Studies on Heterocage Compounds. IV.[1] The Through-σ-Bond Interaction of β-Amino Ketone Moiety in 1,3-Diazaadamantan-6-one and 3,6-Diazahomoadamantan-9-one Systems. Structure and Reactivity

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Received October 3, 1972

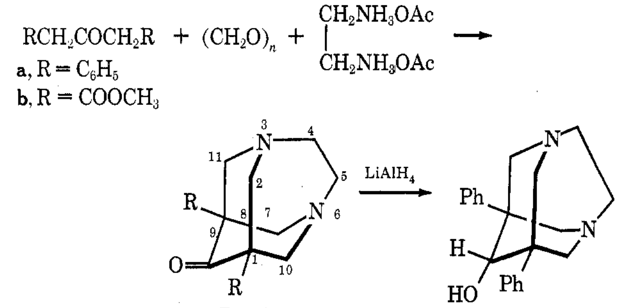
Some characteristic structural features of 5,7-diphenyl- (**1a**) and 5,7-dicarbomethoxy-1,3-diazaadamantan-6-one (**1b**) and 1,8-diphenyl- (**2a**) and 1,8-dicarbomethoxy-3,6-diazahomoadamantan-9-one (**2b**) are discussed in terms of uv, nmr, and ir spectral data, and pK_a' values. The β-amino ketone moiety in these compounds was shown to behave as an amide analog because of the through-σ-bond interaction of the lone electron pair on the nitrogen atom with the carbonyl π orbitals. Reaction of **1a** with tosylhydrazide afforded no trace of the corresponding hydrazone but only 6-alcohol **8**. Reaction of **1a** with excess hydrazine hydrate in refluxing diethylene glycol gave hydrazone **7**, which, on treatment with potassium *tert*-butoxide in dimethyl sulfoxide, gave also **8**.

Although the through-σ-bond interaction of the appropriately oriented β-amino ketone moiety is well recognized by recent theoretical and spectroscopic (uv and CD) studies,[2-4] structure–reactivity correlations of such systems have not been extensively studied.[5] In a continuation of our recent studies on heterocage compounds,[6] this paper deals with some characteristic structural features and reactions of 1,3-diazaadamantan-6-one and 3,6-diazahomoadamantan-9-one systems, in which both the lone electron pair on nitrogen and the π orbitals of the C=O group can interact with the same C–C σ bond.

Results and Discussion

Synthesis.—5,7-Diphenyl- (**1a**) and 5,7-dicarbomethoxy-1,3-diazaadamantan-6-one (**1b**) were prepared by the Mannich condensation of dibenzyl ketone and dimethyl acetonedicarboxylate with formaldehyde and ammonia according to reported procedures.[7] By using ethylenediamine instead of ammonia in the above Mannich reactions, 1,8-diphenyl- (**2a**) and 1,8-dicarbomethoxy-3,6-diazahomoadamantan-9-one (**2b**) were obtained in 8 and 6% yields, respectively (Scheme I). Although the yields are very low, this reaction provides a facile one-step synthesis of the homoadamantane skeleton.[8]

SCHEME I



$$RCH_2COCH_2R + (CH_2O)_n + \begin{matrix} CH_2NH_3OAc \\ | \\ CH_2NH_3OAc \end{matrix} \longrightarrow$$

a, R = C_6H_5
b, R = $COOCH_3$

2a, R = C_6H_5
b, R = $COOCH_3$

3

Compound **2a** had a formula $C_{21}H_{22}N_2O$ from analysis and a mass spectral molecular ion peak at *m/e* 318. An ir absorption at 1700 cm^{-1} indicated the presence of a carbonyl group in **2a** (Table I), which, on reduction with lithium aluminum hydride, was converted to the corresponding alcohol **3**. In the nmr spectrum, **2a** revealed an AB-pattern quartet (8 H) centered at τ 6.35 assignable to methylene protons at C_2, C_7, C_{10}, and C_{11}, and a singlet (4 H) at τ 6.70 due to the ethanobridge protons as well as a singlet (10 H) at τ 2.77 due to phenyl protons.

The mass spectral fragmentation pattern of **2a** was different from that of **1a**. Compound **2a** revealed some ion peaks corresponding to methyl piperidone and piperidine derivatives at *m/e* 268 and 251, although fragment peaks of pyridone derivatives at *m/e* 261, 260, and 247 are abundant for **1a**. An ion peak at *m/e* 58 appeared as a base peak for **2a**, while an ion peak at *m/e* 103 appeared for **1a**.

The methano bridge in **1a** is known to be cleaved very readily on treatment with acetic anhydride, affording *N,N'*-diacetylbispidin-9-one (**6b**).[7a] However, the same treatment of **2a** did not cleave the ethano bridge at all, even under more drastic conditions.

All of these spectral and chemical data are in good agreement with the assigned diphenyldiazahomoadamantanone structure for **2a**. The structural assignment of **2b** was performed similarly.

Spectral Properties.—In the uv spectra, **1a, 1b, 2a,** and **2b** all showed characteristic strong absorptions in the 224–260-nm region (Table I and Figure 1). An absorption of **1b** at 255 nm can be assigned to the σ-coupled (π–π^*) transition[3,4] that arises when the lone electron pair of nitrogen is antiperiplanar to the C_α–C_β bond of a carbonyl group. This absorption moves to shorter wavelengths on protonation of one of the nitrogen lone pairs in *ca.* 0.2 *N* ethanolic hydro-

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(1) Part III of this series: T. Sasaki, S. Eguchi, and T. Kiriyama, *Tetrahedron Lett.*, 2651 (1971).

(2) (a) R. Hoffmann, A. Imamura, and W. J. Hehre, *J. Amer. Chem. Soc.*, **90**, 1499 (1968); (b) R. Hoffmann, *Accounts Chem. Res.*, **4**, 1 (1971); (c) W.-D. Stohrer and R. Hoffmann, *J. Amer. Chem. Soc.*, **94**, 779 (1972).

(3) R. C. Cookson, J. Henstock, and J. Hudec, *ibid.*, **88**, 1060 (1966).

(4) J. Hudec, *Chem. Commun.*, 829 (1970).

(5) (a) However, for the lone-pair σ_{cc} interactions in electrochemical oxidation of tertiary amines, see S. F. Nelson and P. J. Hintz, *J. Amer. Chem. Soc.*, **94**, 7114 (1972). (b) For the reactivity in the Grob fragmentation, see C. A. Grob, *Angew. Chem., Int. Ed. Engl.*, **8**, 535 (1969), and references cited therein; R. Gleiter, W.-D. Stohrer, and R. Hoffmann, *Helv. Chim. Acta*, **55**, 893 (1972).

(6) T. Sasaki, S. Eguchi, and T. Kiriyama, *J. Org. Chem.*, **36**, 2061 (1971).

(7) (a) H. Stetter, J. Schafer, and K. Dieminger, *Chem. Ber.*, **91**, 598 (1958); (b) J. Kutham and J. Palecock, *Collect. Czech. Chem. Commun.*, **28**, 2260 (1963); (c) S. Chiavarelli, F. Toffler, P. Mazzeo, and L. Gramiccioni, *Farmaco, Ed. Sci.*, **23**, 360 (1968).

(8) The ring-expansion reaction of adamantane derivatives is a general route to homoadamantane derivatives: R. C. Bingham and P. v. R. Schleyer, "Chemistry of Adamantanes," Springer-Verlag, New York, N. Y., 1971, p 30, and references cited therein. For azahomoadamantane, see T. Sasaki, S. Eguchi, and T. Toru, *J. Org. Chem.*, **35**, 4109 (1970), and references cited therein.

TABLE I

SPECTRAL PROPERTIES AND pK_a' VALUES OF 1,3-DIAZAADAMANTAN-6-ONE AND 3,6-DIAZAHOMOADAMANTAN-9-ONE DERIVATIVES

Compd	Uv, nm (ϵ) (EtOH)	Ir, cm^{-1} (KBr)	Nmr, τ (CDCl$_3$, 25°)	In H$_2$O (19°)	
				pK_{a1}'	pK_{a2}'
1a	250 (1640)	1700 (CO)	2.81 (m, 10, 2C_6H_5), 5.82 (s, 2, NCH_2N), 6.25 (s, 8, other CH_2)	4.45	3.30
	(EtOH-HCl)$^{a-c}$	(monohydrochloride)			
	249 (1130) 256 (1050)	1728 (CO)			
1b	255 (1380)	1694 (CO) 1725 ($COOCH_3$)	5.94 (s, 2, NCH_2N), 6.23 (s, 8, other CH_2), 6.35 (s, 6, $COOCH_3$)	5.15	3.43
	(EtOH-HCl)^{a,c} 227 (1200) (DMCS-HCl)^d 224 (654) 285 (164)				
2a	250 (1840)^e 256 (1670)^e 263 (1350)^e	1700 (CO)	2.77 (s, 10, 2C_6H_5), 6.35 (AB q, 8, J = 14 Hz, $J/\Delta\tau$ = 0.486, 4CH_2), 6.70 (s, 4, NCH_2CH_2N)	5.03	3.46
	(EtOH-HCl)^{a,c}	(dihydrochloride)			
	250 (1170) 262 (1250)	1748			
2b	259 (1670) (end type)	1696 (CO) 1725 ($COOCH_3$)	6.27 (s, 6, 2$COOCH_3$), 6.83 (s, 4, NCH_2CH_2N), 6.47 (AB q, 8, J = 14 Hz, $J/\Delta\tau$ = 0.376, 4CH_2)	5.33	3.51
	(EtOH-HCl)^{a,c} 259 (1000) (DMCS-HCl)^d 260–285^f				
4	250 (1015) 256 (955) 262 (670)	1722 (CO) 970 (NO)	4.25 (m, 10, 2C_6H_5), 6.22 (s, 2, NCH_2NO), 6.74 (AB q, 4, J = 12 Hz, $J/\Delta\tau$ = 0.364, 2CH_2 at C_8 and C_9), 7.32 (s, 4, 2CH_2 at C_4 and C_{10})^g		
5	250 (910) 256 (820) 263 (585) 285 (87, broad)	1725 (CO)			
8	250 (740) 256 (625) 262 (425)	3400 (OH)	2.55 (s, 10, 2C_6H_5), 5.37 (s, 1, CHOH), 5.95 (s, 2, NCH_2N), 6.05–6.90 (m, 8, other CH_2), 7.45 (broad s, 1, OH)	7.20	3.47

[a] *Ca.* 0.2 *N* hydrochloric acid in ethanol. [b] An ethanolic solution of the isolated monohydrochloride of **1a** gave the same absorptions. [c] No characteristic n–π^* absorption was observed owing to the facile formation of diethyl ketal in *ca.* 1.5 *N* hydrochloric acid in ethanol. [d] Into dimethyl Cellosolve solution, dry hydrogen chloride gas was bubbled and the spectral change was followed by time. [e] As shoulder. [f] Because of lower solubility of **2b**, only broad weak absorption was observed qualitatively. [g] In CF_3COOH by using $CHCl_3$ as an internal reference.

chloric acid. The n–π^* transition of a carbonyl group in these systems is too weak to be observed because of symmetry.[9] Further addition of hydrochloric acid until *ca.* 1.5 *N* ethanolic hydrochloric acid for complete protonation of both nitrogen lone pairs resulted in no unequivocal absorption in uv spectra.[10] However, in dimethyl Cellosolve saturated with dry hydrogen chloride, the carbonyl n–π^* transition was observed at 285 nm (Table I). A similar absorption of σ-coupled transition for **1a** was observed, although the B band of the phenyl chromophore overlapped. However, the spectra of homoadamantane derivatives **2a** and **2b** were quite different from those of **1a** and **1b**, exhibiting only strong end absorption in this region. Addition of hydrochloric acid to the ethanolic solutions of **2a** and/or **2b** caused a dramatic change in the spectra: the broad end absorption changed to an unequivocal peak at 259 nm for a monoprotonated derivative of **2b** and finally disappeared on further addition of hydrochloric acid;[10] a similar change was observed for **2a**, although the benzene B band overlapped in the same region.

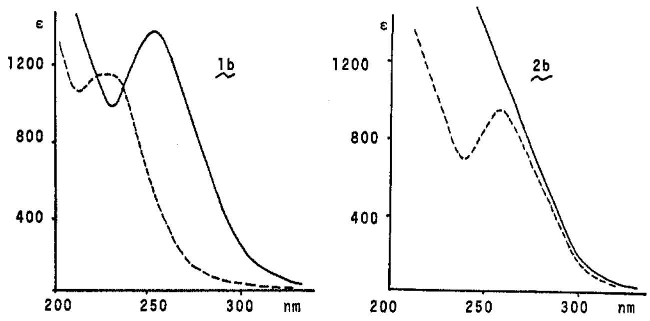

Figure 1.—Uv spectra of **1b** and **2b**: ——, in EtOH; ----, *ca.* 0.2 *N* hydrochloric acid in EtOH.

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(9) This phenomenon was also reported in symmetrical molecules such as tropinone; see ref 4.

(10) This is due to the formation of diethyl ketal in such a strongly acidic solution, as demonstrated by no characteristic carbonyl absorption in the ir spectrum and a molecular ion peak at *m/e* 342 in the mass spectrum.

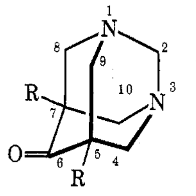
The broadening of the σ-coupled transition absorption of **2a** or **2b** is of interest in comparison with the relatively sharp absorption of **1a** or **1b**, since this difference suggests the presence of another through-σ-bond interaction between two lone electron pairs on two nitrogen atoms; the mixing of the interaction with the π orbitals on the carbonyl group may result in the splitting[2] of the σ-coupled transition of the β-amino ketone chromophore, and hence the broadening of the absorption. The interaction between two lone electron pairs on two nitrogen atoms in **2a** and **2b** should disappear on protonation of one of the nitrogen atoms. As the result, the spectra of **2a** and **2b** in weakly acidic solutions (*cf.* pK_a' values in Table I) showed the simple σ-coupled transition similar to those of **1a** and **1b**.[11-13]

In the ir spectra, **1a**, **1b**, **2a**, and **2b** showed considerably lower carbonyl stretching frequencies at around 1694–1700 cm^{-1} (Table I) compared to those of 4-piperidone derivatives,[14] while the corresponding hydrochlorides, trifluoroacetate, or some other derivatives such as **4** and **6a** had normal values. These facts suggest through-σ-bond interaction of the nitrogen lone electron pair with the carbonyl group in **1a**, **1b**, **2a**, and **2b** in the ground state, which is also supported by the basicity measurements as described below.

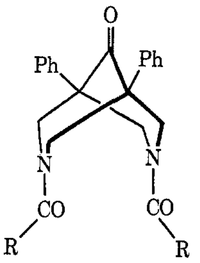
pK_a' Study.—The pK_a' values of **1a**, **1b**, **2a**, **2b**, and **8** were measured potentiometrically in water at 19° and the values obtained are summarized in Table I. The pK_{a1}' values for the carbonyl compounds **1a**, **1b**, **2a**, and **2b** are considerably lower compared to that for alcohol **8**, though the pK_{a2}' values are more or less similar for all compounds. Pseudopelletierine, with a similar piperidone system, has a pK_a' value of 7.55 in water,[15] which is also much higher than those of the present β-amino ketone derivatives.

All of these spectral and pK_a' data indicate that β-amino ketone systems in **1a**, **1b**, **2a**, and **2b** should be regarded as an amide analog rather than independent *tert*-amine and keto groups. Therefore, examination of the carbonyl reactivity in these ring systems is of interest in connection with the structure–reactivity correlation.

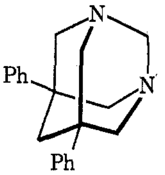
Chemical Reactivity of 1a.—Reactions of **1a** with several carbonyl reagents were examined. Previously, the successful reductions of **1a** to alcohol **8** with $LiAlH_4$ or sodium alkoxide, and to amine **9** with hydrazine hydrate–sodium acetate, have been reported by Stetter[7a] as well as the facile ring fission to the bispidinones **6b** and **6c** with acetic anhydride and benzoyl chloride, respectively. Some of the other reactions examined are summarized in Scheme II. As expected, **1a** did not react with the usual carbonyl reagents such as 2,4-dinitrophenylhydrazine and hydroxylamine, but with hydrazine hydrate **1a** gave the corresponding hydrazone **7** in a moderate yield only under very drastic conditions in refluxing diethylene glycol. With a large excess of



1a, R = C_6H_5
b, R = $COOCH_3$



6b, R = CH_3
c, R = C_6H_5



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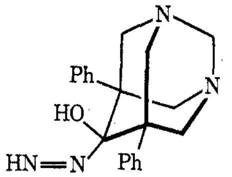

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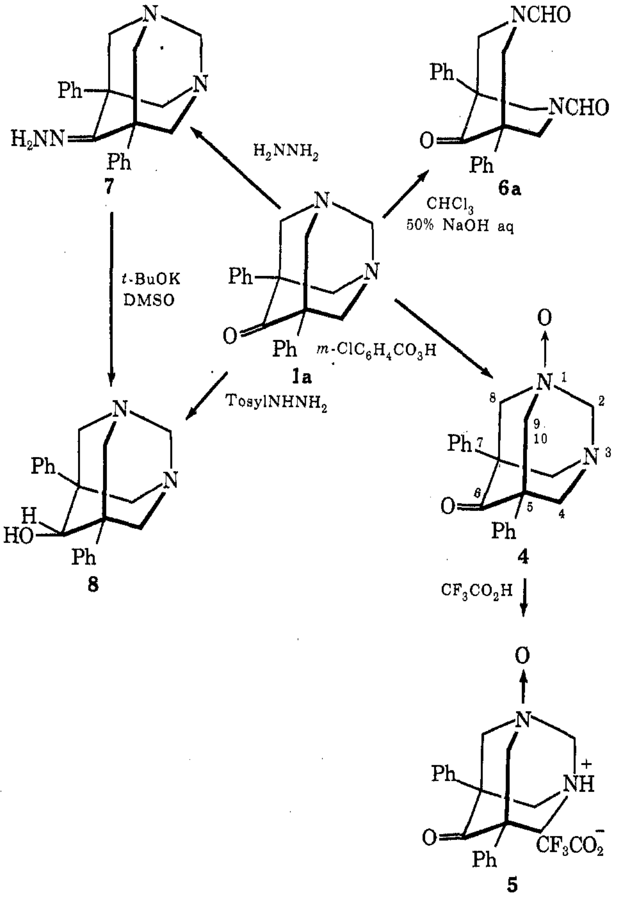
SCHEME II



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(11) The through-σ-bond interaction between two nitrogen atoms is expected to be operative effectively only in an eclipsed conformation of the ethano bridge in **2a** and **2b**; *cf.* ref 2.

(12) The untwisted conformation of the NCH_2CH_2N group in **2a** was suggested by the nmr spectra, since the protons of the ethano bridge at τ 6.70 exhibited no broadening on cooling until at −70° in CH_2Cl_2. The nmr measurement at below −70° was unsuccessful because of the lower solubility of **2a**. Furthermore, **2a** and **2b** had J_{gem} of 14 Hz for CH_2 at C_2, C_7, C_{10}, and C_{11}. This larger J_{gem} value of the homoadamantane system compared to those of the adamantane series (mono-*N*-oxide **4**, for example, had J_{gem} = 12 Hz) is indicative of somewhat flattened cyclohexane ring structures in **2a** and **2b**; for detailed nmr studies on related azacyclic compounds, see (a) S. P. Nelsen, P. J. Hintz, and R. T. Landis, II, *J. Amer. Chem. Soc.*, **94**, 7105 (1972); (b) R. C. Cookson, T. A. Crabb, J. J. Frankel, and J. Hudec, *Tetrahedron, Suppl.*, **No. 7**, 355 (1966).

(13) Homoadamantane itself has been reported recently to have a broad energy minimum between skewing angles of ±33° from calculations; E. M. Engler, L. Chang, and P. v. R. Schleyer, *Tetrahedron Lett.*, 2525 (1972). For the preferred untwisted conformation of *cis*-4,5-homoadamantandiol and homoadamantan-4,5-dione, see P. v. R. Schleyer, E. Funke, and S. H. Liggero, *J. Amer. Chem. Soc.*, **91**, 3965 (1969); J. L. M. A. Schlatmann, J. G. Korsloot, and J. Schut, *Tetrahedron*, **26**, 949 (1970).

(14) For example, *N*-methyl-4-piperidone has a carbonyl frequency at 1725 cm^{-1}: C. J. Pouchert, "The Aldrich Library of Infrared Spectra," Aldrich Chemical Co., Inc., 1970.

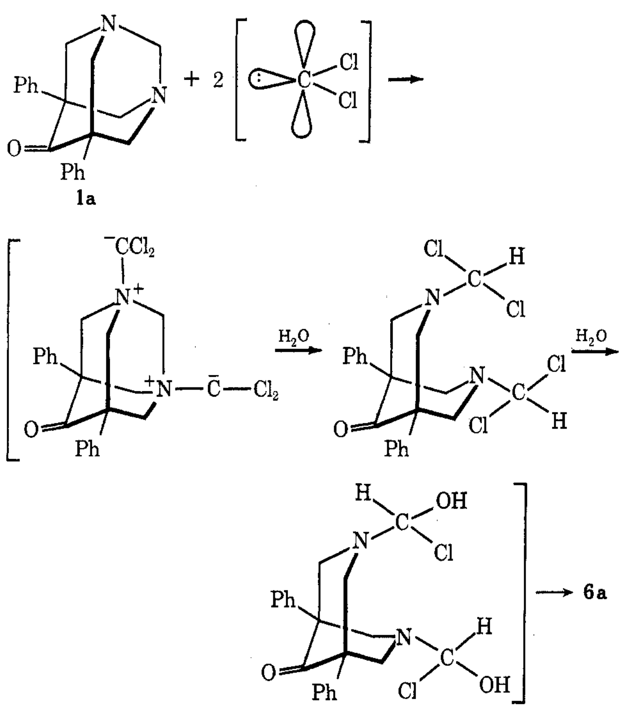
(15) T. Sasaki, S. Euchi, and T. Kiriyama, *Bull. Chem. Soc. Jap.*, **44**, 3410 (1971).

diazomethane, **1a** did not react at all. These facts point to a lower reactivity of the carbonyl group; however, steric hindrance by the 5,7-diphenyl substituents is considered to be another reason.[16]

Reaction of **1a** with excess *m*-chloroperbenzoic acid or hydrogen peroxide afforded no Baeyer–Villiger product but only mono-*N*-oxide **4**. The mono-*N*-oxide structure of **4** was supported by the formation of the monotrifluoroacetate **5**.

Reaction of **1a** with dichlorocarbene in an alkaline micelle[17] afforded a ring-fission product, 1,5-diphenyl-*N*,*N'*-diformylbispidinone (**6a**). The formation of **6a** could be explained by an initial attack of dichlorocarbene on nitrogen followed by ring fission and hydrolysis as illustrated in Scheme III.

SCHEME III



When a mixture of *p*-toluenesulfonylhydrazide (tosylhydrazide), **1a**, and barium oxide in ethanol was heated at 65°, no trace of the corresponding tosylhydrazone was produced but alcohol **8** was produced in a low yield. The formation of **8** from **1a** and tosylhydrazide can be explained reasonably by diimide type reduction or by decomposition of a hydroxyazene intermediate (**10**).[18–20] This is the first example of novel reduction of a very inert alicyclic ketone with tosylhydrazide, though an example for an aromatic ketone has been reported.[20]

When **7** was treated with potassium *tert*-butoxide in dimethyl sulfoxide, only alcohol **8** was produced but no Wolff–Kishner reduction product **9**. This reaction might proceed similarly as above *via* diimide type reduction.

These results on the facile formation of **8** are in good accord with the expected lower reactivity of the carbonyl group in **1a**.

Experimental Section[21]

5,7-Diphenyl-1,3-diazaadamantan-6-one (1a).—This was prepared by the known method:[7a] mp 255–258° (lit.[7a] mp 257°); mass spectrum *m/e* (rel intensity) 304 (13, M$^+$), 261 (43), 260 (12), 247 (10), 233 (15), 146 (13), 144 (18), 131 (42), 103 (100), 91 (33), 77 (36), 57 (35), and 42 (65).

5,7-Dicarbomethoxy-1,3-diazaadamantan-6-one (1b).—A mixture of ammonium acetate (5.00 g, 65.0 mmol), dimethyl acetonedicarboxylate (3.58 g, 20.0 mmol), and paraformaldehyde (3.28 g, 108 mmol) in ethanol (30 ml) was refluxed for 3 hr. Removal of the solvent and extraction with benzene (5 × 20 ml) followed by evaporation afforded a solid product which was recrystallized from ethanol–benzene to give **1b** as colorless crystals (340 mg, 6.4%): mp 175–177°; mass spectrum *m/e* (rel intensity) 268 (7, M$^+$), 241 (14), 240 (30), 239 (15), 237 (41), 226 (13), 209 (15), 208 (22), 194 (18), 181 (12), 177 (18), 167 (8), 142 (6), 140 (8), 114 (12), 113 (100), 96 (26), 69 (12), 59 (74), and 57 (93).

Anal. Calcd for $C_{12}H_{16}N_2O_5$: C, 53.72; H, 6.01; N, 10.44. Found: C, 53.91; H, 6.00; N, 10.26.

1,8-Diphenyl-3,6-diazahomoadamantan-9-one (2a).—A mixture of dibenzyl ketone (4.20 g, 20.0 mmol), paraformaldehyde (3.60 g, 120 mmol), and ethylenediammonium diacetate (3.60 g, 30.0 mmol) prepared from ethylenediamine and acetic acid in ethanol (30 ml) was refluxed for 1 day. After removal of the solvent, the crude product was extracted with benzene (5 × 20 ml) and the combined benzene extracts were purified on a silica gel column eluting with a $CHCl_3$–EtOH system to afford **2a** as colorless crystals (510 mg, 8.1%): mp 182–185°; mass spectrum *m/e* (rel intensity) 318 (72, M$^+$), 287 (15), 268 (15), 251 (10), 240 (15), 160 (62), 117 (33), 113 (41), 103 (71), 77 (42), and 58 (100).

Anal. Calcd for $C_{21}H_{22}N_2O$: C, 79.21; H, 6.96; N, 8.80. Found: C, 79.44; H, 7.04; N, 8.59.

1,8-Dicarbomethoxy-3,6-diazahomoadamantan-9-one (2b).—A mixture of ethylenediammonium diacetate (4.32 g, 24.0 mmol), dimethyl acetonedicarboxylate (3.48 g, 20 mmol), and paraformaldehyde (3.60 g, 120 mmol) in methanol (30 ml) was refluxed for 20 hr. After removal of the solvent, the crude product was extracted with benzene (5 × 20 ml) and the benzene extract was washed once with 10% aqueous sodium carbonate and dried (Na_2SO_4). Removal of the solvent and recrystallization from carbon tetrachloride afforded **2b** as colorless crystals (310 mg, 5.7%): mp 134–135°; mass spectrum *m/e* (rel intensity) 282 (20, M$^+$), 251 (10), 241 (5), 240 (5), 226 (8), 223 (6), 218 (6), 195 (5), 183 (5), 180 (5), 167 (5), 153 (5), 152 (6), 150 (8), 142 (11), 140 (10), 126 (10), 113 (51), 69 (28), 59 (69), 57 (70), and 43 (100).

Anal. Calcd for $C_{13}H_{18}N_2O_5$: C, 55.31; H, 6.43; N, 9.92. Found: C, 55.23; H, 6.29; N, 9.66.

1,8-Diphenyl-3,6-diazahomoadamantan-9-ol (3).—A mixture of **2a** (170 mg, 0.530 mmol) and lithium aluminum hydride (30 mg, 0.79 mmol) in dry tetrahydrofuran (20 ml) was refluxed for 4 hr. The excess reagent was decomposed by adding water (50 ml) and the mixture was extracted with methylene chloride (5 × 20 ml) and dried (Na_2SO_4). Removal of the solvent and recrystallization from methanol afforded **3** as colorless crystals (120 mg, 75%): mp 233–237°; ir (KBr) 3400 cm^{-1}; nmr ($CDCl_3$) τ 2.72 (s, 10, 2 C_6H_5), 5.42 (s, 1, C_9H), 6.18 (d of d, 2, J = 14 and 3 Hz, C_7H_{ax} and $C_{10}H_{ax}$ anti to OH), 6.79 (s, 4, NCH_2CH_2N), 7.20 (d, 4, J = 14 Hz, C_2H_{eq}, C_7H_{eq}, $C_{10}H_{eq}$, and $C_{11}H_{eq}$), and 7.95 (s, 1, OH); mass spectrum *m/e* (rel intensity) 320 (100, M$^+$), 303 (30), 291 (35), 248 (21), 246 (17), 232 (22), 231 (24), 217 (30), 160 (37), 111 (35), 97 (50), 85 (53), and 83 (43).

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(16) The ready formation of the diethyl ketal of **2a** in strongly acidic ethanol suggests that the steric hindrance of 5,7-diphenyl substituents is not extremely severe; see ref 10.

(17) M. Makosza and M. Warzyniewiez, *Tetrahedron Lett.*, 4659 (1969).

(18) For reviews on diimide reductions, see (a) A. Furst, R. C. Berlo, and S. Hooton, *Chem. Rev.*, **65**, 51 (1965); (b) S. Hünig, H. R. Miller, and W. Thier, *Angew. Chem.*, **77**, 368 (1965); (c) C. E. Miller, *J. Chem. Educ.*, **42**, 254 (1965); (d) H. O. House, "Modern Synthetic Reactions," 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1972, p 248.

(19) For the formation of diimide from tosylhydrazide, see R. S. Dewery and E. E. van Tamelen, *J. Amer. Chem. Soc.*, **83**, 3729 (1961).

(20) For an example of such a novel reduction of a very inert aromatic ketone with tosylhydrazide, see J. J. Looker, *J. Org. Chem.*, **32**, 472 (1967).

(21) All melting points were obtained on a hot-stage type Yanagimoto micromelting point apparatus and are uncorrected. Nmr spectra were recorded on a JEOL JNM-C-60HL spectrometer at 60 MHz and mass spectra on a JEOL JMS-01SG mass spectrometer at 75 eV. Ir spectra were obtained with a JASCO IR-S spectrometer and uv spectra on a JASCO ORD/UV-5 spectrometer. Microanalyses were carried out with a Perkin-Elmer 240 Elemental Analyzer.

Anal. Calcd for $C_{21}H_{24}N_2O$: C, 78.71; H, 7.55; N, 8.74. Found: C, 78.42; H, 7.55; N, 8.45.

5,7-Diphenyl-1,3-diazaadamantan-6-one *N*-Oxide (4).—A mixture of **1a** (300 mg, 0.987 mmol) and *m*-chloroperbenzoic acid (520 mg, 3.00 mmol) in chloroform (20 ml) was refluxed for 13 hr. After cooling, excess peracid was decomposed by adding 10% aqueous sodium bisulfite solution and the mixture was extracted with 10% aqueous sodium carbonate solution (3 × 10 ml). The organic layer was dried (Na_2SO_4) and the solvent was removed to afford a crude product which was purified on a silica gel column eluting with a $CHCl_3$–EtOH system to give **4** as colorless crystals (100 mg, 32%): mp 258–261°; mass spectrum *m/e* (rel intensity) 320 (12, M^+), 304 (72), 261 (100), 260 (57), 247 (24), 233 (24), 159 (19), 144 (23), 131 (32), and 103 (46). Treatment of **4** with trifluoroacetic acid gave quantitatively trifluoroacetate salt **5**: mp 177–181°; ir (KBr) 1725 (CO), 1670 (COO^-), and 1190 cm^{-1} (CF_3).

Anal. Calcd for $C_{22}H_{21}N_2O_4F_3$: C, 52.76; H, 3.69; N, 5.12. Found: C, 52.81; H, 3.93; N, 5.12.

***N,N'*-Diformylbispidin-9-one (6a).**—To a vigorously stirred mixture of **1a** (300 mg, 0.987 mmol), triethylbenzylammonium chloride (20 mg, 0.088 mmol), benzene (5 ml), and 50% sodium hydroxide aqueous solution (10 ml) was added dropwise a mixture of benzene (5 ml) and chloroform (0.80 ml, 9.9 mmol) at 25° in *ca.* 0.5 hr. After the addition was completed, the stirring was continued for a further 22 hr, and the mixture was diluted with water (60 ml) and extracted with chloroform (2 × 30 ml). The combined extracts were dried (Na_2SO_4) and evaporated to give a crude product, which was chromatographed on a silica gel column ($CHCl_3$–EtOH) to afford **6a** as colorless crystals (80 mg, 23%): mp 229–232°; ir (KBr) 1720 (CO) and 1680 cm^{-1} (NCHO); nmr ($CDCl_3$) τ 1.98 (s, 2, 2 CHO), 2.69 (s, 10, 2 C_6H_5), 4.80 (d of d, 2, J = 13 and 2 Hz, C_2H_{eq} anti to oxygen atom of the formyl carbonyl), 5.95 (AB q, 4, J = 13 Hz, $J/\Delta\tau$ = 0.542, 2 CH_2 at C_4 and C_8 syn to oxygen atom of the formyl carbonyl), and 6.55 (d of d, 2, J = 13 and 2 Hz, C_2H_{ax} and C_6H_{ax} anti to the formyl carbonyl);[22] mass spectrum *m/e* (rel intensity) 348 (100, M^+), 320 (36), 277 (73), 276 (95), 248 (32), 233 (26), 207 (34), 205 (32), 105 (62), 103 (51), 97 (41), 85 (41), 83 (45), 71 (57), 69 (47), 57 (95), 44 (53), 43 (85), 41 (42), and 40 (38).

Anal. Calcd for $C_{21}H_{20}N_2O_3$: C, 72.39; H, 5.79; N, 8.04. Found: C, 72.40; H, 6.04; N, 7.88.

5,7-Diphenyl-1,3-diazaadamantan-6-one Hydrazone (7).—A mixture of **1a** (600 mg, 1.97 mmol) and 80% hydrazine hydrate (5.00 g, 80.0 mmol) in diethylene glycol (20 ml) was refluxed with a Dean–Stark trap for 18 hr. The cooled mixture was diluted with water (50 ml) and extracted with chloroform (20 ml). The extract was washed with water (2 × 10 ml) and dried (Na_2SO_4). Removal of the solvent and chromatography of the crude product on a silica gel column ($CHCl_3$–EtOH) afforded **7** as colorless crystals (390 mg, 62%): mp 249–251°; mass spectrum *m/e* (rel intensity) 318 (19, M^+), 275 (32), 247 (14), 223 (15), 205 (14), 175 (13), 150 (34), 141 (15), 119 (13), 105 (13), 104 (20), 97 (14), 95 (12), 93 (13), 91 (14), 85 (17), 83 (17), 81 (14), 76 (20), 71 (30), 69 (26), 57 (70), 56 (40), 55 (34), 44 (32), 43 (32), 41 (62), and 40 (100); ir (KBr) 3425 and 3305 cm^{-1}; nmr ($CDCl_3$) τ 2.65 (s, 5, C_6H_5), 2.83 (s, 5, C_6H_5), 5.70 (s, 2, disappeared on deuteration, NH_2), 5.89 (s, NCH_2N), 6.15 (d of d, 4, J = 12 and 4 Hz, C_4H_{ax}, C_8H_{ax}, C_9H_{ax}, and $C_{10}H_{ax}$), and 6.53 (d of d, 4, J = 12 and 3 Hz, C_4H_{eq}, C_8H_{eq}, C_9H_{eq}, and $C_{10}H_{eq}$).

Anal. Calcd for $C_{20}H_{22}N_4$: C, 75.44; H, 6.96; N, 17.60. Found: C, 75.21; H, 6.96; N, 17.82.

Reaction of 1a with Tosylhydrazide.—A mixture of **1a** (160 mg, 0.83 mmol), tosylhydrazide (200 mg, 1.08 mmol), and barium oxide (2.0 g, 13.1 mmol) in ethanol was heated at 65° with occasional stirring for 3 days. After removal of the solids by filtration, the filtrate was evaporated to dryness to give crude product, which on purification by preparative tlc (silica gel, 5% MeOH–$CHCl_3$) afforded recovered **1a** (110 mg, 80% recovery) and 5,7-diphenyl-1,3-diazaadamantan-6-ol (**8**) (30 mg, 20%), mp 282–284° (lit.[7a] mp 274°), identified by spectral (ir and nmr) comparison with an authentic sample.[7a]

Treatment of 7 with Potassium *tert*-Butoxide in Dimethyl Sulfoxide.—To a solution of potassium *tert*-butoxide (40 mg, 0.36 mmol) in freshly distilled (from KOH) dimethyl sulfoxide (4 ml) was added **7** (60 mg, 0.19 mmol) and the resulting solution was stirred for 22 hr at room temperature under nitrogen atmosphere. The mixture was poured onto ice-water (30 ml) and extracted with methylene chloride (4 × 20 ml). The combined extracts were dried (Na_2SO_4) and evaporated to afford **8** (47 mg, 80%).

pK_a' Measurements.—pK_a' measurements were carried out by titrating potentiometrically an acidic solution of each amine (prepared by dissolving *ca.* 2.5 mg of amine into 3.00 ml of 0.01 *N* hydrochloric acid) with 0.1 *N* potassium hydroxide aqueous solution at 19°. The titration was performed on a Radiometer Model TT1.

Registry No.—**1a**, 19066-35-4; **1b**, 38740-11-3; **2a**, 38740-12-4; **2b**, 38740-13-5; **3**, 38740-14-6; **4**, 38740-15-7; **5**, 38740-16-8; **6a**, 38740-17-9; **7**, 38740-18-0; **8**, 3576-75-8; ammonium acetate, 631-61-8; dimethyl acetonedicarboxylate, 1830-54-2; dibenzyl ketone, 1083-30-3; ethylenediammonium acetate, 38734-69-9; trifluoroacetic acid, 76-05-1; tosylhydrazide, 1576-35-8.

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[22] The formyl group seems to rotate not freely at room temperature, and hence two formyl groups in **6a** take preferably the anti conformation to each other by dipole–dipole interaction, though further details on this problem will be published elsewhere: *cf.* ref 6 and references cited therein.

Azodicarboxylic Acid Esters as Dealkylating Agents[1]

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Received March 10, 1972

The use of azodicarboxylic acid esters as dealkylating agents has been studied. The isolation and structure proof of the intermediate adducts obtained from the reaction of the azo esters with secondary and tertiary amines is reported. Dealkylation of compounds other than amines by this method is also discussed.

The diesters of azodicarboxylic acid (**1**, **2**) react with aliphatic primary amines to give amides,[2-4] while primary aromatic amines yield either triazan addition compounds[4-6] or ring-substituted systems.[6,7] It was reported that whereas piperidine reacts with diethyl azodicarboxylate (**1**) to yield the corresponding azodicarboxamide, other secondary amines combined with one molecule of this ester to give a stable addition product.[3,4] On acidic hydrolysis these adducts produced aldehydes in relatively low yields. Diels[3] assigned structure **3** to these adducts and later Kenner and Stedman,[8] utilizing infrared evidence, proposed the triazan structure **4**.

Diels was the first to investigate the reaction of the

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[1] Taken in part from the dissertation presented by A. Makriyannis, March 1967, to the Graduate School of the University of Kansas in partial fulfillment of the requirements for the Doctor of Philosophy degree.

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