Iodine Cyanide Promoted Iodination of Aromatic Compounds. A Simple Synthesis of 1-Iodopyrene
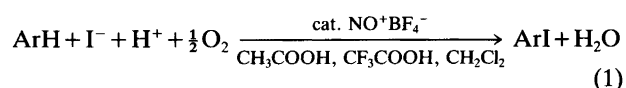
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A simple method for the iodination of reactive aromatic compounds, using ICN in the presence of a Lewis acid as the source of iodine, is presented. 1-Iodopyrene is obtained in 81 % isolated yield from the reaction of pyrene and ICN with $AlCl_3$ in $CH_3NO_2/(C_2H_5)_2O$. Anthracene undergoes partial chlorination in the presence of $AlCl_3$, but with BF_3, 9-iodoanthracene is obtained in 48 % isolated yield.

I recently reported a convenient procedure for the iodination of aromatic compounds [eqn. (1)].[1] By this method compounds with as

$$ArH + I^- + H^+ + \tfrac{1}{2}O_2 \xrightarrow[\text{CH}_3\text{COOH, CF}_3\text{COOH, CH}_2\text{Cl}_2]{\text{cat. NO}^+\text{BF}_4^-} ArI + H_2O \tag{1}$$

different reactivities as the halobenzenes and 1-methoxynaphthalene were successfully iodinated. However, when applied to certain polycyclic aromatic hydrocarbons (PAHs) the method either failed, as with anthracene, or gave low yields of iodinated products as in the case of pyrene. Since the methods available for synthesis of 1-iodopyrene and 9-iodoanthracene generally give poor yields and/or complex reaction mixtures,[1,2] an alternative method was sought and found in the treatment of the PAH with a Lewis acid (L) and ICN in $CH_3NO_2/(C_2H_5)_2O$ [eqn. (2)].

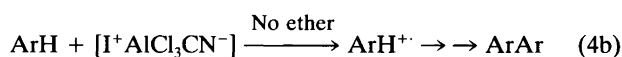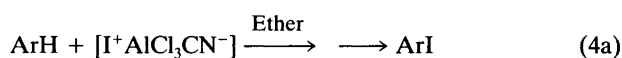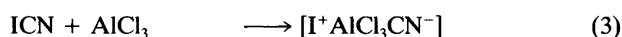$$ArH + ICN + L \rightarrow ArI + H^+ + LCN^- \tag{2}$$
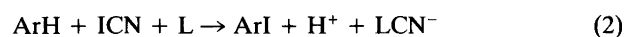
Results and discussion

In the previous paper pyrene was noted to undergo iodination much more slowly than a number of aromatic hydrocarbons, e.g., mesitylene.[1] Considering the fact that the reactivity of pyrene in electrophilic substitution is generally very high, the reverse order ($k_{pyrene} \gg k_{mesitylene}$) would be expected. The low value of k_{rel} for pyrene was presumably caused by the formation of pyrene/I_2 molecular complexes[3] or mixed-valence compounds[4] of approximate composition $C_{16}H_{10}(I_2)_2$. The formation of 1-iodopyrene was accompanied by the formation of 1-nitropyrene[1] and, occasionally, 1-acetylpyrene, and the yields of 1-iodopyrene could never be raised above 35 %, regardless of how the reaction conditions were altered.

In order to avoid the formation of pyrene/I_2 complexes, a source of electrophilic iodine other than I_2 had to be employed. ICN, in the presence[5a,6] or absence[5b,7] of $AlCl_3$, has

been reported to iodinate aromatic compounds[5] and to add I^+CN^- across the multiple bonds of certain alkenes[6] and alkynes,[7] but no detailed investigation of these reactions has been published.* In my hands treatment of cyclohexene with ICN/$AlCl_3$ gave excellent yields of *trans*-1-chloro-2-iodocyclohexane, whereas pyrene under the proper conditions readily gave 1-iodopyrene (Table 1).

Prolonged reaction times, as well as heat, generally had a detrimental effect on the material balances, and the highest yields were generally obtained when the molar ratio of ArH:ICN:$AlCl_3$ was 1:2:5 or 1:3:5. Table 1 also demonstrates the necessity of using diethyl ether as a cosolvent for a successful outcome of the reaction; obviously the system ICN/$AlCl_3$/CH_3NO_2 possesses powerful oxidizing properties which can be moderated by the addition of diethyl ether. This effect was even more evident in the case of 1-methoxynaphthalene (Table 2); in the presence of diethyl ether only iodination was observed [eqn. (4a)], while in its absence oxidative biaryl coupling resulted# [eqn. (4b)].

$$ICN + AlCl_3 \longrightarrow [I^+AlCl_3CN^-] \tag{3}$$

$$ArH + [I^+AlCl_3CN^-] \xrightarrow{\text{Ether}} \longrightarrow ArI \tag{4a}$$

$$ArH + [I^+AlCl_3CN^-] \xrightarrow{\text{No ether}} ArH^{+\cdot} \rightarrow \rightarrow ArAr \tag{4b}$$

With substrates such as naphthalene and fluoranthene, which are less readily oxidized, only iodination was observed in the absence of diethyl ether; in its presence no reaction occurred.

Anisole was very cleanly iodinated by this method and yielded iodoanisoles with an isomer distribution indicative of an electrophilic attack by some 'I$^+$' species [e.g., via

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* For the use of ICN as a cyanating agent, see Ref. 8.

ICN must be involved in these oxidation processes, since $AlCl_3$/CH_3NO_2 alone causes only very slow biaryl formation (or degradation) from 1-methoxynaphthalene or pyrene. For studies on oxidative biaryl coupling, see Ref. 9.

Table 1. Reaction of pyrene with ICN under different conditions. [ArH] = 0.040 M.[a]

[ICN]/M	[AlCl₃]/M	Reaction period/h	[C₂H₅)₂O][b]/ vol %	Yield of ArI/%[c]	Recovered ArH/%[c]
0.044	0.044	20	20	20	79
0.044	0.200	20	20	51	47
0.080	0.200	20	20	79	17
0.120	0.200	20	20	92	3
0.080	0.200	2	0	0	0
0.080	0.200	2	[d]	0	0
[e]	0.200	20	20	0	99

[a]Reaction in 25 ml solvent in tightly stoppered flasks at 25 °C. [b]Vol % of $(C_2H_5)_2O$ in CH_3NO_2. [c]Determined by GLC. [d]CH_2Cl_2 (20 vol %) in place of $(C_2H_5)_2O$. [e]I_2 (0.080 M) in place of ICN.

Table 2. Reaction of aromatic compounds with ICN under different conditions. [ArH] = 0.040 M.[a]

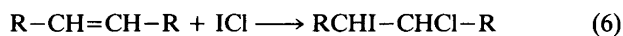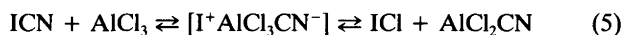| Substrate	Reaction period/h	[(C₂H₅)₂O][c]/ vol %	Reaction product (yield/%)[d]
Naphthalene	72	20	ArH (97)
Naphthalene	72	0	ArI (84)[f]
1-Methoxynaphthalene	20	20	ArI (92)[f]
1-Methoxynaphthalene	20	0	Ar–Ar (> 80)
Fluoranthene	48	0	ArI (> 80)[g]
Anisole	48	20	ArI (95)[h]
Phenol[e]	60	20	ArI (91)[i]

[a]Reaction in 25 ml solvent in tightly stoppered flasks at 25 °C. [b][ICN] = 0.080 M, [AlCl₃] = 0.200 M except in e. [c]Vol % of $(C_2H_5)_2O$ in CH_3NO_2. [d]Determined by GLC. [e][ICN] = [AlCl₃] = 0.044 M. [f]No isomers other than 1-iodonaphthalene and 1-iodo-4-methoxy-naphthalene were detected. [g]Isomer distribution not determined. [h]$o:p$ = 3:97. [i]$o:p$ = 6:94.

eqns. (3) + (4a)]. Phenol was reactive enough to undergo exhaustive iodination when a close-to-stoichiometric ratio of reactants was utilized, and on a larger scale (20 mmol) 1-iodopyrene was obtained in 81 % isolated yield using a molar ratio of pyrene:ICN:AlCl₃ of 1:1.25:1.5.

When anthracene was treated with ICN/AlCl₃ chlorination interfered with, and sometimes dominated, the outcome of the reaction as summarized in Table 3. The use of AlCl₃ in large excess, and the presence of a hindered base (Table 4) increased the iodination/chlorination ratio, but the formation of 9-chloroanthracene could never be completely suppressed when AlCl₃ was employed. Hence, other Lewis acids were examined and while AlI₃ was found to be ineffective, BF₃ gave acceptable yields. Unfortunately, at high conversions, up to 50 % of the initial amount of anthracene was lost in side reactions when BF₃ was used, but the side-products formed did not interfere with the work-up procedure. In the absence of diethyl ether, AlCl₃ as well as BF₃ caused complete degradation of anthracene upon treatment with ICN.

In Table 4 the effects of the addition of different tetraalkylammonium salts to the anthracene/ICN/AlCl₃ system are summarized. The efficient production of 9-bromo- and 9-chloroanthracene in the presence of R₄NBr and R₄NCl was presumably caused by the AlCl₃-catalyzed formation of I⁺X⁻ as discussed below.

Anthracene was the only compound from which chlorinated products were obtained,[*] and since pyrene and anthracene have nearly identical oxidation potentials this peculiarity almost certainly resides in the ability of anthracene to undergo 1,4-addition across the 9,10-positions. Cyclohexene gave quantitative yields of the ICl addition product, probably via the reactions shown in eqns. (5) and (6).

$$ICN + AlCl_3 \rightleftharpoons [I^+AlCl_3CN^-] \rightleftharpoons ICl + AlCl_2CN \qquad (5)$$

$$R-CH=CH-R + ICl \longrightarrow RCHI-CHCl-R \qquad (6)$$

Analogously, the formation of 9-chloroanthracene probably resulted from 1,4-addition of ICl to yield 9-chloro-10-iodo-9,10-dihydroanthracene, followed by loss of HI. On delibrate addition of Cl⁻ ions, the formation of ICl was even more favored (Table 4, 5th entry). Also note that when BF₃ was used as the Lewis acid or when R₄NF was added the corresponding formation of 'IF' apparently did not interfere.

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[*] In the presence of diethyl ether, perylene yielded complex reaction mixtures containing chloroperylenes, which might have been formed in a similar manner. Other ways of forming chloroperylenes, e.g., reaction of PeH⁺ with Cl⁻ cannot be excluded in the absence of a detailed study.

Table 3. Iodination of anthracene with ICN under different conditions. [ArH] = 0.040 M.[a]

[ICN]/M	Lewis acid (conc./M)	Reaction period/h	[(C₂H₅)₂O][b]/ vol %	Yield/%[c] ArCl	Yield/%[c] ArI	Recovered ArH/%[c]
0.044	AlCl₃ (0.200)	20	20	25	52	21
0.080	AlCl₃ (0.044)	60	20	61	29	6
0.120	AlCl₃ (0.400)	2	10	28	61	1
0.080	AlCl₃ (0.200)	2	0	0	0	0
0.080	AlI₃ (0.200)	20	20	0	0	100
0.080	BF₃ (0.400)	150	20	0	36	30
0.200	BF₃ (0.120)	120	20	0	39	3
[d]	BF₃[d]	216	15	0	48[e]	3
0.080	BF₃ (0.200)	2	0	0	0	0

[a]Reaction in 25 ml solvent in tightly stoppered flasks at 25 °C. [b]Vol % of (C₂H₅)₂O in CH₃NO₂. [c]Determined by GLC. [d]ArH = 0.10 M, [ICN]$_{tot}$ = 0.40 M, [BF₃] = 0.55 M. Total volume = 100 ml; see the Experimental section. [e]Isolated yield.

Table 4. Reaction of anthracene with ICN, AlCl₃ and different additives. [ArH] = 0.040 M, [ICN] = 0.080 M, [AlCl₃] = 0.200 M, [additive] = 0.040 M.[a]

Additive	Yield %[b] ArCl	Yield %[b] ArI	Yield %[b] ArBr	Recovered ArH/%[b]
(C₄H₉)₄NPF₆	30	64		4
(C₄H₉)₄NCN	6	24	[c]	65
(C₄H₉)₄NI	27	25		40
(CH₃)₄NF	41	0	[c]	51
(C₄H₉)₄NCl	85	10		1
(C₄H₉)₄NBr	6	1	88	2
2,6-Di-t-butylpyridine	23	70		2

[a]Reaction in 20 ml of CH₃NO₂/5 ml of (C₂H₅)₂O in tightly stoppered flasks at 25 °C for 20 h. [b]Determined by GLC. [c]No ArCN or ArF was detected.

Finally it may be noted that ICN can be replaced by I₂ and a catalytic amount of CN⁻. Thus, from 2.5 mmol pyrene, 2.0 mmol I₂, 0.2 mmol (C₄H₉)₄NCN and 10 mmol AlCl₃, 1.4 mmol 1-iodopyrene (70 % based on I₂) were obtained. When applied to anthracene this approach yielded mainly 9-chloroanthracene. The reaction probably proceeds via ICN since I₂ and CN⁻ rapidly yield ICN and I⁻.[10]

Experimental

Materials and methods. Nitromethane (Merck) was passed through silica gel prior to use. Diethyl ether was distilled from sodium. Dichloromethane (Merck) was dried over 3 Å molecular sieves. Aromatic compounds were used as received or were purified by chromatography (purity > 98 %). Iodine cyanide was prepared by the method described.[10] Commercial iodine cyanide (Fluka), used as received, generally gave inferior, albeit acceptable, results. Iodine, tetraalkylammonium salts, anhydrous aluminium chloride and gaseous boron trifluoride were commercial samples and were used as supplied. Solutions of boron

trifluoride were prepared by saturating known volumes of nitromethane and the concentration was determined by differential weighing. Commerical boron trifluoride–diethyl ether was not effective in these reactions. Aluminium triiodide was prepared according to a literature method.[11]

Column chromatography was performed and ¹H NMR and mass spectra were recorded as previously described.[1] Product identification was performed and GLC yields were obtained as in Ref. 1, but 1-acetylpyrene and 9-bromoanthracene were used as reference compounds.

General iodination procedure. The aromatic compound and ICN were weighed into an Erlenmeyer flask and (C₂H₅)₂O and most of the CH₃NO₂ were added. The flask was stoppered and after 10 min of stirring, AlCl₃ dissolved in CH₃NO₂ was added in one portion.

After being stirred for the appropriate reaction period at room temperature, the reaction mixture was poured onto aq. Na₂S₂O₃/CH₂Cl₂. the aqueous layer was washed with CH₂Cl₂, and the combined organic layers were washed with water, aq. NaHCO₃, and water and dried (MgSO₄). After evaporation and passage through a short column the yield was determined by GLC, or work-up followed by chromatography on silica gel with pentane/0–20 % CH₂Cl₂.

Iodination of pyrene. Pyrene (0.020 mol) and ICN (0.025 mol) were treated with AlCl₃ (0.030 mol) in 40 ml of (C₂H₅)₂O/150 ml of CH₃NO₂ for 72 h. After work-up as described above, 1-iodopyrene (0.016 mol, 80 %, recrystallized from ethanol) was obtained.

Iodination of anthracene. Anthracene (0.010 mol) and ICN (0.015 mol; a total of 0.040 mol was added) were dissolved in 15 ml of (C₂H₅)₂O/15 ml of CH₃NO₂ by gentle warming. BF₃ (0.055 mol) in 65 ml of CH₃NO₂ was added and the stoppered flask was stirred for 9 days; on days 3 and 6 additional portions of ICN were added. After work-up as described above, 9-iodoanthracene (0.0048 mol, 48 %, recrystallized from ethanol) was obtained.

Iodination of 1-methoxynaphthalene. Following the general procedure and with the experimental details given in Table 2, 1-iodo-4-methoxynaphthalene was formed in 92 % yield (GLC) in the presence of ether (20 vol%). In the absence of ether, but under otherwise identical conditions, the major product was 4,4'-dimethoxy-1,1'-binaphthyl [>80% yield (GLC)] and no starting material remained. On treatment of 1-methoxynaphthalene with $AlCl_3$ in CH_3NO_2 (i.e. in the absence of ether and ICN) under the same conditions only 5 % of the biaryl was formed and >90 % of the starting material remained unchanged.

Iodination of phenol and anisole. Following the general procedure the yields reported in Table 2 were determined by GLC. Isomer distributions were determined by comparison with authentic samples by capillary GLC on Superox 10. In the absence of ether, all starting material was rapidly consumed, but no identified products were formed.

Iodination of fluoranthene and perylene. Following the general procedure fluoranthene yielded monoiodofluoranthenes in the absence of ether. The yield was estimated to be >80 % by GLC, but the products were only identified by MS. No attempts to isolate the individual isomers or to determine the isomer distribution were made. In the case of perylene complicated reaction mixtures containing mono- and di-chlorinated perylenes (GLC/MS) were formed in the presence of ether. The chloroperylene mixtures were not further investigated.

Attempted iodination of cyclohexane. When cyclohexene was treated with $ICN/AlCl_3$ according to the general procedure, excellent yields of *trans*-1-chloro-2-iodocyclohexane [identified by MS, NMR; yield (GLC) 91%] were obtained. No 1-cyano-2-iodocyclohexane was detected by MS. Replacement of $AlCl_3$ by BF_3 resulted in no reaction.

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