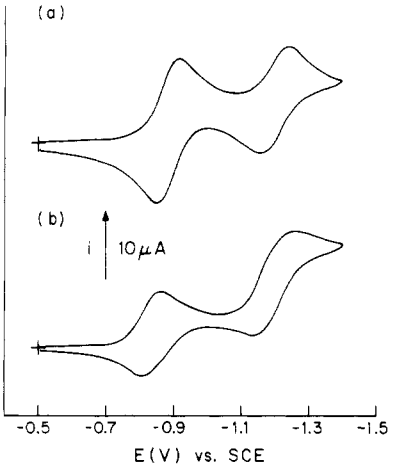

Figure 2. (a) Cyclic voltammogram of 1.0 mM 2-methyl-9,10-anthraquinone (**10**) in DMF (0.10 M $LiClO_4$) at a sweep rate of 20 mV s^{-1}. (b) Cyclic voltammogram of **3a** in DMF (0.10 M $LiClO_4$) at a sweep rate of 20 mV s^{-1}.

and this allows shorter times for electrolysis.

In Scheme IV are outlined several likely pathways leading to the major anthraquinone cleavage product **10**. Reduction of **3a** (**4**) at -0.88 V gives the radical anion $\mathbf{3a}^{-\cdot}$ ($\mathbf{4}^{-\cdot}$) which undergoes cleavage to the neutral radical **12**. Since $\mathbf{3a}^{-\cdot}$ ($\mathbf{4}^{-\cdot}$) is reduced at -1.2 V, it is reasonable to conclude that **12** is rapidly reduced to **13** at -0.88 V. One-electron reduction of **12** produces the anion **13** which is presumably protonated by trace amounts of water in the DMF medium or by the electrolyte to give **10**. Alternatively, reduction of **12** could occur by electron transfer from $\mathbf{3a}^{-\cdot}$ ($\mathbf{4}^{-\cdot}$) and $\mathbf{10}^{-\cdot}$. Reduction of **3a** (**4**) at -1.2 V gives its dianion $\mathbf{3a}^{2-}$ ($\mathbf{4}^{2-}$) which can cleave to give **13** directly. Indeed, the cyclic voltammetric peak currents at 20 and 100 mV s^{-1} suggest that this cleavage occurs on the time scale of seconds.

One possible route to the minor anthraquinone cleavage product, the alcohol **11**, is nucleophilic attack of water or hydroxide ion on **12** or **13**. However, this pathway does not appear to be operative. Reduction of **3a** in DMF containing 1% water gave **10** and **11** in approximately the same relative yields as in dry DMF. Furthermore, reduction of **3a** at -0.88 V in the presence of 0.10 M potassium ethyl xanthate, a nucleophile that has been used to successfully trap the quinone methide derived from 11-deoxydaunomycin,[5] gave only **10** and **11** as anthraquinone products in yields that were similar to those obtained in the absence of the nucleophile. A second possible source of **11** is the base catalyzed hydrolysis (saponification) of **3a** (**4**). Reductive cleavage of **3a** (**4**) to **10** in DMF increases the basicity of the medium (see Scheme IV). It follows then that electrolysis of increasing concentrations of **3a** (**4**) should lead to increasing basicity and presumably higher yields of **11**. This was not found to be the case. Electrolysis at **3a** at -0.88 V in the concentration range of 2-8 mM produced **11** in yields of 27-34%. A more serious problem with the saponification mechanism, though, is that very little free GABA is formed in the electrolysis of **3a** or **4**. It is unlikely that only the ester adjacent to the Maq group in **3a** and **4** would be hydrolyzed without hydrolysis of the ester at the opposite end of the chain also occurring in at least one case. As a final probe into the question of how **11** is formed, **3a** (2.0 mM) was reduced at -0.88 V in the presence of varying concentrations of **10** (2.0-13.0 mM). The yield of **11** nearly doubled. Thus, **10** or $\mathbf{10}^{-\cdot}$ somehow catalyzes the "hydrolytic" conversion of **3a** to **11**. We have not explored this further.

As mentioned in the introduction one of our goals in this work was to use the GABA-bound Maq esters as drug delivery systems. This work shows that these systems will have limited use in this application. Very slow cleavage rates in aqueous media will make GABA delivery under physiological conditions impractical. A second goal in this work was to provide an alternative method for deprotecting Maq esters of carboxylic acids used in the synthesis of peptides. The high yield of cleavage products from the electroreduction of **3a** in DMF at only moderately negative potentials clearly shows that this goal was accomplished. Furthermore, synthesis of **4** and its reductive cleavage to the benzyl ester of GABA in high yields demonstrates that Maq esters of carbamates can serve as excellent protecting groups of primary amines.

Acknowledgment. This work was supported by the National Institutes of Health.

Registry No. **3a**, 92013-50-8; **3b**, 92013-56-4; **4**, 92013-54-2; **5**, 5105-78-2; **5** Bu_4N^+ salt, 92013-58-6; **6**, 86272-16-4; **7**, 92013-51-9; **8**, 92013-52-0; **9**, 92013-55-3; **11**, 17241-59-7; $NH_2(CH_2)_3CO_2H$, 56-12-2; $PhCH_2OC(O)Cl$, 501-53-1; $2,4,5\text{-}Cl_3C_6H_2OC(O)Cl$, 16947-69-6; $ClSiMe_3$, 75-77-4; $2,4,5\text{-}Cl_3C_6H_2OSiMe_3$, 1014-29-5; $PhCH_2OC(O)(CH_2)_3N{=}C(OSiMe_3)O\text{-}2,4,5\text{-}Cl_3C_6H_2$, 92013-53-1; $PhCH_2OC(O)(CH_2)_3NH_3^+$, 92013-59-7; 2-(bromomethyl)-9,10-anthraquinone, 7598-10-9; 2-methyl-9,10-anthraquinone, 84-54-8; 2-benzyl-9,10-anthraquinone, 49658-23-3.

Synthesis of the Non-K-Region Dihydrodiols of 7-Methylbenz[*c*]acridine

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The syntheses of the four non-K-region *trans*-dihydrodiols of 7-methylbenz[*c*]acridine (**2**) are described. The *trans*-8,9- and -10,11-dihydrodiols **13** and **16** were prepared from 7-methyl-8,9,10,11-tetrahydrobenz[*c*]acridine (**3**) via the *trans*-8,9-diacetoxy-7-methyl-8,9,10,11-tetrahydrobenz[*c*]acridine (**10**) and its 10,11-isomer (**14**) by selective benzylic bromination followed by dehydrobromination. The *trans*-tetrahydro diacetates were obtained through the alkenes **6** and **7** and their epoxide derivatives. *trans*-1,2- and -3,4-dihydrodiols **22** and **24** were similarly prepared from the *trans*-1,2- and -3,4-diacetates of 7-methyl-1,2,3,4-tetrahydrobenz[*c*]acridine (**19** and **20**). The latter were products of the Prevost reaction on mixed 3,4- and 1,2-dihydro-7-methylbenz[*c*]acridines (**17** and **18**).

7-Methylbenz[*c*]acridine (**2**) is a polycyclic azaaromatic compound with significant carcinogenic potency[1] and is structurally analogous to 7-methylbenz[*a*]anthracene, a potent carcinogenic polycyclic hydrocarbon.[2] For poly-

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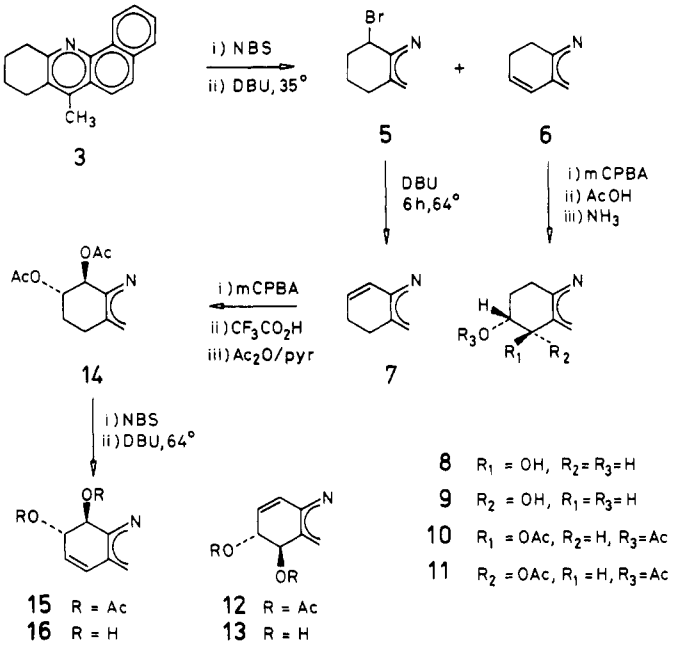
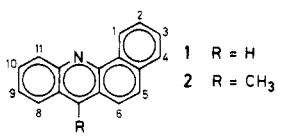
Scheme I

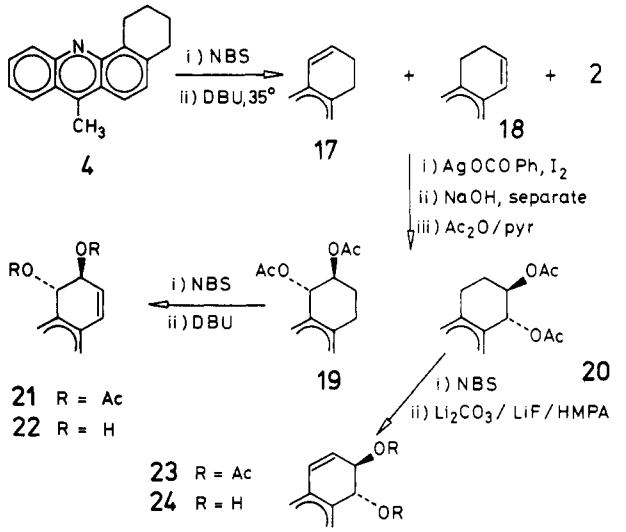


cyclic hydrocarbons biological activation of carcinogens proceeds through dihydrodiols and diol epoxides,[3] but apart from some work with benz[a]- and benz[c]acridine such pathways have not yet been clearly demonstrated for azaaromatic compounds.[4] Investigations into azaaromatics have identified several metabolites of 7-methylbenz[c]acridine including four of the possible five *trans*-dihydrodiols.[5] These are *trans*-1,2-dihydro-1,2-dihydroxy-7-methylbenz[c]acridine (**22**) and the 5,6, 8,9 (**13**), and 10,11 (**16**) isomers. Synthetic work with the parent systems, benz[a]acridine and benz[c]acridine (**1**) has afforded the five *trans*-dihydrodiols of **1**[6,7] and the *trans*-3,4-dihydrodiol of benz[a]acridine.[7] Dihydrodiols have also been reported for dibenz[c,h]acridine.[8]



This paper reports the synthesis of the four non-K-region *trans*-dihydrodiols of **2**, namely, **13**, **16**, **22**, and *trans*-3,4-dihydro-3,4-dihydroxy-7-methylbenz[c]acridine

Scheme II



(**24**). Syntheses of these compounds enabled metabolite structures to be confirmed and has allowed carcinogenicity testing and mutagenicity testing studies to commence.

Results and Discussion

Many methods are reported for the synthesis of dihydrodiols and other derivatives of polycyclic aromatic hydrocarbons.[9] A method successfully used to prepare the non-K-region dihydrodiols of benz[c]acridine (**1**) employs the 1,2,3,4- and 8,9,10,11-tetrahydrobenz[c]acridines as synthetic starting points.[6] 7-Methyl-1,2,3,4- and 7-methyl-8,9,10,11-tetrahydrobenz[c]acridine (**4** and **3**) were therefore chosen as starting points in the synthesis of the non-K-region dihydrodiols of **2** with the expectation that reduction of 7-bromomethyl derivatives would be necessary.[9c] Syntheses of **3** and **4** have been reported previously.[10]

The routes employed closely follow those previously described for the dihydrodiols of **1** by Lehr and Kumar,[6] who noted that the Prevost reaction was unsatisfactory for the synthesis of *trans*-10,11-diacetoxy-8,9,10,11-tetrahydrobenz[c]acridine. Bromination of **3** followed by mild treatment with DBU allowed the isolation of 11-bromo-7-methyl-8,9,10,11-tetrahydrobenz[c]acridine (**5**) and 10,11-dihydro-7-methylbenz[c]acridine (**6**) (Scheme I). Prolonged DBU treatment of **5** at higher temperatures afforded 8,9-dihydro-7-methylbenz[c]acridine (**7**). Structures of **6** and **7** were assigned from their ^{13}C NMR spectra, the ^{13}C NMR spectrum of **5**, and the synthesis of **7** from **5**. In **5**, signals observed from C_{11}, C_{10}, C_9, and C_8 at 54.2, 32.3, 18.3, and 25.9 were similar to the calculated values of an 11-bromo derivative of **3** (54.4, 33.6, 19.5, and 26.7).[11] Calculated values of the 8-bromo derivative were 46.6, 33.2, 19.9, and 34.3. The alkene **6** was epoxidized with *m*-chloroperbenzoic acid, and subsequent treatment of the product with acetic acid and methanolic ammonia gave a separable 2:1 mixture of *trans*- and *cis*-8,9-dihydroxy-7-

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methyl-8,9,10,11-tetrahydrobenz[c]acridine, **8** and **9**. Stereochemistry was assigned from the spin–spin couplings of H_8 with H_9, H_9 with H_{10}, and H_9 with $H_{10'}$ in the diols and their diacetates, **10** and **11**. The C_8 substituent is assumed to have a quasi-axial position due to steric hindrance from the 7-methyl group.[12] A cis isomer was not previously isolated in the benz[c]acridine series.[6] Treatment of **10** with NBS followed by DBU afforded *trans*-8,9-diacetoxy-8,9-dihydro-7-methylbenz[c]acridine (**12**). Similar treatment of 8,9-dihydro-7-methylbenz[c]acridine (**7**) afforded only *trans*-10,11-diacetoxy-7-methyl-8,9,10,11-tetrahydrobenz[c]acridine (**14**) which was brominated to give 8α-bromo-10β,11α-diacetoxy-7-methyl-8,9,10,11-tetrahydrobenz[c]acridine (structure assigned from ^1H NMR spin–spin couplings). Dehydrobromination of the latter gave *trans*-10,11-diacetoxy-10,11-dihydro-7-methylbenz[c]acridine (**15**).

Bromination of 7-methyl-1,2,3,4-tetrahydrobenz[c]-acridine followed by dehydrobromination yielded two alkenes (**17** and **18**) (Scheme II). The structure of **17** was assigned from the downfield position of the H_1 signal (δ 8.04). The ^1H NMR spectra of crude bromination products showed no signal attributable to a bromomethyl group (δ 5.3) as was found in the preparation of 7-methylbenz[a]-anthracene 1,2- and -3,4-dihydrodiol.[9c] The Prevost reaction was performed with silver benzoate on mixtures of **17** and **18** to afford, after hydrolysis and acetylation, *trans*-1,2-diacetoxy-1,2,3,4-tetrahydro-7-methylbenz[c]-acridine (**19**) and its 3,4-isomer (**20**). Reaction of **17** with CPBA as performed for **6** also lead to mixtures of cis and trans products. NBS treatment of **19** and **20** was followed by dehydrobromination to yield *trans*-1,2-diacetoxy-1,2-dihydro-7-methylbenz[c]acridine and *trans*-3,4-diacetoxy-3,4-dihydro-7-methylbenz[c]acridine, **21** and **23**, respectively. Better yields of **23** were obtained by use of Li_2CO_3/LiF/HMPA in the dehydrobromination step.

The dehydrobromination reactions to the *trans*-diacetoxy dihydro derivatives were always accompanied by some concurrent loss of acetic acid to form 2-,[13] 4-,[13] 9-,[10] and 11-acetoxy-7-methylbenz[c]acridine[10] from **19**, **20**, **10**, and **14**, respectively. Hydrolysis of the *trans*-diacetoxy dihydro derivatives afforded the required *trans*-dihydrodiols **22**, **24**, **13**, and **16**.

The dihydrodiols **16**, **22** and **24**, showed comparable ^1H NMR spectra to the corresponding benz[c]acridine dihydrodiols[6] except for minor differences due to 7-methyl substitution. In the dihydrodiol **13**, differences to the corresponding benz[c]acridine dihydrodiol were more profound as the small value for $J_{8,9}$ of 2.1 Hz indicated a quasi-diaxial arrangement of the 8,9-dihydroxy group due to the additional steric effect of the 7-methyl group. For the benz[c]acridine 8,9-dihydrodiol, without the 7-methyl group, a quasi-diequatorial arrangement of the hydroxyl groups was indicated by a strong coupling $J_{8,9}$ of 10 Hz.[6] The ultraviolet spectra, recorded in methanol, of the dihydrodiols **13**, **16**, **22**, and **24** were very similar to those of the corresponding benz[c]acridine dihydrodiols.[6]

Experimental Section

Ultraviolet spectra of **13**, **16**, **22**, and **24** were recorded on a Varian Techtron Series 634 spectrophotometer. Nuclear magnetic resonance spectra were recorded on JEOL FX-90Q and Bruker 400-MHz spectrometers. Unless noted otherwise, spectra were recorded at 90 MHz. Coupling constants (J) are recorded in hertz, chemical shifts in parts per million (δ) with Me_4Si as an internal standard. Where possible, assignments were confirmed in ^1H NMR spectra by homodecoupling and in ^{13}C NMR by the attached proton test (APT)[14] (Table II, see supplementary material section). Chemical ionization mass spectra (CIMS) were recorded on a Finnigan 3200E mass spectrometer using methane as reagent gas. High-resolution electron impact mass spectra were recorded on an AEI MS-9 mass spectrometer. Melting points are uncorrected. Purification of compounds was carried out by short column vacuum chromatography,[15] a method modified from vacuum chromatography.[16] Preparative-layer chromatography (PLC) was carried out with Merck silica gel PF_{254} (TLC grade) coated onto glass plates in 1-mm layers.

11-Bromo-7-methyl-8,9,10,11-tetrahydrobenz[c]acridine (5) and 10,11-Dihydro-7-methylbenz[c]acridine (6). A mixture of **3** (4.99 g), NBS (3.96 g), and CCl_4 (100 mL) was refluxed under N_2 for 2 h. Succinimide was removed by filtration, and the residue after evaporation of solvent was dissolved in a mixture of tetrahydrofuran (100 mL) and CH_2Cl_2 (40 mL). DBU (3.1 mL) was added and the solution was refluxed for 1 h under N_2. The solution was concentrated and filtered through silica gel H, the silica was washed wth CH_2Cl_2/EtOAc (10:1), and the filtrate and washings were concentrated to give a red brown syrup (5.4 g). Chromatography (bed 70 mm in diameter × 35 mm; solvent gradient, hexane/CH_2Cl_2, CH_2Cl_2, CH_2Cl_2/EtOAc) gave **5** (0.98 g), **6** (0.94 g), and **3** (1.21 g). Compound **5** was recrystallized from hexane/CH_2Cl_2 to give colorless crystals: mp 230–260 °C dec; ^1H NMR (16 mg/0.3 mL, $CDCl_3$) δ 1.90–2.28 (m, 2 H_9), 2.28–2.68 (m, 2 H_{10}), 2.54 (s, 3 H), 2.80–2.32 (m, 2 H_8), 5.85 (m, H_{11}), 7.60–7.96 (m, 5 H), 9.26–9.40 (m, H_1); CIMS, m/e (relative intensity) 328 (M + 1, 51), 326 (M + 1, 53), 257 (27), 255 (12), 248 (33), 247 (38), 246 (100). Anal. Calcd for $C_{18}H_{16}BrN$: C, 66.27; H, 4.94; N, 4.29. Found: C, 66.43; H, 5.28; N, 3.98. Compound **6** was recrystallized from MeOH to give pale yellow needles: mp 88–89 °C; ^1H NMR (3 mg/0.3 mL, $CDCl_3$) δ 2.39–2.70 (m, 2 H_{10}), 2.66 (s, 3 H), 3.10–3.37 (m, 2 H_{11}), 6.27 (dt, H_9), 6.92 (dt, H_8), 7.57–8.01 (m, 5 H), 9.23–9.38 (m, H_1); $J_{8,9}$ = 9.8 Hz, $J_{9,10}$ = $J_{9,10'}$ = 4.4 Hz, $J_{8,10}$ = $J_{8,10'}$ = 1.8 Hz; CIMS, m/e (relative intensity) 246 (M + 1, 100), 245 (20), 244 (33). Anal. Calcd for $C_{18}H_{15}N$: C, 88.13; H, 6.16; N, 5.71. Found: C, 87.84; H, 5.93; N, 5.49.

8,9-Dihydro-7-methylbenz[c]acridine (7). A solution of **5** (1.10 g), DBU (1.5 mL), and THF (35 mL) was refluxed under N_2 for 7 h. CH_2Cl_2 was added to dissolve the product which partially crystallized during reflux, and the solution was filtered through a bed of silica gel H and the silica washed with CH_2Cl_2. Removal of the solvent gave **7** (0.825 g, 99%). Recrystallization from EtOH gave colorless needles: mp 141–142 °C; ^1H NMR (2 mg/0.3 mL, $CDCl_3$) δ 2.30–2.67 (m, 2 H_9), 2.64 (s, 3 H), 2.97–3.21 (m, 2 H_8), 6.50 (dt, H_{10}), 6.93 (dt, H_{11}), 7.52–7.99 (m, 5 H), 9.22–9.40 (m, H_1); $J_{9,10}$ = $J_{9',10}$ = 4.2 Hz, $J_{10,11}$ = 9.8 Hz, $J_{9,11}$ = $J_{9',11}$ = 1.8 Hz; CIMS, m/e (relative intensity) 246 (M + 1, 100), 245 (22). Anal. Calcd for $C_{18}H_{15}N$: C, 88.13; H, 6.16; N, 5.71. Found: C, 87.93; H, 6.24; N, 6.02.

3,4-Dihydro-7-methylbenz[c]acridine (17) and 1,2-Dihydro-7-methylbenz[c]acridine (18). A mixture of **4** (4.26 g), finely powdered NBS (3.68 g), CCl_4, and α,α′-azobis(isobutyronitrile) (AIBN, 0.43 g) was refluxed under N_2 for 30 min. After DBU (5.25 mL) treatment for 1 h at 35 °C, chromatography (bed 100 mm in diameter × 50 mm, solvent gradient, pentane/CH_2Cl_2 (1:1) to CH_2Cl_2/EtOAc (10:1)) gave **2** (0.41 g), **17** (1.03 g), **18** (0.17 g), and **4** (0.89 g). Recrystallization of **17** from hexane/CH_2Cl_2 gave yellow crystals: mp 112–113 °C; ^1H NMR (2 mg/0.3 mL $CDCl_3$) δ 2.32–2.64 (m, 2 H_3), 2.96–3.16 (m, 2 H_4), 3.10 (s, 3 H), 6.34 (dt, H_2), 8.09 (d, H_1), 7.35–8.32 (m, 6 H); $J_{1,2}$ = 9.9 Hz, $J_{2,3}$ = $J_{2,3'}$ = 4.3 Hz; CIMS, m/e (relative intensity) 246 (M + 1, 100), 245 (21), 244 (9). Anal. Calcd for $C_{18}H_{15}N$: C, 88.13; H, 6.16; N, 5.71. Found: C, 88.35; H, 5.97; N, 5.77. Recrystallization of **18** from hexane gave yellow crystals: mp 92–94 °C; ^1H NMR (2 mg/3 mL, $CDCl_3$) δ 2.36–2.72 (m, 2 H_2), 3.10 (s, 3 H), 3.60–3.82 (m, 2 H_1), 6.35 (dt, H_3), 6.66 (dt, H_4), 7.29–8.36 (m, 6 H); $J_{2,3}$ = $J_{2',3}$ = 4.5 Hz, $J_{2,4}$ = $J_{2',4}$ = 1.8 Hz, $J_{3,4}$ = 9.3 Hz; CIMS, m/e

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(relative intensity) 246 (M + 1, 100), 245 (15), 244 (14). Anal. Calcd for $C_{18}H_{15}N$: C, 88.13; H, 6.16; N, 5.71. Found: C, 88.20; H, 6.12; N, 5.74.

***trans*-8,9-Diacetoxy-7-methyl-8,9,10,11-tetrahydrobenz[*c*]acridine (10) and *cis*-8,9-Diacetoxy-7-methyl-8,9,10,11-tetrahydrobenz[*c*]acridine (11).** To an ice-cold solution of **6** (1.49 g) in CH_2Cl_2 was added CPBA (85%, 1.34 g), and the mixture was stirred at 0 °C for 10 min and then allowed to warm to 20 °C over 50 min. The mixture was then cooled to 0 °C, washed with ice-cold 5% NaOH and water, then dried (anhydrous Na_2SO_4), filtered, and concentrated to give 8,9-epoxy-7-methyl-8,9,10,11-tetrahydrobenz[c]acridine (**25**) (1.61 g). Recrystallization from EtOAc gave colorless needles: mp 160–163 °C; ^1H NMR (5 mg/0.4 mL, $CDCl_3$) δ 1.84–2.20 (m, H_{10}), 2.40–2.60 (m, $H_{10'}$), 2.78 (s, 3 H), 3.00–3.24 (m, 2 H_{11}), 3.81 (m, H_9), 4.33 (d, H_8), 7.56–8.00 (m, 5 H), 9.20–9.40 (m, H_1); $J_{8,9}$ = 4.3 Hz; CIMS, *m/e* (relative intensity) 262 (M + 1, 100), 261 (15).

Treatment of **25** with 88% formic acid followed by acetylation using acetic anhydride and pyridine as described for the corresponding benz[c]acridine derivatives[6] gave *trans*-9-acetoxy-8-(formyloxy)-7-methyl-8,9,10,11-tetrahydrobenz[c]acridine as a major product. Recrystallization from hexane/EtOAc gave colorless crystals: mp 200 °C dec; ^1H NMR (1.0 mg/0.3 mL $CDCl_3$) δ 2.04 (s, 3 H), 2.20–2.48 (m, 2 H_{10}), 2.63 (s, 3 H), 3.35 (t, 2 H_{11}), 5.42 (dd, H_9), 6.48 (br d, H_8), 7.64–8.08 (m, 5 H), 8.21 (d, formyl H), 9.28–9.58 (m, H_1); $J_{8,9}$ = 3.6 Hz, $J_{9,10}$ = 3.6 Hz, $J_{10,11}$ = 6.7 Hz, H_8 coupled to formyl H, J = 1.1 Hz; CIMS, *m/e* (relative intensity) 350 (M + 1, 95), 304 (100), 303 (8), 290 (17), 262 (57). Instead, **25** was treated with AcOH (14 mL) for 17 h at 25 °C, and after workup, the residue was dissolved in MeOH (70 mL) and concentrated aqueous NH_3 (14 mL). After 3 days at 25 °C, concentration of the solution left a solid residue (1.77 g) which gave two major components by chromatography (solvent gradient CH_2Cl_2, CH_2Cl_2/EtOAc). These were *cis*-8,9-dihydroxy-7-methyl-8,9,10,11-tetrahydrobenz[c]acridine (**9**) [0.33 g; ^1H NMR (2 mg/0.4 mL $(CD_3)_2CO$) δ 2.10–2.55 (m, 2 H_{10}), 2.87 (s, 3 H), 3.16–3.36 (m, 2 H_{11}), 4.04 (dt, H_9), 5.12 (d, H_8), 7.64–8.20 (m, 5 H), 9.25–9.42 (m, H_1); $J_{8,9}$ = 3.8 Hz, $J_{9,10}$ = 11.5 Hz, $J_{9,10'}$ = 3.8 Hz] and *trans*-8,9-dihydroxy-7-methyl-8,9,10,11-tetrahydrobenz[c]acridine (**8**) [0.79 g; ^1H NMR (2 mg/0.4 mL $(CD_3)_2CO$) δ 2.16–2.58 (m, 2 H_{10}), 2.84 (s, 3 H), 3.10–3.44 (m, 2 H_{11}), 4.18–4.36 (m, H_9), 5.03 (d, H_8), 7.60–8.17 (m, 5 H), 9.24–9.44 (m, H_1); $J_{8,9}$ = 3.2 Hz]. Acetylation of **9** (0.33 g) gave **11** (0.27 g) as colorless crystals: mp 188–190 °C from hexane/EtOAc; ^1H NMR (5 mg/0.3 mL, $CDCl_3$) δ 2.10 (s, 3 H), 2.12 (s, 3 H), 2.20–2.60 (m, 2 H_{10}), 2.65 (s, 3 H), 3.00–3.75 (m, 2 H_{11}), 5.32 (dt, H_9), 6.71 (dd, H_8), 7.60–8.02 (m, 5 H), 9.20–9.46 (m, H_1); $J_{8,9}$ = 3.6 Hz, $J_{9,10}$ = 12.1 Hz, $J_{9,10'}$ = 3.6 Hz, $J_{8,10}$ = 1.1 Hz; CIMS, *m/e* (relative intensity) 364 (M + 1, 100), 304 (82), 262 (37), 246 (12). Anal. Calcd for $C_{22}H_{21}NO_4$: C, 72.71; H, 5.82; N, 3.85. Found: C, 72.93; H, 5.68; N, 3.71. Acetylation of **8** (0.79 g) gave **10** (0.63 g) as colorless crystals: mp 147–149 °C from hexane/EtOAc; ^1H NMR (2 mg/0.3 mL, $CDCl_3$) δ 2.03 (s, 3 H), 2.12 (s, 3 H), 2.20–2.46 (m, 2 H_{10}), 2.64 (s, 3 H), 3.20–3.44 (m, H_{11}), 5.38 (q, H_9), 6.33 (d, H_8), 7.65–8.06 (m, 5 H), 9.28–9.46 (m, H_1); $J_{8,9}$ = $J_{9,10}$ = $J_{9,10'}$ = 3.4 Hz; CIMS, *m/e* (relative intensity) 364 (M + 1, 60), 304 (100), 262 (13), 246 (26). Anal. Calcd for $C_{22}H_{21}NO_4$: C, 72.71; H, 5.82; N, 3.85. Found: C, 72.81; H, 5.79; N, 3.93.

***trans*-10,11-Diacetoxy-7-methyl-8,9,10,11-tetrahydrobenz[*c*]acridine (14).** A solution of **7** (0.33 g) in CH_2Cl_2 (10 mL) was treated with CPBA (85%, 0.3 g) using a two-phase system with 5% $NaHCO_3$. Workup as previously described for **10** gave 10,11-epoxy-7-methyl-8,9,10,11-tetrahydrobenz[c]acridine (**26**): mp 160–164 °C from EtOAc; ^1H NMR (2 mg/0.4 mL, $CDCl_3$) δ 1.64–2.10 (m, H_9), 2.40–3.20 (m, 3 H), 2.64 (s, 3 H), 3.92 (t, H_{10}), 5.40 (d, H_{11}), 7.60–8.04 (m, 5 H), 9.35–9.62 (m, H_1); $J_{9,10}$ = $J_{10,11}$ = 4.3 Hz; CIMS, *m/e* (relative intensity) 262 (M + 1, 100), 261 (7), 246 (4). A solution of **26** (0.31 g) in AcOH (4 mL) and trifluoroacetic acid (0.1 mL) was left standing at room temperature overnight. After removal of the acids and acetylation, chromatography (solvent gradient hexane/EtOAc) gave **14** as a solid (0.28 g) which was recrystallized from hexane/EtOAc, giving crystals: mp 202–212 °C dec; ^1H NMR (5 mg/0.3 mL, $CDCl_3$) δ 2.10 (s, 3 H), 2.26 (s, 3 H), 2.14–2.42 (m, 2 H_9), 2.63 (s, 3 H), 2.96–3.14 (m, 2 H_8), 5.24–5.50 (m, H_{10}), 6.37 (d, H_{11}), 7.60–8.00 (m, 5 H), 9.14–9.30 (m, H_1); $J_{10,11}$ = 7.3 Hz; CIMS, *m/e* (relative intensity) 364 (M + 1, 100), 304 (60), 262 (25), 246 (11). Anal. Calcd for $C_{22}H_{21}NO_4$: C, 72.71; H, 5.82; N, 3.85. Found: C, 72.84; H, 5.96; N, 3.91.

***trans*-1,2-Diacetoxy-7-methyl-1,2,3,4-tetrahydrobenz[*c*]acridine (19).** Silver benzoate (1.21 g) was mixed with benzene (10 mL) under N_2, iodine (0.615 g) was added, and mixing was continued until all the iodine had formed pale yellow silver iodobenzoate. A benzene solution of **17** (5 mL, 0.585 g) was added, and the mixture was stirred under N_2 for 30 min and then refluxed 2 h. EtOAc (5 mL) was added and the suspension filtered through a short bed of silica gel H. The filtrate and EtOAc washings of the silica were concentrated to give a light brown crystalline solid (1.21 g). Recrystallization from hexane/EtOAc gave *trans*-1,2-bis(benzoyloxy)-7-methyl-1,2,3,4-tetrahydrobenz[c]acridine (**27**) as pale yellow crystals: mp 188–189 °C; ^1H NMR (4 mg/0.4 mL, $CDCl_3$) δ 2.32–2.60 (m, 2 H_3), 3.10 (s, 3 H), 3.06–3.32 (m, 2 H_4), 5.85 (q, H_2), 7.20–7.76 (m, 10 H), 7.88–8.40 (m, 7 H); $J_{1,2}$ = $J_{2,3}$ = $J_{2,3'}$ = 3.5 Hz; CIMS, *m/e* (relative intensity) 488 (M + 1, 9), 366 (15), 246 (4), 245 (2), 244 (3), 163 (2), 151 (57), 123 (100), 105 (20). Hydrolysis under N_2 of a solution of **27** (1.21 g) in freshly distilled THF (35 mL) and MeOH (10 mL) with 5% NaOH was followed by acetylation. Chromotography (solvent gradient hexane/CH_2Cl_2, CH_2Cl_2, CH_2Cl_2/EtOAc) gave **19** (0.46 g). Recrystallization from EtOAc yielded pale yellow crystals: mp 194–207 °C dec; ^1H NMR (15 mg/0.3 mL, $CDCl_3$) δ 2.00 (s, 6 H), 2.10–2.38 (m, 2 H_3), 2.90–3.16 (m, 2 H_4), 3.07 (s, 3 H), 5.47 (q, H_2), 7.08 (d, H_1), 7.24–7.85 (m, 4 H), 8.04–8.32 (m, 2 H); $J_{1,2}$ = $J_{2,3}$ = $J_{2,3'}$ = 3.6 Hz; CIMS, *m/e* (relative intensity) 364 (M + 1, 43), 304 (100), 262 (18), 246 (14), 244 (18). Anal. Calcd for $C_{22}H_{21}NO_4$: C, 72.71; H, 5.82; N, 3.85. Found: C, 72.53; H, 6.04; N, 3.89.

***trans*-3,4-Diacetoxy-7-methyl-1,2,3,4-tetrahydrobenz[*c*]acridine (20).** Treatment of **18** (0.14 g, containing 20% **17**) using the Prevost conditions described for the preparation of **19** gave, after alkaline hydrolysis, a pale brown solid (0.15 g). Chromatography (solvent gradient CH_2Cl_2/EtOAc (10:1) to EtOAc) gave *trans*-3,4-dihydroxy-7-methyl-1,2,3,4-benz[c]acridine (92 mg) and *trans*-1,2-dihydroxy-7-methyl-1,2,3,4-benz[c]acridine (21 mg) as pale yellow crystalline solids. Acetylation gave **20** and **19**, respectively. Recrystallization of **20** from EtOAc gave pale yellow crystals: mp 170–170 °C; ^1H NMR (70 mg/0.3 mL, $CDCl_3$) δ 2.06 (s, 3 H), 2.18 (s, 3 H), 2.14–2.40 (m, 2 H_2), 2.90 (s, 3 H), 3.60 (t, H_3), 5.23–5.43 (m, H_3), 6.26 (d, H_4), 7.18–8.24 (m, 6 H); $J_{3,4}$ = 5.6 Hz, $J_{1,2}$ = 6.5 Hz; CIMS, *m/e* (relative intensity) 364 (M + 1, 14), 304 (67), 262 (32), 246 (38), 245 (24), 244 (100). Anal. Calcd for $C_{22}H_{21}NO_4$: C, 72.71; H, 5.82; N, 3.85. Found: C, 72.64; H, 5.69; N, 4.02.

***trans*-8,9-Diacetoxy-8,9-dihydro-7-methylbenz[*c*]acridine (12).** A mixture of **10** (403 mg), NBS (234 mg), AIBN (5 mg), and CCl_4 (100 mL) was refluxed under N_2 for 35 min. The bromination products (550 mg) were isolated by chromatography (solvent gradient CCl_4 to CH_2Cl_2/EtOAc, 25:1) and dissolved in CH_2Cl_2 (10 mL) and DBU (170 μL) was added. The solvent was removed and the residue heated at 35 °C for 1 h. Chromatography (solvent gradient CH_2Cl_2 to CH_2Cl_2/EtOAc, 100:1) gave **12** (222 mg) and 9-acetoxy-7-methylbenz[c]acridine (**28**) (45 mg). Recrystallization of **12** from hexane/EtOAc gave colorless crystals: mp 186–188 °C; ^1H NMR (see Table I); CIMS, *m/e* (relative intensity) 362 (M + 1, 78), 302 (80), 260 (100), 244 (60). Anal. Calcd for $C_{22}H_{19}NO_4$: C, 73.12; H, 5.30; N, 3.88. Found: C, 73.17; H, 5.35; H, 3.76. Recrystallization of **28** from CH_2Cl_2 gave pale yellow needles: mp 168–170 °C (lit. mp 168–170 °C); ^1H NMR (2 mg/0.3 mL, $CDCl_3$) δ 2.44 (s, 3 H), 3.08 (s, 3 H), 7.63 (dd, H_{10}), 7.75–8.20 (m, 6 H), 8.44 (d, H_{11}), 9.53–9.67 (m, H_1), $J_{10,11}$ = 9.1 Hz, $J_{8,10}$ = 2.5 Hz; CIMS, *m/e* (relative intensity) 302 (M + 1, 75), 301 (13), 260 (100). Analyses for $C_{20}H_{15}NO_2$.[10]

***trans*-10,11-Diacetoxy-10,11-dihydro-7-methylbenz[*c*]acridine (15).** Bromination of **14** (479 mg) as described for the preparation of **12** gave 8α-bromo-10β,11α-diacetoxy-7-methyl-8,9,10,11-tetrahydrobenz[c]acridine (676 mg). Recrystallization from hexane/CH_2Cl_2 gave colorless crystals: mp 135 °C dec; ^1H NMR (2 mg/0.4 mL, $CDCl_3$) δ 2.16 (s, 3 H), 2.36 (s, 3 H), 2.44–3.06 (m, 2 H_9), 2.75 (s, 3 H), 5.76 (t, H_8), 6.10 (ddd, H_{10}), 6.52 (d, H_{11}), 7.60–8.00 (m, 5 H), 9.04–9.24 (m, H_1); $J_{8,9}$ = $J_{8,9'}$ = 3.5 Hz, $J_{9,10}$ = 11.6 Hz, $J_{9',10}$ = 4.0 Hz, $J_{10,11}$ = 9.5 Hz; CIMS, *m/e* (relative intensity) 444 (M + 1, 22), 443 (12), 442 (M + 1, 24), 441 (10), 364 (26), 363 (25), 362 (87), 361 (7), 302 (100), 301 (7), 260 (47),

Table I. ^{1}H NMR Spectral Data of Diesters and Diols (J values are in hertz)

compound	ester/carbinol hydrogen		vinyl hydrogen		7-methyl hydrogens	acetyl hydrogens	aromatic hydrogens
	benzylic	non-benzylic	benzylic	non-benzylic			
12; 2 mg/0.3 mL, $CDCl_3$	6.56 (H_8) m	5.46 (H_9) m	7.25 (H_{11}) d	6.58 (H_{10}) m	2.76	2.01, 2.08	7.6–8.1 (5 H), 9.40 (1 H, H_1)
2 mg/0.3 mL, C_6H_6	6.75 (H_8)	$J_{10,11}$ = 9.6 Hz 5.69 (H_9)	7.35 (H_{11})	6.54 (H_{10})	2.32	1.50, 1.52	7.3–7.8 (5 H) , 9.84 (1 H, H_1)
13; 2 mg/0.3 mL, $(CD_3)_2CO$	$J_{8,9}$ = 2.1, $J_{8,10}$ = 1.2, $J_{9,10}$ = 5.4, $J_{10,11}$ = 9.8 5.25 (H_8)	4.45 (H_9)	7.01 (H_{11})	6.62 (H_{10})	2.85		7.7–8.2 (5 H) , 9.38 (1 H, H_1)
15; 2 mg/0.3 mL, $CDCl_3$	$J_{8,9}$ = 2.1, $J_{9,10}$ = 5.4, $J_{10,11}$ = 10.0, $J_{8,10}$ = 1.3 6.51 (H_{11})	5.95 (H_{10})	7.09 (H_8)	6.17 (H_9)	2.75	2.15, 2.36	7.6–8.1 (5 H) , 9.27 (1 H, H_1)
16; 5 mg/0.3 mL $(CD_3)_2CO/(CD_3)_2SO$	$J_{8,9}$ = 10.0, $J_{10,11}$ = 8.8, $J_{9,10}$ = 3.2, $J_{8,10}$ = 1.4 4.88 (H_{11})	4.60 (H_{10})	7.00 (H_8)	6.22 (H_9)	2.77		7.6–8.2 (5 H), 9.44 (1 H, H_1)
21; 9 mg/0.3 mL, $CDCl_3$	$J_{8,9}$ = 10.2, $J_{9,10}$ = 2.0, $J_{10,11}$ = 10.4, $J_{8,10}$ = 2.3 7.47 (H_1)	5.57 (H_2)	6.91 (H_4)	6.42 (H_3)	3.09	1.99, 2.00	7.4–7.8 (3 H), 8.1–8.4 (3 H)
22; 2 mg/0.3 mL, $(CD_3)_2CO/D_2O$	$J_{1,2}$ = 1.5, $J_{1,3}$ = 1.1, $J_{2,3}$ = 6.2, $J_{3,4}$ = 9.6 5.75 (H_1)	4.70 (H_2)	6.62 (H_4)	6.29 (H_3)	3.17		7.3–8.5 (6 H)
23; 3 mg/0.3 mL, $CDCl_3$	$J_{1,2}$ = 9.4, $J_{2,3}$ = 2.8, $J_{3,4}$ = 9.8, $J_{2,4}$ = 2.0 6.39 (H_4)	5.74 (H_3)	8.34 (H_1)	6.29 (H_2)	3.11	2.06, 2.14	7.4–7.9 (3 H), 8.1–8.3 (3 H)
24; 2 mg/0.3 mL, $(CD_3)_2CO/D_2O$	$J_{1,2}$ = 9.9, $J_{2,3}$ = 4.1, $J_{3,4}$ = 5.5, $J_{1,3}$ = 1.1 5.00 (H_4)	4.62 (H_3)	7.99 (H_1)	6.24 (H_2)	3.16		7.5–8.5 (6 H)
	$J_{1,2}$ = 10.2, $J_{2,3}$ = 2.3, $J_{3,4}$ = 12.0, $J_{1,3}$ = 2.3						

259 (7), 244 (10), 243 (5). The bromo compound, dissolved in THF (15 mL), was treated with DBU (233 μL) at room temperature for 17 h. After chromatography (solvent gradient, CH_2Cl_2/EtOAc, 50:1) **15** (173 mg) and 11-acetoxy-7-methylbenz[*c*]acridine (**29**) (93 mg) were obtained. Recrystallization of **15** from hexane/EtOAc gave colorless needles: mp 186–199 °C dec; ^{1}H NMR (see Table I); CIMS, *m/e* (relative intensity) 362 (M + 1, 38), 302 (100), 260 (20), 244 (33). Anal. Calcd for $C_{22}H_{19}NO_4$: C, 73.12; H, 5.30; N, 3.88. Found: C, 73.10; H, 5.29; N, 3.85. Recrystallization of **29** from hexane/CH_2Cl_2 gave yellow needles: mp 179–82 °C; ^{1}H NMR (2 mg/0.3 mL, $CDCl_3$) δ 2.72 (s, 3 H), 3.12 (s, 3 H), 7.56–7.96 (m, 6 H), 8.07 (d, H_6), 8.22 (dd, H_8), 9.36–9.50 (m, H_1), $J_{5,6}$ = 9.3 Hz, $J_{8,9}$ = 7.2 Hz, $J_{8,10}$ = 3.9 Hz; CIMS, *m/e* (relative intensity) 302 (M + 1, 100), 260 (25). Analyses for $C_{20}H_{15}NO_2$.[10]

***trans*-1,2-Diacetoxy-1,2-dihydro-7-methylbenz[*c*]acridine (21).** Conversion of **19** (0.41 g) to **21** was effected as described for the preparation of **12**. Chromatography (solvent gradient CH_2Cl_2 to CH_2Cl_2/EtOAc, 20:1) gave **19** (81 mg), 2-acetoxy-7-methylbenz[*c*]acridine (**30**) (25 mg), and **21** (188 mg). Recrystallization of **21** from EtOAc gave pale yellow crystals: mp 198–201 °C dec; ^{1}H NMR (see Table I); CIMS, *m/e* (relative intensity) 362 (M + 1, 5), 302 (100), 260 (9), 244 (50). Anal. Calcd for $C_{22}H_{19}NO_4$: C, 73.12; H, 5.30; N, 3.88. Found: C, 73.40; H, 5.25; N, 3.78. Recrystallization of **30** from hexane/CH_2Cl_2 gave pale yellow prisms: mp 152–154 °C (lit. mp 154 °C); mixed melting point with an authentic sample[13] was not depressed; ^{1}H NMR (10 mg/0.3 mL, $CDCl_3$) δ 2.42 (s, 3 H), 3.03 (s, 3 H), 7.46 (dd, H_3), 7.60–7.90 (m, 4 H), 7.95 (d, H_6), 8.16–8.37 (m, H_8, H_{11}), 9.20 (d, H_1); $J_{1,3}$ = 2.4 Hz, $J_{3,4}$ = 8.4 Hz, $J_{5,6}$ = 9.4 Hz; CIMS, *m/e* (relative intensity) 302 (M + 1, 100), 260 (10).

***trans*-3,4-Diacetoxy-3,4-dihydro-7-methylbenz[*c*]acridine (23).** Compound **20** (50 mg) was brominated as described for the preparation of **12**. The product was treated under N_2 with LiF (101 mg) and Li_2CO_3 (152 mg) in freshly distilled HMPA (2.5 mL) at 95–100 °C for 6 h. After being cooled, the mixture was partitioned between water and CH_2Cl_2, and the CH_2Cl_2 phase gave a residue (62 mg) which was fractionated by PLC (two plates, 20 × 20 cm, CH_2Cl_2) to give **20** (11.5 mg) and **23** (26 mg, 51%). Recrystallization of **23** from hexane/EtOAc gave pale yellow crystals: mp 171–172 °C; ^{1}H NMR (see Table I); CIMS, *m/e* (relative intensity) 362 (M + 1, 13), 302 (100), 260 (57), 244 (55). Anal. Calcd for $C_{22}H_{19}NO_4$: C, 73.12; H, 5.30; N, 3.88. Found: C, 73.34; H, 5.42; N, 3.97. When the dehydrobromination was effected with DBU, 4-acetoxy-7-methylbenz[*c*]acridine (**31**), **20**, and **23** were isolated. Recrystallization of **31** from hexane/CH_2Cl_2 gave pale yellow prisms: mp 187–189 °C (lit. mp 188 °C); mixed melting point with an authentic sample[13] was not depressed; ^{1}H NMR (400 MHz, 10 mg/0.4 mL, $CDCl_3$) δ 2.50 (s, 3 H), 3.08 (s, 3 H), 7.49 (d, H_3), 7.62 (ddd, H_9), 7.75 (t, H_2), 7.75 (d, H_5), 7.82 (ddd, H_{10}), 8.06 (d, H_6), 8.26 (ddd, H_8), 8.36 (ddd, H_{11}), 9.46 (dt, H_1); $J_{1,2}$ = 8.2 Hz, $J_{1,3}$ = 1.1 Hz, $J_{1,2}$ = $J_{2,3}$ = 8.3 Hz, $J_{5,6}$ = 10.0 Hz, $J_{8,9}$ = 8.8 Hz, $J_{8,10}$ = 1.4 Hz, $J_{8,11}$ = 0.7 Hz, $J_{9,10}$ = 6.8 Hz, $J_{9,11}$ = 1.4 Hz; CIMS, *m/e* (relative intensity) 302 (M + 1, 100), 260 (35).

***trans*-8,9-Dihydro-8,9-dihydroxy-7-methylbenz[*c*]acridine (13).** A mixture of **12** (75 mg), MeOH (10 mL), and concentrated NH_3 (3 mL) was stirred at room temperature for 18 h to give a homogeneous solution. Concentration of the solution left a solid residue which was dried under vacuum (64.5 mg) and recrystallized from hexane/EtOAc, giving **13** as fine colorless needles: mp 172–174 °C; ^{1}H NMR (see Table I); CIMS, *m/e* (relative intensity) 278 (M + 1, 82), 277 (10), 260 (100); UV spectrum in MeOH (λ_{max}, nm (ϵ_{max})) 250 (47 000), 277 (25 500), 313 (14 000), 327 (10 500, sh), 343 (6400), 360 (6600). Anal. Calcd for $C_{18}H_{15}NO_2$: C, 77.96; H, 5.45; N, 5.05. Found: C, 78.16; H, 5.47; N, 4.92.

***trans*-10,11-Dihydro-10,11-dihydroxy-7-methylbenz[*c*]acridine (16).** Treatment of **15** (32 mg) as described for **13** gave **16**. Recrystallization from MeOH gave buff needles: mp 185–195 °C dec; ^{1}H NMR (see Table I); CIMS, *m/e* (relative intensity) 278 (M + 1, 100), 277 (10), 276 (5), 260 (95); UV spectrum in MeOH (λ_{max}, nm (ϵ_{max})) 226 (18 700), 268 (49 000), 277 (5000), 300 (20 000), 312 (11 500), 332 (2000), 347 (3300), 366 (3500). Anal. Calcd for $C_{18}H_{15}NO_2$: C, 77.96; H, 5.45; N, 5.05. Found: C, 77.54; H, 5.69; N, 5.14.

***trans*-1,2-Dihydro-1,2-dihydroxy-7-methylbenz[*c*]acridine (22).** The product from hydrolysis of **21** (96 mg) required

chromatography (solvent gradient, CH_2Cl_2/EtOAc (2:1 to 1:1)) and gave a yellow solid (53 mg). Recrystallization from MeOH gave **22** as yellow needles: mp 190–192 °C dec; ^1H NMR (see Table I); CIMS, *m/e* (relative intensity) 278 (M + 1, 100), 277 (14), 276 (11), 260 (60); UV spectrum in MeOH (λ_{max}, nm (ϵ_{max})) 255 (41 500), 280 (48 000), 288 (43 000), 344 (4000 sh), 363 (8200), 381 (11 300). Anal. Calcd for $C_{18}H_{15}NO_2$: C, 77.96; H, 5.45; N, 5.05. Found: C, 77.68; H, 5.48; N, 4.97.

***trans*-3,4-Dihydro-3,4-dihydroxy-7-methylbenz[*c*]acridine (24).** Similar treatment of **23** (38 mg) gave a yellow solid which on fractionation by PLC (three plates, 20 × 20 cm, CH_2Cl_2/EtOAc, 1:1) gave **24** (20 mg). Recrystallization from EtOAc gave pale yellow needles: mp 186–191 ° dec; ^1H NMR (see Table I); CIMS, *m/e* (relative intensity) 278 (M + 1, 45), 277 (14), 276 (4), 260 (100); UV spectrum in MeOH (λ_{max}, nm (ϵ_{max})) 261 (103 000), 348 (5600), 366 (9900), 393 (6700); high-resolution electron impact MS, *m/e* 277.1111 ($C_{18}H_{15}NO_2$ requires 277.1102). In dilute MeOH solution **24** was unstable when exposed to white fluorescent light ($t_{1/2} \sim 1$ h).

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Registry No. **2**, 3340-94-1; **3**, 86538-46-7; **4**, 86538-47-8; **5**, 92145-10-3; **6**, 92145-11-4; **7**, 92145-12-5; **8**, 92145-13-6; **9**, 92145-14-7; **10**, 92145-15-8; **11**, 92145-16-9; **12**, 92145-17-0; **13**, 82962-56-9; **14**, 92145-18-1; **15**, 92145-19-2; **16**, 88797-47-1; **17**, 92145-20-5; **18**, 92145-21-6; **19**, 92145-22-7; **20**, 92145-23-8; **21**, 92145-24-9; **22**, 88797-48-2; **23**, 92145-25-0; **24**, 92145-26-1; **25**, 92145-27-2; **26**, 92145-28-3; **27**, 92145-29-4; **28**, 92145-30-7; **29**, 86538-51-4; **30**, 83876-60-2; **31**, 83876-62-4; *trans*-9-acetoxy-8-(formyloxy)-7-methyl-8,9,10,11-tetrahydrobenz[*c*]acridine, 92145-09-0; (8α,10β,11α)-8-bromo-10,11-diacetoxy-7-methyl-8,9,10,11-tetrahydrobenz[*c*]acridine, 92145-31-8.

Supplementary Material Available: ^{13}C NMR data for **2–7** **10–12**, **14**, **15**, **17–19**, **21**, and **23** (Table II) (2 pages). Ordering information is given on any current masthead page.

Platinum Complex Catalyzed Reductive N-Acylation of Nitro Compounds

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Aromatic and aliphatic nitro compounds reacted with carboxylic acids at 180 °C for 4 h in the presence of a catalytic amount of $PtCl_2(PPh_3)_2$ combined with tin(IV) chloride under 60 atm of carbon monoxide pressure to give corresponding N-substituted amides in moderate to fairly good yields. From nitrobenzene, acetanilide was obtained in 91% yield. Tin(IV) chloride can be substituted by other Lewis acids such as $SnCl_2$, $FeCl_3$, VCl_3, $AlCl_3$, and $ZnCl_2$. The reaction appears to include the formation of nitrene and isocyanate as key intermediates.

One of the most widely applicable methods of amide formation is an acylation of primary or secondary amine with an acylating agent, R^1COX, where X = halogen, R^1COO, R^2O, R^2R^3N, N_3, or BF_4.[1] On the other hand, several attempts have been made in order to prepare amide derivatives from nitro compounds. This so-called reductive N-acylation seems more important industrially for aromatic nitro compounds. These direct anilide formations from nitroarenes were attained by employing various reducing agents. Ho utilized molybdenum hexacarbonyl ($Mo(CO)_6$) as the reducing agent.[2] This reaction, however, required excess $Mo(CO)_6$ (2.0 equiv) and a long reaction time (20 h at 120 °C). Owsley et al. employed metallic iron and succeeded in dissolving iron salts after the reaction.[3] Furthermore, a patent literature claimed that a large excess of acetic acid (40 equiv) reduced nitrobenzene to afford acetanilide at 250 °C.[4] As for catalytic reaction, Kajimoto and Tsuji investigated the anilide formation under carbon monoxide pressure in the presence of group VIII first-row transition-metal-carbonyl catalysts. The reaction proceeded readily at temperatures higher than 300 °C, while the anilides were not obtained at all at 285 °C.[5]

Table I. Reductive N-Acylation of Nitrobenzene Catalyzed by Pt Complexes[a]

run	platinum complex	Lewis acid	CO, atm	convn,[b] %	yield,[b] % acetanilide	yield,[b] % aniline
1			0	0	0	0
2			60	0	0	0
3		$SnCl_4$	60	0	0	0
4	$PtCl_2(PPh_3)_2$		60	81	46	18
5	$PtCl_2(PPh_3)_2$	$SnCl_4$	0	0	0	0
6	$PtCl_2(PPh_3)_2$	$SnCl_4$	30	60	29	17
7	$PtCl_2(PPh_3)_2$	$SnCl_4$	60	100	91	0
8[c]	$PtCl_2(PPh_3)_2$	$SnCl_4$	60	100	77	8
9[d]	$PtCl_2(PPh_3)_2$	$SnCl_4$	60	100	59	28
10	$PtCl_2(PhCN)_2$	$SnCl_4$	60	100	59	5

[a] A mixture of nitrobenzene (10 mmol), acetic acid (40 mmol), platinum complex (0.1 mmol), $SnCl_4$ (1.0 mmol), and dioxane (18 mL) was stirred at 180 °C for 4 h. [b] Determined by GLC based on the amount of nitrobenzene charged. [c] Triethylamine (1.8 mmol) was added. [d] H_2O (1.0 mL) was added.

In this paper, we report an alternative catalytic system for the synthesis of N-substituted amides from aromatic or aliphatic nitro compounds under carbon monoxide pressure.

Results

The platinum complex–tin(IV) chloride system showed much higher catalytic activity than that of the catalyst

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