Table I. Synthesis of 4-Methylene-3-tosyloxazolidin-2-ones[a]

propargylic alcohol 1	product 2	isolated yield (%)
1a	2a	80
1b	2b	81
1c	2c	82
1d	2d	82
1e	2e	83
1f	2f	81

[a] Conditions: propargylic alcohol (10 mmol), *p*-toluenesulfonyl isocyanate (10 mmol), CuI (0.1 mmol), Et_3N (0.5 mmol), and CH_2Cl_2 (10 mL) at 25 °C for 20 h. Ts = *p*-toluenesulfonyl.

pentyn-2-ol (**4b**)[12] were prepared by the reported methods. THF and CH_2Cl_2 were freshly distilled from benzophenone ketyl and CaH_2, respectively, before use. Commercially available *p*-toluenesulfonyl isocyanate, cuprous iodide, and triethylamine were used without further purification.

Typical Procedure for Preparation of 4-Alkylidene-3-tosyloxazolidin-2-ones. In a 30-mL round-bottomed flask with a septum inlet was placed cuprous iodide (0.02 g, 0.1 mmol) under argon, and a dry dichloromethane (7 mL) solution of triethylamine (0.05 g, 0.5 mmol) and propargylic alcohol (10 mmol) was added. A dry dichloromethane (3 mL) solution of *p*-toluenesulfonyl isocyanate (1.97 g, 10 mmol) was added dropwise to the solution by syringe at 0 °C. After the mixture was stirred for 20 h at room temperature, a white solid was filtered. Evaporation of the filtrate left a crude product, which was subjected to column chromatography (EtOAc/hexane, 1:3) and recrystallized from CH_2Cl_2/hexane or EtOH.

4-Methylene-3-tosyloxazolidin-2-one (2a): yield 2.45 g (80%); white solid; mp 149–152 °C; IR 1796 (C=O) cm^{-1}; ^1H NMR (270 MHz) δ 2.46 (s, 3 H), 4.53 (dt, J = 2.2, 2.7 Hz, 1 H), 4.79 (t, J = 2.2 Hz, 2 H), 5.53 (dt, J = 2.4, 2.7 Hz, 1 H), 7.37 (d, J = 8.4 Hz, 2 H), 7.95 (d, J = 8.4 Hz, 2 H); ^{13}C NMR δ 21.8 (q), 67.1 (t), 90.8 (t), 128.2 (d, Ts, C(2)), 129.9 (d, Ts, C(3)), 134.2 (s, Ts, C(4)), 135.0 (s), 146.3 (s, Ts, C(1)), 151.7 (s, C=O). Anal. Calcd for $C_{11}H_{11}NO_4S$: C, 52.16; H, 4.38; N, 5.53; S, 12.66. Found: C, 52.09, H, 4.31; N, 5.46; S, 12.57.

5-Methyl-4-methylene-3-tosyloxazolidin-2-one (2b): yield 2.45 g (81%); white solid; mp 100–104 °C; IR 1791 (C=O) cm^{-1}; ^1H NMR (270 MHz) δ 1.47 (d, J = 6.3 Hz, 3 H), 2.46 (s, 3 H), 4.47 (dd, J = 2.2, 2.2 Hz, 1 H), 4.99 (ddq, J = 2.2, 2.2, 6.3 Hz, 1 H), 5.53 (dd, J = 2.2, 2.2 Hz, 1 H), 7.36 (d, J = 8.2 Hz, 2 H), 7.95 (d, J = 8.2 Hz, 2 H); ^{13}C NMR δ 20.8 (q), 21.7 (q), 75.3 (d), 90.8 (t), 128.1 (d, Ts, C(2)), 129.6 (s), 129.8 (d, Ts, C(3)), 134.2 (s, Ts, C(4)), 140.8 (s), 146.2 (s, Ts, C(1)). Anal. Calcd for $C_{12}H_{13}NO_4S$: C, 53.92; H, 4.90; N, 5.24; S, 12.00. Found: C, 53.86; H, 4.78; N, 5.20; S, 12.01.

5,5-Dimethyl-4-methylene-3-tosyloxazolidin-2-one (2c): yield 2.31 g (82%); white crystalline solid; mp 82–84 °C; IR 1786 (C=O) cm^{-1}; ^1H NMR (270 MHz) δ 1.46 (s, 6 H), 2.46 (s, 3 H), 4.46 (d, J = 3.0 Hz, 1 H), 5.51 (d, J = 3.0 Hz, 1 H), 7.36 (d, J = 8.1 Hz, 2 H), 7.95 (d, J = 8.1 Hz, 2 H); ^{13}C NMR δ 21.8 (q), 27.8 (q), 83.3 (s), 90.2 (t), 128.1 (d, Ts, C(2)), 129.6 (d, Ts, C(3)), 134.4 (s, Ts, C(4)), 145.1 (s), 146.1 (s, Ts, C(1)), 150.2 (s, C=O). Anal. Calcd for $C_{13}H_{15}NO_4S$: C, 55.50; H, 5.37; N, 4.98; S, 11.40. Found: C, 55.11; H, 5.27; N, 4.97; S, 11.35.

5-(3-Butenyl)-5-methyl-4-methylene-3-tosyloxazolidin-2-one (2d): yield 2.64 g (82%); pale yellow oil; IR 1798 (C=O) cm^{-1}; ^1H NMR (270 MHz) δ 1.44 (s, 3 H), 1.67–1.91 (m, 4 H), 2.45 (s, 3 H), 4.43 (d, J = 3.0 Hz, 1 H), 4.88 (ddt, J = 10.7, 1.5, 1.5 Hz, 1 H), 4.90 (ddt, J = 16.6, 1.5, 1.5 Hz, 1 H), 5.56 (d, J = 3.0 Hz, 1 H), 5.64 (ddt, J = 16.6, 10.7, 5.9 Hz, 1 H), 7.36 (d, J = 8.6 Hz, 2 H), 7.94 (d, J = 8.6 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.6 (q), 26.8 (q), 26.9 (t), 39.7 (t), 85.0 (s), 90.3 (t), 115.3 (t), 127.9 (d, Ts, C(2)), 129.8 (d, Ts, C(3)), 136.4 (d), 143.4 (s, Ts, C(4)), 146.1 (s, Ts, C(1)), 150.3 (s, C=O). Anal. Calcd for $C_{16}H_{19}NO_4S$: C, 59.79; H, 5.96; N, 4.36; S, 9.98. Found: C, 60.19; H, 6.01; N, 4.29; S, 9.69.

5-Methyl-4-methylene-5-phenyl-3-tosyloxazolidin-2-one (2e): yield 2.85 g (83%); pale yellow solid; mp 91–92 °C (CH_2Cl_2/hexane); IR 1800 (C=O) cm^{-1}; ^1H NMR (270 MHz) δ 1.81 (s, 3 H), 2.43 (s, 3 H), 4.60 (d, J = 2.8 Hz, 1 H), 5.64 (d, J = 2.8 Hz, 1 H), 7.26–7.32 (m, 7 H), 7.86 (d, J = 8.4 Hz, 2 H); ^{13}C NMR δ 21.7 (q), 26.9 (q), 85.6 (s), 93.7 (t), 124.8 (d, Ph, C(2)), 128.1 (d, Ts, C(2)), 128.7 (d, Ph, C(4)) 128.8 (d, Ph, C(3)), 129.8 (d, Ts, C(3)), 134.3 (s, Ts, C(4)), 140.0 (s, Ph, C(1)), 144.1 (s), 146.1 (s, Ts, C(1)), 150.6 (s, C=O). Anal. Calcd for $C_{18}H_{17}NO_4S$: C, 62.96; H, 4.99; N, 4.08; S, 9.34. Found: C, 62.62; H, 4.92; N, 4.11; S, 9.33.

4-Methylene-5,5-pentamethylene-3-tosyloxazolidin-2-one (2f): yield 2.59 g (81%); white solid; mp 87–89 °C (EtOH); IR 1779 (C=O) cm^{-1}; ^1H NMR (270 MHz) δ 1.51–1.79 (m, 10 H), 2.45 (s, 3 H), 4.42 (d, J = 2.8 Hz, 1 H), 5.51 (d, J = 2.8 Hz, 1 H), 7.35 (d, J = 8.0 Hz, 2 H), 7.94 (d, J = 8.0 Hz, 2 H); ^{13}C NMR δ 21.1 (t), 21.6 (q), 24.2 (t), 36.6 (t), 84.8 (s), 90.1 (t), 127.9 (d, Ts, C(2)), 129.7 (d, Ts, C(3)), 134.3 (s, Ts, C(4)), 144.9 (s), 145.9 (s, Ts, C(1)), 150.2 (C=O). Anal. Calcd for $C_{16}H_{19}NO_4S$: C, 59.79; H, 5.96; N, 4.36; S, 9.98. Found: C, 59.63; H, 5.99; N, 4.41; S, 9.92.

(*Z*)-4-Ethylidene-3-tosyloxazolidin-2-one (6a): yield 1.95 g (73% based on **4a**); white solid; mp 84–85 °C (CH_2Cl_2/hexane); IR 1782 (C=O) cm^{-1}; ^1H NMR (270 MHz) δ 1.88 (dt, J = 7.2, 1.7 Hz, 3 H), 2.46 (s, 3 H), 4.66 (dq, J = 1.7, 1.7 Hz, 2 H), 5.27 (tq, J = 7.2, 1.7, 1 H), 7.36 (d, J = 8.2 Hz, 2 H), 7.96 (d, J = 8.2 Hz, 2 H); ^{13}C NMR δ 14.5 (q), 21.7 (q), 70.1 (t), 112.3 (d), 128.1 (s), 128.2 (d, Ts, C(2)), 129.8 (d, Ts, C(3)), 135.3 (s, Ts, C(4)), 145.7 (s, Ts, C(1)), 153.5 (s, C=O). Anal. Calcd for $C_{12}H_{13}NO_4S$: C, 53.92; H, 4.90; N, 5.24; S, 11.99. Found: C, 53.78; H, 4.85; N, 5.23; S, 12.18.

(*Z*)-4-Ethylidene-5-methyl-3-tosyloxazolidin-2-one (6b): yield 2.22 g (79% based on **4b**); white solid; mp 103–105 °C (CH_2Cl_2/hexane); IR 1790 (C=O) cm^{-1}; ^1H NMR (270 MHz) δ 1.46 (d, J = 6.4 Hz, 3 H), 1.87 (dd, J = 7.3, 1.7 Hz, 3 H), 2.45 (s, 3 H), 4.91 (dqq, J = 6.4, 1.7, 1.7 Hz, 1 H), 5.21 (dq, J = 7.3, 1.7 Hz, 1 H), 7.36 (d, J = 8.3 Hz, 2 H), 7.97 (d, J = 8.3 Hz, 2 H); ^{13}C NMR δ 14.7 (q), 19.4 (q), 21.7 (q), 78.1 (d), 111.6 (d), 127.0 (s), 128.5 (d, Ts, C(2)), 129.7 (d, Ts, C(3)), 133.7 (s, Ts, C(4)), 135.2 (s, Ts, C(1)), 145.6 (s, C=O). Anal. Calcd for $C_{13}H_{15}NO_4S$: C, 55.50; H, 5.37; N, 4.98; S, 11.40. Found: C, 55.40; H, 5.39; N, 4.93; S, 11.52.

Acknowledgment. This work is supported in part by Grants from Ministry of Education, Science and Culture, Japan. Thanks are also due to the Analytical Center, Faculty of Engineering, Osaka University, for the use of JEOL GSX-400 and Bruker AM600 spectrometers.

(11) Beumel, O. F.; Harris, R. F. *J. Org. Chem.* **1964**, *29*, 1872.
(12) Fleming, I.; Takaki, K.; Thomas, A. P. *J. Chem. Soc., Perkin Trans. 1* **1987**, 2269.

Studies on Polycyclic Azaarenes. 3.[1] Stereoselective Synthesis of *trans*-10,11-Dihydroxy-10,11-dihydrodibenz[*a*,*h*]-acridine and *trans*-10,11-Dihydroxy-10,11-dihydroacenaphtho-[1,2-*b*]quinoline

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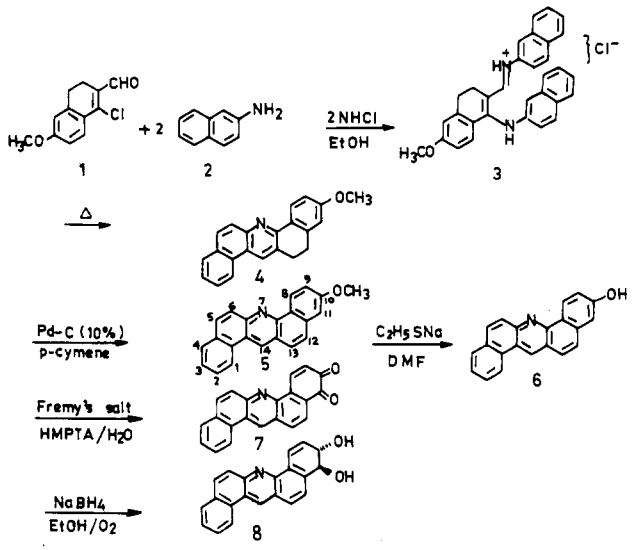
Received June 18, 1990

Dibenz[*a*,*h*]acridines are found to be mutagenic and carcinogenic.[2] There is substantial evidence that they are metabolically activated to reactive diol epoxide intermediates that bind to DNA in vivo. The diastereomeric 10,11-diol 8,9-epoxide is 20–40 times more mutagenic than the related 3,4-diol 1,2-epoxide.[2,3]

(1) Part 2: Ramesh, D.; Kar, G. K.; Chatterjee, B. G.; Ray, J. K. *J. Org. Chem.* **1988**, *53*, 212.
(2) Wood, A. W.; Chang, R. L.; Katz, M.; Conney, A. H.; Jerina, D. M.; Sikka, H. C.; Levin, W., Kumar, S. *Cancer Res.* **1989**, *49*, 6981.
(3) Sayer, J. M.; Lehr, R. E.; Kumar, S.; Yagi, H.; Yeh, H. J. C.; Holder, G. M.; Duke, C. C.; Silverton, J. V.; Gibson, C.; Jerina, D. M. *J. Am. Chem. Soc.* **1990**, *112*, 1177.
(4) Kar, G. K.; Karmakar, A. C.; Ray, J. K. *Tetrahedron Lett.* **1989**, *30*, 223.

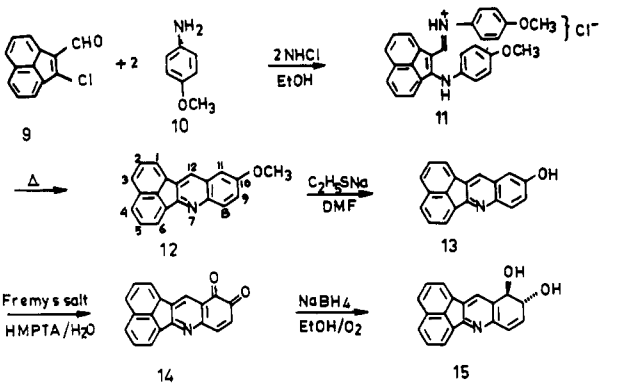
0022-3263/91/1956-2268$02.50/0

We report a convenient method of synthesis of the title compounds. Our method involves treatment of the chloro aldehyde **1** with 2 equiv of 2-naphthylamine in ethanol followed by treatment with excess of 2 N HCl to make the anil hydrochloride **3** in 82% yield. The enamino imine hydrochloride **3** cyclizes regioselectively on heating (225–230 °C) for 3–4 min, with the exclusion of 1 equiv of 2-naphthylamine hydrochloride to produce 10-methoxy-12,13-dihydrodibenz[*a*,*h*]acridine (**4**). Aromatization of the dihydro compound **4** by heating with Pd/C (10%) in *p*-cymene produces **5** in quantitative yield. The methoxy derivative **5** undergoes conversion to phenol **6** by refluxing in DMF with the sodium salt of ethyl mercaptan[5] in 92% yield. Fremy's salt[6] oxidation of phenol **6** gives the *o*-quinone **7** in 97% yield. Finally, sodium borohydride reduction in the presence of oxygen of *o*-quinone **7** produces the title compound **8** in 25% yield.



The synthesis of **8** described provides a more convenient route to this dihydrodiol than the previous method.[10]

Although the dihydrodiol of benzo[*k*]fluoranthene has been reported,[7] the corresponding aza analogue has not been synthesized and tested for mutagenic activity. Our finding that the nitro derivative of acenaphthoquinoline[8] is mutagenic without metabolic oxidation[9] prompted us to undertake the synthesis of the oxidized metabolite of acenaphtho[1,2-*b*]quinoline. Our method involves synthesis of anil hydrochloride **11** from chloro aldehyde **9**[9] and 4-methoxyaniline (**10**). Thermal cyclization of **11** produces 10-methoxyacenaphtho[1,2-*b*]quinoline **12** in 52% yield. The methoxy derivative **12** is converted to phenol in 92% yield, which in turn is converted to quinone **14** in quantitative yield. Borohydride reduction of *o*-quinone **14** produces the title compound in 40% yield.



Experimental Section

General Notes. Fremy's salt (potassium nitroso disulfonate) was prepared according to the method described by Zimmer.[6] Compounds **1** and **9** were prepared by following the method of Ray et al.[9,11] The NMR spectra were recorded on a Varian EM 390 (90 MHz) or on a Bruker 250 (250 MHz) spectrometer with tetramethyl silane as internal standard. All the melting points are uncorrected.

General Method for the Preparation of Anil Hydrochlorides 3 and 11. To a stirred solution of 6 mmol of the arylamine (**2** or **10**) in 20 mL of ethanol was added 3–3.5 mL of 2 N HCl, and the mixture was stirred at 5–10 °C. To this 2.5 mmol of the chloro aldehyde (**1** or **9**) in 10 mL of ethanol was added. Stirring was continued for 3 h at room temperature, and the mixture was cooled in ice bath and filtered. The residue was washed with little cold ethanol and dried in air to get the anil hydrochloride (**3** or **11**).

6-Methoxy-1-(β-naphthylamino)-2-((β-naphthylimino)methyl)-3,4-dihydronaphthalene hydrochloride (3): red solid; mp 208–209 °C dec (ethanol); yield 81.5%; IR (KBr) ν_{max} 1590, 1595, 2900, 3375 cm^{-1}.

1-((*p*-Methoxyphenyl)amino)-2-(((*p*-methoxyphenyl)imino)methyl)acenaphthylene hydrochloride (11): dark red solid; mp 202–203 °C dec; yield 97%; IR (Nujol) ν_{max} 1615, 1640, 3435 cm^{-1}.

General Method for the Preparation of 4 and 12. The anil derivative (**3** or **11**) was heated slightly above its melting point for 3–4 min in a long-neck tube. Arylamine hydrochloride, deposited in the cooler part of the test tube was removed. The cooled residue was extracted with chloroform or benzene, washed with water, and dried (Na_2SO_4), and solvent was removed to get the crude product which was further purified by column filtration (neutral Al_2O_3/benzene) followed by recrystallization from suitable solvent.

10-Methoxy-12,13-dihydrodibenz[*a*,*h*]acridine (4): colorless solid; mp 162–163 °C (EtOH); yield 61%; ^{1}H NMR ($CDCl_3$) δ 2.9–3.3 (m, 4 H), 3.8 (s, 3 H), 6.7–7.0 (m, 2 H), 7.7–8.1 (m, 3 H), 8.5–8.8 (m, 3 H) ppm.

Anal. Calcd for $C_{22}H_{17}NO$: C, 84.9; H, 5.4; N, 4.5. Found: C, 84.6; H, 5.1; N, 4.2.

10-Methoxyacenaphtho[1,2-*b*]quinoline (12): light yellow solid; mp 168–169 °C (benzene–hexane); yield 52%; ^{1}H NMR (CD_3CN + CF_3CO_2D) δ 3.85 (s, 3 H), 7.05 (d, 1 H), 7.25 (dd, 1 H), 8.4 (s, 1 H) ppm; MS (*m*/*e*) 283 (M^+), 268, 240.

Anal. Calcd for $C_{20}H_{13}NO$: C, 84.8; H, 4.6; N, 5.0. Found: C, 84.6; H, 4.4; N, 4.7.

10-Methoxydibenz[*a*,*h*]acridine (5). The dihydromethoxy derivative **4** (1 g), Pd–C (10%) (300 mg), and *p*-cymene (15 mL) were refluxed together for 4–5 h and filtered to remove Pd–C. Filtrate on evaporation afforded **5** as a light yellow solid (1 g, 100%): mp 213–214 °C (EtOH); ^{1}H NMR ($CDCl_3$) δ 4.0 (s, 3 H), 7.3–8.4 (m, 8 H), 8.75 (d, 1 H), 8.8 (d, 1 H), 9.4 (s, 1 H), 9.5 (d, 1 H) ppm.

Anal. Calcd for $C_{22}H_{15}NO$: C, 85.4; H, 4.8; N, 4.5. Found: C, 85.2; H, 4.7; N, 4.2.

General Procedure for the Preparation of the Phenols 6 and 13. To C_2H_5SNa (prepared from 1.08 mmol of Na) a solution of the methoxyazaarene (**5** or **12**) in 5 mL of dry DMF was added. The mixture was refluxed under N_2 for 7 h, cooled, poured in ice water, and acidified with acetic acid. The solid separated was either filtered (in case of **6**) or extracted with ethyl acetate (in case of **13**) to give the desired phenol **6** or **13** in excellent yield.

10-Hydroxydibenz[*a*,*h*]acridine (6): cream-colored solid; mp 287–288 °C; yield 92%; MS (*m*/*e*) 295 (M^+), 266.

Anal. Calcd for $C_{21}H_{13}NO$: C, 85.4; H, 4.4; N, 4.7. Found: C, 85.3; H, 4.1; N, 4.5.

(5) Feutrill, G. I.; Mirrington, R. N. *Tetrahedron Lett.* **1970**, 1327.
(6) Zimmer, H.; Lankin, D. C.; Horgan, S. W. *Chem. Rev.* **1971**, *71*, 229.
(7) Amin, S.; Bedenko, V.; La Voie, E.; Hecht, S. S.; Hoffman, D. *J. Org. Chem.* **1981**, *46*, 2573.
(8) Kar, G. K.; Ray, J. K., unpublished results.
(9) Ray, J. K.; Kar, G. K.; Chatterjee, B. G. *Tetrahedron* **1984**, *40*, 2959.
(10) Kumar, S. *J. Org. Chem.* **1985**, *50*, 3070.
(11) Ray, J. K.; Sharma, S.; Chatterjee, B. G. *Synth. Commun.* **1979**, *9*, 727.

10-Hydroxyacenaphtho[1,2-*b*]quinoline (13): light yellow solid; mp 309–310 °C (ethyl acetate); yield 92%; ^{1}H NMR (DMSO-d_6) δ 7.4–8.5 (m, 10 H), 8.95 (s, 1 H) ppm.

Anal. Calcd for $C_{19}H_{11}NO$: C, 84.7; H, 4.1; N, 5.2. Found: C, 84.6; H, 4.0; N, 5.0.

General Method for the Preparation of Quinones 7 and 14. To an aqueous solution of Fremy's salt $(SO_3K)_2NO$ (3.9 mmol) in 100 mL of 0.16 M KH_2PO_4 at 5 °C was added dropwise with stirring a solution of the phenol (6 or 13) in 50 mL of HMPA. The mixture was stirred at 5–7 °C for 2–2.5 h and then left overnight at 0 °C. The solid separated was filtered, washed well with water, and dried.

10,11-Dioxo-10,11-dihydrodibenz[*a*,*h*]acridine (7): purple violet solid; mp 235–237 °C dec; yield 97%; IR (KBr) ν_{max} 1615, 1645, 1660 cm^{-1}.

Anal. Calcd for $C_{21}H_{11}NO$: C, 81.5; H, 3.5; N, 4.5. Found: C, 81.3; H, 3.4; N, 4.2.

10,11-Dioxo-10,11-dihydroacenaphtho[1,2-*b*]quinoline (14): brick red solid; mp >350 °C; yield 100%; IR (KBr) ν_{max} 1615, 1640, 1655 cm^{-1}.

Anal. Calcd for $C_{19}H_9NO_2$: C, 80.5; H, 3.2; N, 5.0. Found: C, 80.3; H, 2.9; N, 4.7.

General Procedure for the Preparation of the *trans*-Dihydrodiols 8 and 15. To a suspension of the quinone (7 or 14) (0.3 mmol) in ethanol (15 mL) was added an excess of $NaBH_4$ (200 mg). The mixture was stirred at 25 °C for 48 h with a constant blow of oxygen and keeping the volume of solvent constant by addition of ethanol. The color of the reaction mixture changed from orange to faint yellow during this time. After decomposing the complex with ice–water, the organic portion was extracted with an ethyl acetate–ether mixture, washed with water, and dried ($MgSO_4$). Removal of solvent in vacuo followed by purification by preparative TLC (silica gel/ethyl acetate–ether, 1:1) furnished the *trans*-diols.

***trans*-10,11-Dihydroxy-10,11-dihydrodibenz[*a*,*h*]acridine (8)**: faint yellow solid; mp 226–229 °C (lit.[10] mp 230–231 °C; yield 25%; MS (*m*/*e*) 313 (M$^+$); ^{1}H NMR (DMSO-d_6 + D_2O) δ 4.3 (d, 1 H), 4.9 (d, 1 H), 6.1 (dd, 1 H), 7.6–8.5 (m, 8 H), 8.9 (d, 1 H), 9.7 (s, 1 H) ppm.

***trans*-10,11-Dihydroxy-10,11-dihydroacenaphtho[1,2-*b*]quinoline (15)**: faint yellow solid; mp 225–227 °C; yield 40%; ^{1}H NMR (DMSO-d_6 + D_2O) δ 4.1 (m, 1 H), 5.2 (d, 1 H, J = 7 Hz), 6.5 (m, 1 H), 7.2 (d, 1 H, J = 7 Hz), 7.3–8.5 (m, 5 H), 8.6 (d, 1 H, J = 6 Hz), 9.1 (s, 1 H) ppm.

Anal. Calcd for $C_{19}H_{19}NO_2$: C, 79.4; H, 4.5; N, 4.9. Found: C, 79.1; H, 4.3; N, 4.5.

Acknowledgment. Thanks to CSIR, New Delhi, for financial support.

A Case of Self-Induced Anisochrony in the Proton Nuclear Magnetic Resonance Spectra of 1,5-Benzothiazepines

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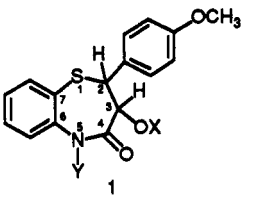
Received June 13, 1990

The NMR spectra of enantiomers may be different when they are of solutions in a nonracemic chiral solvent[1a] or of solutions in an achiral solvent containing a nonracemic chiral additive, such as a lanthanide shift reagent.[1b] In the absence of any added nonracemic chiral substance, the notion that enantiomers and racemates show identical NMR spectra holds true only at high dilution. To the extent that there is some degree of solute aggregation, they may exhibit different NMR spectra.[1a,2-8] Generally, the differences under such circumstances are so small that they are not detectable.

Now, we report a new example of the self-discrimination of enantiomers which can be conveniently used for the determination of the enantiomeric purity of 1,5-benzothiazepines 1 (Figure 1) by ^{1}H NMR methods. In this case, enantiomeric purity is of particular importance because



1

X=OCCH$_3$	Y=CH$_2$CH$_2$N(CH$_3$)$_2$·HCL	Cis	2S,3S	(+)-1a
X=H	Y=H	Cis	2S,3S	(+)-1b
X=H	Y=H	Cis	2R,3R	(-)-1b
X=OCCH$_3$	Y=H	Cis	2S,3S	(+)-1c
X=OCCH$_3$	Y=H	Cis	2R,3R	(-)-1c
X=H	Y=CH$_3$	Cis	2S,3S	(+)-1d
X=H	Y=CH$_3$	Cis	2R,3R	(-)-1d
X=H	Y=H	Trans	2S*,3R*	(+)-1e
X=H	Y=H	Trans	2S*,3R*	(-)-1e

Figure 1.

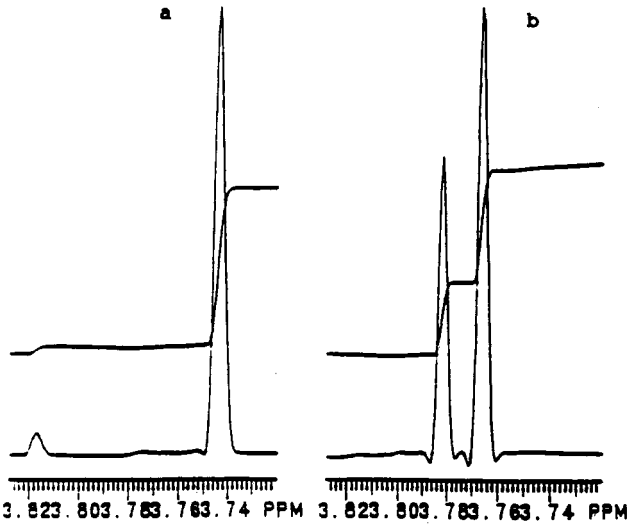


Figure 2. *p*-Methoxy proton resonances of (a) 95% (+)-**1b**, 5% (-)-**1b**, and (b) 60% (+)-**1b**, 40% (-)-**1b**.

(1) Morrison, J. D., Ed. *Asymmetric Synthesis*; Academic Press Inc.: New York, 1983. (a) Weismann, G. R, Chapter 8, pp 153–171. (b) Fraser, R. R., Chapter 9, p 173.

(2) Williams, T.; Pitcher, R. G.; Bommer, P.; Gutzwiller, J.; Uskokovič, M. *J. Am. Chem. Soc.* **1969**, *91*, 1871.

(3) Horeau, A.; Guetté, J. P. *Tetrahedron* **1974**, *30*, 1923.

(4) Harger, M. J. P. *J. Chem. Soc., Chem. Commun.* **1976**, 555. Harger, M. J. P. *J. Chem. Soc., Perkin Trans. 2* **1977**, 1882; **1978**, 326.

(5) Kabachnik, M. I.; Mastryukova, T. A.; Fedin, E. I.; Vaisberg, M. S.; Morozov, L. L.; Petrovsky, P. V.; Shipov, A. E. *Tetrahedron* **1976**, *32*, 1719; *Russ. Chem. Rev.* **1978**, *47*, 821.

(6) Thong, C. M.; Marraud, M.; Neel, J. *C. R. Seances Acad. Sci., Ser. C* **1975**, *281C*, 691.

(7) Dobashi, A.; Saito, N.; Motoyama, Y.; Hara, S. *J. Am. Chem. Soc.* **1986**, *108*, 307.

(8) For an example of chiral self-recognition by NMR in the presence of an achiral amplifying agent, see: Luchinat, C.; Roelens, S. *J. Am. Chem. Soc.* **1986**, *108*, 4873.

0022-3263/91/1956-2270$02.50/0