Table I. Half-Life Values for Hydrodehalogenation of Halo Aromatic Products in the Presence of $CoO/MoO_3/Al_2O_3$ Hydrodesulfurization Catalyst[a]

| compd | $t_{1/2}$, min | products[b] |
|---|---|---|
| 1, phenyl chloride | 49 | benzene |
| 2, phenyl bromide | 43 | benzene |
| 3, α-naphthyl chloride | 38 | naphthalene |
| 4, α-naphthyl bromide | 29 | naphthalene |
| 5, benzyl chloride | 2 | toluene |
| 6, benzyl bromide | 2 | toluene |
| 7, (2-bromoethyl)benzene | 5 | ethylbenzene |
| 8, phenacyl bromide | 2 | ethylbenzene |
| 9, 2-bromobenzo[*b*]thiophene | 6 | benzo[*b*]thiophene, 2,3-dihydrobenzo[*b*]thiophene, ethylbenzene |
| 10, 3-bromobenzo[*b*]thiophene | 6 | benzo[*b*]thiophene, 2,3-dihydrobenzo[*b*]thiophene, ethylbenzene |
| 11, 2,3-dibromobenzo[*b*]thiophene | 4 | benzo[*b*]thiophene, 2,3-dihydrobenzo[*b*]thiophene, ethylbenzene |
| 12, 3-chlorobenzo[*b*]thiophene | 23 | benzo[*b*]thiophene, 2,3-dihydrobenzo[*b*]thiophene, ethylbenzene |
| 13, 2,3-dichlorobenzo[*b*]thiophene | 18 | benzo[*b*]thiophene, 2,3-dihydrobenzo[*b*]thiophene, ethylbenzene |
| 14, 3-bromobenzo[*b*]thiophene *S,S*-dioxide[c] | 0.6 | benzo[*b*]thiophene *S,S*-dioxide, 2,3-dihydrobenzo[*b*]thiophene *S,S*-dioxide |

[a] $P(H_2)$ = 50 atm; $t$ = 250 °C; wt % of S based on charge = 0.3 in dodecane, decane, or Decalin. [b] For **9-14**, see text for data on the relative percentages of the products formed. [c] This rate was measured by competition with **10** at 190 °C and 50 atm.

Table II. Half-Life Values for Hydrodehalogenation of α-Naphthyl Bromide over Different Catalysts[a]

| catalyst | $t_{1/2}$, min |
|---|---|
| Co-Mo unsulfurized (HR 306) | 690 |
| Co-Mo sulfurized (HR 306) | 29 |
| Ni-Mo sulfurized (HR 346) | 19 |

[a] $P(H_2)$ = 50 atm; $t$ = 250 °C; wt % of S based on charge = 0.3 in dodecane.

the presence of different catalysts: sulfided and unsulfided HR 306 (Co–Mo) and sulfided HR 346 (Ni–Mo), under the same conditions as described below. In all cases naphthalene was the only product formed, and all the reactions were first order. The half-life values are listed in Table II.

The unsulfided HR 306 catalyst (Co–Mo) was at least 20 times less active than the sulfided one; in other words, for hydrodehalogenation, the active catalytic species is the sulfurized one as in HDS. The slight difference between the activity of sulfided Co–Mo (HR 346) catalysts is probably due to the better hydrogenating ability of the Ni–Mo catalyst.[10]

## Experimental Section

The catalysts were desulfurization catalysts used industrially, HR 306 and HR 346, obtained from Procatalyse, having the following composition $CoO/MoO_3/Al_2O_3$ (3:14:83, w/w) and $NiO/MoO_3/Al_2O_3$ (3:14:83, w/w), respectively; the pressure was 1 atm; the gas flow rate was 100 l/h per 80 g of catalyst, and the initial temperature was 150 °C. It was increased from 150 to 350 °C and maintained at 350 °C for 2 h.

The halo compounds and the catalyst were introduced into the reactor in a dodecane, decane, or Decalin solution. The apparatus used was an agitated autoclave of 0.3-L capacity. This autoclave was equipped with sample inlets, was heated by an external oven, and could be agitated at different speeds. The characteristics of this batch operation have been given by elsewhere.[7] Air was removed by purging with nitrogen at 5-atm pressure. Hydrogen was introduced at 10–15 °C below the working temperature (usually 250 °C). For all the experiments the product content was kept at 0.3 wt % of the charge. All products were analyzed by gas–liquid chromatography and identified by comparison with reference samples (IR, $^1H$ NMR, and $^{13}C$ NMR spectra).

**Registry No.** **1**, 108-90-7; **2**, 108-86-1; **3**, 90-13-1; **4**, 90-11-9; **5**, 100-44-7; **6**, 100-39-0; **7**, 103-63-9; **8**, 70-11-1; **9**, 5394-13-8; **10**, 7342-82-7; **11**, 6287-82-7; **12**, 7342-86-1; **13**, 5323-97-7; **14**, 16957-97-4; CoO, 1307-96-6; $MoO_3$, 1313-27-5; NiO, 1313-99-1; benzene, 71-43-2; naphthalene, 91-20-3; toluene, 108-88-3; ethylbenzene, 100-41-4; benzo[*b*]thiophene, 95-15-8; 2,3-dihydrobenzo[*b*]thiophene, 4565-32-6; benzo[*b*]thiophene *S,S*-dioxide, 825-44-5; 2,3-dihydrobenzo[*b*]thiophene *S,S*-dioxide, 14315-13-0.

(10) Lepage, J. F. "Catalyse de contact"; Technip: Paris, 1978; pp 441–535.

## Reaction of Various Nucleophiles with 2-Bromo-*p*-xylene and 4-Bromoveratrole via Aryne Reaction

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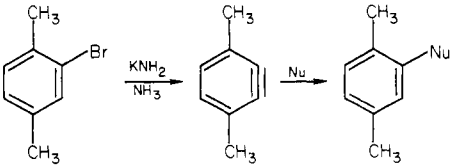
The orientation and reactivity of monosubstituted arynes has been studied extensively;[1] however, little has been reported on such investigations of polysubstituted arynes. By selecting appropriately substituted aryne precursors, high yields of a pure product should be obtained. This paper reports on the aryne reaction of two such compounds, 2-bromo-*p*-xylene, **1**, and 4-bromoveratrole, **2**, with primary and secondary amines, aliphatic nitriles, and potassium amide as base.

Compound **1** will yield the symmetrically substituted aryne 3,6-dimethylbenzyne, **3**, which will yield only 2-substituted *p*-xylenes upon nucleophilic addition. On the




**1** **3** **5**

other hand, **2** should afford predominately 3,4-dimeth-

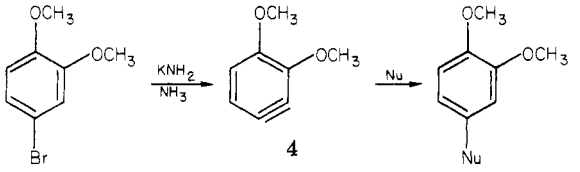
(1) See Hoffman, R. W. "Dehydrobenzene and Cycloalkane"; Academic Press: New York, 1969, and references therein.

0022-3263/83/1948-4397$01.50/0 

Table I. Reaction of 2-Bromo-*p*-xylene or 4-Bromoveratrole with Various Primary and Secondary Amines and Potassium Amide

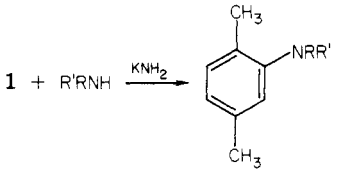
| bromo compd | amine | time, h | yield, % | bp, °C/torr |
|---|---|---|---|---|
| 2-bromo-*p*-xylene | *n*-propyl | 2 | 92 | 71/0.4 |
| | *n*-butyl | 2 | 89 | 88/0.5 |
| | isobutyl | 2 | 71 | 80/0.5 |
| | *sec*-butyl | 2 | 73 | 73/0.4 |
| | *tert*-butyl | 2 | 64 | 62/0.5 |
| | diethyl | 4 | 78 | 56/0.5 |
| | di-*n*-propyl | 4 | 65 | 76/0.5 |
| | diisopropyl | 6 | 51 | 66/0.4 |
| | di-*n*-butyl | 4 | 70 | 97/0.5 |
| | methyl-*n*-butyl | 4 | 78 | 77/0.7 |
| | ethyl-*n*-butyl | 4 | 74 | 78/0.5 |
| 4-bromoveratrole | *sec*-butyl | 2 | 79 | 114/0.3 |
| | *tert*-butyl | 2 | 73 | 106/0.3 |
| | diisopropyl | 2 | 90 | 96/0.2 |
| | methyl-*n*-butyl | 2 | 91 | 116/0.3 |
| | ethyl-*n*-butyl | 2 | 91 | 116/0.2 |

oxybenzyne, **4**, due to the greater acidity of the hydrogen atom on carbon 3 than that on carbon 5.[2] Subsequent nucleophilic addition to **4** should occur predominantly at carbon 1 to form the more stable of the possible carbanions (with the negative charge closer to the methoxy group), which upon neutralization would yield the corresponding 4-substituted veratroles.




**2** **4** **6**

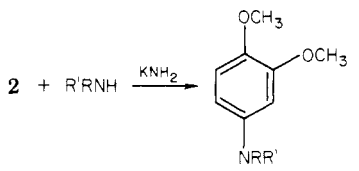
Table I lists the results of the reaction of compounds **1** and **2** with various primary and secondary amines. With one exception, **1** was converted to the corresponding 2,5-dimethylaniline in good to excellent yields (65–92%), using reaction times of 2 and 4 h for primary and secondary amines, respectively. The reaction of **1** with diisopropylamine required heating for 6 h at 60 °C to obtain a modest yield (51%) of product.




**7**

R' = H or alkyl

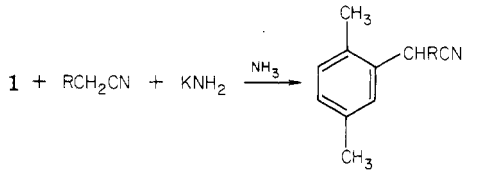
In all cases, **2** was converted to the corresponding aminoveratroles in good to excellent yields (73–91%) at room temperature and reaction time of 2 h.




**8**

The products were identified on the basis of their IR, MS, and NMR spectra. GC analysis indicated that the reaction mixtures from the reaction of **1** and **2** with secondary amines yielded only 2,5-dimethyl-*N*,*N*-dialkylanilines and 4-(dialkylamino)veratroles, respectively, whereas reaction mixtures from the reaction of **1** and **2** with primary amines consisted primarily of 2,5-dimethyl-*N*-alkylanilines and 4-(aminoalkyl)veratroles, respectively, contaminated with small quantities of diarylated products.

Table II lists the results from the reaction of **1** with various carbanions derived from nitriles and potassium amide in liquid ammonia. In each reaction excellent yields




**9**

of the corresponding nitrile (78–83%) and low yields of 2,5-dimethylaniline (10–15%), the product formed by addition of ammonia, were obtained. Unfortunately, the reaction of **2** with certain anions derived from nitriles with potassium amide in liquid ammonia gave only 2,5-dimethylaniline. We[3] had shown previously that –I groups (withdrawing by induction) increase the reactivity of benzyne to such an extent that ammonia or amide ion competed more successfully than the carbanion derived by acetonitrile for benzyne. For example, the reaction of *o*-bromoanisole with acetonitrile anion and sodium amide in methylamine gave a 73% yield of *N*-methyl-*m*-anisidine and only 13% yield of (*m*-methoxyphenyl)acetonitrile. Apparently, the two methoxy groups increase the reactivity of aryne **4** to such an extent that only the more abundant but less reactive ammonia solvent reacts with **4** to the total exclusion of the less abundant but more reactive nitrile anion.

Table II. Reaction of 1 with Various Anions of Nitriles and Potassium Amide

| nitrile | yield,[a] % | bp, °C/torr |
|---|---|---|
| acetonitrile | 81 | 79/0.3 |
| propionitrile | 78 | 82/0.3 |
| butyronitrile | 79 | 98/0.3 |
| valeronitrile | 80 | 102/0.5 |

[a] Spectral data were consistent with proposed structure of product; satisfactory elemental analysis (C, H, N) was obtained.

## Experimental Section

GLC analyses were performed on a Gow Mac Series 550 instrument with a thermal conductivity detector using a 6 ft × $^1/_8$ in. 10% SP-2100 column.

Proton NMR spectra were measured in $CDCl_3$ solutions on a Perkin-Elmer R32 spectrometer at 90 MHz. Infrared (IR) spectra were recorded on a Perkin-Elmer 283 grating spectrophotometer and mass spectra were obtained with a Dupont Dymaspec gas chromatograph/EI CI mass spectrometer with a 6 ft × $^1/_4$ in. column packed with 10% SE 30 on 80/100 HP Chromosorb W.

**Starting Materials.** Amines, nitriles, **1**, and **2** were purchased from Aldrich Chemical Co. and were dried and distilled prior to use. Liquid ammonia and potassium metal were available from previous studies.

**General Procedure for the Reaction of 1 and 2 with Primary and Secondary Amines.** Potassium metal (3.9 g, 0.1 mol) was added to a 250-mL flask equipped with a dry ice condenser and mechanical stirrer and containing 100 mL of anhydrous ammonia and 0.1 g of ferric nitrate. After the formation of

(2) Roberts, J. D.; Vaughan, C. W.; Carlsmith, L. A.; Semenov, D. A. *J. Am. Chem. Soc.* **1956**, *78*, 601, 611.

(3) Biehl, E. R.; Nieh, E.; Hsu, K. C. *J. Org. Chem.* **1969**, *34*, 3495.

potassium amide, as evidenced by the discharge of the blue solution to gray, the appropriate amine was added and the ammonia was evaporated by heating with a steam bath and under a gentle flow of dry nitrogen. Compound **1** or **2** was added then and the reaction mixture stirred for either 2 h for **1** with primary amines or **2** with primary and secondary amines or 4 h for **1** and secondary amines; the reaction of **1** with diisopropylamine required 6 h of stirring at 60 °C. The amine products were obtained by passing the reaction mixture through a column packed with silica G, concentrating the appropriate fraction (rotary evaporator), and then distilling the residue under vacuum.

**General Reaction of 1 with Nitriles.** Potassium amide (0.2 mol) was prepared in the same manner described above. The appropriate nitrile (0.1 mol) was added over a period of 5 min and the solution stirred for 10 min at which time **1** (0.05 mol) was added dropwise and the resulting solution stirred for 1 h. Then the ammonia was evaporated by heating with a steam bath, and the residue was dissolved in ether and extracted with two 100-mL portions of 6 N HCl. The ether was dried ($Na_2SO_4$) and evaporated and the residue distilled to yield the amine product.

**Acknowledgment** is made to the Robert A. Welch Foundation, Houston, TX, for partial support of this research (Grant N-118).

**Registry No.** **1**, 553-94-6; **2**, 2859-78-1; **7** (R = H; $R^1$ = Pr), 87282-05-1; **7** (R = H; $R^1$ = Bu), 87282-06-2; **7** (R = H; $R^1$ = *i*-Bu), 87282-07-3; **7** (R = H; $R^1$ = *sec*-Bu), 60388-37-6; **7** (R = H; $R^1$ = *t*-Bu), 87282-08-4; **7** (R,$R^1$ = Et), 3995-37-7; **7** (R,$R^1$ = Pr), 87282-09-5; **7** (R,$R^1$ = *i*-Pr), 87282-10-8; **7** (R,$R_1$ = Bu), 87282-11-9; **7** (R = Me; $R^1$ = Bu), 87282-12-0; **7** (R = Et; $R_1$ = Bu), 87282-13-1; **8** (R = H; $R^1$ = Bu), 87282-14-2; **8** (R = H; $R^1$ = *t*-Bu), 87282-15-3; **8** (R,$R^1$ = *i*-Pr), 87282-16-4; **8** (R = Me;$R^1$ = Bu), 87282-17-5; **8** (R = Et; $R^1$ = Bu), 87282-18-6; **9** (R = H), 16213-85-7; **9** (R = Me), 16213-86-8; **9** (R = Et), 16213-87-9; **9** (R = Pr), 16213-88-0; propylamine, 107-10-8; butylamine, 109-73-9; isobutylamine, 78-81-9; *sec*-butylamine, 13952-84-6; *tert*-butylamine, 75-64-9; diethylamine, 109-89-7; dipropylamine, 142-84-7; diisopropylamine, 108-18-9; dibutylamine, 111-92-2; *N*-methylbutylamine, 110-68-9; *N*-ethylbutylamine, 13360-63-9; acetonitrile, 75-05-8; propionitrile, 107-12-0; butyronitrile, 109-74-0; valeronitrile, 110-59-8.

## Synthesis of Porphyrinoctakis(dialkylcarboxamides)

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*Received May 2, 1983*

Certain water-soluble porphyrins have been reported as attractive alternatives to currently employed sensitizers in the photochemical reduction of water to hydrogen.[1] They have also been found to accumulate in tumors,[2] and their use as diagnostic[3] and thereapeutic agents has been examined.[4] All of these porphyrins owe their water solubility to the presence of readily ionized substituents (carboxylate,[4] sulfonate,[5] or quaternary ammonium[6] salts). We report here the synthesis of porphyrinoctakis(diethylcarboxamide) **7a** and porphyrinoctakis(dimethylcarboxamide) **7b**, two neutral, meso, unsubstituted porphyrins, which display considerable solubility in water as well as in organic solvents ranging in polarity from toluene to ethanol.

Scheme I

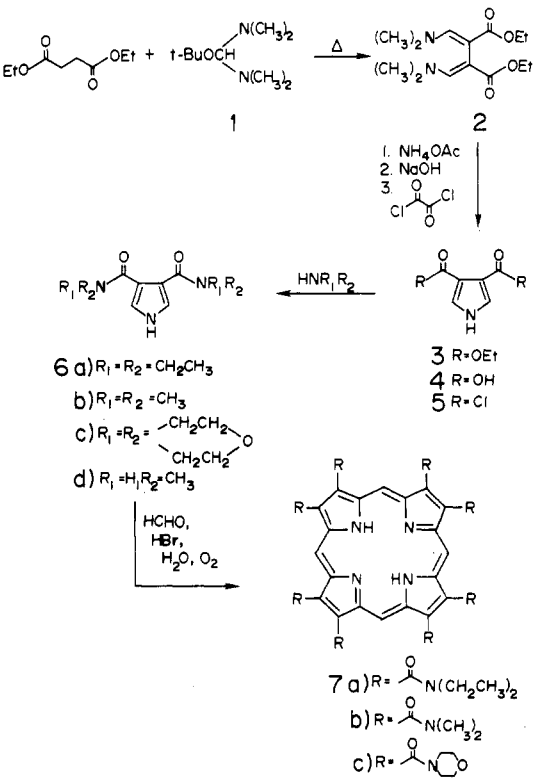


Table I. Maximum Solubilities of Porphyrins 7a and 7b in Selected Solvents

| | solubility, g/L (mol/L at 25 °C) | |
|---|---|---|
| solvent | 7a | 7b |
| $H_2O$[a] | 0.013 ($1.2 \times 10^{-5}$) | 2.4 ($2.7 \times 10^{-3}$) |
| EtOH | 3.5 ($3.2 \times 10^{-2}$) | 1.6 ($1.8 \times 10^{-3}$) |
| EtOAc | 2.2 ($2.0 \times 10^{-3}$) | 0.097 ($1.1 \times 10^{-4}$) |
| $CH_2Cl_2$ | 96 ($8.7 \times 10^{-2}$) | 65 ($7.4 \times 10^{-2}$) |
| $Et_2O$ | 0.051 ($4.6 \times 10^{-5}$) | 0.004 ($4.3 \times 10^{-6}$) |
| toluene | 7.9 ($7.2 \times 10^{-3}$) | 0.05 ($5.7 \times 10^{-5}$) |

[a] Plots of the absorbance of the Soret band vs. the concentration of **7a** ($1.2 \times 10^{-5}$ to $1.0 \times 10^{-7}$ M) and **7b** ($7.4 \times 10^{-5}$ to $2.6 \times 10^{-6}$ M) obey Beer's law, implying a lack of self-aggregation at these low concentrations. Higher concentrations of **7b** were not tested.

Recently, we described the acid-catalyzed condensations of formaldehyde and various 3,4-disubstituted pyrroles in ethanol as a convenient route to octasubstituted porphyrins.[7] Pyrroles bearing two strongly deactivating benzoyl, carbethoxy,[8] or trifluoromethyl[9] groups fail to undergo this reaction. The condensation of slightly less deactivated pyrroledicarboxamides with formaldehyde, however, had not been explored.[10] Scheme I summarizes the syntheses of a series of pyrrole-3,4-dicarboxamides **6a–d** and their conversion to porphyrins **7a–c**.

(1) Rillema, D. P.; Nagle, J. K.; Barringer, Jr., L. F.; Meyer, T. J. *J. Am. Chem. Soc.* **1981**, *103*, 56. Kalyanasundaram, K.; Grätzel, M. *Helv. Chim. Acta* **1980**, *63*, 478.
(2) Gomer, C. J.; Dougherty, T. J. *Cancer Res.* **1973**, *39*, 146.
(3) Sanderson, D. R.; Fontana, R. S.; Lipson, R. L.; Baldes, E. J. *Cancer (Amsterdam)* **1972**, *30*, 1368.
(4) Bonnett, R.; Ridge, R. J.; Scourides, P. A.; Berenbaum, M. C. *J. Chem. Soc., Perkin Trans. 1* **1981**, 3135. Hambright, P.; Fawwaz, R.; Valk, P.; McRae, J.; Bearden, A. J. *Bioinorg. Chem.* **1975**, *5*, 87. Diamond, I.; McDonagh, A. F.; Wilson, C. B.; Granelli, S. G.; Nielsen, S.; Jaenicke, R. *Lancet* **1972**, 1175.
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(8) Cheng, D. O. Ph.D. Thesis, Michigan State University, 1977.
(9) Kaesler, R. W.; LeGoff, E. *J. Org. Chem.* **1982**, *47*, 4779. Leroy, J.; Cantacuzene, D.; Wakselman, C. *Synthesis* **1982**, 313.
(10) Concurrent with this work was the reported synthesis of **7a** and several metalloderivatives: private communication from R. S. Marianelli and G. D. Sturgeon. See: Shirazi, A., Ph.D. Thesis, University of Nebraska, Lincoln, NE, 1982.

0022-3263/83/1948-4399$01.50/0 