large excess of DTBMP. The addition of DTBMP to the reaction system caused the rapid completion of reaction. Unused oxime was not obtained and the yields of isoxazole increased in each case (runs 6, 8, and 10). At the same time, the formation of ketone was diminished, suggesting that the ketone to some extent arose from hydrolysis of a complex that had been formed between oxime and $Th^{\bullet+}$, analogous to our experience with aldoximes.[1] However, we have this time been unable to relate ketone formation quantitatively to the formation of ThO, nor have we used $H_2[^{18}O]$, as we did earlier with aldehydes, as a diagnostic aid in tracing the source of the ketone.

Experimental Section

Reactions of Oximes with $Th^{\bullet+}ClO_4^-$. A general procedure was adopted. Solid $Th^{\bullet+}ClO_4^-$ and the oxime in the mole ratio 2:1 were placed under argon in a septum-capped flask into which 20 mL of acetonitrile was injected by syringe. The mixture was stirred for 48 h. In all cases, the dark purple color of $Th^{\bullet+}$ faded with time but did not entirely disappear. When reaction was carried out in the presence of 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP), the mole ratio used was 2:1:3, and the DTBMP was placed in the flask with the $Th^{\bullet+}ClO_4^-$ and oxime before solvent was added. In each of these cases the color of $Th^{\bullet+}$ disappeared completely within 5 min, but the yellow solution was stirred overnight. Thereafter, 5 mL of water was added followed by aqueous $NaHCO_3$ to neutralize $HClO_4$ that had been formed in reaction and in hydrolysis of unused $Th^{\bullet+}ClO_4^-$. The solution was extracted with 4 × 20 mL of CH_2Cl_2, and the dried ($MgSO_4$) CH_2Cl_2 solution was evaporated. The tared residue thus obtained was taken up in a standard volume of CH_2Cl_2, and the solution was analyzed by GC and GC-MS. Concentration factors for all products were determined with authentic materials. Each reaction was run twice, and the averaged yields of products are given in Tables I and II. All other experimental procedures have been described earlier.[1]

Preparation of Oximes. Oximes were prepared in standard ways from mixtures of the carbonyl compound, $NH_2OH{\cdot}HCl$, and a base in aqueous ethanol. No attempts were made to separate *E* and *Z* isomers.

Preparation of 5-Methyl-3-styryl-1,2,4-oxadiazole (5a). Cinnamaldehyde oxime (2.7 g, 18.4 mmol) in 26 mL of ice-cold 37% HCl solution, was converted into its α-chloro derivative by dropwise addition of 30 mL of commercial bleach (5.25% NaOCl). After standing for 1 h, the solution was poured into a slurry of ice (300 g) and water. The oil that separated was extracted with 30 mL of CH_2Cl_2, and the CH_2Cl_2 solution was washed twice with 30 mL of water and dried over $MgSO_4$. Removal of the CH_2Cl_2 left 2.1 g (11.6 mmol, 63%) of a yellow oil: ^1H NMR ($CDCl_3$) δ 6.85 (d, 1 H, *J* = 16 Hz), 7.30-7.44 (m, 6 H). To an ice-cold solution of the oil (2.0 g) in dry ether was added dropwise with stirring 1.5 mL of triethylamine. After 10 min the precipitate of Et_3NHCl was removed and the ether solution was washed with 200 mL of 5% H_2SO_4, 100 mL of 5% $NaHCO_3$, and 3 × 50 mL of water. It was then dried over $MgSO_4$. To the dried ether solution was added 4.5 mL of $BF_3{\cdot}Et_2O$ complex and 40 mL of dry CH_3CN. The ether was removed at 50 °C, and the remaining solution was heated under reflux for 8 h. Evaporation of the solvent under reduced pressure left 2.1 g of dark oil. This was chromatographed on a column of silica gel, with elution by ethyl acetate/hexane, 1:9. Among 15 30-mL fractions, fractions 8 and 9 were found by GC to contain the desired, but impure, oxadiazole. The fractions were purified by TLC on a silica plate with the same solvent development, to give 80 mg of yellow oil that was again subjected to TLC, giving 20 mg (0.115 mmol, 1% based on the α-chlorooxime) of a yellow solid, 98% pure by GC analysis. Crystallization from hexane gave 5 mg of **5a** as yellow needles: mp 80-81 °C; mass required for $C_{11}H_{10}N_2O$ 186.2152, found 186.0788.[3] This oxadiazole has been prepared earlier by (apparently) the dehydrochlorination and cyclization of *N*-acetyl-*N'*-chlorocinnamic acid amidine in basic solution (lit.[4] mp 78 °C).

(3) Midwest Center for Mass Spectrometry, a regional NSF facility, University of Nebraska, Lincoln, NE.

Acknowledgment. We thank the Robert A. Welch Foundation (Grant D-028) and the National Science Foundation (Grant CHE 86-12031) for support.

Supplementary Material Available: Details of preparation of the oximes and of authentic samples of **4a**, **6a**, **6b**, **7a** and **8** and the ^1H NMR data for **5a** (3 pages). Ordering information is given on any current masthead page.

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A New Synthetic Route to 4-Alkylpyrenes from 2,7-Di-*tert*-butyl-*trans*-10b,10c-dimethyl-10b,10c-dihydropyrenes

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Received May 14, 1990

Introduction

It is well known that electrophilic reagents attack positions 1, 3, 6, and 8 of pyrene, but not the other positions (2, 4, 5, 7, 9, and 10). Therefore, pyrenes substituted at the latter positions must be obtained in ways other than by electrophilic substitution of pyrene itself.[4-6]

It was reported[7-9] that 2,7-di-*tert*-butyl-*trans*-10b,10c-dimethyl-10b,10c-dihydropyrene, which is easily obtained from toluene, reacted with iodine in boiling benzene to afford 2,7-di-*tert*-butylpyrene. It was also reported[9] that positions 4, 5, 9, and 10 of the 10b,10c-dihydropyrene were reactive toward electrophilic reagents. We report a synthetic route to 4-substituted pyrenes that are not easily obtained by previously reported methods.

Results and Discussion

Electrophilic substitutions, such as nitration, formylation, acylation, and bromination, of 2,7-di-*tert*-butyl-*trans*-10b,10c-dimethyl-10b,10c-dihydropyrene (**1a**) gave the 4-substituted derivatives (**1b-f**) (Scheme I).

The 4-formyl- (**1b**), 4-acyl- (**1c-d**), and 2,7-di-*tert*-butyl-4-nitro-*trans*-10b,10c-dimethyl-10b,10c-dihydropyrenes (**1e**) were obtained from **1a** under mild conditions (Scheme I). However, bromination of **1a**, with an equimolar amount of bromine, afforded a mixture of mono- and disubstituted products and unreacted **1a**. Isolation of **1f** from the reaction mixture was unsuccessful.

4-Alkyl derivatives **1g-i** were prepared by reduction of the carbonyl derivatives **1b-d** with $LiAlH_4$-$AlCl_3$, and the

(1) Department of Molecular Science and Technology.
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(6) Streitwieser, A.; Lawler, R. G.; Schwaab, D. *J. Org. Chem.* **1965**, *30*, 1470.
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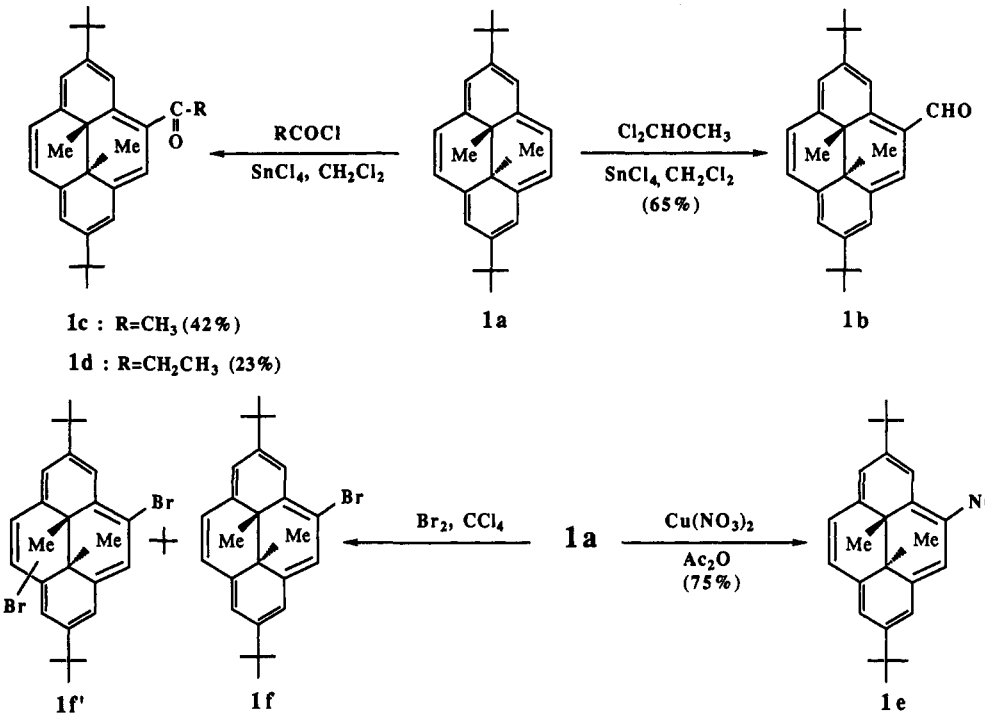
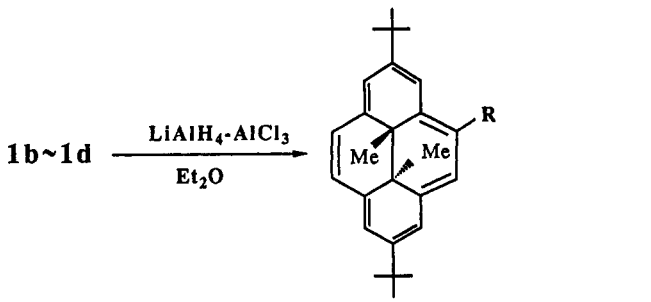
0022-3263/91/1956-1334$02.50/0

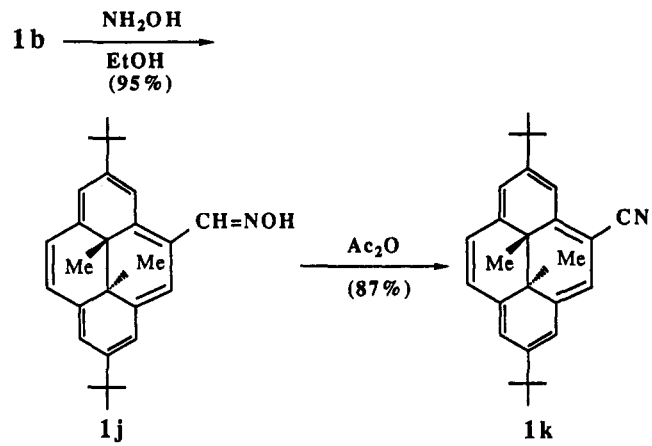
Scheme I



Scheme II



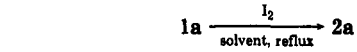
1g : R=CH_3 (94%)
1h : R=CH_2CH_3 (97%)
1i : R=$CH_2CH_2CH_3$ (96%)



4-cyano derivative (**1k**) was prepared from **1b** via **1j** (Scheme II).

Although the preparation of 2,7-di-*tert*-butylpyrene (**2a**) from **1a** by treatment with iodine was described earlier,[8] the reaction of **1a** with iodine under various conditions was reinvestigated to obtain more information about the best reaction conditions for formation of **2a**. The results are summarized in Table I. Toluene proved to be a more suitable solvent than benzene for the preparation of **2a**.

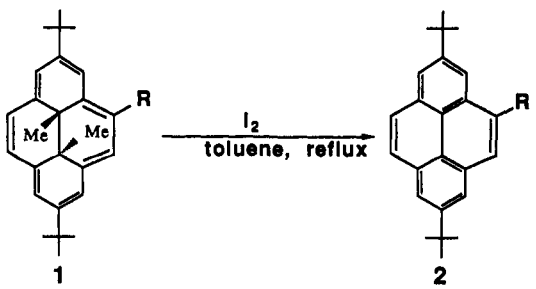
Table I. Reaction of 2,7-Di-*tert*-butyl-*trans*-10b,10c-dimethyl-10b,10c-dihydropyrenes (1a) with Iodine in Boiling Solvent



entry	solvent	I_2/1a, mol/mol	time, h	yield of 2a,[a] %
1	benzene	4	60	95
2	toluene	4	48	97
3	toluene	8	24	98
4	toluene	12	14	96
5	toluene	24	6	97

[a] Isolated yields are shown.

Table II. Reaction of 2,7-Di-*tert*-butyl-4-substituted-*trans*-10b,10c-dimethyl-10b,10c-dihydropyrenes with Iodine in Boiling Toluene



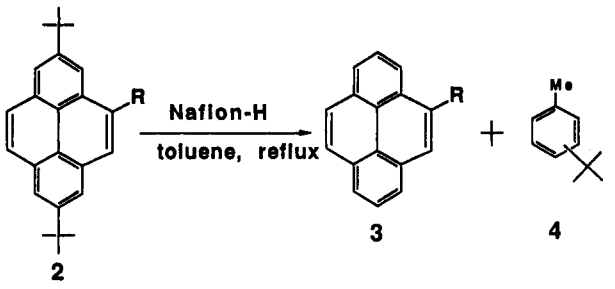
entry	substrate (R)	time, h	product, (%)[a]
1	**1b** (CHO)	120	**2b** (60)
2	**1c** ($COCH_3$)	120	**2c** (72)
3	**1e** (NO_2)	120	tar
4	**1g** (CH_3)	36	**2g** (87)
5	**1h** (CH_2CH_3)	48	**2h** (73)
6	**1i** ($CH_2CH_2CH_3$)	48	**2i** (75)
7	**1k** (CN)	120	tar

[a] Isolated yields are shown.

Also it was found that an increase in the amount of iodine shortened the reaction time. However, isolation of product **2a** was difficult in the presence of a large excess of iodine.

Reactions of 4-substituted dihydropyrenes **1b–i** and **1k** with iodine were performed in boiling toluene. The results

Table III. The Nafion-H-Catalyzed Trans-*tert*-butylation of 2,7-Di-*tert*-butyl-4-substituted-pyrenes (2) in Boiling Toluene



entry	substrate (R)	time, h	product (%)
1	**2a** (H)	24	**3a** (90),[a] **4** (95)[b]
2	**2b** (CHO)	48	no reaction
3	**2c** ($COCH_3$)	48	no reaction
4	**2g** (CH_3)	24	**3g** (86),[a] **4** (90)[b]
5	**2h** (CH_2CH_3)	24	**3h** (81),[a] **4** (89)[b]
6	**2i** ($CH_2CH_2CH_3$)	24	**3a** (8),[a] **3i** (72),[a] **4** (93)[b]

[a] Isolated yields are shown. [b] Yields were determined by GLC analysis.

are summarized in Table II. The reactions of **1e** and **1k** with iodine did not afford any of the desired products. Only resinuous material was produced. In the other cases, the expected products **2b**, **2c**, **2g**, **2h**, and **2i** were obtained.

When **2a** was treated with $AlCl_3$–CH_3NO_2,[10] pyrene (**3a**) was not obtained. Instead a large amount of resinous material was produced.

However it was reported[11] that when *tert*-butylbenzene derivatives were treated with Nafion-H in boiling toluene, trans-*tert*-butylated benzenes and *tert*-butyltoluene were formed in excellent yields.

Thus, trans-*tert*-butylation of **2**, in the presence of Nafion-H as a catalyst, was carried out in boiling toluene to obtain the 4-substituted pyrenes **3**. The results are summarized in Table III.

Unfortunately, the expected products **3b** and **3c** were not obtained by trans-alkylation of **2b** and **2c**, respectively. Pyrene (**3a**) itself and the 4-alkylpyrenes **3g**, **3h**, and **3i** were obtained by trans-*tert*-butylation of **2a**, **2g**, **2h**, and **2i**, respectively. However, **2i** unexpectedly afforded a mixture of pyrene (**3a**) and the desired product **3i**, in a 1:9 ratio.

Compound **3a** might be formed in the trans-alkylation of **2i** under the conditions used by trans-propylation of **3i**. The above results indicate that the preparative route of **1a** → (**1b–d**) → (**1g–i**) → (**2g–i**) → (**3g–i**) should be useful for the preparation of 4-alkylpyrenes.

Experimental Section

Melting points are uncorrected. ^1H NMR spectra of $CDCl_3$ solutions were recorded at 270 MHz with a Nippon Denshi JNM-GX270 NMR spectrometer. Me_4Si served as an internal reference. IR spectra of KBr pellets were recorded with a Nippon Denshi JIR-AQ20M spectrometer. Electron-impact mass spectra (EIMS) were obtained with a Nippon Denshi JMS-01 SA-2 spectrometer at 75 eV using a direct inlet. Wako C-300 silica gel was used for column chromatography. Nafion-H is a registered trademark of E. I. du Pont de Nemours and Co., Inc.

2,7-Di-*tert*-butyl-4-formyl-*trans*-10b,10c-dimethyl-10b,10c-dihydropyrene (1b). To a solution of 1.0 g (2.91 mmol) of **1a** and 443 mg (3.85 mol) of dichloromethyl methyl ether in 200 mL of dry dichloromethane, held at 0 °C, was added 1 mL of $SnCl_4$. The mixture was warmed to room temperature and was stirred for 2 h. Then it was poured into ice–water and was extracted with 100 mL of dichloromethane. The extract was washed with water, dried (Na_2SO_4), and concentrated. The residue was dissolved in dichloromethane and was chromatographed on silica gel (hexane, then benzene) to give 300 mg (33%) of unreacted **1a** (eluted with hexane) and 700 mg (65%) of **1b** (eluted with benzene). **1b**: deep brown prisms (hexane); mp 193–194 °C; IR 3040, 2960, 2720, 1630, 1590, 1520, 1460, 1440, 1380, 1340, 1230, 1180, 1020, 890, 850, 720 cm^{-1}; ^1H NMR ($CDCl_3$) δ –3.87 (3 H, s), –3.84 (3 H, s), 1.67 (9 H, s), 1.71 (9 H, s), 8.44 (1 H, d, J = 8 Hz), 8.56 (1 H, d, J = 8 Hz), 8.58 (2 H, s), 8.70 (1 H, d, J = 1 Hz), 8.93 (1 H, s), 9.80 (1 H, d, J = 1 Hz), 11.12 (1 H, s); EIMS m/e 372 (M^+). Anal. Calcd for $C_{27}H_{32}O$: C, 87.50; H, 8.66. Found: C, 87.20; H, 8.83.

2,7-Di-*tert*-butyl-4-acetyl-*trans*-10b,10c-dimethyl-10b,10c-dihydropyrene (1c). To a solution of 300 mg (0.87 mmol) of **1a** and 1.4 mL of $SnCl_4$ in 100 mL of dichloromethane was added 0.16 mL (2.3 mmol) of acetyl chloride at room temperature. After the reaction mixture was stirred at room temperature for 3 h, it was poured into ice–water and was extracted with 30 mL of dichloromethane. The extract was washed with water, dried (Na_2SO_4), and concentrated. The residue was dissolved in 5 mL of dichloromethane and was chromatographed on silica gel (hexane, then benzene) to give 120 mg (40%) of unreacted **1a** (eluted with hexane) and 169 mg (42%) of **1c** (eluted with benzene). **1c**: deep brown prisms (hexane); mp 183–185 °C (lit.[9] mp 185–187 °C).

2,7-Di-*tert*-butyl-4-propionyl-*trans*-10b,10c-dimethyl-10b,10c-dihydropyrene (1d). To a solution of 300 mg (0.87 mmol) of **1a** and 1.4 mL of $SnCl_4$ in 100 mL of dichloromethane was added 0.2 mL (2.3 mmol) of propionyl chloride at room temperature. After 2 h, the mixture was treated in the same manner as described above for **1c** to give 181 mg (60%) of unreacted **1a** (eluted with hexane) and 80 mg (23%) of **1d** (eluted with benzene). **1d**: pale brown prisms (hexane); mp 189–192 °C; IR 3050, 2950, 2850, 1665, 1590, 1525, 1480, 1450, 1350, 1235, 1200, 1110, 1050, 890, 805, 790, 680, 660 cm^{-1}; ^1H NMR δ –3.92 (3 H, s), –3.91 (3 H, s), 1.48 (3 H, t, J = 7 Hz), 1.70 (9 H, s), 1.71 (9 H, s), 3.50 (2 H, q, J = 7 Hz), 8.50 (5 H, m), 8.93 (1 H, s), 9.74 (1 H, s); EIMS m/e 400 (M^+). Anal. Calcd for $C_{29}H_{36}O$: C, 86.95; H, 9.06. Found: C, 86.93; H, 9.09.

2,7-Di-*tert*-butyl-4-nitro-*trans*-10b,10c-dimethyl-10b,10c-dihydropyrene (1e). To a solution of 200 mg (0.58 mmol) of **1a** in 40 mL of acetic anhydride, held at 0 °C, was added 145 mg (0.60 mmol) of powdered cupric nitrate trihydrate. In about 10 min, the color of the solution changed from deep green to deep brown. The reaction mixture was warmed to room temperature (20 °C) and was stirred for 90 min. Then 5 g of ice and 20 mL of ether were added. When the reaction of the excess acetic anhydride with water was complete, the ether layer was separated, washed with water, dried (Na_2SO_4), and concentrated. The residue was dissolved in dichloromethane and was chromatographed on silica gel (benzene) to give 170 mg (75%) of **1e**: deep brown prisms (hexane) mp 211–212 °C; IR 3040, 2960, 1590, 1520, 1450, 1385, 1335, 1300, 1260, 1230, 1180, 960, 850, 770 cm^{-1}; ^1H NMR δ –3.78 (3 H, s), –3.77 (3 H, s), 1.66 (9 H, s), 1.70 (9 H, s), 8.49 (1 H, d, J = 8 Hz), 8.60 (2 H, s), 8.62 (1 H, d, J = 8 Hz), 8.68 (1 H, d, J = 1 Hz), 9.19 (1 H, s), 9.71 (1 H, d, J = 1 Hz); EIMS m/e 389 (M^+). Anal. Calcd for $C_{26}H_{31}O$: C, 80.17; H, 8.02; N, 3.60. Found: C, 80.28; H, 8.08; N, 3.89.

General Procedure for the Reduction of 1b, 1c, and 1d To Give 4-Alkyl Derivatives. To a suspension of 191 mg (5.0 mmol) of $LiAlH_4$ in 2.5 mL of absolute ether at room temperature was added a solution of 667 mg (5.0 mmol) of $AlCl_3$ in 2.5 mL of ether. To the resulting suspension was added a solution of 358 mg (0.96 mmol) of **1b** in 15 mL of ether. The mixture was refluxed for 1 h. After the mixture was cooled to room temperature, it was poured into a large amount of ice–water and was extracted with 50 mL of dichloromethane. The extract was washed with water and 10% aqueous HCl, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed on silica gel (hexane) to give 340 mg (94%) of **1g**: deep green prisms (hexane); mp 210–211 °C; IR 3050, 2960, 1590, 1435, 1360, 1340, 1230, 1215, 1120, 880, 790, 670 cm^{-1}; ^1H NMR δ –3.96 (3 H, s), –3.92 (3 H, s), 1.67 (9 H, s), 1.70 (9 H, s), 3.22 (3 H, s), 8.2–8.7 (7 H, m); EIMS m/e 358 (M^+). Anal. Calcd for $C_{27}H_{34}$: C, 90.44; H, 9.56. Found: C, 89.98; H, 9.40.

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(11) Olah, G. A.; Prakash, G. K. S.; Iyer, P. S.; Tashiro, M.; Yamato, T. *J. Org. Chem.* **1987**, *52*, 1881.

1h (97%): deep green prisms (hexane); mp 117–119 °C; IR 3050, 2950, 1590, 1455, 1340, 1225, 1110, 1060, 970, 930, 880, 790, 660 cm^{-1}; ^1H NMR δ -3.97 (3 H, s), -3.92 (3 H, s), 1.59 (3 H, t, J = 7 Hz), 1.68 (9 H, s), 1.69 (9 H, s), 3.64 (2 H, q, J = 7 Hz), 8.4–8.7 (7 H, m); EIMS m/e 372 (M^+). Anal. Calcd for $C_{28}H_{36}$: C, 90.26; H, 9.74. Found: C, 90.01; H, 9.82.

1i (96%): deep green prisms (ethanol); mp 129–130 °C; IR 3050, 2980, 2950, 2880, 1600, 1470, 1440, 1380, 1360, 1340, 1230, 1120, 880 cm^{-1}; ^1H NMR δ -3.99 (3 H, s), -3.94 (3 H, s), 1.07 (3 H, t, J = 7 Hz), 1.68 (9 H, s), 1.69 (9 H, s), 2.05 (2 H, tq, J = 8 Hz, J = 7 Hz), 3.58 (2 H, t, J = 8 Hz), 8.36–8.48 (6 H, m), 8.70 (1 H, s); EIMS m/e 386 (M^+). Anal. Calcd for $C_{29}H_{38}$: C, 90.09; H, 9.91. Found: C, 90.34; H, 9.85.

2,7-Di-*tert*-butyl-*trans*-10b,10c-dimethyl-10b,10c-dihydropyrene-4-aldoxime (1j). To a solution of 420 mg (1.09 mmol) of **1b** in 40 mL of ethanol was added 2.0 g (28.6 mmol) of hydroxylamine hydrochloride. The pH of the solution was adjusted to pH 7 with 10% aqueous Na_2CO_3. After the mixture was warmed on steam bath for 1 h, it was cooled to room temperature. A green precipitate was removed by filtration. This solid was recrystallized from ethanol to give 417 mg (95%) of **1j**: green prisms; mp 214–216 °C; IR 3350, 3050, 2950, 2350, 1900, 1500, 1450, 1360, 1225, 930, 880, 660 cm^{-1}; ^1H NMR δ -3.78 (3 H, s), -3.94 (3 H, s), 1.57 (9 H, s), 1.67 (9 H, s), 5.30 (1 H, s), 8.50 (4 H, m), 8.52 (1 H, s), 8.81 (1 H, s), 9.47 (1 H, s); EIMS m/e 387 (M^+). Anal. Calcd for $C_{27}H_{33}NO$: C, 83.68; H, 8.58; N, 3.61. Found: C, 83.14; H, 8.47; N, 3.59.

2,7-Di-*tert*-butyl-4-cyano-*trans*-10b,10c-dimethyl-10b,10c-dihydropyrene (1k). A solution of 301 mg (1.16 mmol) of **1j** in 20 mL of acetic anhydride was refluxed for 3 h. After cooling to room temperature, the mixture was poured into water. When the reaction of excess acetic anhydride with water was completed, the mixture was extracted with 30 mL of dichloromethane. The extract was washed with saturated aqueous NaCl and then was concentrated. The residue was recrystallized from methanol to give 283 mg (87%) of **1k**: green prisms (methanol); mp 212–213 °C; IR 3020, 2950, 2200, 1590, 1455, 1380, 1345, 1230, 1150, 1065, 930, 880, 790, 680, 670 cm^{-1}; ^1H NMR δ -3.96 (3 H, s), -3.95 (3 H, s), 1.69 (9 H, s), 1.73 (9 H, s), 8.5–8.7 (6 H, m), 8.91 (1 H, s); EIMS m/e 369 (M^+). Anal. Calcd for $C_{27}H_{31}N$: C, 87.75; H, 8.46; N, 3.79. Found: C, 87.47; H, 8.39; N, 3.89.

General Procedure for Reaction of 1 with Iodine. A solution of 400 mg (1.16 mmol) of **1a** and 1220 mg (4.8 mmol, 4.2 equiv) of iodine in 30 mL of toluene was refluxed for 48 h. The cooled mixture was washed with 10% aqueous sodium thiosulfate and water. The organic layer was then evaporated. The residue was dissolved in a small amount of benzene and was chromatographed on silica gel (hexane) to give 360 mg (97%) of **2a** as a colorless solid, which was recrystallized from ethanol. **2a**: colorless prisms (ethanol); mp 209–210 °C (lit.[12] mp 208–209 °C). Compounds **2b**, **2c**, **2g**, **2h**, and **2i** were prepared in a similar manner.

2b (60%): yellow prisms (hexane); mp 175–177 °C; IR 3050, 2950, 2700, 1675, 1590, 1450, 1380, 1350, 1200, 1165, 890, 710 cm^{-1}; ^1H NMR δ 1.59 (9 H, s), 1.61 (9 H, s), 8.03 (1 H, d, J = 6 Hz), 8.07 (1 H, d, J = 6 Hz), 8.27 (1 H, d, J = 1.6 Hz), 8.34 (1 H, d, J = 1.4 Hz), 8.36 (1 H, d, J = 1.4 Hz), 8.59 (1 H, s), 9.73 (1 H, d, J = 1.6 Hz), 10.54 (1 H, s); EIMS m/e 342 (M^+). Anal. Calcd $C_{25}H_{26}O$: C, 87.67; H, 7.65. Found: C, 87.58; H, 7.64.

2c (72%): brown yellow prisms (chloroform); mp 121–122 °C; IR 3000, 2940, 1680, 1610, 1490, 1470, 1400, 1370, 1275, 1235, 1210, 890, 730, 695 cm^{-1}; ^1H NMR δ 1.58 (18 H, s), reduced, 2.93 (3 H, s), 7.99 (1 H, d, J = 9 Hz), 8.04 (1 H, d, J = 9 Hz), 8.25 (1 H, d, J = 2 Hz), 8.27 (1 H, s), 8.59 (2 H, s), 9.23 (1 H, d, J = 2 Hz); EIMS m/e 356 (M^+). Anal. Calcd for $C_{26}H_{28}O$: C, 87.59; H, 7.92. Found: C, 87.51; H, 7.97.

2g (87%): colorless prisms (ethanol); mp 172–175 °C; IR 3050, 2950, 1600, 1470, 1450, 1360, 1220, 880, 790, 715 cm^{-1}; ^1H NMR δ 1.56 (9 H, s), 1.59 (9 H, s), 2.89 (3 H, s), 7.88 (1 H, s), 8.00 (2 H, s), 8.12 (2 H, s), 8.19 (1 H, d, J = 1.8 Hz), 8.29 (1 H, d, J = 1.8 Hz); EIMS m/e 328 (M^+). Anal. Calcd for $C_{25}H_{28}$: C, 91.41; H, 8.59. Found: C, 91.70; H, 8.68.

2h (73%): colorless prisms (methanol); mp 110–113 °C; IR 3020, 2920, 2850, 1590, 1445, 1385, 1350, 1260, 1220, 1195, 870, 710 cm^{-1}; ^1H NMR δ 1.56 (3 H, t, J = 7.0 Hz), 1.57 (9 H, s), 1.59 (9 H, s), 3.32 (2 H, q, J = 7.0 Hz), 7.90 (1 H, s), 8.01 (2 H, s), 8.12 (1 H, d, J = 2.0 Hz), 8.14 (1 H, d, J = 2.0 Hz), 8.18 (1 H, d, J = 2.0 Hz), 8.38 (1 H, d, J = 2.0 Hz); EIMS m/e 342 (M^+). Anal. Calcd for $C_{26}H_{30}$: C, 91.17; H, 8.83. Found: C, 91.04; H, 8.89.

2i (75%): colorless prisms (methanol); mp 87–90 °C; IR 3020, 2900, 2850, 1590, 1445, 1380, 1350, 1265, 1220, 1190, 870, 710 cm^{-1}; ^1H NMR δ 1.13 (3 H, t, J = 7.3 Hz), 1.57 (9 H, s), 1.59 (9 H, s), 1.98 (2 H, tq, J = 6.5, 7.3 Hz), 3.26 (2 H, t, J = 6.5 Hz), 7.88 (1 H, s), 8.00 (2 H, s), 8.13 (2 H, s), 8.17 (1 H, d, J = 1.6 Hz), 8.36 (1 H, d, J = 1.6 Hz); EIMS m/e 356 (M^+). Anal. Calcd for $C_{27}H_{32}$: C, 90.95; H, 9.05. Found: C, 90.83; H, 9.00.

General Procedure for Trans-*tert*-butylation of 2,7-Di-*tert*-butyl-4-substituted-pyrenes in the Presence of Nafion-H with Toluene as an Acceptor. A mixture of 2,7-di-*tert*-butyl-4-substituted-pyrenes (200 mg) and Nafion-H (200 mg) in toluene (5 mL) was refluxed until completion of the reaction. Progress was monitored by GLC (2-m OV-1 column). The Nafion-H was then filtered from the cooled mixture, and the filtrate was concentrated in vacuo. The residue was chromatographed on silica gel (hexane) to afford a colorless solid, which was recrystallized from ethanol in all cases.

3a (90%): colorless prisms; mp 150–151 °C (lit.[13] mp 149–150 °C).

3g (86%): colorless prisms; mp 148–151 °C (lit.[14] mp 147.5–148 °C).

3h (81%): colorless prisms; mp 58–62 °C; IR 3050, 2950, 2930, 1600, 1590, 1450, 1370, 1180, 880, 830, 710 cm^{-1}; ^1H NMR δ 1.55 (3 H, t, J = 6.3 Hz), 3.35 (2 H, q, J = 6.3 Hz), 7.9–8.4 (9 H, m); EIMS m/e 230 (M^+). Anal. Calcd for $C_{18}H_{14}$ (M^+): C, 93.87; H, 6.13. Found: C, 93.65; H, 6.26.

3i (72%): colorless oil; IR 3050, 2950, 2930, 1600, 1590, 1450, 1370, 1180, and 880 cm^{-1}; ^1H NMR δ 1.06 (3 H, t, J = 7.3 Hz), 1.96 (2 H, sex, J = 7.3 Hz), 3.20 (2 H, t, J = 7.3 Hz), 7.9–8.3 (9 H, m); high resolution EIMS calcd for $C_{19}H_{16}$ (M^+) 244.1251, found 244.1252.

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Antineoplastic Agents. 200. Absolute Configuration of the Bryostatins[1]

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Received July 3, 1990

By 1755 the phylum Bryozoa was firmly placed in the animal kingdom and three years later the marine bryozoan *Bugula neritina* (Gymnolamota class, contains some 3000 of the 4000 known Bryozoa) was recorded.[2] In 1968, we detected[3] the presence of highly active antineoplastic constituents in this otherwise unpretentious appearing organism. Fourteen years later the isolation and structure of bryostatin 1 (**1a**),[4] the first member of a new class of remarkable antineoplastic,[5] immunopotentiating,[6,7] and

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0022-3263/91/1956-1337$02.50/0