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On the Reactions of Dibenz[*b*,*f*]oxireno[*d*]azepine Derivatives[1)]

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The chemical properties of the epoxy ring in 1a,10b-dihydro-6*H*-dibenz[*b*,*f*]oxireno-[*d*]azepines (**1**) are dependent on the nature of the substituents on the nitrogen at the 6-position. Treatment with acids or alkalis led to either the normal cleavage of the epoxy ring or the rearrangement to the acridine ring.

Keywords——dibenzoxirenazepine; dibenzazepine; epoxide; halohydrin; peracid; rearrangement; acridine

The synthesis and pharmacological activities of the dibenz[*b*,*f*]oxireno[*d*]azepine derivatives **1**, a novel class of tetracyclic compounds, have recently been described by the present authors.[3)] In the course of the synthetic study, some chemical properties of the ring system attracted the attention of the authors, which are the subject of the present paper. The chemical properties of the epoxy ring in **1** are dependent on the nature of the substituents on the nitrogen at the 6-position. Treatment with acids or alkalis led to either the normal cleavage of the epoxy ring or the rearrangement to the acridine ring.

The epoxy ring in 1a, 10b-dihydro-6*H*-dibenz[*b*,*f*]oxireno[*d*]azepines (**1**) can be cleaved normally by acids if the N–H group at the 6-position is protected by the chlorocarbonyl or acetyl groups. Thus, **1a** was converted into the halohydrins **2a** and **2b** by reaction with hydrochloric or hydrobromic acids, while the ring opening by thiocyanic acid[4)] transformed **1b** into **2c** (Chart 1). The *trans* relationship between X and hydroxyl groups in **2** was suggested by

1

a: R=COCl
b: R=$COCH_3$

2

a: X=Cl; R=COCl
b: X=Br; R=COCl
c: X=SCN; R=$COCH_3$

Chart 1

the large values of coupling constants between C10-H and C11-H in the nuclear magnetic resonance (NMR) spectra of **2**: 10 Hz for **2a**, 11 Hz for **2b** and 10 Hz for **2c**, as well as the facile ring closure of **2a** and **2b** to afford **1c** (=**1**, R=$CONH_2$) and **1d** (=**1**, R=$CONH(CH_2)_2$-CH_3) upon treatment with ammonia and *n*-propylamine, respectively.

Epoxidation of 5*H*-dibenz[*b*,*f*]azepine-5-carboxylic acid 3-chloropropyl ester (**3**) gave no corresponding epoxide **4** but led to the rearranged products **5** and **6** (Chart 2). Some infor-

1) A part of this study was presented at the 94th Annual Meeting of Pharmaceutical Society of Japan, Sendai, April, 1974.
2) Location: *17–85, Juso-honmachi 2-chome, Yodogawa-ku, Osaka 532, Japan.*
3) K. Kawashima, T. Ishiguro, S. Chiba, and Y. Nagawa, *J. Takeda Res. Lab.*, accepted.
4) T. Komeno, *Chem. Pharm. Bull.* (Tokyo), **8**, 672 (1960).

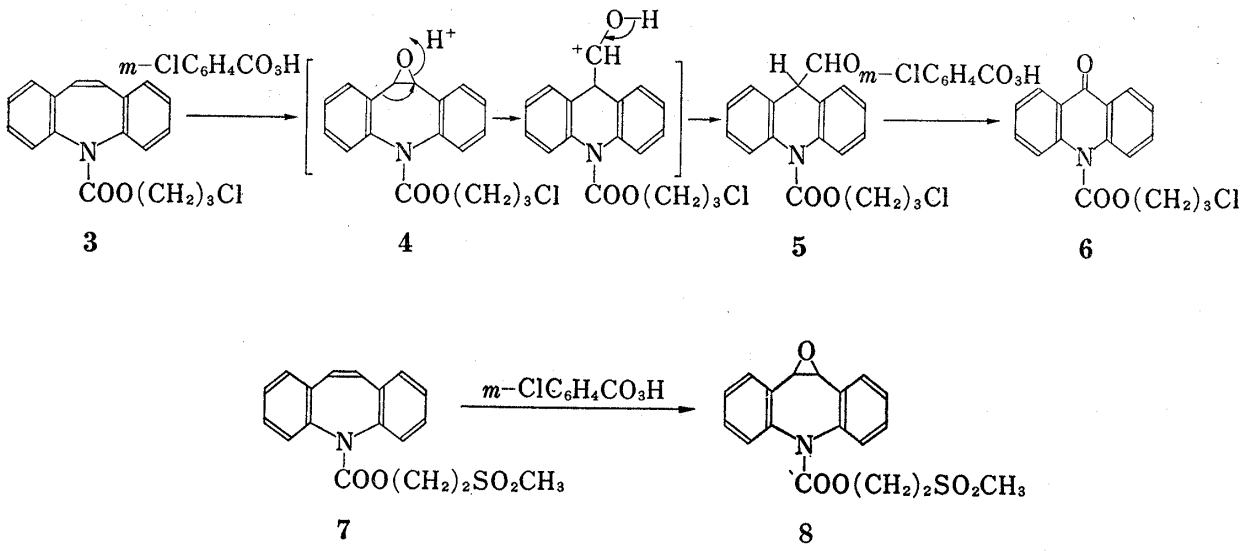

Chart 2

mation was obtained concerning the mechanism of the rearrangement when the oxidation was followed by the measurement of the NMR spectra; a signal at δ 6.93 (–CH=CH–) was first replaced gradually by a signal at δ 4.25 (epoxy protons), and new signals at δ 4.70 and δ 9.48 (–CH(CHO)–) then appeared at the expense of the latter signal. This fact suggests that the epoxide **4** once formed would have rearranged to **5** probably by a catalytic action of *m*-chlorobenzoic acid as shown in Chart 2. Further oxidation of **5** with *m*-chloroperbenzoic acid afforded **6**. The facile rearrangement of **4** is surprising because the related epoxide **8** with a similar substituent is stable under the reaction conditions.[3]

The unsubstituted 1a,10b-dihydro-6*H*-dibenz[*b*,*f*]oxireno[*d*]azepine (**10**) is highly unstable and prone to rearrangement both under acidic and basic conditions. Thus, all attempts to

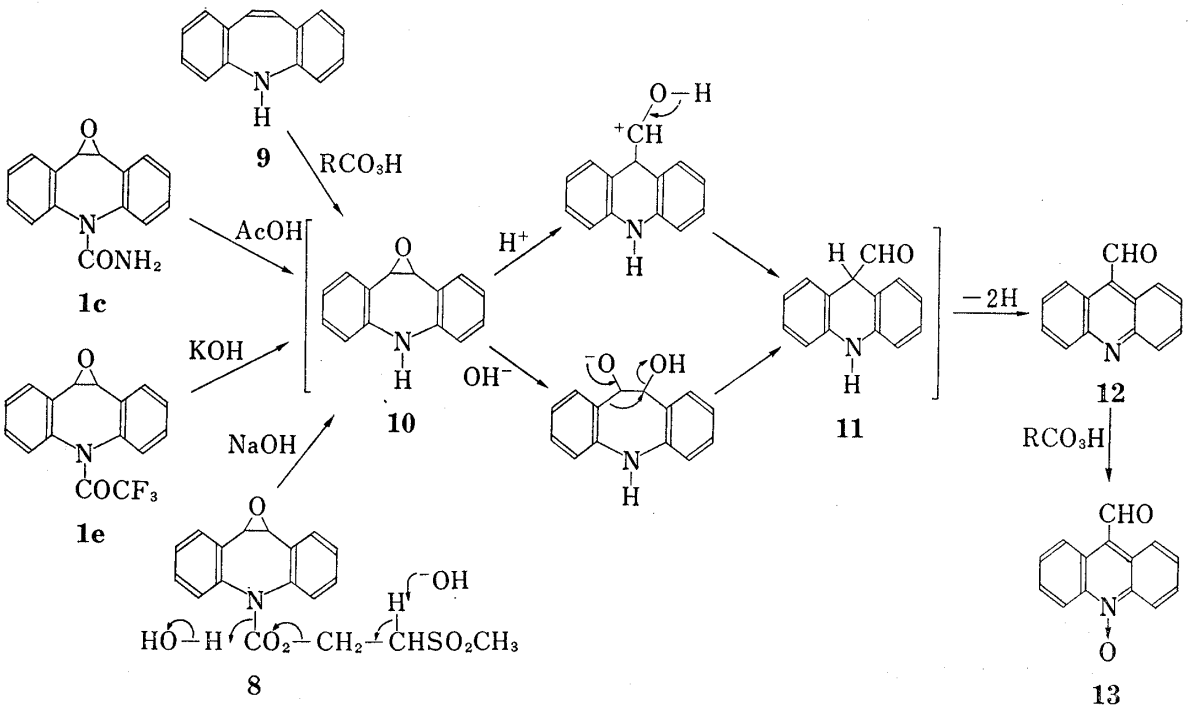

Chart 3

isolate **10** were unsuccessful. When 5*H*-dibenz[*b*,*f*]azepine[5] (**9**) was reacted with organic peracids, 9-acridinecarbaldehyde (**12**) and its N-oxide (**13**) were obtained in stead of **10**. A plausible mechanism of the reaction is shown in Chart 3. The intermediate **10** appears to be involved also in the transformation of the carboxamide **1c** into **12** by boiling acetic acid.[3,6] Although trifluoroacetyl group is known to be removed under mild alkaline conditions,[7] it became resistant to hydrolysis when attached to aromatic amines as in **1e**. Thus, **1e** was not affected by potassium carbonate but converted by potassium hydroxide to **12**. Another protecting group tested was [2-(methylsulfonyl)ethyl]oxycarbonyl, a representive of the amino-protecting groups which can be cleaved under mild alkaline conditions accompanied by β-elimination.[8] However, the protecting group in **8** was cleaved only by strong alkali; treatment of **8** with sodium hydroxide afforded **12** as the sole product. These facts suggest that the rearrangement of **10** into **11** is induced also by an alkali as shown in Chart 3.

Experimental

Melting points are uncorrected. IR spectra were taken with a Hitachi EPI-S2 model. NMR spectra were recorded with Varian T-60 (60 MHz) and HR-100 (100 MHz) models, the chemical shifts being expressed in ppm relative to internal tetramethylsilane (δ). Abbreviations are as follows: s, singlet; d, doublet; t, triplet; m, multiplet; br, broad. Mass spectra were measured with a Hitachi RMU-6D double focussing mass spectrometer.

6-Acetyl-1a,10b-dihydro-6*H*-dibenz[*b*,*f*]oxireno[*d*]azepine (**1b**)——To a flask containing 5-acetyl-5*H*-dibenz[*b*,*f*]azepine[5] (92.3% purity, 12.8 g; 50 mmol) was added under ice-cooling a solution of perbenzoic acid in $CHCl_3$ (108 ml; containing *ca.* 60 mmol of the peracid) prepared following the method described in the literature.[9] After standing at room temperature for 3 days, the solution was successively washed with 5% $NaHSO_3$ aq. (30 ml), saturated $NaHCO_3$ aq. (70 ml) and water (50 ml). The solution was dried over Na_2SO_4 and evaporated under reduced pressure to afford an oil (18.3 g), which was crystallized by addition of benzene (20 ml) to yield **1b** (7.48 g; 59.6% yield). Recrystallization from EtOH afforded pure **1b**, mp 151—152°. IR ν_{max}^{Nujol} cm^{-1}: 1671 (C=O). NMR (100 MHz) δ^{CDCl_3}: 1.89 (s, $COCH_3$), 4.19 (s, epoxy), 6.8—7.5 (m, aromatic). *Anal.* Calcd. for $C_{16}H_{13}NO_2$: C, 76.47; H, 5.22; N, 5.57. Found: C, 76.61; H, 5.14; N, 5.61.

10-Chloro-10,11-dihydro-11-hydroxy-5*H*-dibenz[*b*,*f*]azepine-5-carbonyl Chloride (**2a**)——To a solution of 1a,10b-dihydro-6*H*-dibenz[*b*,*f*]oxireno[*d*]azepine-6-carbonyl chloride[3] (**1a**) (0.529 g) in THF (10 ml) was added 10% HCl aq. (1 ml) and the mixture was heated under reflux for 1 hr. The solution was concentrated, water was added and the product was extracted with $CHCl_3$. The $CHCl_3$ solution was dried over Na_2SO_4 and evaporated under reduced pressure to yield a yellow oil, which was crystallized from MeOH to give **2a** (0.262 g), mp 165—167°. IR ν_{max}^{Nujol} cm^{-1}: 3500 (OH), 1730, 1715 (NCOCl). NMR (60 MHz) δ^{CDCl_3}: 5.08 (d, J=10 Hz, CHCl), 5.52 (d, J=10 Hz, CHOH), 7.2—8.0 (m, aromatic). *Anal.* Calcd. for $C_{15}H_{11}Cl_2NO_2$: C, 58.46; H, 3.60; N, 4.54. Found: C, 58.59; H, 3.58; N, 4.40.

10-Bromo-10,11-dihydro-11-hydroxy-5*H*-dibenz[*b*,*f*]azepine-5-carbonyl Chloride (**2b**)——To a solution of **1a** (2.00 g) in THF (10 ml) was added 48% HBr aq. (0.7 ml) and the mixture was heated under reflux for 1 hr. The solution was concentrated, and water and $CHCl_3$ were added to the residue. The $CHCl_3$ layer separated was dried over Na_2SO_4 and evaporated under reduced pressure to yield a white powder, which was recrystallized from MeOH to give **2b** (1.36 g), mp 147—148°. IR ν_{max}^{Nujol} cm^{-1}: 3490 (OH), 1730, 1718 (NCOCl). NMR (60 MHz) δ^{CDCl_3}: 5.26 (d, J=11 Hz, CHBr), 5.66 (d, J=11 Hz, CHOH), 7.2—7.9 (m, aromatic). *Anal.* Calcd. for $C_{15}H_{11}BrClO_2$: C, 51.09; H, 3.14; N, 3.97. Found: C, 51.09; H, 3.01; N, 3.94.

1a,10b-Dihydro-6*H*-dibenz[*b*,*f*]oxireno[*d*]azepine-6-carboxamides (**1**) **by Ring Closure Reaction of 10-Halo-10,11-dihydro-11-hydroxy-5*H*-dibenz[*b*,*f*]azepine-5-carbonyl Chlorides** (**2**)——a) A mixture of **2a** (56 mg) and 10% NH_3 in MeOH (15 ml) was stirred for 2.5 hr at room temperature. The solvent was evaporated under reduced pressure, and $CHCl_3$ (15 ml) and water (7 ml) were added. The $CHCl_3$ solution was dried over Na_2SO_4 and evaporated under reduced pressure to yield 1a,10b-dihydro-6*H*-dibenz[*b*,*f*]oxireno[*d*]azepine-6-

5) W. Schindler and H. Blattner, *Helv. Chim. Acta*, **44**, 753 (1961).
6) The same transformation had been observed when **1c** was subjected to the gas-liquid chromatographic analysis (K.M. Baker, A. Frigerio, P.L. Morselli, and G. Pifferi, *J. Pharm. Sci.*, **62**, 475 (1973)).
7) L.F. Fieser and M. Fieser, "Reagents for Organic Synthesis," John Wiley and Sons, Inc., New York, N.Y., 1967, p. 1226.
8) A.T. Kader and C.J.M. Stirling, *J. Chem. Soc.*, **1964**, 258; S. Terao, T. Matsuo, S. Tsushima, T. Miyawaki, and M. Miyamoto, Japan. Patent 38995 (1972).
9) G. Braun, "Organic Syntheses," Col. Vol. 1, 2nd ed., ed. by H. Gilman, John Wiley and Sons, Inc., New York, N.Y., 1951, p. 431.

carboxamide (**1c**) (38 mg), mp 195—197° (dec.), which was identical in all respects with the authentic sample described earlier.[3]

b) A mixture of **2b** (0.572 g) and 10% NH_3 in MeOH (30 ml) was stirred for 1 hr at room temperature. The solvent was evaporated under reduced pressure, and water (10 ml) and $CHCl_3$ (30 ml) were added. The $CHCl_3$ solution was dried over Na_2SO_4 and evaporated under reduced pressure. The residue was recrystallized from EtOH to yield **1c** (297 mg), mp 195—197° (dec.).

c) To a solution of **2b** (0.703 g) in EtOH (25 ml) was added *n*-propylamine (0.354 g) and the mixture was stirred for 1 hr at room temperature. The solvent was evaporated under reduced pressure to yield a brown oil (0.625 g), which was purified by column chromatography on silica gel to give 1a,10b-dihydro-N-propyl-6*H*-dibenz[*b*,*f*]oxireno[*d*]azepine-6-carboxamide (**1d**) (0.187 g), mp 128—130°, which was identical in all respects with the authentic sample described earlier.[3]

5-Acetyl-10,11-dihydro-10-hydroxy-11-thiocyanato-5*H*-dibenz[*b*,*f*]azepine (**2c**)——To a solution of **1b** (0.627 g; 2.5 mmol) in $CHCl_3$ (5 ml) was added a solution of HSCN in ether[4] (5 ml; containing *ca.* 25 mmol of HSCN) under ice-cooling and the mixture was left standing for 2 days at room temperature. Crystals deposited were collected and washed first with $CHCl_3$–ether and then with ether to yield **2c** (0.486 g; 62.8% yield). Recrystallization from EtOH gave pure **2c**, mp 175—179° (dec.). IR ν_{max}^{Nujol} cm^{-1}: 3350 (OH), 2170 (SCN), 1642 ($NCOCH_3$). NMR (100 MHz) $\delta^{DMSO\text{-}d_6}$: 2.20 (s, $COCH_3$), 4.67 (d, J=10 Hz, CHS), 5.30 (d, J=10 Hz, CHO), 6.58 (br, OH), 7.0—7.8 (m, aromatic). *Anal.* Calcd. for $C_{17}H_{14}N_2O_2S$: C, 65.78; H, 4.55; N, 9.03; S, 10.33. Found: C, 65.80; H, 4.54; N, 8.90; S, 10.48.

5*H*-Dibenz[*b*,*f*]azepine-5-carboxylic Acid 3-Chloropropyl Ester (**3**)——A mixture of 5*H*-dibenz[*b*,*f*]-azepine[5] (**9**) (0.483 g; 2.5 mmol), 3-chloropropyl chloroformate[10] (0.43 g; 2.75 mmol) and benzene (4.8 ml) was heated under reflux for 12 hr. Additional chloroformate (0.36 g; 2.25 mmol) was added and additional 5 hr refluxing was effected. Evaporation of the solvent yielded an oil (1.175 g), which was purified by chromatography on silica gel (24 g). From the fractions eluted with $CHCl_3$ was isolated **3**, mp 58—63°. IR ν_{max}^{Nujol} cm^{-1}: 1712 (NCO_2). NMR (60 MHz) δ^{CDCl_3}: 1.93 (quintet, J=6 Hz, C–CH_2–C), 3.35 (t, J=6 Hz, CH_2Cl), 4.20 (t, J=6 Hz, OCH_2), 6.93 (s, olefinic), 7.1—7.6 (m, aromatic). *Anal.* Calcd. for $C_{18}H_{16}ClNO_2$: C, 68.90; H, 5.14; N, 4.46; Cl, 11.30. Found: C, 68.82; H, 5.02; N, 4.41; Cl, 11.38.

Attempted Epoxidation of 5*H*-Dibenz[*b*,*f*]azepine-5-carboxylic Acid 3-Chloropropyl Ester (**3**)——a) 9-Formyl-10-acridancarboxylic Acid 3-Chloropropyl Ester (**5**): To a solution of **3** (66.0% pure, 1.43 g; 3 mmol) in $CHCl_3$ (14 ml) was added *m*-chloroperbenzoic acid (85% pure, 0.610 g; 3 mmol) in portions over a period of 5 min with stirring under ice-cooling. After 15 min, all the peracid had been dissolved and an orange-yellow solution was obtained. The mixture was left standing for 3 days at −9° and then overnight at room temperature. To the mixture were added 5% $NaHSO_3$ aq. (3 ml) and saturated $NaHCO_3$ aq. (5 ml), successively. The $CHCl_3$ layer was washed with saturated $NaHCO_3$ aq. (3 ml) and saturated NaCl aq. (5 ml), dried over Na_2SO_4 and evaporated under reduced pressure to yield a crude product (1.428 g). The crude product was purified by column chromatography on silica gel (28.6 g); $CHCl_3$–AcOEt (95: 5) first eluted the unreacted **3** (0.315 g; 33.4%) and then oily **5** (0.715g; 72.2% yield). IR $\nu_{max}^{Liq.}$ cm^{-1}: 2830, 2730, 1725 (CHO), 1714 (NCO_2). NMR (60 MHz) δ^{CDCl_3}: 2.12 (quintet, J=6 Hz, C–CH_2–C), 3.58 (t, J=6 Hz, CH_2Cl), 4.45 (t, J=6 Hz, OCH_2), 4.70 (d, J=2 Hz, –CHCHO), 7.2—7.9 (m, aromatic), 9.48 (d, J=2 Hz, CHO).

b) 9-Oxo-10-acridancarboxylic Acid 3-Chloropropyl Ester (**6**): To a solution of **3** (0.471 g; 1.5 mmol) in $CHCl_3$ (4.7 ml) was added *m*-chloroperbenzoic acid (85% pure, 0.610 g; 3 mmol) and the mixture was stirred overnight at room temperature and then heated under reflux for 1 hr. Additional *m*-chloroperbenzoic acid (0.305 g; 1.5 mmol) was added and additional 2 hr refluxing was effected. To the mixture were added 5% $NaHSO_3$ aq. (2 ml) and saturated $NaHCO_3$ aq. (7 ml), successively. The $CHCl_3$ solution was washed with saturated $NaHCO_3$ aq. (2 ml) and saturated NaCl aq. (3 ml), dried over Na_2SO_4 and evaporated under reduced pressure to yield a crude product (0.591 g). The crude product was purified by column chromatography on silica gel (11.8 g); from the fractions eluted with $CHCl_3$ was obtained **6** (0.344 g; 69.9%). Recrystallization from benzene–hexane yielded pure **6**, mp 63—68°. IR ν_{max}^{Nujol} cm^{-1}: 1757 (NCO_2), 1635 (C=O), 1606 (aromatic). NMR (60 MHz) δ^{CDCl_3}: 2.20 (quintet, J=6 Hz, C–CH_2–C), 3.60 (t, J=6 Hz, CH_2Cl), 4.62 (t, J=6 Hz, OCH_2), 7.2—7.9 (m, aromatic). *Anal.* Calcd. for $C_{17}H_{14}ClNO_3$: C, 64.66; H, 4.47; N, 4.44; Cl, 11.23. Found: C, 64.54; H, 4.47; N, 4.28; Cl, 11.07. MS *m/e*: 315; 317 (M^+).

Attempted Epoxidation of 5*H*-Dibenz[*b*,*f*]azepine (**9**)——a) To a solution of **9** (0.483 g; 2.5 mmol) in dioxane (7 ml) was added *m*-chloroperbenzoic acid (85% pure, 0.610 g; 3 mmol) and the mixture was left standing overnight. Additional *m*-chloroperbenzoic acid (0.406 g; 2 mmol) was added and the mixture was left standing for 80 min. Water (7 ml) was added and the product was extracted twice with $CHCl_3$ (10 and 5 ml). The $CHCl_3$ solution was washed first with saturated $NaHCO_3$ aq. (5 and 2 ml) and then with saturated NaCl aq. (5 ml), dried over Na_2SO_4 and evaporated under reduced pressure to yield a crude product (0.692 g). The crude product was purified by column chromatography on silica gel (34.6 g); $CHCl_3$ eluted first unreacted **9** (0.054 g; 11.2%), secondly 9-acridinecarbaldehyde (**12**) (0.129 g; 24.9% yield) and lastly 9-acridinecarbal-

10) J.S. Pierce and R. Adams, *J. Am. Chem. Soc.*, **45**, 790 (1923).

dehyde 10-oxide (**13**). **12**, mp 138—140° (lit.[11] 139—140°; 145—146°). IR ν_{max}^{Nujol} cm^{-1}: 1686 (CHO). NMR (100 MHz) δ^{CDCl_3}: 7.4—8.8 (m, aromatic), 11.44 (s, CHO). *Anal.* Calcd. for $C_{14}H_9NO$ (**12**): C, 81.14; H, 4.38; N, 6.76. Found: C, 81.50; H, 4.36; N, 7.01. **13**, mp 200° (dec.). (lit.[12] 250°; 261°). IR ν_{max}^{Nujol} cm^{-1}: 1665 (CHO), 1272 (N→O). NMR (100 MHz) δ^{CDCl_3}: 7.5—9.1 (m, aromatic), 11.34 (s, CHO). *Anal.* Calcd. for $C_{14}H_9NO_2$ (**13**): C, 75.32; H, 4.06; N, 6.28. Found: C, 75.87; H, 3.87; N, 6.06.

b) To a solution of **9** (1.93 g) in $CHCl_3$ (8.1 ml) were added 40% peracetic acid in AcOH (8.1 ml) and AcONa (250 mg), successively, and the mixture was heated at 40° for 24 hr. The reaction solution was washed first with saturated $NaHCO_3$ aq. (40 ml) and then with 5% $NaHSO_3$ aq. (40 ml) and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (50 g); $CHCl_3$–AcOEt (9: 1) eluted **12** (0.82 g; 42.0% yield).

Reaction of 1a,10b-Dihydro-6*H*-dibenz[*b,f*]oxireno[*d*]azepine-6-carboxamide (1c) with AcOH——A solution of **1c**[3] (1.0 g) in AcOH (25 ml) was heated for 10 min under reflux. The resulting blue-black solution was evaporated under reduced pressure to give a black oil, which was extracted with $CHCl_3$. The $CHCl_3$ solution was washed with water, dried over Na_2SO_4 and evaporated under reduced pressure to give a black oil. The oil was chromatographed on silica gel (20 g); a fraction eluted with $CHCl_3$–AcOEt (90: 5) afforded a crystalline substance. Recrystallization from MeOH yielded 9-acridinecarbaldehyde (**12**) (0.25 g; 28.5% yield).

5-(Trifluoroacetyl)-5*H*-dibenz[*b,f*]azepine[13]——To a suspension of 5*H*-dibenz[*b,f*]azepine (**9**) (0.386 g; 2 mmol) in pyridine (0.32 ml; 4 mmol) and $CHCl_3$ (3.9 ml) was added $(CF_3CO)_2O$ (0.56 ml; 4 mmol) with stirring under ice-cooling resulting in immediate dissolution of **9**. After stirring for 20 min, ice-water (*ca.* 10 ml) and $CHCl_3$ were added. The $CHCl_3$ layer was washed twice with water (10 ml) and once with saturated NaCl aq., dried over Na_2SO_4 and evaporated to yield crude crystals (0.596 g). Recrystallization from hexane (4 ml) gave 5-(trifluoroacetyl)-5*H*-dibenz[*b,f*]azepine (0.509 g; 88.1% yield), mp 91—93°. IR ν_{max}^{Nujol} cm^{-1}: 1702 (NCOCF$_3$). NMR (60 MHz) δ^{CDCl_3}: 6.99 (s, olefinic), 7.3—7.5 (m, aromatic). *Anal.* Calcd. for $C_{16}H_{10}F_3NO$: C, 66.43; H, 3.48; N, 4.83. Found: C, 66.49; H, 3.54; N, 4.63.

1a,10b-Dihydro-6-(trifluoroacetyl)-6*H*-dibenz[*b,f*]oxireno[*d*]azepine (1e)——To a solution of 5-(trifluoroacetyl)-5*H*-dibenz[*b,f*]azepine (5.02 g; 17.4 mmol) in $CHCl_3$ (50 ml) was added *m*-chloroperbenzoic acid (85% pure, 7.05 g; 34.7 mmol). After refluxing for 3.5 hr, the solution was successively washed with 5% $NaHSO_3$ aq. (10 ml), saturated $NaHCO_3$ aq. (60 ml) and saturated NaCl aq. (30 ml). The solution was dried over Na_2SO_4 and evaporated under reduced pressure to afford a crude product (5 g), which was recrystallized from EtOH (30 ml) to yield **1e** (3.49 g; 65.9%). From the mother liquor was obtained an additional crop of **1e** (0.40 g; 7.6%). **1e**, mp 137—140°. IR ν_{max}^{Nujol} cm^{-1}: 1702 (C=O). NMR (60 MHz) δ^{CDCl_3}: 4.30 (s, epoxy), 7.2—7.6 (m, aromatic). *Anal.* Calcd. for $C_{16}H_{10}F_3NO_2$: C, 62.95; H, 3.30; N, 4.59; F, 18.67. Found: C, 63.15; H, 3.31; N, 5.26; F, 17.56.

Reaction of 1a,10b-Dihydro-6-(trifluoroacetyl)-6*H*-dibenz[*b,f*]oxireno[*d*]azepine (1e) with KOH——To a solution of **1e** (0.400 g) in hot EtOH (4 ml) was added 50% KOH aq. (0.4 ml) and the mixture was left standing at room temperature for 50 min. The reaction solution was concentrated under reduced pressure and water (10 ml) was added. The precipitates formed were collected and washed with water to yield a crude product (0.242 g), a part of which (0.202 g) was recrystallized from EtOH to give 9-acridinecarbaldehyde (**12**) (0.074 g; 32.8% yield).

Reaction of 1a,10b-Dihydro-6*H*-dibenz[*b,f*]oxireno[*d*]azepine-6-carboxylic Acid 2-(Methylsulfonyl)ethyl Ester (8) with NaOH——To a solution of **8**[3] (359 mg) in acetone (10 ml) was added 0.1 N NaOH aq. (10 ml) and the mixture was stirred for 30 min at room temperature. Water (40 ml) was added and the product was extracted with $CHCl_3$. The $CHCl_3$ solution was dried over Na_2SO_4 and evaporated under reduced pressure to yield a brown oil. Crystallization from EtOH gave **12** (82 mg; 39% yield), mp 140—142°.

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