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Tetrahedron Letters 47 (2006) 7011–7015

Tetrahedron Letters

Oxidative-substitution reactions of polycyclic aromatic hydrocarbons with iodine(III) sulfonate reagents

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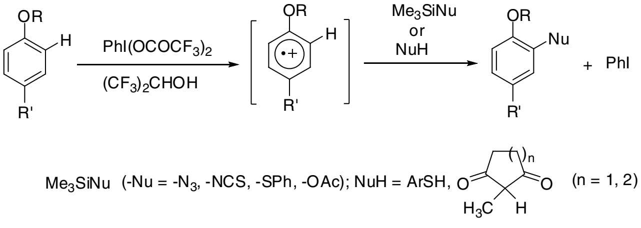
Received 30 June 2006; revised 17 July 2006; accepted 21 July 2006

Abstract—Polycyclic aromatic hydrocarbons (PAH) undergo regioselective oxidative-substitution reactions with iodine(III) sulfonate reagents in dichloromethane to give the corresponding aryl sulfonate esters. The use of [hydroxy(tosyloxy)iodo]benzene in conjunction with trimethylsilyl isothiocyanate leads to thiocyanation of the PAH nucleus.

The capacity of phenyliodine(III) bis(trifluoroacetate), PIFA, to promote oxidative-substitution and oxidative-coupling reactions of electron-rich aromatic compounds through arene radical–cation intermediates has been amply demonstrated over the past 15 years. For example, PIFA oxidations of aromatic ethers in $(CF_3)_2$-$CHOH$ permit the introduction of selected nucleophiles into the aromatic nucleus; Eq. 1.[1–4] The nature of the solvent is crucial to the success of these two-electron oxidation–reduction reactions. It has been shown, for example, that the use of CH_2Cl_2 instead of $(CF_3)_2CHOH$ reduces the yields of nuclear substitution products to trace levels or less.[2,4]



(1)

The treatment of PIFA with $Et_2O \cdot BF_3$ affords a more reactive iodine(III) species, and, in this case, CH_2Cl_2 is the solvent of choice. These conditions have been employed for nuclear azidations of naphthalene and polymethylbenzenes with Me_3SiN_3,[1] nuclear cyanations of thiophenes, pyrroles, and indoles with Me_3SiCN,[5] and heterocyclizations of aromatic ethers containing alkylsulfanyl sidechains.[6] When nucleophiles are not available, oxidative-coupling occurs. Hence, thiophenes,[7,8] polyalkylbenzenes,[9] and aromatic ethers[10] are converted to biaryl products with BF_3—activated PIFA in CH_2Cl_2. Intramolecular coupling reactions of this type provide access to various benzo-annulated heterocyclic compounds.[11]

We know of one reported example of aryl trifluoroacetate formation during PIFA oxidations of aromatic compounds; namely, EPR observation of the 9-trifluoroacetoxyanthracene radical–cation when anthracene was treated with PIFA in trifluoroacetic acid at −11 °C.[12] Other polycyclic aromatic hydrocarbons such as pyrene, perylene, pentacene, and 9,10-dimethylanthracene gave unsubstituted radical–cations ($ArH^{\cdot+}$) under the same conditions.[12]

In contrast to PIFA, the use of iodine(III) sulfonate reagents, $ArI(OH)OSO_2R$, for nuclear oxidations of aromatic substrates has been little explored. Indeed, whereas benzene and toluene are unreactive with PhI(OH)OTs, electron-rich aromatics (e.g., anisole, thiophenes, trimethylsilylarenes, and trimethylsilylfurans) undergo electrophilic substitution reactions with ArI(OH)OTs, leading to iodonium salts $Ar(Ar')I^{+}$ ^{-}OTs.[13]

We now report that iodine(III) sulfonates undergo direct oxidative-substitution reactions with polycyclic

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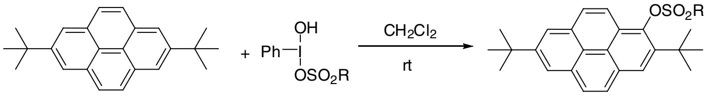
doi:10.1016/j.tetlet.2006.07.114

aromatic hydrocarbons. This was discovered when an attempt to phenyliodinate 2,7-di-*tert*-butylpyrene (**1**, 2,7-DTBP) with [hydroxy(tosyloxy)iodo]benzene (**2a**, HTIB) gave 1-tosyloxy-2,7-di-*tert*-butylpyrene (**3a**) instead. Similar treatment of 2,7-di-*tert*-butylpyrene with the phenyl λ^3-iodanes **2b**–**2d**, containing mesylate (OMs), (+)-10-camphorsulfonate (OCs), and 2,4-dinitrobenzenesulfonate (ODNs) ligands, led regioselectively to the 1-sulfonyloxy-2,7-DTBP derivatives **3b**–**3d** shown in Eq. 2 and Table 1. These reactions proceed readily in CH_2Cl_2 at room temperature and do not require activation of the iodine(III) reagent.

The structures of **3a**–**d**, including the location of the sulfonate group, are clearly evident by ^{1}H and ^{13}C NMR analysis. For example, in addition to two *tert*-butyl singlets (δ 1.59 and 1.73) and one methyl singlet (δ 3.43) in the aliphatic region, the ^{1}H spectrum (300 MHz, $CDCl_3$) of **3b** features a 2H AB multiplet at δ 8.02 (H-4 and H-5), 1H doublets at δ 8.13 ($J = 9.3$ Hz, H-9) and δ 8.48 ($J = 9.5$ Hz, H-10), a 2H 'singlet' at δ 8.23 (H-6 and H-8) and a 1H singlet at δ 8.28 (H-3).[15] Furthermore, the structures of the tosylate,[16] mesylate,[17] and camphorsulfonate[16] analogs were established unequivocally by single crystal X-ray analysis.



1 2 3 (2)

a (-OTs, R = 4-MeC_6H_4) **b** (-OMs, R = Me) **c** (-OCs, R = (1R)-10-camphoryl)
d (-ODNs, R = 2,4-$(NO_2)_2C_6H_3$)

The yields of **3a**–**d** (and all other oxidative-substitution products) reported herein are based on chromatographically isolated compounds, sometimes after further purification by recrystallization. For example, in one experiment, a mixture of 2,7-DTBP (0.315 g, 1.0 mmol) and **2a** (0.432 g, 1.1 mmol) in CH_2Cl_2 (20 mL) was stirred magnetically under N_2 for 45 min at room temperature. After aqueous workup (H_2O; 5% $NaHCO_3$; $MgSO_4$) and solvent removal, a red oil (0.72 g) containing PhI was obtained. Column chromatography of the oil on silica gel with 10–25% CH_2Cl_2 in hexanes gave a pale-yellow solid (0.371 g). Recrystallization of this material from methanol returned 1-tosyloxy-2,7-DTBP as a white solid; yield, 0.329 g (68%); mp 175.5–176.5 °C.

Table 1. Reactions of 2,7-di-*tert*-butylpyrene with iodine(III) sulfonate reagents in CH_2Cl_2 at rt

Reactants[a] (mmol)	CH_2Cl_2 (mL), time (h)	OSO_2R	Product, yield[b] (%)
1 (1.0), **2a** (1.2)	20, 24	OTs	**3a**, 82[c]
1 (1.0), **2a** (1.1)	20, 0.75	OTs	**3a**, 68
1 (1.0), **2a** (1.1)	15, 0.5	OTs	**3a**, 65
1 (1.0), **2b** (1.2)	15, 17	OMs	**3b**, 64[d]
1 (0.64), **2b** (0.70)	15, 1.7	OMs	**3b**, 63
1 (0.65), **2c** (0.72)	15, 17	OCs	**3c**, 67[e] (77)
1 (0.64), **2c** (0.70)	20, 1.5	OCs	**3c**, 50 (59)
1 (1.0), **2d** (1.2)	30, 3	ODNs	**3d**, 73[f]

[a] Rounded-off to two significant figures.

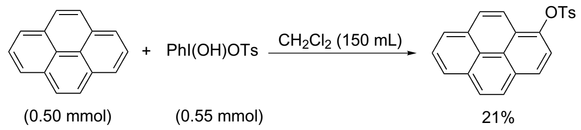
[b] Isolated yields; The yields in parentheses are corrected for recovered hydrocarbon.

[c] Anal. Calcd for $C_{31}H_{32}O_3S$: C, 76.82; H, 6.66; found: C, 76.47; H, 6.71;[14] mp 180–181 °C.

[d] Anal. Calcd for $C_{25}H_{28}O_3S$: C, 73.50; H, 6.91; found: C, 73.08; H, 6.93; mp 209–211 °C.

[e] Anal. Calcd for $C_{34}H_{40}O_4S$: C, 74.96; H, 7.40; found: C, 74.90; H, 7.33; mp 146–150 °C.

[f] Mp 184–186 °C (dec).

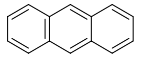
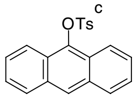
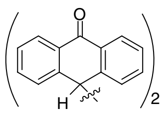
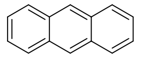
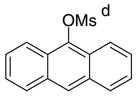
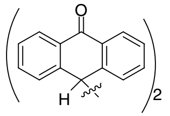
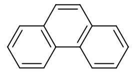
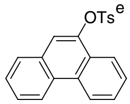
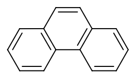
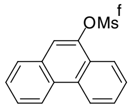
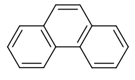
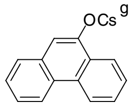
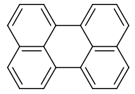
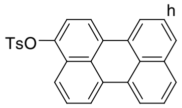


(3)

The starting concentrations of 2,7-DTBP in the foregoing experiments ranged from about 0.03 to 0.07 M and provided good yields of the oxidative-substitution products. However, when **2a** was added to a 0.05 M solution of parent pyrene in CH_2Cl_2, *p*-toluenesulfonic acid and a highly insoluble olive-green solid co-precipitated. Treatment of the mixture with acetone (under reflux) allowed separation of the individual components in 78% ($TsOH\cdot H_2O$) and 75% (by mass) yields, respectively. The insoluble solid did not melt at temperatures up to 300 °C and, based on comparison of its solid-state ^{13}C NMR spectrum with that of pyrene,[18] appears to be a mixture of pyrene oligomers. Column chromatography (silica gel; hexanes, 5–10% EtOAc–hexanes) of the oil recovered from the filtrate gave 1-tosyloxypyrene in 7% yield. When **2a** was allowed to react with a more dilute solution of pyrene ($C_0 = 3.3 \times 10^{-3}$ M), the oligomeric material was still produced, but in this case, 1-tosyloxypyrene was isolated in 21% yield (Eq. 3) and identified by single crystal X-ray analysis.[16]

Whether oxidative-substitution reactions of this type extend to other polycyclic ring systems was tested by the treatment of anthracene, phenanthrene, and perylene with selected iodine(III) sulfonate reagents in CH_2Cl_2. In these exploratory studies, starting concentrations of the substrates were in the range 0.02–0.10 M and dilution effects were not examined. As shown in Table 2, all three hydrocarbons were converted regioselectively to the indicated sulfonate derivatives, although the yields of the 9-anthryl sulfonates were limited by the

Table 2. Reactions of anthracene, phenanthrene, and perylene with iodine(III) sulfonate reagents in CH_2Cl_2 at rt

Reactants[a] (mmol)	CH_2Cl_2 (mL), time	Product, yield[b] (%)
 , **2a** (1.0) (1.2)	20, 0.75 h	 [c] 21.5  43.5
 , **2b** (1.0) (1.2)	50, 3 h	 [d] 33  24
 , **2a** (1.0) (1.2)	25, ca. 4 d	 [e] 60 (66)
 , **2b** (1.0) (1.2)	25, 4 d	 [f] 54 (62)
 , **2c** (1.0) (1.2)	10, ca. 5 d	 [g] 41 (55)
 , **2a** (0.50) (0.60)	10, 1 h	 [h] 44 (55)

[a] Rounded-off to two significant figures.

[b] Isolated yields; The yields in parentheses are corrected for recovered hydrocarbon.

[c] Mp 164–166 °C.

[d] Anal. Calcd for $C_{15}H_{12}O_3S$: C, 66.16; H, 4.44; found: C, 66.13; H, 4.58; mp 176–177 °C.

[e] Anal. Calcd for $C_{21}H_{16}O_3S$: C, 72.39; H, 4.63; found: C, 72.33; H, 4.64; mp 155–156 °C.

[f] Anal. Calcd for $C_{15}H_{12}O_3S$: C, 66.16; H, 4.44; found: C, 66.30; H, 4.52; mp 111–112 °C.

[g] Mp 99.5–101 °C.

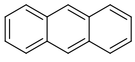
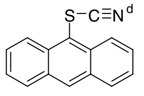
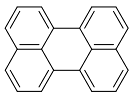
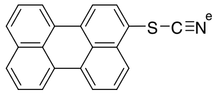
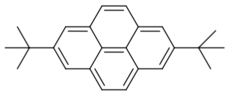
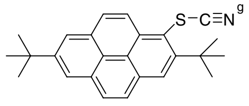
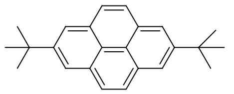
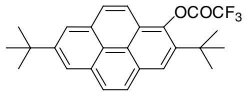
[h] Mp 200–202 °C (dec).

competing formation of bianthronyl. Phenanthrene reacts more slowly with **2** than the other ring systems, but this had little or no effect on product yields. Finally, in addition to NMR (^1H, ^{13}C) characterization of the sulfonate products shown in Table 2, single crystal X-ray structures of the tosylate derivative of perylene and the mesylate derivatives of anthracene and phenanthrene were determined.[16]

The possibility that iodine(III) sulfonate reagents might be employed without activation in CH_2Cl_2 for the introduction of external nucleophiles into polycyclic aromatic hydrocarbons was demonstrated by the conversion of anthracene, perylene, and 2,7-DTBP to the thiocyanato derivatives shown in Table 3. This was accomplished by treatment of the hydrocarbons with **2a** (HTIB) in the presence of a 5-fold excess of trimethylsilyl isothiocyanate. In view of significant bianthronyl production during direct reactions of anthracene with **2a** and **b**, the high yield of 9-thiocyanatoanthracene when Me_3SiNCS is available is noteworthy. However, a similar attempt to prepare the thiocyanate derivative of phenanthrene was unsuccessful.

We finally report that PIFA reacts with 2,7-DTBP in CH_2Cl_2 to give the trifluoroacetate derivative shown in Table 3, the structure of which was verified by single crystal X-ray analysis.[17] A mechanism for the oxysulfonylation of polycyclic aromatic hydrocarbons with iodine(III) sulfonate reagents has not yet been

Table 3. Thiocyanation and trifluoroacetoxylation of polycyclic aromatic hydrocarbons with iodine(III) reagents in CH_2Cl_2

Reactants[a] (mmol)	CH_2Cl_2 (mL), time	Product, yield[b] (%)
 ,**2a**, Me_3SiNCS (1.0) (1.2) (5.0)	20[c]	 84
 ,**2a**, Me_3SiNCS (0.50) (0.60) (2.5)	10, 5 h	 48, (65)
 ,**2a**, Me_3SiNCS (0.50) (0.60) (2.5)	10[f]	 89
 , $PhI(OCOCF_3)_2$ (3.1) (3.5) (0.50) (0.55)	30, 20 h 10, 2.7 h	 73.5 71[h]

[a] Rounded-off to two significant figures.

[b] Isolated yields; The yields in parentheses are corrected for recovered hydrocarbon.

[c] 1.5 h at 0 °C, overnight at rt.

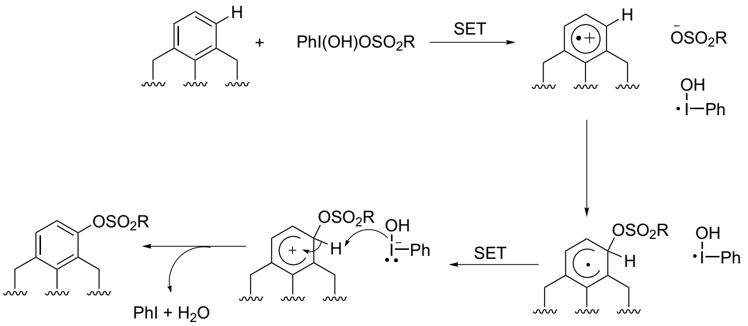
[d] Anal. Calcd for $C_{15}H_9NS$: C, 76.56; H, 3.86; found: C, 76.26; H, 4.05; mp 182.5–184 °C.

[e] HRMS Calcd for $C_{21}H_{11}NS{+}Na$: 332.0510; found: 332.0504; mp 180.5–182 °C.

[f] 0.5 h at 0 °C, 24 h at rt.

[g] Anal. Calcd for $C_{25}H_{25}NS$: C, 80.82; H, 6.78; found: C, 80.92; H, 7.11; mp 118–120 °C.

[h] Anal. Calcd for $C_{26}H_{25}F_3O_2$: C, 73.22; H, 5.91; found: C, 72.86; H, 5.88; mp 123–126 °C.



Scheme 1.

established. However, based on analogy with PIFA, the radical–cation mechanism shown in Scheme 1 seems plausible, and is suggested as a preliminary model.

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13. Moriarty, R. M.; Vaid, R. K.; Koser, G. F. *Synlett* **1990**, 365–383, See pp 378–379 and references cited therein.
14. The elemental analyses reported herein were performed by Galbraith Laboratories, Inc., Knoxville, TN; Microanalysis Laboratory, University of Illinois, Urbana, IL; or Midwest Microlab, LLC, Indianapolis, IN.
15. The proton assignments are based on analysis of the COSY and NOESY spectra of **3b**. The spectra were recorded by Silapong Baiagern at The University of Akron on a 400 MHz Spectrometer (Inova 400).
16. Semih Durmus and Wiley J. Youngs; The University of Akron, unpublished results.
17. Jered C. Garrison and Wiley J. Youngs; The University of Akron, unpublished results.
18. The solid-state ^{13}C NMR spectra were recorded by Todd A. Wagler at The University of Akron.