Transannular reactions in the dibenzo[*a,d*]cycloheptene series. II. Preparation of 10,11-dihydro-10,5-(epoxymethano)-5*H*-dibenzo[*a,d*]cyclohepten-13-one and derivatives

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Received September 7, 1967

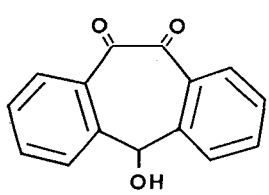
The reaction of electrophilic reagents with the 5-substituted 5*H*-dibenzo[*a,d*]cycloheptene derivatives (**13***a–e*) and with their 10,11-dihydro analogues (**19***a–b*) occurs with transannular participation of the 5-substituent to yield derivatives of 10,11-dihydro-10,5-(epoxymethano)-5*H*-dibenzo[*a,d*]cycloheptene. The epimeric 10,11-dihydro-10-hydroxy-5*H*-dibenzo[*a,d*]cycloheptene-5-carboxamides (**22**, **23**) are described. The *syn*-hydroxy isomer **22** is readily transformed to the lactone **16***c* under neutral conditions whereas the *anti* isomer **23** requires acid catalysis for this conversion. Treatment of *anti*-11-bromo-10,11-dihydro-10,5-(epoxymethano)-5*H*-dibenzo[*a,d*]cyclohepten-13-one (**16***b*) with ammonia or primary aliphatic amines gives the epoxyamides **21***a–d* which can react with secondary aliphatic amines to give the *anti*-11-dialkylamino-10,11-dihydro-10,5-(epoxymethano)-5*H*-dibenzo[*a,d*]cyclohepten-13-ones (**25***a–d*). The epimeric *syn*-11-dialkylamino compounds **24***a–e* are obtained from the interaction of **16***b* with secondary aliphatic amines. The nuclear magnetic resonance spectra of the products are tabulated.

Canadian Journal of Chemistry, 46, 2843 (1968)

The dibenzo[*a,d*]cycloheptene ring system serves as a convenient template for the study of transannular reactions. Thus, 5-hydroxy-5*H*-dibenzo[*a,d*]cycloheptene-10,11-dione (1) exists, in part, as the hemiketal **2** and derivatives of both forms have been prepared (1). Similar behavior is exhibited by both *cis*- and *trans*-10,11-dihydroxy-10,11-dihydro-5*H*-dibenzo-[*a,d*]cyclohepten-5-ones which, in alkaline media, exist and react as the hemiketals **3***a* and **3***b* respectively (2). These early observations have recently found practical utility in the preparation of a number of pharmacologically active dibenzo[*a,d*]cycloheptene derivatives, **4** (3). A number of more complex examples have been reported. Thus, treatment of the acid chloride **5** with 1-methylpiperazine gave, as a minor by-product, the chloroketone **6** (4). The diazoketone **7** has been converted into 2,3:7,8-dibenzotricyclo[3·3·1·$0^{4,6}$]nona-2,7-dien-9-one, **8**, furnishing an example of transannular attack by an α-ketocarbene intermediate (5). Base-promoted cyclization of **9***a* and **9***b* gave **10***a* and **10***b* respectively (6). Treating the bromoacid **11** with silver nitrate caused concommitant skeletal rearrangement and formation of the lactone **12** (7). Transannular reactions in related tricyclic systems, in some cases leading to scission of the central ring, have been reported to occur with derivatives of dibenzo[*a,e*]cyclooctane (8*a*), dibenzo[*b,e*]thiocin (8*b*), and dibenz[*b,f*]azepin (8*c*). It has recently been observed that 10,11-dihydro-5*H*-dibenzo[*a,d*]cycloheptene-5-carboxamide is metabolized in animals and man to 10-hydroxy and 10,11-dihydroxy analogues which are readily transformed to derivatives of 10,11-dihydro-10,5-(epoxymethano)-5*H*-dibenzo[*a,d*]-cyclohepten-13-one (9). This observation prompted us to investigate further the transannular reactions of 5-substituted dibenzo[*a,d*]cycloheptene derivatives.

Hydroxylation of 5*H*-dibenzo[*a,d*]cycloheptene-5-carboxamide (**13***a*) with silver acetate and iodine according to the method of Woodward and Brutcher (10*a*) gave *syn*-11-acetoxy-10,11-dihydro-10,5-(epoxymethano)-5*H*-dibenzo[*a,d*]-cyclohepten-13-one (**14***a*) (for numbering, see Fig. 1). Saponification of this compound gave the *syn*-hydroxylactone **14***b* which was reconverted to **14***a* with pyridine and acetic anhydride. The *syn* orientation of the 11-substituent in **14***a*, and therefore in **14***b*, was assigned from its mode of introduction which has repeatedly been shown to result in *cis* hydroxylation (10). The *syn*-hydroxylactone **14***b* was oxidized with chromium trioxide – sulfuric acid to the ketolactone **14***c* which regenerated **14***b* upon catalytic hydrogenation.

A minor by-product from the silver acetate – iodine oxidation of **13***a* was 10,11-diacetoxy-10,11-dihydro-5*H*-dibenzo[*a,d*]cycloheptene-5-carboxamide (**15**) of uncertain geometry. Traces of anthracene derivatives were also formed but these could not be fully characterized.



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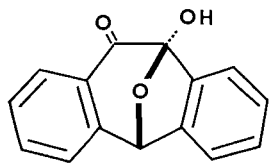

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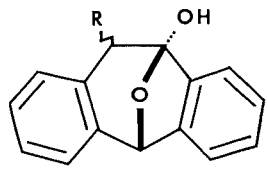
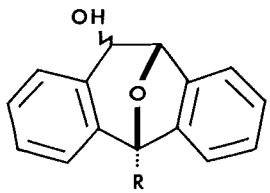
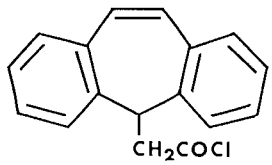


3*a*, R=cis-OH
b, R=trans-OH



4, R=dialkylaminopropyl



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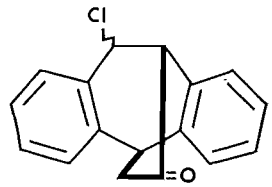

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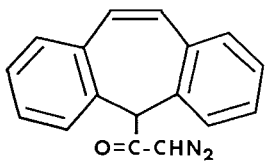

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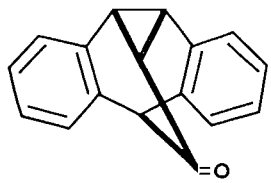

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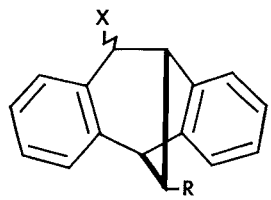
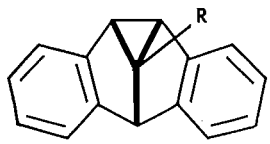
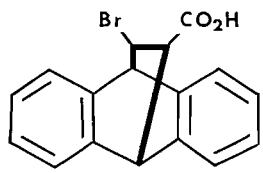


9*a*, R=anti-SO_2Ph, X=endo-Cl
b, R=anti-CO_2CH_3, X=exo-Cl



10*a*, R=SO_2Ph
b, R=CO_2H



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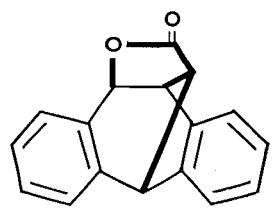

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Attempted *trans*-hydroxylation of the same amide **13*a*** with silver acetate and iodine under the anhydrous conditions of the Prévost reaction (10*c*,11) gave only trace amounts of lactonic products. Successful *trans* hydroxylation of **13*a*** was achieved with 3-chloroperbenzoic acid to give the *anti*-11-hydroxylactone **16*a***. This compound was oxidized with chromium trioxide – sulfuric acid to the ketolactone **14*c*** thereby demonstrating the epimeric relationship of **14*b*** and **16*a***.

A number of reaction pathways are possible for the genesis of the *syn*-acetoxylactone **14*a*** as shown on p. 2847. The route **13*a*** → **A** → **B** → **14*a*** is the normal pathway of the Woodward hydroxylation reaction (10) followed by an 'OH-6' (12) anchimerically-assisted hydrolysis of the amide group. The hydroxyl-assisted hydrolysis of amides is well known (13) and inspection of a Drieding molecular model of **B** shows the hydroxyl and amide functions to be in close proximity. The alternative pathway

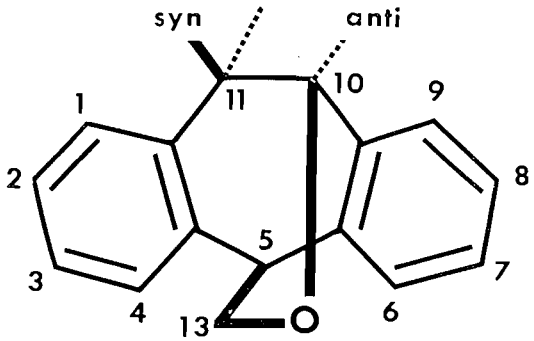


FIG. 1. The 10,11-dihydro-10,5-(epoxymethano)-5*H*-dibenzo[*a*,*d*]cycloheptene ring system.

13*a* → **A** → **C** → **14***a* is followed in the conversion of halogen-containing amides to lactones (14).

The *anti*-11-hydroxylactone **16***a* is probably derived from the transient *anti*-10,11-epoxide **D**[1] *via* the iminolactone intermediate **E** as shown on p. 2847. An alternate pathway, involving *trans*-hydration of **D** and subsequent 'OH-6' cyclization of the resulting glycol was rendered unlikely by the observation that the *syn*-10,11-epoxyamide **21***b* (see later) was unaffected by a mixture of 3-chloroperbenzoic and 3-chlorobenzoic acids in chloroform.

Addition of bromine to a solution of the amide **13***a* in chloroform gave rapidly, and in almost quantitative yield, the *anti*-11-bromo-iminolactone hydrobromide **17**. The structure of this compound is supported by its nuclear magnetic resonance (n.m.r.) spectrum which is consistent with a *trans* arrangement of the protons at C-10 and C-11, and by its very ready hydrolysis to the *anti*-11-bromolactone **16***b*. The same bromolactone was also obtained, in poor yield, from the interaction of the *syn*-11-hydroxylactone **14***b* and phosphorus tribromide and pyridine, and from displacement of the tosyl derivative of **14***b* with calcium bromide.

The geometry of **17** indicates that its formation from the amide **13***a* must involve the carboxamide function in either a concerted addition process or in an intramolecular displacement (17,18) of a bromonium ion. The intermediacy of a *trans*-10,11-dibromide would, obviously, lead to an isomeric *syn*-11-bromo-iminolactone hydrobromide.

[1]In contrast, epoxidation of 5*H*-dibenzo[*a*,*d*]cyclohepten-5-ol has been reported to give the corresponding *syn*-epoxide (15). Allylic hydroxyl groups are, however, known to promote the formation of *cis*-epoxyalcohols (16).

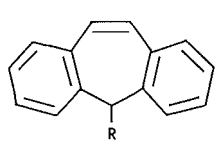
The propensity for transannular reaction was not confined to the amide **13***a*. Thus, addition of bromine to the diethylamide **13***d* and subsequent hydrolysis of the crude product gave the bromolactone **16***b*. Treatment of both the unsaturated acid **13***b* and its methyl ester **13***c* with bromine also gave the bromolactone. The participation of carboxyl and carboalkoxy groups in halogen and pseudohalogen additions is well known (18,19).

Addition of bromine to the unsaturated alcohol **13***e* involved participation of the hydroxyl function since the *anti*-11-bromoether **18** was produced. Bromine addition to α,α-dimethylallyl alcohol is known to proceed in a similar fashion (20).

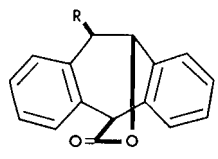
Transannular reactions also occurred when 10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene derivatives were used as substrates. Thus, irradiation and subsequent hydrolysis of a solution of the amide **19***a* and bromine in chloroform gave the unsubstituted lactone **16***c*. Treatment of the 5-hydroxyester **19***b* with either bromine or *N*-bromosuccinimide gave the 5-hydroxylactone **20**.

The *anti*-11-bromolactone **16***b* contains a potential bromohydrin system and, with this feature in view, its reactions with basic reagents were investigated. Treatment of **16***b* with aqueous sodium hydroxide solution gave the epoxyacid **21***a* whereas treatment of **16***b* with either liquid ammonia or warm ammonium hydroxide gave the *syn*-10,11-epoxyamide **21***b*. The analogous amides **21***c* and **21***d* respectively were obtained when methylamine and *t*-butylamine were employed in place of ammonia. These products undoubtedly arose by a common mechanism involving attack at the carbonyl group of **16***b* by the basic reagent, and their formation supports the geometry assigned to this compound. Both **21***a* and **21***b* reacted rapidly with hydrogen bromide to give **16***b* and with hydrogen chloride to give the *anti*-11-chlorolactone **16***d*. The *anti*-11-methoxylactone **16***e* was prepared by the acid-catalyzed reaction of methanol with both **21***a* and **21***b*.

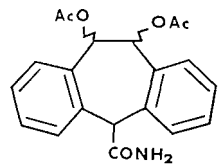
Hydration of the epoxyamide **21***b* with dilute sulfuric acid in either dioxane or dimethyl sulfoxide gave an approximately equimolar mixture of the epimeric hydroxylactones **14***b* and **16***a*. The non-stereospecificity of the hydration performed in dimethyl sulfoxide is in contrast to the acid-catalyzed stereospecific



13*a*, R=$CONH_2$ *d*, R=$CON(C_2H_5)_2$
b, R=CO_2H *e*, R=CH_2OH
c, R=CO_2CH_3



14*a*, R=OAc
b, R=OH
c, R=(=O)



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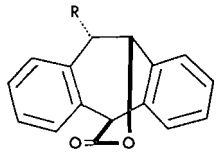
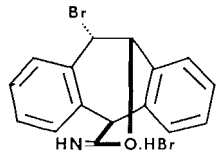


16*a*, R=OH *d*, R=Cl
b, R=Br *e*, R=OCH_3
c, R=H *f*, R=OAc



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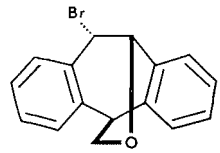

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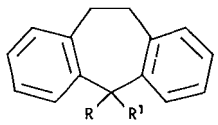
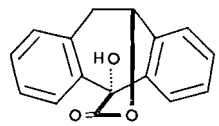


19*a*, R=H, R^1=$CONH_2$
b, R=OH, R^1=CO_2CH_3



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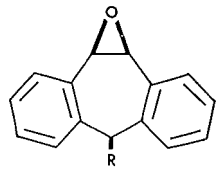
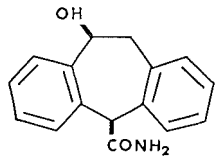


21*a*, R=CO_2H *c*, $CONHCH_3$
b, R=$CONH_2$ *d*, $CONHBu^t$



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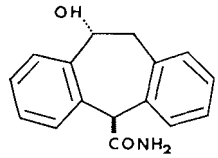

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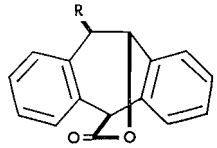
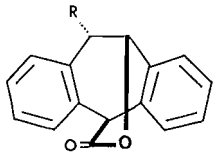
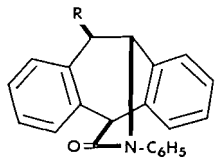


24*a*, R=dimethylamino
b, R=morpholino
c, R=piperidino
d, R=N-methylpiperazino
e, R=N-phenylpiperazino
f, R=anilino



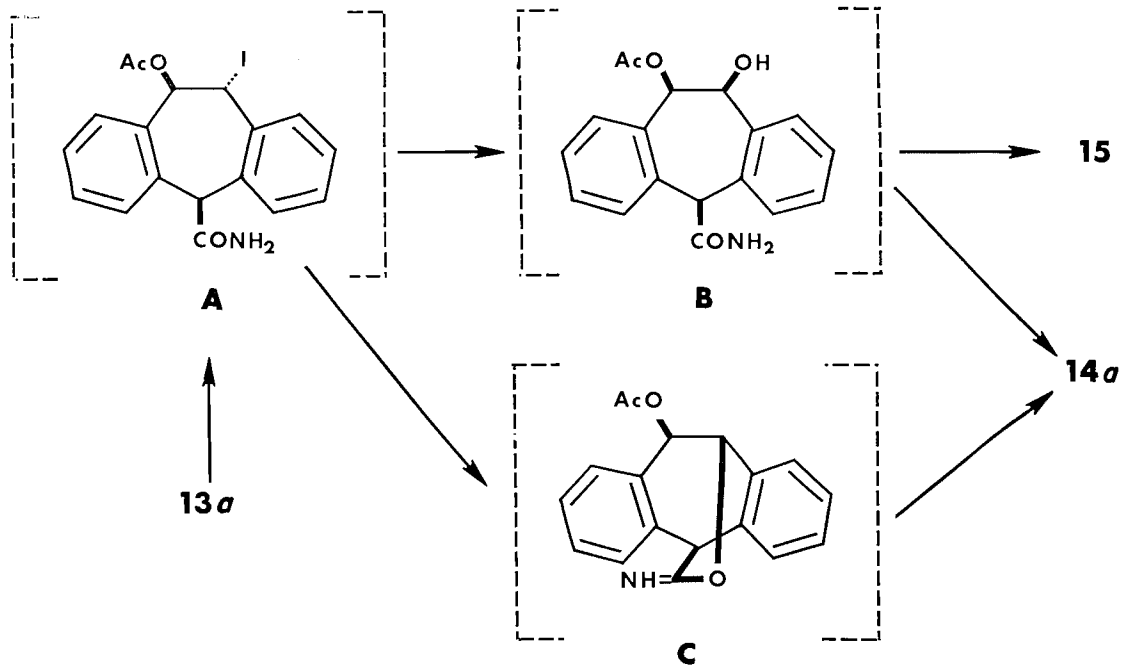
25*a*, R=morpholino
b, R=piperidino
c, R=N-methylpiperazino
d, R=N-phenylpiperazino
e, R=anilino



26*a*, R=OH
b, R=(=O)

hydration of both *cis* and *trans* stilbene oxides in this solvent (21). A similar hydration of the epoxyacid gave the *anti*-hydroxylactone as the predominant product.

Hydrogenation of the epoxyamide **21***b* gave the unstable *syn*-11-hydroxyamide **22**. This compound readily evolved ammonia in both the solid state and in solution to give the unsubstituted lactone **16***c* undoubtedly *via* an intramolecular attack of the hydroxyl group upon the amide function (13). It is noteworthy that the unsubstituted amide **19***a* is relatively resistant to



hydrolysis (22). The epimeric *anti*-11-hydroxyamide **23** was prepared in poor yield by hydroboration of the unsaturated amide **13***a*. In contrast to **22**, the *anti*-hydroxy epimer **23** was stable up to a temperature of 140°. Treatment of **23** with dilute mineral acid gave, however, the unsubstituted lactone **16***c* accompanied by a small amount of the unsaturated acid **13***b*. This cyclization may proceed *via* epimerization at either C-5 or C-10 to give **22** or it could proceed *via* a transient iminolactone.

In contrast to the behavior of the *anti*-11-bromolactone **16***b* with primary aliphatic amines, the reactions of the same substrate with secondary aliphatic amines did *not* involve the lactone ring. The products obtained were the *syn*-11-dialkylaminolactones **24**. The geometry of these products, which was inferred from their n.m.r. spectra (see Table I), is that expected to arise from direct displacement of the bromine atom of **16***b* by the secondary amine. To confirm further the structure of **24***a–e* the epoxyacid **21***a* and the *syn*-epoxyamide **21***b* were treated with several secondary amines. No reaction occurred at room temperature, even in the presence of mineral acid (23), but at elevated temperatures, the *anti*-11-dialkylaminolactones **25***a–d* were formed, as evidenced by the n.m.r. spectra of the products (see Table I).

Aniline, in its reaction with the bromolactone **16***b*, behaved as a secondary amine rather than as a primary amine since the product was the *syn*-11-anilinolactone **24***f*. The structure of this compound was demonstrated by its ready acid-catalyzed rearrangement to the *syn*-11-hydroxylactam **26***a* which is only possible with a *syn*-arrangement of anilino and lactone groups. Oxidation of **26***a* with chromium trioxide–sulfuric acid furnished the ketone **26***b* which regenerated only the parent hydroxy compound

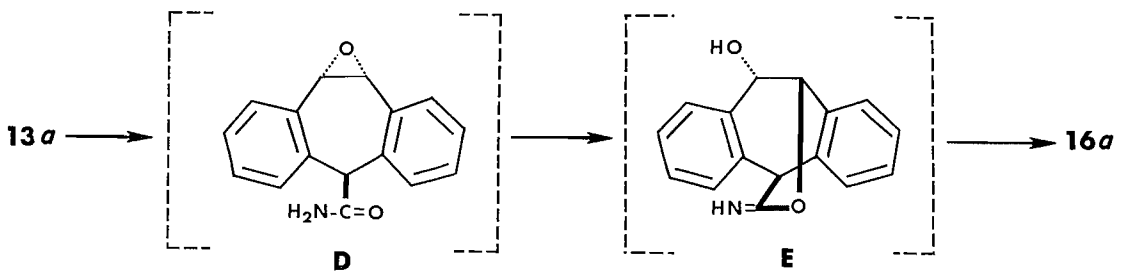


TABLE I

Proton assignments in the 11-substituted-10,11-dihydro-10,5-(epoxymethano)-5*H*-dibenzo[*a*,*d*]cyclohepten-13-one system

11-Substituent	No.	Chemical shift*, τ					$J_{10,11}$ c.p.s.
		syn-11-H	*anti*-11-H	10-H	5-H	Other	
syn-11-Acetoxy	**14***a*		4.00	4.18	5.03	7.92 (Acetate)	2.6
syn-11-Hydroxy†	**14***b*		5.21	4.30	5.11		2.5
11-Keto	**14***c*			4.16	5.07		
anti-11-Hydroxy†	**16***a*	4.54		5.01	5.40		5.0
anti-11-Bromo	**16***b*	4.37		4.23	5.37		5.2
11-Hydrogen	**16***c*	6.26	6.78	4.36	5.31		4.1, 2.6
anti-11-Chloro	**16***d*	4.36		4.36	5.32		?
anti-11-Methoxy	**16***e*	5.28		4.33	5.42	6.31 (Methyl)	4.9
anti-11-Acetoxy	**16***f*	3.63		4.37	5.37	7.89 (Acetate)	5.1
5-Hydroxy	**20**	6.24	6.80	4.28		5.76 (Hydroxy)	4.5, 2.5
syn-11-Dimethylamino	**24***a*		6.02	4.13	5.36	7.18 (Methyl)	1.8
syn-11-Morpholino	**24***b*		6.00	4.10	5.35	6.30, 7.17 (Methylene)	1.8
syn-11-Piperidino	**24***c*		6.03	4.11	5.37	7.21, 8.47 (Methylene)	1.8
syn-11-(*N'*-Methylpiperazino)	**24***d*		6.08	4.22	5.45	7.80 (Methylene and methyl)	1.8
syn-11-(*N'*-Phenylpiperazino)	**24***e*		5.92	4.11	5.35	6.90 (Methylene)	1.8
syn-11-Anilino	**24***f*		5.02	4.23	5.27	6.18 (NH)	2.0
anti-11-Morpholino	**25***a*	5.50		4.33	5.37	6.44, 7.58 (Methylene)	5.0
anti-11-Piperidino	**25***b*	5.58		4.40	5.43	7.65, 8.67 (Methylene)	4.9
anti-11-(*N'*-Methylpiperazino)	**25***c*	5.47		4.37	5.39	7.76 (Methylene and methyl)	5.0
anti-11-(*N'*-Phenylpiperazino)	**25***d*	5.42		4.34	5.37	6.87 (Methylene)	5.0
anti-11-Anilino	**25***e*	4.73		4.39	5.38	6.60 (NH)	4.8

*Spectra were determined using a Varian A-60A instrument. All spectra were obtained in deuteriochloroform solution unless otherwise noted. All compounds showed aromatic absorption at 2.5–3.0.
†Spectrum determined in dimethyl sulfoxide solution.

26*a* upon catalytic hydrogenation. The *anti*-11-anilinolactone **25***e*, isomeric with **24***f* and obtained by the interaction of the *syn*-epoxyamide **21***b* and aniline, was not rearranged by treatment with either aqueous acid or alkali.

Empirical confirmation of the geometry of many of the compounds described herein has been obtained from their n.m.r. spectra (Table I). Compounds assigned the *syn*-configuration show $J_{10,11}$ 1.8–2.6 c.p.s. whereas the compounds assigned the *anti*-configuration show $J_{10,11}$ 4.1–5.2 c.p.s. These coupling constants are similar to those reported for dibenzobicyclo[3·2·1]octadienes (24).

Experimental

*syn-11-Acetoxy-10,11-dihydro-10,5-(epoxymethano)-5H-dibenzo[a,d]cyclohepten-13-one (**14***a*)

To a well-stirred solution of the amide **13***a* (22) (50.0 g, 0.2 mole) in acetic acid (1 l) was added silver acetate (82.0 g, 0.05 mole) and then iodine (56.0 g, 0.22 mole) which was added portionwise, and then water (10 ml). The mixture was heated on the steam bath for 3 h and then solid sodium chloride was added. The mixture was cooled, filtered, and the filtrate was evaporated to dryness *in vacuo*. The residue was triturated with water and the solids were then dissolved in chloroform. This solution was washed with water, dried, and evaporated and the residue was crystallized from ethanol to give the product (30.2 g), m.p. 145–146°; ν_{max}($CHCl_3$) 1757 (lactone) and 1740 cm^{-1} (acetate).

Anal. Calcd. for $C_{18}H_{14}O_4$: C, 73.46; H, 4.80. Found: C, 73.65; H, 4.87.

From a sparingly soluble fraction of the above crude product there was obtained 1.6 g of 10,11-diacetoxy-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene-5-carboxamide (**15**), m.p. 229–230° (from ethanol or chloroform); ν_{max}(Nujol) 1770, 1750 (acetate), 1692, 1665, and 1635 cm^{-1} (amide); ν_{max}($CHCl_3$) 3480, 3370 (NH), 1760 (ester), and 1675 cm^{-1} (amide).

Anal. Calcd. for $C_{20}H_{19}NO_5$: C, 67.98; H, 5.43; N, 3.96. Found: C, 67.85; H, 5.55; N, 4.08.

Chromatography of the above crude product on silica gel gave an anthracene derivative, λ_{max}(EtOH) 263, 354, 378mμ (ε 165 700, 4670, 11 550), which gave inconsistent analytical data.

*syn-11-Hydroxy-10,11-dihydro-10,5-(epoxymethano)-5H-dibenzo[a,d]cyclohepten-13-one (**14b**)*

A solution of **14***a* (30.2 g) in methanol (600 ml) and water (300 ml) was treated with 50% sodium hydroxide solution (30 ml) and kept overnight. The methanol was removed *in vacuo*, water (200 ml) was added, and the filtered solution was acidified. The product (23.8 g), m.p. 156–157° tenaciously retained solvent of crystallization when recrystallized from ethanol or ethyl acetate – hexane. Purification was effected by dissolution in aqueous alkali or ammonium hydroxide followed by partial evaporation and acidification to give material of the above m.p. ν_{max}(Nujol) 3440 (OH) and 1725 cm^{-1} (lactone).

Anal. Calcd. for $C_{16}H_{12}O_3$: C, 75.18; H, 4.80. Found: C, 76.00; H, 4.93.

Acetylation of the hydroxylactone by acetic anhydride and pyridine gave **14***a*, m.p. 143–144°.

The *syn*-11-*p*-toluenesulfonyl derivative was prepared from **14***b* and *p*-toluenesulfonyl chloride in pyridine at 25°; m.p. 139–140° (decomp.).

Anal. Calcd. for $C_{23}H_{18}O_5S$: C, 67.97; H, 4.46; S, 7.88. Found: C, 68.06; H, 4.54; S, 7.90.

*10,5-(Epoxymethano)-5H-dibenzo[a,d]cycloheptene-11,13-(10H)-dione (**14c**)*

Jones' reagent (25) (74 ml) was added dropwise and with stirring to an ice-cold solution of a mixture of the *syn*- and *anti*-hydroxylactones **14***b* and **16***a* (61.0 g, 0.24 mole) in acetone (900 ml). The brown suspension so obtained was filtered and the filtrate was chilled, diluted with water (900 ml), and the precipitated product was recrystallized from aqueous acetone to give 48.5 g (79%), m.p. 166–167°; ν_{max}($CHCl_3$) 1758 (lactone) and 1685 cm^{-1} (ketone); λ_{max}(EtOH) 262mμ (ε 8550).

Anal. Calcd. for $C_{16}H_{10}O_3$: C, 76.79; H, 4.03. Found: C, 76.91; H, 4.09.

Hydrogenation of the ketolactone (250 mg) in dioxane (15 ml) with 10% palladium on charcoal at 25° and 1 atm gave chiefly the *syn*-hydroxylactone **14***b*, m.p. 155–156° and a little of the unsubstituted lactone **16***c*, m.p. 168–170° (from ethanol). The latter product predominated when the reduction was carried out in methanol at 50°.

*anti-11-Hydroxy-10,11-dihydro-10,5-(epoxymethano)-5H-dibenzo[a,d]cyclohepten-13-one (**16a**)*

Method (a)

A solution of the epoxyamide **21***b* (47.7 g) in dioxane (500 ml) and 1*N* H_2SO_4 (650 ml) was kept at room temperature for 2 h. The bulk of the dioxane was removed *in vacuo* and the residue was extracted with dichloromethane. This solution was extracted with water, then dried and evaporated. Crystallization of the residual oil from ethyl acetate – hexane gave a mixture (38.0 g) of the *syn* and *anti* hydroxylactones, m.p. 130–172°. Recrystallization afforded the pure *anti* isomer **16***a* (13.1 g), m.p. 187–188°; ν_{max}(Nujol) 3420 (OH), 1730 cm^{-1} (lactone).

Anal. Calcd. for $C_{16}H_{12}O_3$: C, 76.18; H, 4.80. Found: C, 76.13; H, 4.71.

The *syn* isomer **14***b* was obtained in solvated form from the above mother liquors by recrystallization from ethanol; desolvation as described above gave 8.0 g, m.p. 155–156°.

The *anti*-11-acetyl derivative **16***f*, prepared from **16***a* and acetic anhydride – pyridine, had m.p. 201–202° (from ethanol).

Anal. Calcd. for $C_{18}H_{14}O_4$: C, 73.46; H, 4.08. Found: C, 73.57; H, 5.01.

The *anti*-11-*p*-toluenesulfonyl derivative had m.p. 140–141° (decomp.).

Anal. Calcd. for $C_{23}H_{18}O_5S$: C, 67.97; H, 4.46; S, 7.88. Found: C, 68.25; H, 4.65; S, 7.81.

Method (b)

A solution of the epoxyacid **21***a* (5.6 g) in dioxane (175 ml) and 1*N* sulfuric acid (80 ml) was kept overnight at room temperature. It was processed as described above except that the crude product was extracted with dilute sodium bicarbonate solution. Recrystallization from

ethanol–hexane afforded 2.4 g of the *anti*-hydroxylactone, m.p. 188–189°; no significant amounts of the *syn* isomer were observed.

Method (c)

A solution of the amide **13***a* (10.0 g, 0.04 mole) and 85% 3-chloroperbenzoic acid (8.8 g, 0.04 mole) in dichloromethane (550 ml) was kept at room temperature until no more of the amide was consumed (14 days). A 100 ml aliquot was extracted with sodium bisulfite solution followed by sodium bicarbonate and then water. Evaporation of the solvent and recrystallization from dichloromethane–hexane gave unchanged amide, m.p. 208–210° (1.5 g). Chromatography of the mother liquors on silica gel from 75% chloroform–benzene afforded crude **16***a* as an oil (177 mg); recrystallization from ethyl acetate – pentane gave a sample m.p. 187–189°.

Treatment of another 100 ml aliquot with an additional 1.8 g of the peracid caused consumption of the remaining amide but gave no increase in yield of the hydroxylactone.

*anti-11-Bromo-10,11-dihydro-10,5-(epoxymethano)-5H-dibenzo[a,d]cyclohepten-13-imine Hydrobromide (**17**)*

A solution of bromine (16.0 g, 0.1 mole) in chloroform (50 ml) was added dropwise during 20 min to a stirred suspension of the amide **13***a* (23.5 g, 0.1 mole) in chloroform (50 ml). A red solution was obtained which soon deposited the product as pale-yellow crystals (36.0 g), m.p. 215–220° (decomp.); ν_{max}(Nujol) 1675 (C=N) and 1105 cm^{-1} (ether).

Anal. Calcd. for $C_{16}H_{13}BrNO$: Br, 40.46. Found: Br, 42.73.

The n.m.r. spectrum of this compound in dimethyl sulfoxide showed an eight-proton multiplet at 2.6 (aromatic), two one-proton doublets at 3.88 and 4.13 respectively (Ar—C(Br)—C(H)—Ar, $J_{10,11}$ 5.0 c.p.s.), a one-proton singlet at 5.04 (Ar—C(H)—Ar), and a broad two-proton singlet at 6.08 (O—C=NH·HBr).

*anti-11-Bromo-10,11-dihydro-10,5-(epoxymethano)-5H-dibenzo[a,d]cyclohepten-13-one (**16***b*)*

Method (a)

A mixture of **17** (300 g) and ethanol (1 l) containing water (50 ml) was heated on a steam bath for 6 h. The solvent was removed *in vacuo* and the residue was thoroughly washed with hot water. The residue was crystallized from ethanol to give the product (210 g), m.p. 160–161°; $\nu_{max}(CHCl_3)$ 1765 cm^{-1} (lactone).

Anal. Calcd. for $C_{16}H_{11}BrO_2$: C, 60.96; H, 3.72; Br, 25.35. Found: C, 60.85; H, 3.96; Br, 25.43.

Method (b)

A solution of bromine (160 mg) in chloroform (3.0 ml) was added to a stirred suspension of 5*H*-dibenzo[*a,d*]-cycloheptene-5-carboxylic acid (**13***b*) (23) (236 mg) in chloroform (10 ml). The mixture was kept at room temperature for 2 h and then evaporated to dryness. The residue was crystallized from ethanol to give **16***b* (220 mg) identified by m.p. and mixture m.p.

Method (c)

The acid **13***b* was esterified with methanol saturated with hydrogen chloride. The ester **13***c* was purified from methanol as needles, m.p. 110–111°.

Anal. Calcd. for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.30; H, 5.43.

The acid **13***b* used in the above method was replaced by **13***c* (248 mg). The same product was obtained, identified by m.p. and mixture m.p.

Method (d)

The diethylamide **13***d* was prepared from the corresponding acid chloride (22) and diethylamine in the usual manner. It was crystallized from chloroform–hexane, m.p. 141–144°.

Anal. Calcd. for $C_{20}H_{21}NO$: C, 82.44; H, 7.26; N, 4.81. Found: C, 82.20; H, 6.99; N, 4.93.

This product (1.45 g) was dissolved in chloroform (8.0 ml) and a solution of bromine (0.8 g) in chloroform (5.0 ml) was then added to it. The mixture was kept at room temperature overnight and then evaporated to dryness. The residue was repeatedly crystallized from ethanol to give **16***b* (1.0 g) identified by m.p. and mixture m.p.

Method (e)

A solution of the epoxyacid **21***a* (1.6 g) in chloroform (20 ml) was saturated with dry hydrogen bromide. The solution was kept at room temperature overnight, evaporated to dryness and the residue was crystallized from ethanol to give **16***b* (800 mg) identified by m.p. and mixture m.p.

Method (f)

The epoxyacid in the foregoing method was replaced by the epoxyamide **21***b* (1.0 g). The same product was obtained.

Method (g)

A solution of the *syn*-hydroxylactone **14***b* (1.0 g, 0.004 mole) and pyridine (0.2 ml) in dry dioxane (5 ml) was treated with phosphorus tribromide (0.5 ml) and kept overnight. Water was added and the dioxane was removed *in vacuo*. The product was extracted into benzene and the solution was washed with dilute sodium bicarbonate solution and then evaporated. Recrystallization of the residue from ethanol–hexane gave the bromolactone (150 mg), m.p. 150–151°, undepressed on admixture with an authentic specimen.

Method (h)

A solution of the *p*-toluenesulfonate ester of **14***b* (0.5 g, 0.001 mole) in dry dioxane (20 ml) was added to dry calcium bromide (0.25 g, 0.001 mole) in ethanol (2 ml). The mixture was heated under reflux for 18 h and processed as in method *g*. Recrystallization from chloroform–hexane gave **16***b* (78 mg), m.p. 153–155°.

*anti-11-Bromo-10,11-dihydro-10,5-(epoxymethano)-5H-dibenzo[a,d]cycloheptene (**18**)*

A solution of 5*H*-dibenzo[*a,d*]cycloheptene-5-methanol (**13***e*) (2.0 g, 0.01 mole; prepared from **13***c* and $LiAlH_4$) and triethylamine (1.0 g, 0.01 mole) in carbon tetrachloride (75 ml) was treated with a 10% w/v solution of bromine in the same solvent (20 ml, 0.01 mole). It was

stirred at room temperature for 3 h, then filtered and evaporated. Recrystallization of the residue from ethanol and then from carbon tetrachloride afforded **18** (0.4 g), m.p. 165–166°; ν_{max}($CHCl_3$) 1080 cm^{-1} (ether).

Anal. Calcd. for $C_{16}H_{13}BrO$: C, 63.80; H, 4.35; Br, 26.53. Found: C, 64.09; H, 4.70; Br, 26.72.

Attempted displacement of the halogen atom by heating the bromo ether with dimethylamine was unsuccessful.

*10,11-Dihydro-10,5-(epoxymethano)-5H-dibenzo[a,d]-cyclohepten-13-one (**16c**)*

Method (a)

The epoxyamide **21***b* (10 g) was hydrogenated as described above. The filtered solution was heated under reflux until ammonia evolution had ceased (6 h) and then concentrated whereupon the product crystallized as prisms (8.0 g), m.p. 169–170.5°.

Anal. Calcd. for $C_{16}H_{12}O_2$: C, 81.34; H, 5.12. Found: C, 81.27; H, 5.26.

Method (b)

The bromolactone **16***b* (4.9 g) in ethanol (550 ml) was hydrogenated with palladium–charcoal catalyst until hydrogen uptake ceased. Removal of the catalyst and evaporation of the filtrate gave an oil which was chromatographed upon silica gel. Evaporation of the chloroform eluates and crystallization of the residue gave the product (1.9 g) identified by m.p. and mixture m.p.

Method (c)

A mixture of the *anti*-hydroxyamide **23** (200 mg) and 1 *N* HCl was heated under reflux for 1 h. The solids were collected and partitioned between chloroform and 2 *N* Na_2CO_3. Evaporation of the organic phase and crystallization of the residue gave the product (170 mg) identified by m.p. and mixture m.p.

The aqueous layer was acidified and the precipitate was crystallized from methanol to give 5*H*-dibenzo[*a,d*]cycloheptene-5-carboxylic acid (10 mg), m.p. 241–242° (lit. (22) m.p. 241–242°).

Method (d)

A solution of bromine (8.0 g, 0.05 mole) and the amide **19***a* (22) (11.85 g, 0.95 mole) in chloroform (100 ml) was maintained at 45–50° and irradiated with a photoflood lamp for 8 h. The solvent was removed *in vacuo* and the residue was dissolved in a mixture of methanol (200 ml) and water (10 ml). The solution was heated under reflux for 2 h, evaporated to dryness and the residue was crystallized from methanol to give the title product (3.2 g), identified by m.p. and mixture m.p.

*Methyl 5-hydroxy-10,11-dihydro-5H-dibenzo[a,d]cycloheptene-5-carboxylate (**19b**)*

Method (a)

A solution of methyl 10,11-dihydro-5*H*-dibenzo[*a,d*]-cycloheptene-5-carboxylate (26) (3.0 g, 0.01 mole) in ether (50 ml) was added to a suspension of sodium amide (from 0.3 g, 0.01 g-atom of sodium) in liquid ammonia (125 ml). A stream of dry air was passed through the mixture for 5 h and the ammonia was allowed to evaporate overnight. Water was added and the ether layer was separated, washed with sodium bicarbonate solution, dried, and concentrated. Recrystallization of the residue from carbon tetrachloride – hexane gave 2.0 g (63% yield) of the hydroxy ester, m.p. 134–135° (lit. (27) m.p. 139–140°).

Method (b)

Following a general procedure (28), a solution of 10,11-dihydro-5*H*-dibenzo[*a,d*]cyclohepten-5-one (41.6 g, 0.2 mole) in 1,2-dimethoxyethane (150 ml) was added to sodium (11.6 g, 0.5 g-atom) suspended in the same solvent (70 ml). The mixture was stirred at room temperature for 4 h and then treated with dimethyl carbonate (20.0 g, 0.2 mole) dissolved in ether (150 ml). An additional 300 ml of ether was added and next morning the excess of sodium was destroyed by the cautious addition of water. Separation and evaporation of the organic phase gave 25 g (47%) of **19***b*, m.p. 135–137° after crystallization from carbon tetrachloride – hexane.

*5-Hydroxy-10,11-dihydro-10,5-(epoxymethano)-5H-dibenzo[a,d]cyclohepten-13-one (**20**)*

A mixture of the ester **19***b* (20.0 g, 0.075 mole), *N*-bromosuccinimide (14.2 g, 0.08 mole) and a little benzoyl peroxide in carbon tetrachloride (450 ml) was stirred under a heat lamp for 25 min and then heated under reflux for 1.5 h. It was kept overnight, filtered, and evaporated. Chromatography of the residue on silica with 25% chloroform–benzene gave the hydroxylactone (4.4 g, 23%), m.p. 130–131° (from carbon tetrachloride – hexane); ν_{max}($CHCl_3$) 3530 (OH), 1740 cm^{-1} (lactone). The compound existed in a second crystalline form, m.p. 113–114°; the solution spectra were identical.

Anal. Calcd. for $C_{16}H_{12}O_3$: C, 76.18; H, 4.80. Found: C, 76.18; H, 4.80.

The early fractions from the chromatography gave a yellow solid, m.p. 165–169° (77 mg). Recrystallization from ether–hexane gave a sample which was not analytically pure but whose spectral properties agreed with the proposed structure of 10-bromomethyl-9-anthroic acid methyl ester; ν_{max}($CHCl_3$) 1725 cm^{-1} (ester); λ_{max}(EtOH) 255, 357, 375, and 398mμ (ε 127 000; 6580; 9700 and 19 050); molecular weight by mass spectrometry: 328 (^{79}Br), 330 (^{81}Br) (in correct ratio for 1Br); calculated molecular weight, 329.

*10,11-Dihydro-10,11-epoxy-5H-dibenzo[a,d]cycloheptene-5-carboxylic Acid (**21a**)*

To a stirred suspension of the bromolactone **16***b* (19.7 g) in water (100 ml) at 90° was added 2.5 *N* NaOH solution in one portion. The mixture was kept at 90° during 35 min, rapidly cooled to 0°, and then acidified with 2 *N* HCl. The precipitate was thoroughly washed with water, dried, and then crystallized from ethyl acetate to give the product (11.6 g), m.p. 161–163° (decomp.).

Anal. Calcd. for $C_{16}H_{12}O_3$: C, 76.18; H, 4.80. Found: C, 76.33; H, 4.88.

Treating this product with ethereal diazomethane gave methyl-10,11-dihydro-10,11-epoxy-5*H*-dibenzo[*a,d*]cycloheptene-5-carboxylate, purified from methanol as needles, m.p. 179–181.5°.

Anal. Calcd. for $C_{17}H_{14}O_3$: C, 76.67; H, 5.30. Found: C, 76.60; H, 5.08.

*10,11-Dihydro-syn-10,11-epoxy-5H-dibenzo[a,d]cycloheptene-5-carboxamide (**21b**)*

Very finely-powdered bromolactone **16***b* (150 g) was added in small portions to stirred liquid ammonia (750 ml). The suspension was kept for 8 h and then the ammonia was allowed to evaporate. The residue was

thoroughly washed with hot water and the remaining solid was crystallized from ethanol to give the product (110 g), m.p. (after drying at 140°) 191–193°.

Anal. Calcd. for $C_{16}H_{13}NO_2$: C, 76.47; H, 5.22; N, 5.57. Found: C, 76.76; H, 5.27; N, 5.31.

*N-Methyl-10,11-dihydro-syn-10,11-epoxy-5H-dibenzo-[a,d]cycloheptene-5-carboxamide (**21c**)*

A mixture of the bromolactone **16***b* (20 g) and methylamine (50 g) was stirred under reflux for 12 h. The excess methylamine was evaporated and the solids were washed with water. The residue was crystallized from ethanol to give the product as needles (12.0 g), m.p. 192–194.°

Anal. Calcd. for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.45; N, 5.09. Found: C, 76.84; H, 5.45; N, 5.09.

*N-tert-Butyl-10,11-dihydro-3-syn-10,11-epoxy-5H-dibenzo[a,d]cycloheptene-5-carboxamide (**21d**)*

A mixture of the bromolactone **16***b* (2.0 g) and *t*-butylamine (20 ml) was heated under reflux for 6 days. The mixture was evaporated to dryness and the solids were washed with water. The residue was crystallized from benzene–hexane to give needles (1.1 g), m.p. 172–176°; ν_{max}($CHCl_3$) 3440 (NH), 1668 cm^{-1} (C=O).

Anal. Calcd. for $C_{20}H_{21}NO_2$: C, 78.17; H, 6.88; N, 4.55. Found: C, 77.89; H, 6.88; N, 4.84.

*anti-11-Chloro-10,11-dihydro-10,5-(epoxymethano)-5H-dibenzo[a,d]cyclohepten-13-one (**16d**)*

A suspension of the epoxyacid **21***a* (1.0 g) in chloroform (20 ml) was saturated with dry hydrogen chloride. Evaporation of the solution and crystallization of the residue from ethyl acetate gave the product (809 mg), m.p. 172–173°.

Anal. Calcd. for $C_{16}H_{11}ClO_2$: C, 71.00; H, 4.07; Cl, 13.10. Found: C, 70.87; H, 4.06; Cl, 13.12.

*10,11-Dihydro-10,5-(epoxymethano)-anti-11-methoxy-5H-dibenzo[a,d]cyclohepten-13-one (**16e**)*

A solution of the epoxyacid **21***a* (1.0 g) in anhydrous methanol (25 ml) containing 3 drops of sulfuric acid was heated under reflux for 10 h. The solvent was removed *in vacuo* and the residue was partitioned between chloroform and water. Evaporation of the dried chloroform phase and crystallization of the residue gave the product (600 mg), m.p. 191–193°.

Anal. Calcd. for $C_{17}H_{14}O_2$: C, 76.67; H, 5.3. Found: C, 76.76; H, 5.08.

*10,11-Dihydro-syn-11-hydroxy-5H-dibenzo[a,d]cycloheptene-5-carboxamide (**22**)*

The epoxyamide **21***b* (500 mg) in dry methanol (30 ml) was hydrogenated at atmospheric pressure with palladium on charcoal catalyst until hydrogen uptake ceased (20 min). The filtered solution was evaporated to dryness *in vacuo* at room temperature. The residue was crystallized from cold dioxan–hexane to give the product (320 mg), m.p. 163–165° (decomp.).

Anal. Calcd. for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.78; H, 5.85; N, 5.53.

This material rapidly decomposed at room temperature with formation of **16***c*.

*10,11-Dihydro-anti-11-hydroxy-5H-dibenzo[a,d]cycloheptene-5-carboxamide (**23**)*

A solution of the amide **13***a* (22) (5.0 g) in dry tetrahydrofuran (200 ml) was added dropwise to a stirred 0.83 *M* solution of diborane in tetrahydrofuran (80 ml). The mixture was kept at room temperature for 20 h and then cautiously diluted with water. Sodium hydroxide (80 ml, 3 *N*) and hydrogen peroxide (20 ml, 30%) were then added and the mixture was kept at 50° for 1 h. The mixture was saturated with potassium carbonate and the organic layer was collected and evaporated. Repeated crystallization of the residue from ethyl acetate and then from ethanol gave the product (1.3 g), m.p. 183–185°.

Anal. Calcd. for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.86; H, 5.91; N, 5.68.

*syn-11-Dialkylamino Derivatives of 10,11-Dihydro-10,5-(epoxymethano)-5H-dibenzo[a,d]cyclohepten-13-one (**24**)*

General Procedure

The bromolactone **16***b* (0.1 mole) was added portionwise to the appropriate anhydrous secondary amine (0.3 mole). The mixture was stirred overnight, diluted with water, and the crude product which separated was recrystallized.

10,11-Dihydro-*syn*-11-dimethylamino-10,5-(epoxymethano)-5*H*-dibenzo[*a,d*]cyclohepten-13-one (**24***a*) crystallized from isopropanol as needles, m.p. 152–154°, yield 22.0 g.

Anal. Calcd. for $C_{18}H_{17}NO_2$: C, 77.39; H, 6.13; N, 5.01. Found: C, 77.64; H, 6.04; N, 5.03.

10,11-Dihydro-10,5-(epoxymethano)-*syn*-11-morpholino-5*H*-dibenzo[*a,d*]cycloheptene-13-one (**24***b*) crystallized from isopropanol as needles, m.p. 239–242°, yield 23.0 g.

Anal. Calcd. for $C_{20}H_{19}NO_3$: C, 74.74; H, 5.96; N, 4.36. Found: C, 74.78; H, 6.09; N, 4.08.

10,11-Dihydro-10,5-(epoxymethano)-*syn*-11-piperidino-5*H*-dibenzo[*a,d*]cyclohepten-13-one (**24***c*) crystallized from isopropanol as needles, m.p. 204–207°, yield 19.5 g.

Anal. Calcd. for $C_{21}H_{21}NO_2$: C, 78.97; H, 6.63; N, 4.39. Found: C, 79.21; H, 6.75; N, 4.17.

10,11-Dihydro-10,5-(epoxymethano)-*syn*-11-(*N'*-methylpiperazine)-5*H*-dibenzo[*a,d*]cyclohepten-13-one (**24***d*) crystallized from isopropanol as needles, m.p. 178–181°, yield 22.0 g.

Anal. Calcd. for $C_{21}H_{22}N_2O_2$: C, 75.42; H, 6.63; N, 8.38. Found: C, 75.70; H, 6.73; N, 8.09.

10,11-Dihydro-10,5-(epoxymethano)-*syn*-11-(*N'*-phenylpiperazino)-5*H*-dibenzo[*a,d*]cyclohepten-13-one (**24***e*) crystallized from methanol as needles, m.p. 199–202°, yield 25.0 g.

Anal. Calcd. for $C_{26}H_{24}N_2O_2$: C, 78.76; H, 6.10; N, 7.07. Found: C, 78.65; H, 5.99; N, 7.95.

*syn-11-Anilino-10,11-dihydro-10,5-(epoxymethano)-5H-dibenzo[a,d]cyclohepten-13-one (**24f**)*

A mixture of the bromolactone **16***b* (100 g) aniline (140 g) and water (500 ml) was heated in a rocking autoclave at 130° for 8 h. The reaction mixture was extracted with chloroform and the organic phase was extracted with 2 *N* HCl and then washed with water. Evaporation of the chloroform phase and crystallization of the residue from chloroform–isopropanol gave the product as needles (50 g), m.p. 203–205°; ν_{max}($CHCl_3$) 3420 (NH) and 1752 cm^{-1} (lactone).

Anal. Calcd. for $C_{22}H_{17}NO_2$: C, 80.71; H, 5.23; N, 4.28. Found: C, 80.45; H, 5.31; N, 4.02.

*anti-11-Dialkylamino Derivatives of 10,11-Dihydro-10,5-(epoxymethano)-5H-dibenzo[a,d]cycloheptene-13-one (**25**)*

General Procedure

A mixture of either the epoxyacid **21***a* (0.01 mole) or the epoxyamide **21***b* (0.01 mole), the appropriate secondary amine (0.03 mole), and either xylene or toluene (20 ml) was heated under reflux for 5–10 h. The cooled solution was diluted with ether and the precipitate was crystallized.

10,11-Dihydro-10,5-(epoxymethano)-*anti*-11-morpholino-5*H*-dibenzo[*a*,*d*]cycloheptene-13-one (**25***a*) crystallized from methanol as needles, m.p. 171–175°, yield 2.4 g.

Anal. Calcd. for $C_{20}H_{19}NO_3$: C, 74.74; H, 5.96; N, 4.36. Found: C, 74.62; H, 5.73; N, 4.10.

10,11-Dihydro-10,5-(epoxymethano)-*anti*-11-piperidino-5*H*-dibenzo[*a*,*d*]cycloheptene-13-one (**25***b*) crystallized from methanol as needles, m.p. 189–191°, yield 2.8 g.

Anal. Calcd. for $C_{20}H_{21}NO_2$: C, 78.97; H, 6.63; N, 4.39. Found: C, 78.72; H, 6.60; N, 4.35.

10,11-Dihydro-10,5-(epoxymethano)-*anti*-11-(*N'*-methylpiperazino)-5*H*-dibenzo[*a*,*d*]cycloheptene-13-one (**25***c*) crystallized from isopropanol as needles, m.p. 188–190°, yield 2.4 g.

Anal. Calcd. for $C_{21}H_{22}N_2O_2$: C, 75.42; H, 6.63; N, 8.38. Found: C, 75.11; H, 6.89; N, 8.32.

10,11-Dihydro-10,5-(epoxymethano)-*anti*-11-(*N'*-phenylpiperazino)-5*H*-dibenzo[*a*,*d*]cycloheptene-13-one (**25***d*) crystallized from isopropanol as needles, m.p. 181–183°, yield 2.8 g.

Anal. Calcd. for $C_{26}H_{24}N_2O_2$: C, 78.76; H, 6.10; N, 7.07. Found: C, 78.79; H, 5.86; N, 6.92.

*anti-11-Anilino-10,11-dihydro-10,5-(epoxymethano)-5H-dibenzo[a,d]cycloheptene-13-one (**25***e*)*

A mixture of the epoxyamide **21***b* (5.0 g) and aniline (20 ml) was heated under reflux for 20 h. The reaction mixture was partitioned between 1 *N* HCl and chloroform. Evaporation of the chloroform phase and crystallization of the residue from isopropanol gave the product as needles (4.8 g), m.p. 177–179°; ν_{max}(CHCl$_3$) 1750 cm^{-1}.

Anal. Calcd. for $C_{22}H_{17}NO_2$: C, 80.71; H, 5.23; N, 4.28. Found: C, 80.85; H, 5.50; N, 4.55.

*10,11-Dihydro-syn-11-hydroxy-10,5-(iminomethano)-12-phenyl-5H-dibenzo[a,d]cycloheptene-13-one (**26***a*)*

A suspension of the *syn*-anilinolactone **24***f* (10.0 g) in ethanol (150 ml) containing 2 *N* H_2SO_4 (10 ml) was heated under reflux for 6 h. Concentration of the resulting solution gave the product as needles (8.0 g), m.p. 266–267°; ν_{max}(Nujol) 1650 cm^{-1} (C=O).

Anal. Calcd. for $C_{22}H_{17}NO_2$: C, 80.71; H, 5.23; N, 4.28. Found: C, 80.41; H, 5.33; N, 4.38.

The epimeric anilinolactone **25***e* was recovered unchanged after similar treatment.

*10,5-(Iminomethano)-12-phenyl-5H-dibenzo[a,d]cycloheptene-11,13-(10H)-dione (**26***b*)*

Jones' reagent was added dropwise to a cold suspension of **26***a* (5.0 g) in acetone (50 ml) until a slight excess of oxidant was present. The mixture was stirred for 30 min and then ethanol (2.0 ml) was added. The solvent was evaporated at room temperature and the residue was partitioned between water and chloroform. The organic phase was washed, dried, and evaporated and the residue was crystallized from ethanol to give needles (4.2 g), m.p. 180–182°.

Anal. Calcd. for $C_{22}H_{15}NO_2$: C, 81.21; H, 4.65; N, 4.31. Found: C, 80.91; H, 4.56; N, 4.10.

Hydrogenation of this ketone (500 mg) in methanol (20 ml) with palladium on charcoal gave the original hydroxylactam **26***a*.

Acknowledgments

We wish to thank Dr. G. S. Myers and his group for furnishing the tricyclic compounds in quantity. Spectral data were recorded by Mrs. J. Jachner and Mr. M. Boulerice, and analyses were carried out by Mr. W. J. Turnbull. The mass spectra were determined by the Morgan-Schaffer Corporation, Montreal.

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