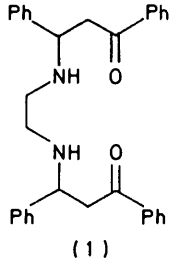
The Formation and Decomposition of 1,4,8,11-Tetra-azacyclotetradeca-4,11-dienes

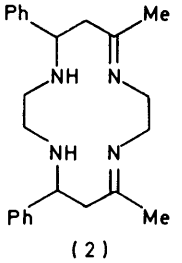
By **Olga H. Hankovszky** and **Kálmán Hideg**, Central Laboratory, Chemistry, University of Pécs, Hungary
Douglas Lloyd,* Department of Chemistry, Purdie Building, University of St. Andrews, St. Andrews, Fife
Hamish McNab, Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh

When ethylenediamine reacts with benzylideneacetone the final product isolated is a tetra-azacyclotetradecadiene (4) but the reaction path is complex and proceeds *via* an equilibrium mixture containing two macrocycles, a tetrahydrodiazepine, and a mono-condensation product. If the macrocycle (4) is heated, or left in solution at room temperature, the same equilibrium mixture is generated. Removal of ethylenediamine from this mixture promotes formation of a bisenimine which on addition of ethylenediamine slowly regenerates the equilibrium mixture. The macrocycle (4) is cleaved by hydroxylamine to give an oxime. Some new tetra-azacyclotetradecadienes have been prepared. The reaction between neat ethylenediamine and enones, previously reported to provide tetrahydrodiazepines, gives either macrocycles or bisoxoenamines as the isolated products.

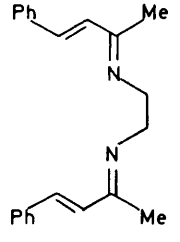
WHEN equimolar quantities of benzylideneacetone and ethylenediamine are heated in cyclohexane–ether in the presence of potassium carbonate, the crystalline product isolated in high yield is a tetra-azacyclotetradecadiene.[1]



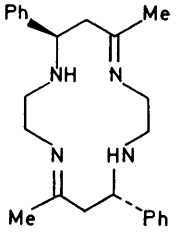
(1)



(2)



(3)



(4)

When benzylideneacetophenone is used as the enone, instead of a macrocycle, the bis-adduct (1) is obtained. On the assumption that a similar bis-adduct might be an intermediate in the formation of the macrocycle from benzylideneacetone a *cisoid* structure (2) was tentatively suggested for this macrocycle,[1] and this suggestion appeared to be confirmed when it was shown that gentle heating of solutions of the macrocycle provided good yields of the bisenimine (3), which reacted with ethylenediamine at room temperature to regenerate the same macrocycle.[2]

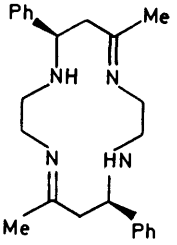
However *X*-ray crystallographic examination of the sodium borohydride reduction product of the macrocycle,[3] its reaction product with glyoxal,[4] and of metal complexes of the macrocycle [3] and of its reduction product [5] leave no doubt but that the macrocycle has the *transoid* structure (4).

The present paper discusses further studies of the formation of (4) from benzylideneacetone and also the conversion of (4) into (3) and of (3) into (4).

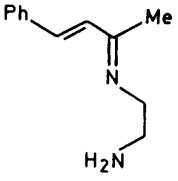
RESULTS AND DISCUSSION

The initial reaction product from benzylideneacetone and ethylenediamine is a yellow oil, which provides crystals of (4) when a solution in ether is kept in a refrigerator. Alternatively, crystals sometimes separate from the neat oil. Monitoring of the reaction by ^{13}C n.m.r. spectra shows that the oil is in fact a mixture containing four major products, believed to be (4), (5), (6), and (7), of which less than half is (4), and that the initially formed crystals are a mixture of (4) and (5) only, from which (5) is removed on recrystallisation from chloroform–ether to leave a product (4) identical to that used to provide the compounds for the *X*-ray examinations.

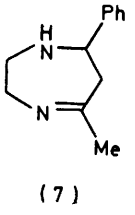
Use of two molar equivalents of benzylideneacetone provided a crude product whose n.m.r. spectrum showed it to be similar to that formed from the 1 : 1 mixture of reactants, but also containing unchanged benzylideneacetone.



(5)



(6)



(7)

The ^{13}C n.m.r. spectra are listed in Table 1, and structures of the compounds were assigned as follows. It was evident that the mixtures contained just four major components by comparisons of the relative intensities of the signals from mixtures containing different proportions of the constituents. Since compound (4) has been obtained pure and characterised by *X*-ray crystallography of derivatives its structure is known and the signals are readily assigned. Compound (5), which co-crystallises with (4) from the initial mixture, obviously

TABLE 1

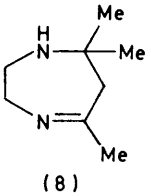
^{13}C N.m.r. spectra (δ, p.p.m. downfield from $SiMe_4$; in $CDCl_3$)

Compound	Me	*C*HPh	CH_2 or CMe_2	C=N	C=C	Ph
(3)	14.06		53.44	166.98	132.75	127.18*m*?
					134.81	128.57*p*
						128.73*o*?
						136.32(1)
(4) †	18.97	59.77	48.19	168.53		126.79*p*
			49.69			127.39*o*?
			49.92			128.31*m*?
						144.36(1)
(5)	19.32	60.66	48.97	169.75		144.52(1)
			49.44			?(*o*,*m*,*p*) *
			50.40			
(6)	13.99		43.04	166.90	132.64	136.26(1)
			55.01		134.75	?(*o*,*m*,*p*) *
(7)	29.97	59.17	45.70	174.02		145.11(1)
			47.65			?(*o*,*m*,*p*,) *
			54.09			
(8) †	28.17(7)		41.31	173.28		
	30.61(5)		49.25(7)			
			49.39			
			54.79(6)			

* Compound not isolated in pure state; phenyl signals not resolvable from those of other components. † Attributions of signals confirmed by off-resonance spectra.

has a structure very closely related to that of (4). Because of its extreme similarity it is assigned the alternative (±)-*transoid* structure (5) rather than the *cisoid* structure (2). This assignment is supported by the two following pieces of circumstantial evidence. Compound (2) would be expected to form very readily from (3) and ethylenediamine whereas, as discussed later, the appearance of this product (5) is very slow. Compound (2) would not be expected to be formed readily from (4) yet (see below) compound (5) is the major component of the mixture formed when (4) decomposes under mild conditions.

The compound to which structure (7) is assigned must, from the nature and number of its signals, represent either a *cisoid* macrocycle (2) or a tetrahydrodiazepine (7). The main differences between the spectra of these alternatives should arise from differences in geometry enforced by the different ring-sizes. To elucidate this problem the ^{13}C n.m.r. spectrum of the known tetrahydrodiazepine (8) [1,6] was recorded. The methyl signal



(8)

from (7) is much further downfield than the signals for methyl groups in similar chemical environment in the macrocycles, but has a chemical shift closely resembling that for the corresponding group in the tetrahydrodiazepine. Also the signal for the imine carbon atom of (7) much more closely resembles that for the analogous atom in (8) than it does the signals for the imine carbon atoms in the macrocycles; the chemical environments of all these imine carbon atoms are the same and differences may be ascribed to geometry. Thus compound (7) is assigned the seven-membered ring structure.

Compound (6) contains an alkene group but no C·CH_2·C grouping. Structure (6) is compatible with this evidence. The ^{1}H n.m.r. spectrum of this compound, observable from a mixture of (3) and ethylenediamine (see below), is also in accord with this structure, since it shows the presence of two dissimilar N·CH_2 groups. Finally, as would be expected from the assigned structure, the ^{13}C n.m.r. spectrum of (6) is almost identical, except for the *C*·N signals, to that of (3).

The ^{13}C n.m.r. spectra of compounds (3) [1] and (8) [1,6] were recorded on pure samples of these compounds, which have been characterised previously.

It thus appears that the initial reaction between benzylideneacetone and ethylenediamine provides an equilibrium mixture consisting largely of compounds (4)—(7). Condensation reactions must be complete at this stage since no water separates subsequently. This equilibrium is disturbed when the macrocycles (4) and (5) crystallise out thus providing finally an excellent yield of the macrocycles.

If compound (4) is kept in chloroform at room temperature a similar equilibrium mixture is slowly established. This also happens when solutions of (4) are heated. The bisenimine (3) results only if reactions or work-up conditions permit the loss of ethylenediamine. This bisenimine is not formed directly from the macrocycle, as had been assumed earlier,[2] but *via* the equilibrium mixture, in particular probably *via* (6).

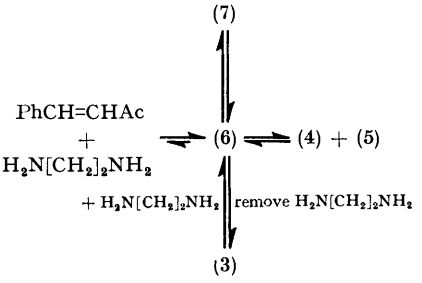
The macrocycle is regenerated from this bisenimine and ethylenediamine in solution in chloroform at room temperature, but only slowly. A similar equilibrium mixture develops and it is possible to track its development from ^{13}C n.m.r. spectra. In the first 2 h the main product observed is (6), then after 3—5 h this is replaced as predominant species by (7). Finally, after the mixture has been left overnight, an equilibrium mixture is present similar to that resulting in the initial preparation of the macrocycle. However in the mixtures obtained both by reaction of the bisenimine (3) with ethylenediamine and by the room temperature decomposition of (4) the alternative stereoisomer (5) is present in greater amount than (4), although the ratio is reversed in the product which crystallises out. Presumably interconversion of these stereoisomers proceeds *via* consecutive retro-Michael and Michael reactions.

All these compounds are thus linked by equilibria as shown in Scheme 1.

Further evidence that the oil initially formed from an arylideneacetone and ethylenediamine is an equilibrium mixture which is displaced towards the macrocycles by their crystallisation comes from crossover experiments. If the oils derived from benzylideneacetone and from *p*-methylbenzylideneacetone are mixed and kept, mass spectra of the crystalline product show the presence

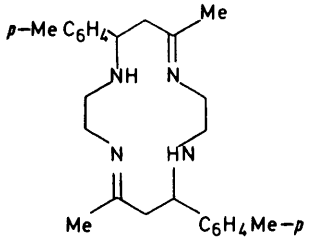
of (4), (9), and (10), thus demonstrating that macrocycle formation is incomplete at the oil stage.

As a control, the mass spectrum of a mixture of the authentic macrocycles (4) and (9) was recorded. This

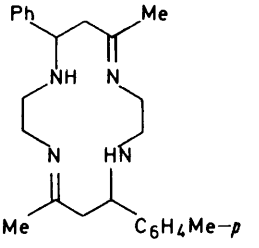


SCHEME 1

showed molecular-ion peaks corresponding to (4) and (9) but none corresponding to (10). However in addition to peaks due to loss of ethylenediamine (M — 60) from (4) and (9) there was also a peak corresponding to the loss of ethylenediamine from (10). This result is explained by equilibration taking place in the mixed melt in the



(9)



(10)

inlet of the spectrometer, and suggests that the (M — 60) peak of the macrocycles, previously attributed to a gas-phase process,[2] in fact derives from equilibration reactions in the melt comparable to those observed for solutions of the macrocycles.

The mass spectrum of (4) is in fact almost identical to that of (3) save for a small molecular ion peak (see Table 2) so that these rearrangement reactions play an important role in the breakdown of the macrocycles in the mass spectrometer. Thenylideneacetone reacts with ethylenediamine to give a macrocycle corresponding to (4),[7] whose mass spectrum is also almost identical to that of the corresponding bisenimine.

When cinnamylidene- or furylidene-acetone react with ethylenediamine neither an adduct nor a macrocycle is isolated but instead the bisenimines corresponding to (3);[7] in these cases the equilibria in Scheme 1 must be biased towards (3).

The formation of (1) rather than a macrocycle from benzylideneacetophenone is presumably a consequence of the much lower reactivity of the carbonyl group in this case, permitting Michael addition reactions to compete successfully with condensation reaction at the carbonyl group.

Hitherto, no example has been reported of both a macrocycle and an adduct like (1) being obtained from

TABLE 2

Mass spectra

Compound (4)

M^+ = 376 (0%); 316 (≡ 3) (2%); 225 (2%); 158 {≡ [½(3)]$^+$} (100%); 129 (35%); 117 (68%); 91 (84%); and 56 (65%) [for further details see entry for (3)]. M^* 113.0 (117→115 requires M^* 113.0); and 86.7 (158→117 requires M^* 86.7).

Compound (3)

M^+ = 316 (18%); 225 ([M − $PhCH_2$]$^+$) (30%); 172 ([M/2 + CH_2]$^+$) (6%); 158 ([M/2]$^+$) (100%); 144 ([M/2 − CH_2]$^+$) (9%); 129 ([M/2 − CH_2NH]$^+$) (32%); 117 ([M/2 − MeCN]$^+$) (75%); 91 ([$PhCH_2$]$^+$) (48%); and 56 (48%) M^* = 160.0 (316→225 requires M^* 160.0); 113.3 (117→115 requires M^* 113.0); and 86.7 (158→117 requires M^* 86.7)

Bisthienyl analogue of (4) (Ph replaced by 2-thienyl)

M^+ = 388 (0%); 352 (3%); 328 ([M − 60]$^+$) (bisenimine) (26%); 164 (≡ [bisenimine/2]$^+$) (100%); 135 (30%); 123 (64%); 97 (56%); 70 (33%); and 56 (72%) (for further details see entry under bisenimine below). M^* 92.5 (164→123 requires M^* 92.3).

Bisthienyl analogue of (3) (Ph replaced by 2-thienyl)

M^+ = 328 (18%); 313 ([M − Me]$^+$) (7%); 231 ([M − $C_4H_3SCH_2$]$^+$) (14%); 217—219 ([M-$C_4H_3SCH{:}CH_2$]$^+$), *etc.* (12%); 164 ([M/2]$^+$) (45%); 150 ([M/2 − CH_2]$^+$) (17%); 135 ([M/2 − CH_2NH]$^+$) (22%); 125 (62%); 124 (40%); 123 ([M/2 − MeCN]$^+$) (31%); 97 ([$C_4H_3SCH_2$]$^+$) (100%); and 70 ([C_3H_2S]$^+$) (100%).

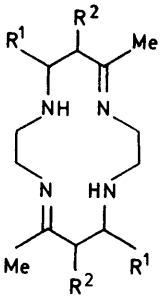
the reaction of an enone with a 1,2-diamine. We now describe a case where either may be obtained, depending on the time allowed for reaction. Although (*E*)-3-methyl-4-phenylbut-3-en-2-one did not react at all with ethylenediamine under standard conditions,[1] (*E*)-3,4-diphenyl- and (*E*)-3-phenyl-4-pyridyl-but-3-en-2-ones provide macrocycles. In the case of the 4-(3-pyridyl)enone, if the reaction is stopped after 4 h a bis-Michael adduct is isolated (68%), but after 24 h the macrocycle is obtained (57%). This indicates that in this case the equilibria involved are more complicated than those given in Scheme 1 and also involve an initial reversible Michael addition reaction; indeed this complication may also be present in other reactions of enones with 1,2-diamines, but without providing a sufficient standing concentration of adduct to have been observed.

In the case of the reaction between mesityl oxide and ethylenediamine the diazepine (8) is the only identified product, since the n.m.r. spectra of the initially formed oil is effectively identical with that of the purified product.

In the course of this investigation a number of new tetra-azacyclotetradecadienes (11) have been prepared and are described in the Experimental section; they include examples of the annellated derivatives (12). A check was also made that the same product was obtained whether ethylenediamine or its perchlorate was used as reactant. When benzylideneacetone and ethylenediamine monoperchlorate were kept overnight in methanol at 0 °C a crystalline product separated out, which, on reduction with sodium borohydride, gave a product which was identical with that obtained by similar reduction of (4).

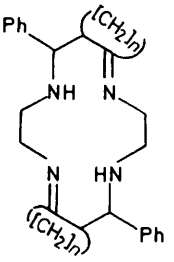
Earlier workers had claimed the preparation of tetrahydrodiazepines rather than 14-membered ring products

when ethylenediamine was heated with a number of enones without solvent; these tetrahydrodiazepines were not isolated but were reduced catalytically to products described as hexahydrodiazepines.[8] Repetition of this work shows that as found under our conditions,[1] benzylideneacetophenone gave the bis-adduct (1) and benzylideneacetone gave the macrocycle (4) as the isolated products.



(11)

(a) R^1 = *p*-FC_6H_4, R^2 = H
(b) R^1 = R^2 = Ph
(c) R^1 = 3,4-$Cl_2C_6H_3$, R^2 = Ph
(d) R^1 = 2-pyridyl, R^2 = Ph
(e) R^1 = 3-pyridyl, R^2 = Ph
(f) R^1 = 4-pyridyl, R^2 = Ph



(12)

(*n* = 3 or 4)

The formation of bisenimines such as (3) by thermal decomposition of the macrocycles has been shown to be a general reaction. The structure of the products follow from their spectra, molecular weights, and elemental analyses; coupling constants indicate that the alkene bonds have *trans* configurations. Re-formation of macrocycles from these bisenimines when they are set aside in solution with ethylenediamine also is general. The bisenimines are readily reduced by sodium borohydride to give bisallylamines.

The macrocycle (4) is cleaved by hydroxylamine to give an oxime which with ethanolic hydrochloric acid provides the crystalline dihydrochloride (13). The presence of two methyl peaks in the ^{1}H n.m.r. spectrum indicates that the alternative geometric isomer is also present but that (13) predominates (4 : 1). The stereochemistry is assigned by comparison with the results obtained[9] on the isomers (14) which result from treatment of the macrocycle (15) with hydroxylamine. Formation of (13) rather than a bisoxime comparable to (14) provides chemical evidence of the *transoid* structure of the macrocycle (4).

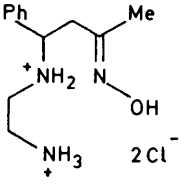
EXPERIMENTAL

N.m.r. spectra were recorded for solutions in deuteriochloroform unless otherwise stated. I.r. spectra were recorded on Nujol mulls.

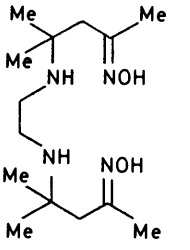
Condensation of Ethylenediamine with Benzylideneacetone.—The reaction between ethylenediamine and benzylideneacetone (1 : 1) in refluxing cyclohexane–ether in the presence of potassium carbonate gave, after filtration and evaporation of the solvents *in vacuo*, a thick yellow oil, which sometimes solidified, τ 2.3—3.1 and 5.6—8.2 (both complex), average molecular weight (cryoscopy in cyclohexane) *ca.* 320. If a solution of this oil in deuteriochloroform was set aside, its n.m.r. spectrum was virtually unchanged after 6 d, but if it was mixed with ether and set aside overnight high yields of the macrocycles (4) and (5), crystallised out which, after two recrystallisations from chloform–ether, gave essentially pure (4).

Crossover Experiments.—Ethereal solutions of the oils obtained from reactions of ethylenediamine with (*a*) benzylideneacetone and (*b*) *p*-tolylideneacetone were mixed immediately after the isolation of the oils, and the mixture kept overnight. The solid which separated out had the following peaks in its mass spectrum in the molecular-ion *M* (macrocycle) and *M* (macrocycle) −60 regions: *m/e* 404 (4%), 390 (10%), 376 (6%), 344 (67%), 330 (100%), and 316 (39%). Under similar operating conditions a mixture of (4) and (9) gave *m/e* 404 (6%), 376 (100%), 344 (100%), 330 (22%), and 316 (22%).

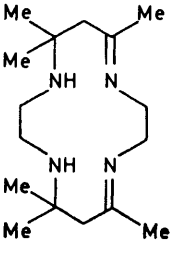
Preparation of New 1,4,8,11-*Tetra-azacyclotetradeca*-4,11-*dienes* (11).—Molar equivalents of enone and ethylenediamine (6.0 g) in cyclohexane–ether (2 : 1; 200 ml), in the presence of anhydrous potassium carbonate (10 g), were heated under reflux for 6 h and then filtered and evaporated *in vacuo*. The residue was mixed with ether (80 ml) and kept overnight in a refrigerator. The following 1,4,8,11-tetra-azacyclotetradecadienes were obtained and recrystallised from chloroform–ether: 5,12-*dimethyl*-7,14-*bis*-p-*fluorophenyl*- (11a) (85%), m.p. 125—127 °C; $\nu_{max.}$ 3 300 and 1 655 cm^{-1}; τ 2.4—3.1 (8 H, complex), 5.7—6.1br (4 H), 6.5—6.9br (4 H), 7.2—7.6 (8 H, complex), and 8.2 (6 H, s) (Found: C, 69.85; H, 7.65; N, 14.1. $C_{24}H_{30}F_2N_4$ requires C, 69.9; H, 7.35; N, 13.6%): 5,12-*dimethyl*-6,7,13,14-*tetraphenyl*- (11b) (38%), m.p. 145—146 °C;



(13)



(14)



(15)

$\nu_{max.}$ 3 320 and 1 660 cm^{-1}; τ 2.6—3.2 (20 H, complex), 5.62 (2 H, d), 6.25—7.6 (12 H, complex), and 8.3 (6 H, s) (Found: C, 81.8; H, 7.6; N, 10.45. $C_{36}H_{40}N_4$ requires C, 81.8; H, 7.65; N, 10.6%): 7,14-*bis*-(3,4-*dichlorophenyl*)-5,12-*dimethyl*-6,13-*diphenyl*- (11c) (70%), m.p. 169 °C

(decomp.); $\nu_{max.}$ 3 300 and 1 650 cm^{-1}; τ 2.8—3.3 (16 H, complex), 5.7 (2 H, d), 6.3—7.6br (12 H), and 8.3 (6 H, s) (Found: C, 64.95; H, 5.75; N, 8.5; Cl, 21.35. $C_{36}H_{36}Cl_4N_4$ requires C, 64.9; H, 5.4; N, 8.4; Cl, 21.3%): 5,12-*dimethyl*-6,13-*diphenyl*-7,14-*di*-(2-*pyridyl*)- (11d) (62%); $\nu_{max.}$ 3 300 and 1 655 cm^{-1}; τ 1.4 (2 H, d), 2.5—3.2 (16 H, complex), 5.44 (2 H, d), 5.98 (2 H, d), 6.2—7.8 (10 H, m), and 8.3 (6 H, s) (Found: C, 77.2; H, 7.1; N, 15.8. $C_{34}H_{38}N_6$ requires C, 76.95; H, 7.2; N, 15.85%): 5,12-*dimethyl*-6,13-*diphenyl*-7,14-*di*-(3-*pyridyl*)- (11e) (68%), m.p. 145—149 °C; $\nu_{max.}$ 3 300 and 1 655 cm^{-1}; τ 1.6 (4 H, complex), 2.5 (4 H, complex), 2.8—3.3 (10 H, complex), 5.6 (2 H, d), 6.8—7.5 (12 H, complex), and 8.3 (6 H, s) (Found: C, 76.65; H, 7.4; N, 15.75. $C_{34}H_{38}N_6$ requires C, 76.95; H, 7.2; N, 15.85%): and 5,12-*dimethyl*-6,13-*diphenyl*-7,14-*di*-(4-*pyridyl*)- (11f) (73%), m.p. 168—177 °C; $\nu_{max.}$ 3 290 and 1 645 cm^{-1}; τ 1.58 (4 H, d), 2.6—3.2 (14 H, complex), 5.63 (2 H, d), 6.0—7.6 (12 H, complex), and 8.3 (6 H, s) (Found: C, 76.85; H, 7.45; N, 15.8. $C_{34}H_{38}N_6$ requires C, 76.95; H, 7.2; N, 15.85%).

Annellated Tetra-azacyclotetradecadienes (12).—The following tetra-azacyclotetradecadienes were prepared by the same method as for the macrocycles (11): 5,6;12,13-*dicyclopentano*-7,14-*diphenyl*- (12, $n = 3$) (37%), m.p. 137—139 °C; $\nu_{max.}$ 3 270 and 1 670 cm^{-1}; τ 2.5—2.7 (10 H, complex), 6.35 (2 H, d), and 6.5—8.8 (24 H, m) (Found: C, 78.35; H, 8.3; N, 13.25. $C_{28}H_{36}N_4$ requires C, 78.45; H, 8.45; N, 13.05%): and 5,6;12,13-*dicyclohexano*-7,14-*diphenyl*- (12, $n = 4$) (70%), m.p. 140—141 °C; $\nu_{max.}$ 3 280 and 1 650 cm^{-1}; τ 2.4—2.8 (10 H, complex), 6.11 (2 H, d), and 6.2—9.0 (28 H, m) (Found: C, 78.65; H, 8.6; N, 12.15. $C_{30}H_{40}N_4$ requires C, 78.9; H, 8.85; N, 12.25%).

Reaction of Ethylenediamine Monoperchlorate with Benzylideneacetone.—Equivalent amounts of the enone and amine monoperchlorate were dissolved in methanol at 0 °C and set aside overnight in a refrigerator. Crystals of the *diperchlorate* of (4) (60%) separated and were washed with ether; m.p. 154—156 °C (decomp.) (Found: C, 50.1; H, 5.55; N, 9.5. $C_{24}H_{34}Cl_2N_4O_8$ requires C, 49.9; H, 5.95; N, 9.7%). When this diperchlorate was reduced with sodium borohydride in ethanol 5,12-dimethyl-7,14-diphenyl-1,4,8,11-tetra-azacyclotetradecane was formed (89%), m.p. 199—200 °C, identical with an authentic sample.[1]

Reaction of Ethylenediamine with Enones in the Absence of Solvent (cf. *Ref.* 8).—Ethylenediamine was set aside at room temperature for 0.25—3 h with (*a*) benzylideneacetone and (*b*) benzylideneacetophenone. Dilution of the mixtures with ether gave (*a*) the macrocycle (4) (40%), m.p. 134—136 °C, and (*b*) 1,8-dibenzoyl-2,7-diphenyl-3,6-diazaoctane (62%), m.p. 98—100 °C, in each case identical with authentic specimens.[1]

Reaction of (E)-3-*Phenyl*-4-(3-*pyridyl*)*but*-3-*en*-2-*one with Ethylenediamine.*—When molar equivalents of these reagents were heated in ether–cyclohexane in the presence of anhydrous potassium carbonate, work-up [*cf.* preparation of (11)] after 4 h provided 1,8-*diacetyl*-1,8-*diphenyl*-2,7-*di*-(3-*pyridyl*)-3,6-*diazaoctane* (68%), m.p. 150—153 °C (from chloroform–ether); $\nu_{max.}$ 3 250 and 1 700 cm^{-1}; τ 1.5—1.8 (4 H, complex), 2.5—3.2 (14 H, complex), 5.65 (2 H, d), 6.06 (2 H, d), 7.5—7.8 (4 H, m), 7.8 (6 H, s), and 7.9—8.2 (2 H, m) (Found: C, 75.95; H, 7.05; N, 11.1. $C_{32}H_{34}N_4O_2$ requires C, 75.85; H, 6.75; N, 11.05%). Work-up after 24 h or longer at room temperature provided mainly the cyclic product (11e), with small quantities of the diazaoctane as an impurity which separated first on recrystallisation. 1,8-*Dipropionyl*-1,8-*diphenyl*-2,7-*di*-(3-*pyridyl*)-3,6-*diazaoctane* was obtained analogously (57%), m.p. 156—157 °C (from chloroform–ether); $\nu_{max.}$ 3 280 and 1 705 cm^{-1}; τ 1.5—1.8 (4 H, complex), 2.5—3.2 (14 H, complex), 5.64 (2 H, d), 6.08 (2 H, d), 7.2—7.9 (8 H, m), 8.06br (2 H), and 8.96 (6 H, t) (Found: C, 76.25; H, 7.1; N, 10.35. $C_{34}H_{38}N_4O_2$ requires C, 76.4; H, 7.15; N, 10.5%).

Decomposition of Macrocycle (4).—When a solution of the macrocycle (50 mg) in chloroform (0.5 ml) was heated under reflux for 3 h the n.m.r. spectra of the resultant solution were similar to that of the oil initially formed in the preparation of (4). After 24 h at room temperature the overall pattern of the spectra was unchanged although some alteration in intensity ratios indicated a further adjustment of the equilibria. No further change was noted after 6 d at room temperature. A similar equilibrium mixture was established if the initial heating was omitted.

Preparation of Bisenimines (3).—A solution of the macrocycle (4) (3.76 g) in chloroform (20 ml) was heated under reflux for 2 h. The solution was cooled and solvent removed *in vacuo*. A small amount of ether was added to the residue, and when this mixture was kept in the refrigerator light yellow crystals of 3,8-*dimethyl*-1,10-*diphenyl* 4,7-*diazadeca*-1,3,7,9-*tetraene* (3) separated out (2.15 g, 68%), m.p. 112—113 °C (from ether or cyclohexane); $\nu_{max.}$ 1 600 cm^{-1}, τ 2.4—2.9 (10 H, m), 3.04 (4 H, AB pattern, J 17 Hz), 6.18 (4 H, s), and 7.89 (6 H, s) (Found: C, 83.35; H, 7.7; N, 9.15. $C_{22}H_{24}N_2$ requires C, 83.5; H, 7.65; N, 8.85%). Alternatively dimethylformamide (60 ml) was used as solvent and the solution was heated at 80 °C. Other macrocycles were decomposed analogously to give the following 4,7-diazadeca-1,3,7,9-tetraenes: 3,8-*dimethyl*-1,10-*di*-p-*tolyl*- (75%), m.p. 140—143 °C (from ether); τ 2.4—3.1 (12 H, m), 6.18 (4 H, s), 7.62 (6 H, s), and 7.89 (6 H, s) (Found: C, 83.7; H, 8.35; N, 8.3. $C_{24}H_{28}N_2$ requires C, 83.7; H, 8.2; N, 8.15%): 1,10-*bis*-p-*chlorophenyl*-3,8-*dimethyl*- (40%), m.p. 129—133 °C (decomp.) (from ether); τ 2.7 (8 H, AA'BB' pattern), 2.87 (4 H, AB, J 17.2 Hz), 6.18 (4 H, s), and 7.89 (6 H, s) (Found: C, 68.6; H, 5.8; Cl, 18.35; N, 7.3. $C_{22}H_{22}Cl_2N_2$ requires C, 68.6; H, 5.75; Cl, 18.4; N, 7.25%); 1,10-*bis*-p-*fluorophenyl*-3,8-*dimethyl*- (68%), m.p. 135—137 °C (from ether); τ 2.3—3.2 (12 H, m), 6.18 (4 H, s), and 7.89 (6 H, s) (Found: C, 75.0; H, 6.75; N, 7.6. $C_{22}H_{22}F_2N_2$ requires C, 75.0; H, 6.3; N, 7.95%): and 1,10-*bis*-p-*methoxyphenyl*-3,8-*dimethyl*- (78%), m.p. 148—149 °C (from ether); τ 2.4—3.2 (12 H, m), 6.18br (10 H), and 7.90 (6 H, s) (Found: C, 76.6; H, 7.5; N, 7.4. $C_{24}H_{28}N_2O_2$ requires C, 76.55; H, 7.5; N, 7.45%).

Reduction of the Bisenimine (3).—The bisenimine (3.16 g) and sodium borohydride (2 g) in ethanol (30 ml) were heated under reflux for 2 h. Water was added, ethanol was distilled off, and the aqueous residue extracted with chloroform (3 × 20 ml). The combined extracts were dried (Na_2SO_4), filtered, and evaporated. The residual oil was dissolved in ethanolic hydrochloric acid. Addition of ether precipitated 3,8-*dimethyl*-1,10-*diphenyl*-4,7-*diazadeca*-1,9-*diene dihydrochloride* (3.5 g, 89%), m.p. 244—247 °C (from ethanol); $\tau(CF_3CO_2H)$ 1.4—2.2 (4 H, complex), 2.68 (10 H, s), 3.03 (2 H, d, J 17 Hz), 3.73 (2 H, dd, J 9 and 17 Hz), 5.5—6.45 (6 H, complex), and 8.30 (6 H, d, J 6 Hz) (Found: C, 67.3; H, 8.0; Cl, 18.15; N, 7.15. $C_{22}H_{30}Cl_2N_2$ requires C, 67.15; H, 7.7; Cl, 18.0; N, 7.1%).

Reaction of the Bisenimine (3) *with Ethylenediamine.*—The reaction was monitored spectroscopically by dissolving equivalent amounts of the reactants in deuteriochloroform

and recording the ^1H and ^{13}C n.m.r. spectra at intervals. Preparatively, a solution of the bisenimine (3.16 g, 0.01 mol) and ethylenediamine (0.6 g, 0.01 mol) in ether (100 ml) was stirred in the presence of anhydrous potassium carbonate (3 g) for 3 d at room temperature. The solution was filtered, evaporated *in vacuo* to one-tenth of its original volume, and then kept in a refrigerator. Crystals of the macrocycle (4) separated out (2.73 g, 73%), m.p. 133—135 °C (from ether), m.p., i.r., and n.m.r. spectra identical with those of an authentic sample.

5-Phenyl-1,4-diazaoctan-7-one Oxime Dihydrochloride (13). —A solution of the macrocycle (4) (3.78 g, 0.01 mol) in ether (50 ml) was added at room temperature to a solution of hydroxylamine hydrochloride (3.47 g, 0.05 mol) and potassium hydroxide (2.8 g, 0.05 mol) in methanol (25 ml). The mixture was stirred for 3 h, kept overnight, filtered, and evaporated *in vacuo*. The residue was dissolved in ether, filtered, and evaporated *in vacuo*. The resultant oil was dissolved in dry ethanol (20 ml) and acidified to pH 4 with saturated ethanolic hydrogen chloride. When kept in a refrigerator, crystals separated which were washed several times with cold ethanol and ether and then dried. The *oxime dihydrochloride* (4.6 g, 78%) had m.p. 154—160 °C (decomp.); $\tau(D_2O)$ 2.5 (5 H, s), 6.4—7.1 (m, 7 H), and 8.24, and 8.45 (83 : 17) (2 s, 3 H) (Found: C, 48.65; H, 7.15; Cl, 24.3; N, 14.05. $C_{12}H_{21}Cl_2N_3O$ requires C, 49.0; H, 7.2; Cl, 24.1; N, 14.3%).

We are grateful to Dr. W. Scheibelein for valuable discussion and we thank Mr. J. Millar for recording the ^{13}C n.m.r. spectra.

[8/952 *Received*, 22*nd May*, 1978]

REFERENCES

[1] K. Hideg and D. Lloyd, *Chem. Comm.*, 1970, 929; *J. Chem. Soc.* (*C*), 1971, 3441.
[2] O. H. Hankovszky, K. Hideg, D. Lloyd, and H. McNab, *J.C.S. Chem. Comm.*, 1974, 378.
[3] G. Ferguson, P. Roberts, D. Lloyd, and K. Hideg, *J.C.S. Chem. Comm.*, 1977, 149; G. Ferguson, P. Roberts, D. Lloyd, K. Hideg, R. W. Hay, and D. P. Piplani, *J. Chem. Res.*, 1978, (*S*) 314, (*M*) 3734.
[4] P. W. R. Caulkett, D. Greatbanks, R. W. Turner, and J. A. J. Jarvis, *J.C.S. Chem. Comm.*, 1977, 150.
[5] D. F. Cook, *Inorg. Nuclear Chem. Letters*, 1967, **12**, 103.
[6] L. K. Mushkolo and Z. I. Shokol, *Zhur. obshchei Khim.*, 1960, **30**, 1023; B.P. 1,108,440/1966 (*Chem. Abs.*, 1968, **69**, 52034).
[7] O. H. Hankovszky, K. Hideg, K. Polgár, and D. Lloyd, *Acta Chim. Acad. Sci. Hung.*, 1975, **85**, 333.
[8] W. Heinrich and W. Heigel, G.P. 1,047,785/1958 (*Chem. Abs.*, 1961, **55**, 4552).
[9] J. L. Love and H. K. J. Powell, *Chem. Comm.*, 1968, 39; J. W. Fraser, G. R. Hedwig, M. M. Morgan, and H. K. J. Powell, *Austral. J. Chem.*, 1970, **23**, 1847.