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Transannular reactions in the dibenzo[*a*,*d*]cycloheptene series. III. Preparation of 11-substituted-10,11-dihydro-10,5-(iminomethano)-5*H*-dibenzo[*a*,*d*]cycloheptenes

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Treatment of the *syn*-epoxyamide **3** with either ammonium hydroxide or sodium hydride gives 10,11-dihydro-*anti*-11-hydroxy-10,5-(iminomethano)-5*H*-dibenzo[*a*,*d*]cyclohepten-13-one (**1***a*). This compound is readily converted to the *syn*-epimer **1***c* by oxidation to **1***b* and subsequent hydrogenation. The ketone **1***b* reacts with Grignard reagents to give the tertiary alcohols **1***k*,*l* which undergo hydrogenolysis to give the 11-substituted lactams **1***q*,*r*. Reduction of the lactams with lithium aluminium hydride gives the corresponding amines.

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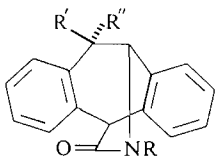
We have recently described the preparation of a number of 10,11-dihydro-10,5-(epoxymethano)-5*H*-dibenzo[*a*,*d*]cyclohepten-13-ones (1, 2). The present paper outlines a general route to 11-substituted-10,11-dihydro-10,5-(iminomethano)-5*H*-dibenzo[*a*,*d*]cycloheptene derivatives **1** and **2**. A different approach has been used by other workers (3–6) to prepare other derivatives and the ring system has been shown to occur naturally in the alkaloids amurensine, amurensinine, and roemfrine (7, 8).



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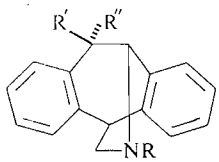

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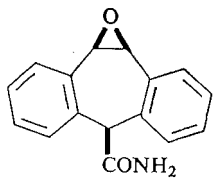
	R	R′(*syn*)	R″(*anti*)
1*a*,**2***a*	H	H	OH
1*b*,**2***b*	H	=O	
1*c*,**2***c*	H	OH	H
1*d*,**2***d*	CH_3	H	OH
1*e*	$CH_2C_6H_5$	H	OH
1*f*	$(CH_2)_3OCH_3$	H	OH
1*g*,**2***g*	CH_3	H	OCH_3
1*h*,**2***h*	$CH_2C_6H_5$	H	OCH_3
1*i*,**2***i*	CH_3	OH	H
1*j*,**2***j*	CH_3	OCH_3	H
1*k*,**2***k*	H	OH	CH_3
1*l*,**2***l*	H	OH	C_6H_5
1*m*	CH_3	=O	
1*n*	CH_3	OH	CH_3
1*o*	CH_3	OH	C_6H_5
1*p*	H	H	H
1*q*	H	H	CH_3
1*r*	H	H	C_6H_5

We have previously found that the *syn*-epoxyamide **3** reacts with secondary amines to give *anti*-11-dialkylaminolactones. In attempts to prepare the unsubstituted *anti*-11-aminolactone **4***a* both the *syn*-epoxyamide **3** and the bromolactone **4***b* were treated with ammonium hydroxide at 140°. The product, obtained in 70% yield in both cases, was not the expected lactone but the *anti*-11-hydroxylactam **1***a*. Oxidation of **1***a* gave the ketolactam **1***b* which regenerated **1***a* upon reduction with sodium borohydride. In contrast, catalytic hydrogenation of **1***b* gave a mixture of 20% **1***a* and 80% of the *syn*-hydroxylactam **1***c*. This hydrogenation parallels that of the ketolactone **4***c* which gives the *syn*-hydroxylactone **4***d* as the major product (2). Reduction of the two epimers **1***a* and **1***c* with lithium aluminium hydride in dimethoxyethane gave the epimeric aminoalcohols **2***a* and **2***c* respectively. Other solvents (see Experimental) were markedly inferior for these reductions in accordance with experience in the preparation of 8-hydroxy-5-phenylbenzomorphan derivatives (9). The infrared (i.r.) hydroxyl absorptions of **2***a* and **2***c* were concentration-dependent, and concentration-independent respectively, indicating that **2***a* was the *anti*-epimer and that **2***c* was the *syn*-epimer (10). These assignments were confirmed by the reaction of the *syn*-aminoalcohol **2***c* with phosgene. The product was the cyclic carbamate **5**, the structure of which was fully supported by its analytical and spectral properties. The geometry of **2***a* and **2***c*, as shown by inspection of molecular models, indicates that only **2***c* can form **5**. Cristol and Bly (11) have cited an analogous cyclic carbonate formation as a structure proof of dibenzobicyclo[3·2·1]octadiene-*exo*-4-*syn*-8-diol. In accord with these assignments only intractable mixtures were obtained when **2***a* was treated with either phosgene or diethyl oxalate (12).



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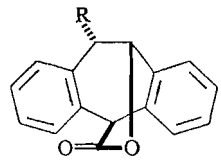
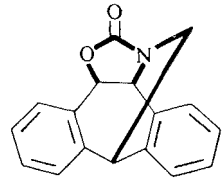


4*a*, R = NH_2; *e*, R = H
b, R = Br; *f*, R = $NHCH_2C_6H_5$
c, R = (=O); *g*, R = NHC_6H_5
d, R = *syn*—OH



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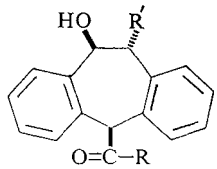
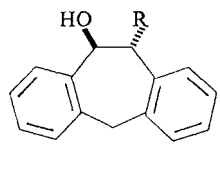
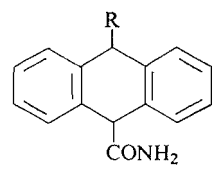


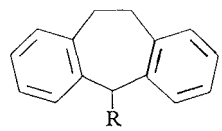
6*a*, R = R′ = $NH(CH_2)_3OCH_3$
b, R = R′ = NH_2
c, R = NH_2, R′ = H



7*a*, R = NHC_6H_5
b, R = $N(CH_3)_2$



8*a*, R = H
b, R = CHO



9*a*, R = CON_3
b, R = NCO

Treatment of the *syn*-epoxyamide **3** with a variety of primary amines at 140° gave the *N*-substituted-*anti*-hydroxylactams **1***d–f*. The same compounds were prepared by monoalkylating **1***a* with sodium hydride and the appropriate alkyl halide confirming that **1***a*, *d–f* belonged to the same epimeric series. Subsequent methylation of **1***d*,*e* gave the ethers **1***g*,*h*. The alkylated derivatives **1***i*,*j* of the *syn*-hydroxylactam were prepared in the same manner. Reduction of **1***d*,*g*,*h* and **1***i*,*j* with lithium aluminium hydride gave the two epimeric series of amines **2***d*,*g*,*h* and **2***i*,*j* respectively. Unlike the nuclear magnetic resonance (n.m.r.) spectra of the previously described lactones (2), the n.m.r. spectra of the lactams and amines described herein cannot be used to distinguish between *syn*- and *anti*-substitution.

Under milder conditions two exceptions to the generality of the amine–epoxyamide reaction were observed. First, treatment of **3** with benzylamine at 100° gave the *anti*-11-benzylaminolactone **4***f*. The geometry of this compound was confirmed by its n.m.r. spectrum (2). Subsequent treatment of **4***f* with either benzylamine or ammonium hydroxide at 140° gave the *N*-benzyl-*anti*-hydroxylactam **1***e*. Second, treatment of **3** with 3-methoxypropylamine at 80° gave a small yield of the secondary amide **6***a*.

These observations suggest that **1***a* arises by normal *trans*-opening of the epoxide function (13) with, most probably, simultaneous lactonization to give the initially expected aminolactone **4***a*. Epimerization of **4***a* at the benzhydrilic carbon atom (C-5) *via* an equilibrium concentration of the amide **6***b* followed by lactam formation would give **1***a*. It is improbable that **6***b* epimerizes without prior lactonization. For example, the *syn*-hydroxyamide **6***c* lactonizes at room temperature (2). The ready lactam formation of the epimerized form of **6***b* is unremarkable in view of the classical methods for forming lactam bridges (14).

It was not possible to convert the *anti*-anilinolactone **4***g* to the corresponding lactam by treatment with ammonium hydroxide since starting material or the aminoalcohol **7***a* were obtained. Presumably the anilino residue was insufficiently basic to undergo lactam formation. Decarboxylation also occurred when the *syn*-epoxyamide **3** was heated with aqueous dimethylamine at 140° since the product was the aminoalcohol **7***b*.

The present studies bear a formal similarity to the preparation of isoquinuclidones recently

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reported by Huffman and co-workers (15). Their procedure requires, however, a *trans*-epoxyester as starting material and subsequent pyrolysis of the intermediate aminoester.

Treatment of the *syn*-epoxyamide **3** with sodium hydride in dry dioxane also gave **1***a*. Presumably this reaction proceeds *via* epimerization at C-5 and subsequent 'N-6' participation (16). Many examples are known of nucleophilic participation by amide nitrogen under basic conditions (17). A by-product from this reaction was 9,10-dihydroanthracene-9-carboxamide **8***a*. This side reaction was undoubtedly a base-promoted conversion of **3** since it was unaffected by both boiling dioxane and boiling water, and the *anti*-hydroxylactam **1***a* was unaffected by sodium hydride in boiling dioxane. Possibly **8***a* arose by initial rearrangement[1] of **3** to the carboxaldehyde **8***b* with subsequent base-catalyzed elimination of the formyl group (11, 19).

Attempts to ammonolyze the lactones **4***d,e* to the corresponding lactams were abortive since starting materials or decarboxylated products were obtained. In contrast, the closely related isochroman-3-one and its 4-phenyl derivative have been successfully ammonolyzed to the corresponding lactams (20, 21).

The ketolactam **1***b* showed normal ketonic properties. Enolization, which sometimes masks the ketonic character of 10,11-dihydro-5*H*-dibenzo[*a,d*]cyclohepten-10-ones (22), is precluded by the presence of the 10,5 bridge system. Thus, **1***b* formed an oxime and a ketal and readily underwent Grignard reactions to give the carbinols **1***k,l*.[2] In these Grignard reactions the lactam function was presumably protected from attack by complex formation (23, p. 876). Grignard reactions with the *N*-methyl-ketolactam **1***m* gave very poor yields of the carbinols **1***n,o* and these compounds were better prepared by methylating **1***k,l*. Lithium aluminium hydride reduction of **1***k,l* gave the aminoalcohols **2***k,l*. The i.r. hydroxyl absorptions of these compounds were concentration-independent indicating that they were *syn*-aminoalcohols. This geometry would be expected assuming that Grignard reagents, like hydrogen, tend to attack the less hindered side of **1***b*.

Hydrogenolysis of the epimeric hydroxylactams **1***a* and **1***c* with sodium in liquid ammonia gave the unsubstituted lactam **1***p* in good yield. Similar hydrogenolyses of the carbinols **1***k,l* gave **1***q,r*. Catalytic hydrogenolyses of **1***a* and **1***k* were unsuccessful, as is the case with similarly substituted benzylic alcohols (9).

The unsubstituted lactam **1***p* was also obtained, in very poor yield, by photolysis of the acyl azide **9***a*. The major product was the isocyanate **9***b* in accord with experience in the photolysis of carbocylic acyl azides (24, 25).

The more important pharmacological properties of some of the compounds described in this paper, particularly those of the amines **2***a–m*, will be described elsewhere.

Experimental

10,11-Dihydro-anti-11-hydroxy-10,5-(iminomethano)-5H-dibenzo[a,d]cyclohepten-13-one (1a)

Method a

A mixture of the *syn*-epoxyamide **3** (50 g) (2) and ammonium hydroxide (200 ml) was kept at 140° for 6 h. The solid product was collected and washed with water, chloroform and ether, and then crystallized from ethanol to give the title product (35 g) as needles, m.p. 260–262° (decomp.); ν_{max} (Nujol) 1670 cm^{-1}.

Anal. Calcd. for $C_{16}H_{13}NO_2$: C, 76.47; H, 5.22; N, 5.57. Found: C, 76.50; H, 5.08; N, 5.57.

Method b

Following the procedure of method *a*, the bromolactone **4***b* (315 g) (2) and ammonium hydroxide (2 l) gave **1***a* (178 g).

Method c

A mixture of the *syn*-epoxyamide **3** (2.51 g), sodium hydride (460 mg of a 52% suspension in mineral oil), and dioxane (50 ml) was heated under reflux for 1 h. The reaction mixture was diluted with water and then concentrated *in vacuo*. The residue was washed with water, and then with hexane, and the residue was crystallized from ethanol to give **1***a* (1.5 g), m.p. 260–262° (decomp.). The infrared (i.r.) spectrum of this material was identical with that of the product from method *a*.

The mother liquors from the above crystallization yielded 9,10-dihydroanthracene-9-carboxamide (**8***a*), m.p. and mixture m.p. with an authentic sample 151–152° (lit. (26), m.p. 151–152°).

10,11-Dihydro-10,5-(iminomethano)-5H-dibenzo[a,d]-cyclohepten-11,13-dione (1b)

Jones reagent (20 ml) (27) was added dropwise to an ice-cold stirred suspension of **1***a* (10.0 g) in acetone (150

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[1]The influence of the 5-proton is manifest in this rearrangement. Thus, 10,11-epoxy-10,11-dihydro-5*H*-dibenzo[*a,d*]cyclohepten-5-one gave the corresponding 5,10-dione on base treatment, and gave 10-hydroxy-9-anthraldehyde on either pyrolysis or acid-treatment (18).

[2]The physical properties and chemical behavior of **1***k,l* confirmed that they were single epimers. The reaction of **1***b* with allyl magnesium bromide appeared to give a mixture of epimers which is being investigated further. Ethyl magnesium bromide reduced **1***b* to the *anti*-hydroxylactam (23, p. 147–158).

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ml). The mixture was kept at 0° for 0.5 h and then diluted with isopropanol (5.0 ml). The mixture was concentrated *in vacuo*, diluted with water, and then extracted with chloroform. The combined extracts were washed with water, dried, evaporated, and the residue was crystallized from ethanol to give **1***b* (9.0 g), m.p. 197–199°; ν_{max} ($CHCl_3$) 3425, 3200, and 1685 cm^{-1}.

Anal. Calcd. for $C_{16}H_{11}NO_2$: C, 77.09; H, 4.45; N, 5.62. Found: C, 77.34; H, 4.36; N, 5.78.

The oxime derivative of **1***b* was prepared in the usual manner and recrystallized from ethanol, m.p. 290–295° (decomp.).

Anal. Calcd. for $C_{16}H_{12}N_2O_2$: C, 72.71; H, 4.58; N, 10.60. Found: C, 72.40; H, 4.69; N, 10.75.

Treatment of **1***b* (1.0 g) with sodium borohydride (0.5 g) in ethanol (30 ml) at room temperature gave **1***a* (0.93 g) identical in all respects with **1***a* prepared by method *a* above.

*10,11-Dihydro-syn-11-hydroxy-10,5-(iminomethano)-5H-dibenzo[a,d]cyclohepten-13-one (**1***c*)

A solution of the ketolactam **1***b* (100 g) in ethanol (3.0 l) was hydrogenated at 50° and 7 atm in the presence of 10% palladium-on-charcoal catalyst (0.5 g) until hydrogen uptake ceased. The catalyst was removed and the solution was concentrated to half-volume whereupon **1***c* (60 g) crystallized as fine needles, m.p. 260–263° (decomp.); ν_{max} (Nujol) 1665 cm^{-1}.

Anal. Calcd. for $C_{16}H_{13}NO_2$: C, 76.47; H, 5.22; N, 5.57. Found: C, 76.35; H, 5.13; N, 5.21.

Fractional crystallization of the residue from the mother liquors gave a further 19.0 g of **1***c* and 17.0 g of **1***a*.

*10,11-Dihydro-10,5-(iminomethano)-5H-dibenzo[a,d]-cyclohepten-anti-11-ol (**2***a*)

Lithium aluminium hydride (7.25 g) was added portionwise to a stirred suspension of **1***a* (25.1 g) in 1,2-dimethoxyethane (150 ml). The mixture was stirred and heated under reflux for 10 h. The excess hydride was destroyed with water and the basic material was isolated in the usual manner. This material was recrystallized from benzene–hexane to give **2***a* (19.0 g), m.p. 130–134°; ν_{max} ($CHCl_3$) 3570, 3325, and 1020 cm^{-1}.

Anal. Calcd. for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90. Found: C, 80.97; H, 6.65; N, 5.71.

The hydrochloride salt of **2***a* was recrystallized from ethanol, m.p. 220–225° (decomp.).

Anal. Calcd. for $C_{16}H_{16}ClNO$: C, 70.30; H, 5.85; Cl, 12.99; N, 5.12. Found: C, 70.52; H, 6.04; Cl, 12.70; N, 4.81.

Reduction of **1***a* with lithium aluminium hydride in ether gave mainly starting material; similar reductions of **1***a* in tetrahydrofuran and in dioxane gave 40% and 22% yields respectively of **2***a*.

*10,11-Dihydro-10,5-(iminomethano)-5H-dibenzo[a,d]-cyclohepten-syn-11-ol (**2***c*)

The *syn*-hydroxylactam **1***c* (30 g) was treated with lithium aluminium hydride (6.0 g) in dimethoxyethane (200 ml) and then processed as described above. The crude basic material was recrystallized from methanol to give **2***c* (24.1 g), m.p. 191–193°; ν_{max} ($CHCl_3$) 3300, 1488, and 1308 cm^{-1}.

Anal. Calcd. for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90. Found: C, 80.78; H, 6.42; N, 5.69.

*3a,12b-Dihydro-3,8-methano-2H,8H-dibenzo[3,4:6,7]-cyclohepta[1,2-d]oxazol-2-one (**5**)*

A 4% solution of phosgene in benzene (30 ml) was added dropwise during 3 h to a solution of **2***c* (2.63 g) in dioxane (100 ml) and pyridine (4 drops). The mixture was kept at room temperature for 1 h and then evaporated to dryness. The residue was partitioned between chloroform and water and the organic phase was evaporated to leave the crude product. This material was recrystallized from methanol to give **5** (1.0 g), m.p. 226–228° (decomp.); ν_{max} ($CHCl_3$) 1758 cm^{-1}.

Anal. Calcd. for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.59; H, 5.00; N, 5.17.

Similar treatment of the *anti*-aminoalcohol **2***a* with phosgene gave a solid product, ν_{max} ($CHCl_3$) 1700 cm^{-1}. This material was shown to be inhomogeneous by thin-layer chromatography and it could not be purified.

*Preparation of the anti-Hydroxylactams **1***d–f*

Method a

Under the conditions described for the preparation of **1***a* (method *a*) the following compounds were obtained.

10,11-Dihydro-*anti*-11-hydroxy-12-methyl-10,5-(iminomethano)-5*H*-dibenzo[*a*,*d*]cyclohepten-13-one (**1***d*) (66.0 g), m.p. 267–270° (from ethanol); ν_{max} (Nujol) 3415, 3260, and 1650 cm^{-1} was obtained from **3** (100 g) and aqueous methylamine (600 ml of a 30% solution).

Anal. Calcd. for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.96; H, 5.53; N, 4.99.

12-Benzyl-10,11-dihydro-*anti*-11-hydroxy-10,5-(iminomethano)-5*H*-dibenzo[*a*,*d*]cyclohepten-13-one (**1***e*) (10.0 g), m.p. 224–226° (from ethanol); ν_{max} ($CHCl_3$) 3570, and 1660 cm^{-1} was obtained from **3** (30 g), benzylamine (30 g) and water (80 ml).

Anal. Calcd. for $C_{23}H_{19}NO_2$: C, 80.91; H, 5.61; N, 4.10. Found: C, 80.99; H, 5.48; N, 4.25.

10,11-Dihydro-*anti*-11-hydroxy-12-(3′-methoxypropyl)-10,5-(iminomethano)-5*H*-dibenzo[*a*,*d*]cyclohepten-13-one (**1***f*) (3.0 g), m.p. 150–152° (from ethyl acetate); ν_{max} ($CHCl_3$) 3570, 1660, and 1100 cm^{-1} was obtained from **3** (5.0 g), 3-methoxypropylamine (9.0 g), and water (40 ml).

Anal. Calcd. for $C_{20}H_{21}NO_3$: C, 74.28; H, 6.55; N, 4.33. Found: C, 74.30; H, 6.48; N, 4.39.

Method b

A mixture of the *anti*-hydroxylactam **1***a* (5.02 g, 0.02 mole), sodium hydride (920 mg of a 52% suspension in mineral oil, 0.02 mole), methyl iodide (3.12 g), and dioxane (60 ml) was stirred and heated under reflux for 4 h. The mixture was evaporated and the residue was washed with hexane and then with water and then recrystallized from ethanol to give **1***d* (4.8 g), m.p. 265–269°. The i.r. spectrum of this material was identical with that of **1***d* prepared by method *a*.

*anti-11-Benzylamino-10,11-dihydro-10,5-(epoxymethano)-5H-dibenzo[a,d]cyclohepten-13-one (**4***f*)

A mixture of the *syn*-epoxyamide **3** (25.0 g), benzylamine (30.0 g), and water (50 ml) was stirred and heated under reflux for 12 h. The reaction mixture was extracted

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with chloroform and the extracts were washed with 2 *N* HCl and then with water, and then dried. The extracts were evaporated and the residue was recrystallized from ethanol to give **4***f* (8.0 g), m.p. 141–143°; ν_{max} ($CHCl_3$) 1745 cm^{-1}.

Anal. Calcd. for $C_{23}H_{19}NO_2$: C, 80.91; H, 5.61; N, 4.10. Found: C, 81.16; H, 5.83; N, 3.98.

From the mother liquors of the above crystallization there was obtained **1***e* (11.0 g), m.p. and mixture m.p. 224–226°.

10,11-Dihydro-10-hydroxy-N-(3-methoxypropyl)-11-[N-(3-methoxypropylamino)]-5H-dibenzo[a,d]cyclohepten-5-carboxamide (6a)

A solution of the *syn*-epoxyamide **3** (10.0 g) and 3-methoxypropylamine (10.0 g) in benzene (100 ml) was stirred and heated under reflux for 18 h. The resulting solution was concentrated and the concentrate was chromatographed upon alumina. The first material eluted was the lactam **1***f* (3.0 g). The second material eluted was the title product **6***a* (2.5 g) which was recrystallized from isopropanol to m.p. 123–125°; ν_{max} ($CHCl_3$) 3420, 3370, 1655, and 1110 cm^{-1}.

Anal. Calcd. for $C_{24}H_{32}N_2O_4$: C, 69.88; H, 7.82; N, 6.79. Found: C, 69.98; H, 8.02; N, 6.67.

10,11-Dihydro-anti-11-methoxy-12-methyl-10,5-(iminomethano)-5H-dibenzo[a,d]cyclohepten-13-one (1g)

A suspension of **1***d* (5.30 g, 0.02 mole), sodium hydride (1.38 g of a 52% suspension in mineral oil), methyl iodide (4.26 g, 0.03 mole), and dioxane (50 ml) was stirred and heated under reflux for 18 h. The mixture was evaporated and the residue was washed with water and then with hexane and then recrystallized from methanol to give **1***g* (5.0 g), m.p. 212–215°; ν_{max} ($CHCl_3$) 1660 cm^{-1}.

Anal. Calcd. for $C_{18}H_{17}NO_2$: C, 77.39; H, 6.13; N, 5.01. Found: C, 77.29; H, 6.05; N, 5.12.

12-Benzyl-10,11-dihydro-anti-11-methoxy-10,5-(iminomethano)-5H-dibenzo[a,d]cyclohepten-13-one (1h)

This compound was obtained from **1***e* and methyl iodide following the procedure described above. The product crystallized from methanol, m.p. 152–154°; ν_{max} ($CHCl_3$) 1652 cm^{-1}.

Anal. Calcd. for $C_{24}H_{21}NO_2$: C, 81.10; H, 5.96; N, 3.94. Found: C, 80.99; H, 6.34; N, 4.24.

10,11-Dihydro-syn-11-hydroxy-12-methyl-10,5-(iminomethano)-5H-dibenzo[a,d]cyclohepten-13-one (1i)

This compound was obtained from the *syn*-hydroxylactam **1***c* (5.02 g) and methyl iodide (3.12 g) under the conditions described for the preparation of **1***d* (method *b*). It was purified from methanol as needles (4.0 g), m.p. 218–220°; ν_{max} (Nujol) 1668 cm^{-1}.

Anal. Calcd. for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.76; H, 5.76; N, 5.20.

10,11-Dihydro-syn-11-methoxy-12-methyl-10,5-(iminomethano)-5H-dibenzo[a,d]cyclohepten-13-one (1j)

This compound was obtained from **1***i* under the conditions described for the preparation of **1***g*. It was recrystallized from benzene as needles, m.p. 189–191°; ν_{max} ($CHCl_3$) 1666 cm^{-1}.

Anal. Calcd. for $C_{18}H_{17}NO_2$: C, 77.39; H, 6.13; N, 5.01. Found: C, 77.13; H, 6.03; N, 4.99.

10,11-Dihydro-syn-11-hydroxy-anti-11-methyl-10,5-(iminomethano)-5H-dibenzo[a,d]cyclohepten-13-one (1k)

A 3 *M* ethereal solution of methyl magnesium bromide (80 ml) was added dropwise to a solution of the ketolactam **1***b* (24.9 g, 0.1 mole) in anhydrous tetrahydrofuran (200 ml). The reaction mixture was stirred and heated under reflux for 6 h and then treated with saturated ammonium chloride solution (300 ml). The organic phase was collected, dried, and evaporated. The residue was recrystallized from methanol to give **1***k* (21.2 g), m.p. 278–280°; ν_{max} (Nujol) 3590, 3210, and 1690 cm^{-1}.

Anal. Calcd. for $C_{17}H_{15}NO_2$: C, 76.97; H, 5.70; N, 5.28. Found: C, 76.88; H, 5.64; N, 5.29.

10,11-Dihydro-syn-11-hydroxy-anti-11-phenyl-10,5-(iminomethano)-5H-dibenzo[a,d]cyclohepten-13-one (1l)

This compound was obtained from **1***b* (10 g) and phenyl magnesium bromide (0.16 mole) under the conditions used for the preparation of **1***k*. The crude product was recrystallized from ethanol to give **1***l* (8.0 g), m.p. 280–285° (decomp.); ν_{max} (Nujol) 1652 cm^{-1}.

Anal. Calcd. for $C_{22}H_{17}NO_2$: C, 80.71; H, 5.23; N, 4.28. Found: C, 80.72; H, 5.30; N, 4.11.

10,11-Dihydro-12-methyl-10,5-(iminomethano)-5H-dibenzo[a,d]cycloheptene-11,13-dione (1m)

Oxidation of **1***d* (10 g) with Jones reagent (20 ml) (27) gave the above product. It was purified from methanol, m.p. 153–155°.

Anal. Calcd. for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.78; H, 4.82; N, 5.30.

*Preparation of the Lactams **1n** and **1o***

Method a

Under the conditions described for the preparation of **1***k* the following compounds were obtained.

10,11-Dihydro-*syn*-11-hydroxy-*anti*-11-methyl-12-methyl-10,5-(iminomethano)-5*H*-dibenzo[*a*,*d*]cyclohepten-13-one (**1***n*) (1.3 g), m.p. 224–227° (from methanol); ν_{max} ($CHCl_3$) 3600, 3430, and 1667 cm^{-1} from the *N*-methyl-ketolactam **1***m* (10.0 g) and methyl magnesium bromide (0.1 mole).

Anal. Calcd. for $C_{18}H_{17}NO_2$: C, 77.39; H, 6.13; N, 5.01. Found: C, 77.25; H, 6.08; N, 5.18.

10,11-Dihydro-*syn*-11-hydroxy-12-methyl-*anti*-11-phenyl-10,5-(iminomethano)-5*H*-dibenzo[*a*,*d*]cyclohepten-13-one (**1***o*) (0.3 g), m.p. 197–199° (from benzene–hexane); ν_{max} (Nujol) 1650 cm^{-1} from **1***m* (5.0 g) and phenyl magnesium bromide (0.05 mole).

Anal. Calcd. for $C_{23}H_{19}NO_2$: C, 80.91; H, 5.61; N, 4.10. Found: C, 80.83; H, 5.54; N, 3.80.

Method b

Methylation of **1***k* (5.3 g, 0.02 mole) with sodium hydride (920 mg of a 52% suspension in mineral oil, 0.02 mole) and methyl iodide (3.32 g, 0.22 mole) in anhydrous dioxane gave **1***n* (5.0 g), m.p. and mixture m.p. 224–227°.

A similar methylation of **1***l* (3.27 g, 0.01 mole) gave **1***o* (3.0 g), m.p. and mixture m.p. 197–199°.

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10,11-Dihydro-10,5-(iminomethano)-5H-dibenzo[a,d]-cycloheptene-13-one (1p)

Method a

Small pieces of sodium were added to a mechanically stirred suspension of the *anti*-hydroxylactam **1a** (50.0 g) in freshly distilled liquid ammonia (500 ml) until the mixture remained blue for 5 min. An excess of ammonium chloride was then added and the ammonia was allowed to evaporate. The residue was extracted with hot water and the insoluble material was recrystallized from ethanol to give **1p** (45.0 g), m.p. 242–245°; ν_{max} (Nujol) 1675 cm^{-1}.

Anal. Calcd. for $C_{16}H_{13}NO$: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.67; H, 5.62; N, 5.91.

The same product was obtained when the *syn*-hydroxylactam **1c** was used as starting material.

Method b

A solution of sodium azide (0.7 g) in water (5 ml) was added to a solution of 10,11-dihydro-5*H*-dibenzo[*a,d*]-cycloheptene-5-carbonyl chloride (2.56 g) (26) in dioxane (10 ml) at 0°. The mixture was stirred at 0° for 45 min, diluted with iced water, and extracted with hexane (3 × 20 ml portion). The combined extracts were washed with cold water and then dried at 0° with molecular sieves. The solution of the acid azide **9a** so obtained was photolyzed at 0° until an aliquot no longer absorbed energy at 2140 cm^{-1}. The precipitate which had formed was crystallized from benzene–hexane and then from ethanol to give **1p** (200 mg). Concentration of the hexane filtrate gave the isocyanate **9b** (1.5 g), m.p. 60–62° (lit. (26), m.p. 62–63°).

Preparation of the Lactams 1q and 1r

Under the conditions used for the preparation of **1p** (method *a*) the following compounds were obtained.

10,11-Dihydro-*anti*-11-methyl-10,5-(iminomethano)-5*H*-dibenzo[*a,d*]cyclohepten-13-one (**1q**) (10.7 g), m.p. 243–246° (from methanol); ν_{max} ($CHCl_3$) 3410, 3200, and 1675 cm^{-1} was obtained from **1k** (12.0 g).

Anal. Calcd. for $C_{17}H_{15}NO$: C, 81.90; H, 6.06; N, 5.62. Found: C, 81.87; H, 5.94; N, 5.70.

10,11-Dihydro-*anti*-11-phenyl-10,5-(iminomethano)-5*H*-dibenzo[*a,d*]cyclohepten-13-one (**1r**) (2.8 g), m.p. 250–252° (from methanol); ν_{max} ($CHCl_3$) 1670 cm^{-1} was obtained from **1l** (3.3 g).

Anal. Calcd. for $C_{22}H_{17}NO$: C, 84.86; H, 5.50; N, 4.50. Found: C, 84.68; H, 5.71; N, 4.36.

Treatment of the Lactones 4d, 4e, and 4g with Ammonium Hydroxide

(*a*) A solution of the *syn*-hydroxylactone **4d** (300 mg) in ammonium hydroxide (10 ml) was heated at 120° for 5 h in an autoclave. The i.r. spectrum of the solid product was devoid of carbonyl absorption. A small amount of the starting material was recovered from the ammoniacal solution.

(*b*) A solution of the unsubstituted lactone **4e** (10 g) in ammonium hydroxide (200 ml) was kept at 160° for 5 h. The reaction mixture was extracted with ether. Evaporation of the washed and dried extracts and recrystallization of the residue from hexane gave 10,11-dihydro-5*H*-dibenzo[*a,d*]cyclohepten-10-ol (7.0 g), m.p. 63–65° (lit. (28), m.p. 64–66°).

Treatment of **4e** with liquid ammonia at 200° gave an intractable resin.

(*c*) A suspension of the *anti*-anilinolactone **4g** (4.0 g) in ammonium hydroxide (80 ml) was heated at 170° for 6 h. The mixture was processed as described above to give 11-anilino-10,11-dihydro-5*H*-dibenzo[*a,d*]cyclohepten-10-ol (**7a**) (2.4 g), m.p. 177–179° (from ethanol).

Anal. Calcd. for $C_{21}H_{19}NO$: C, 83.69; H, 6.35; N, 4.65. Found: C, 83.99; H, 6.20; N, 4.86.

Similar treatment of the *syn*-epoxyamide **3** (10 g) with dimethylamine (10 g) in water (70 ml) gave 10,11-dihydro-11-dimethylamino-5*H*-dibenzo[*a,d*]cyclohepten-10-ol (**7b**) (7.0 g), m.p. 114–116° (lit. (29), m.p. 117–118°).

Preparations of the Amines 2d,g–l

Under the conditions described for the preparation of **2a**, the following compounds were prepared.

10,11-Dihydro-*anti*-11-hydroxy-12-methyl-10,5-(iminomethano)-5*H*-dibenzo[*a,d*]cycloheptene (**2d**) hydrochloride (3.8 g), m.p. 220° (decomp.) (from isopropanol–ether); ν_{max} (Nujol) 3460 and 3300 cm^{-1} was obtained from **1d** (5.0 g).

Anal. Calcd. for $C_{17}H_{18}ClNO$: C, 70.94; H, 6.30; Cl, 12.35; N, 4.87. Found: C, 70.64; H, 6.58; Cl, 12.69; N, 4.73.

10,11-Dihydro-*anti*-11-methoxy-12-methyl-10,5-(iminomethano)-5*H*-dibenzo[*a,d*]cycloheptene (**2g**) (9.7 g), m.p. 122–125° (from benzene–hexane) was obtained from **1g** (12.0 g).

Anal. Calcd. for $C_{18}H_{19}NO$: C, 81.47; H, 7.22; N, 5.28. Found: C, 81.28; H, 7.25; N, 5.14.

12-Benzyl-10,11-dihydro-*anti*-11-methoxy-10,5-(iminomethano)-5*H*-dibenzo[*a,d*]cycloheptene (**2h**) hydrochloride (3.0 g), m.p. 167–170° (decomp.) (from isopropanol) was obtained from **1h** (5.0 g).

Anal. Calcd. for $C_{24}H_{24}ClNO$: C, 76.30; H, 6.40; Cl, 9.38; N, 3.70. Found: C, 76.33; H, 6.06; Cl, 9.32; N, 3.90.

10,11-Dihydro-*syn*-11-hydroxy-12-methyl-10,5-(iminomethano)-5*H*-dibenzo[*a,d*]cycloheptene (**2i**) oxalate (6.4 g), m.p. 183–185° (decomp.) (from isopropanol–ether) was obtained from **1i** (8.0 g).

Anal. Calcd. for $C_{19}H_{19}NO_5$: C, 66.85; H, 5.61; N, 4.10. Found: C, 67.61; H, 5.63; N, 4.24.

10,11-Dihydro-*syn*-11-methoxy-12-methyl-10,5-(iminomethano)-5*H*-dibenzo[*a,d*]cycloheptene (**2j**) oxalate (3.2 g), m.p. 183–186° (decomp.) (from acetonitrile–ether) was obtained from **1j** (5.4 g).

Anal. Calcd. for $C_{20}H_{21}NO_5$: C, 67.59; H, 5.96; N, 3.94. Found: C, 67.29; H, 6.20; N, 3.83.

10,11-Dihydro-*syn*-11-hydroxy-*anti*-11-methyl-10,5-(iminomethano)-5*H*-dibenzo[*a,d*]cycloheptene (**2k**) hydrochloride (4.7 g), m.p. 233–235° (from ethanol) was obtained from **1k** (7.0 g).

Anal. Calcd. for $C_{17}H_{19}ClNO$: Cl, 12.27; N, 4.11. Found: Cl, 11.99; N, 4.60.

10,11-Dihydro-*syn*-11-hydroxy-*anti*-11-phenyl-10,5-(iminomethano)-5*H*-dibenzo[*a,d*]cycloheptene (**2l**) hydrochloride (4.1 g), m.p. 219–224° (decomp.) (from ethanol) was obtained from **1l** (6.0 g).

Anal. Calcd. for $C_{22}H_{20}ClNO$: C, 75.53; H, 5.76; Cl, 10.13; N, 4.00. Found: C, 75.68; H, 5.73; Cl, 10.21; N, 3.88.

10,11-Dihydro-10,5-(iminomethano)-5H-dibenzo[a,d]-cycloheptene-11-one (2b)

A mixture of the ketolactam **1a** (25.0 g), ethylene glycol

(20 ml), *p*-toluenesulfonic acid (250 mg) and benzene was stirred and heated under reflux (Dean–Stark) for 24 h. The resulting suspension was washed with 2*N* NaOH and the solids were collected, washed with water, and dried to give the ethylene ketal of **1***a* (27.0 g), m.p. 265–269° (decomp.). A mixture of the ketal (26.5 g) and lithium aluminium hydride (4.5 g) in tetrahydrofuran was heated under reflux for 18 h. The mixture was treated with water, filtered, and the filtrate was evaporated. The residue was dissolved in 2*N* HCl (200 ml) and kept overnight. The resulting precipitate was collected and recrystallized from ethanol to give **2***b* hydrochloride (17.0 g), m.p. 285° (decomp.); ν_{max} (Nujol) 1685 cm^{-1}.

Anal. Calcd. for $C_{16}H_{14}ClNO$: C, 70.76; H, 5.16; Cl, 13.08; N, 5.16. Found: C, 70.85; H, 5.08; Cl, 13.23; N, 5.22.

Treatment of **2***b* (3.0 g) with a mixture of formic acid (10 ml) and formaldehyde (10 ml) at room temperature overnight gave, after processing in the usual manner, 10,11-dihydro-12-methyl-10,5-(iminomethano)-5*H*-dibenzo[*a*,*d*]cyclohepten-11-one (**2***m*), m.p. 149–151° (from ethanol); ν_{max} ($CHCl_3$) 2800, and 1665 cm^{-1}.

Anal. Calcd. for $C_{17}H_{15}NO$: C, 81.90; H, 6.06; N, 5.62. Found: C, 81.80; H, 6.09; N, 5.56.

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