural Sciences and Engineering Research Council of Canada is gratefully acknowledged.

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