pionic acid (4.85), benzoic acid (4.2), and p-nitrobenzoic acid (3.4). For each diazoalkane the approximate upper limit was >10 (3h), 10 (3b and 3d), 8 (3c), 7 (3a), 10 (3f), and 8 (3g).

Registry No.-1a, 7216-40-2; 1b, 54618-16-5; 1c, 54618-17-6; 1d, 54618-18-7; 1e, 54618-19-8; 2a, 50908-22-0; 2b, 54618-02-9; 2c. 54618-20-1; 2d, 54618-21-2; 2e, 54618-22-3; 2f, 54618-23-4; 2g, 54618-24-5; 3a, 50908-23-1; 3b, 54618-03-0; 3c, 54618-25-6; 3d, 54618-26-7; 3e, 54618-27-8; 3f, 54618-28-9; 3g, 54618-29-0; 4, 35392-65-5; 2-hydroxymethyl-3-methoxypyridine, 51984-46-4; 2methyl-3-methoxypyridine 1-oxide, 35392-65-5; 2-formylquinoline 1-oxide, 54618-45-0; 1-formylisoquinoline 1-oxide, 54618-46-1.

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Cis Azoxy Alkanes. VI. Cis Azo N.N'-Dioxide Synthesis and the Importance of Entropy in the Nitrosoalkane-Azo Dioxide Equilibrium^{1a}

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Received August 6, 1974

A series of nine cis polycyclic azo $N_{N'}$ -dioxides (nitroso dimers) have been prepared by direct oxidation of the corresponding azo and azoxy alkanes with H₂O₂ and m-chloroperbenzoic acid. The synthesis of two bridgehead substituted α -chloro derivatives has also been accomplished by chlorination of polycyclic dioximes. In all cases the corresponding mono-N-oxides (azoxy alkanes) were generated independently either by azo oxidation and/or by hexachlorodisilane reduction of the N,N'-dioxides. A preliminary study of the thermal behavior of the latter in solution and in the solid state shows that in stark contrast to acyclic nitroso dimers the cyclic derivatives do not deliver the nitroso monomer in observable concentrations on warming to 250°. Estimated ΔH 's and ΔS 's for the azo dioxide ring opening suggest the source of the experimental result to lie predominantly in the small ΔS term. For highly strained cycles it is concluded that the lack of dedimerization can be attributed either to a kinetic or to a thermodynamic origin. Specifically either the transition state for fragmentation is nonlinear and therefore significantly congested or ground-state azo dioxide strain energies are markedly less than those for the corresponding unsaturated hydrocarbons.

C-Nitroso compounds and their $N_{N'}$ -dioxide dimers have been of interest since the last century.^{2a,b} The monomer-dimer equilibrium^{2c} operates for a wide range of substituent types and has stimulated the collection of both thermodynamic³ and kinetic data.⁴

Although a detailed mechanistic understanding is still lacking, recent molecular orbital calculations illuminate



certain stereoelectronic facets of the reaction and suggest that dimer formation proceeds by a nonlinear pathway.⁵

Table	I
Physical Data for the Polyc	yclic Cis Azo Dioxides

,,		Mp. °C	Yield.					Calcd/found, %		d , ً%
Compo	l n	(crystn solvent)	%	Ir, $a \mathrm{cm}^{-1}$	Uv, ^b nm (^e)	¹ H NMR, τ (CDCl ₃ , TMS)	Formula	с	н	N
3	1	142–144 dec	16	1490, 1432,	265 (8800)	5.22 (2 H, s, $W_{1/2} = 4$ Hz)	$C_5H_8N_2O_2$	46.9	6.3	21.9
		(EtOH)		1290, 1270		7.3-8.3 (6 H, m)		47.0	6.4	21.9
	2	221222 dec	41	1475, 1425,	265 (9000)	5.25 (2 H, s, $W_{1/2} = 6$ Hz)	$C_{6}H_{10}N_{2}O_{2}$	50.7	7.1	19.7
		(EtOH)		1328, 1309		7.9 (8 H, broad s)		50.8	7.0	19.8
	3	223–224 dec	72	1483, 1412,	268 (10,500)	5.45 (2 H, s, $W_{1/2} = 8$ Hz)	$\mathbf{C}_{7}\mathbf{H}_{12}\mathbf{N}_{2}\mathbf{O}_{2}$	53.8	7.7	17.9
		(EtOH)		1323, 1293		7.3-8.5 (10 H, m)		54.0	7.8	18.0
	4	216–217 dec	86	1465, 1399,	270 (13,700)	5.40 (2 H, s, $W_{1/2} = 12$ Hz)	$\mathbf{C}_{8}\mathbf{H}_{14}\mathbf{N}_{2}\mathbf{O}_{2}$	56.5	8.3	16.5
		(EtOH)		1331, 1291		7.3–8.7 (12 H, m)		56.8	8.3	16.7
4b		182–183 dec	14	1496, 1428,	271 (6900)	5.45 (2 H, s, $W_{1/2} = 5$ Hz)	$C_7H_8N_2O_2$	55.3	5.3	18.4
		(EtOH)		1290, 1258		7.13 (1 H, s), 7.75		55.3	5.4	18.5
						(3 H, s), 8.08 (2 H, s)				
5b		238–240 dec	56	1425, 1290,	272 (9300)		$C_8H_8N_2O_2$	58.5	4.9	17.1
		(MeOH)		1270				58.5	5.0	17.1
6b		182–185 dec	29	1480, 1403,	267 (7500)	5.09 (2 H, 2, $W_{1/2} = 8$ Hz)	$C_7 H_{10} N_2 O_2$	54.5	6.5	18.2
		(EtOH)		1340, 1300		7.7–8.2 (6 H, m)		54.6	6.6	18.2
						8.5–9.0 (2 H, m)				
9		184–186 dec	91	1460, 1408,	274 (9000)	7.80 (4 H, s)	$\mathbf{C}_{8}\mathbf{H}_{16}\mathbf{N}_{2}\mathbf{O}_{2}$	56.0	9.6	16.0
ŧ		(EtOH)		1335, 1275		8.41 (12 H, s)		55.8	9.4	16.3
11′		165 dec		1418, 1370,	275° (7400)	7.41^{d} (br s)				
				1320	<i>.</i>					
15	1	238-239 dec	23	1421, 1369,	273 (7400)	8.67 ^e (m), 7.49 (m),	$C_{11}H_{14}N_2O_2Cl_2$	47.4	5.1	10.1
		(acetone)		1295	<i>.</i>	6.73 (m)		48.0	5.2	10.2
16	1	241-242 dec	42	1410, 1375,	276 (5300)	6.6–7.3 (7 H, m)	$C_{11}H_{10}N_2O_2Cl_2$	48.4	3.7	10.3
		(acetone)		1270, 1241		7.7–9.2 (3 H, m)		48.6	3.7	10.2

^a KBr. ^b 96% EtOH. ^c CH₂Cl₂. ^d CDCl₃, DMSO-d₆. ^e DMSO-d₆. ^f Reference 18.

For the purpose of investigating the dimerization trajectory, the cis dioxide series 3 seemed ideal, since strain energies and thus ring-opening tendencies can be expected to vary markedly as a function of bridge size $[-(CH_2)_n]$.



The present report describes the preparation of series 2 (n = 1-4) and 3 (n = 1-4) and several closely related compounds by direct oxidation of azo precursors. A second azo dioxide series has been investigated by employing the nitroso dimerization route. In addition a preliminary evaluation of the thermal behavior of the dioxides has been undertaken.

Cis Azoxy Alkanes. The production of substances 2 (n = 1-4), **4a**, and **5a** by oxidation of the corresponding azo alkanes⁶ with *m*-chloroperbenzoic acid (MCPBA) in CH₂Cl₂ or CHCl₃ is unexceptional and proceeds in 70–96% isolated yields. For the cyclopropyl derivative **6a** it is necessary to



work at -10° , since the azo parent, generated in situ, has a half-life of 13 min at 12° .⁷

Bicycle 2 (n = 1) has been prepared in an identical fashion,⁸ while 2 (n = 1-4), 4a, and 6a as well as a variety of unsaturated cis azoxy alkanes may by synthesized by a single hydrolysis-oxidation procedure applied to triazoline-dione adduct precursors.⁹

Oxidation. Although azo alkanes are rapidly converted to the corresponding azo N-oxides by MCPBA (0-10°, CH_2Cl_2 , 1-3 hr), the latter when exposed to the same reagent for longer periods (25°, CHCl₃, 2 weeks) allows isolation of low to moderate yields of dioxides 6a (see Experimental Section) and 7.10b The transformation of pyridazines to pyridazine 1,2-dioxides by the action of 50% hydrogen peroxide in acetic acid,¹¹ albeit in poor yields, suggested that the generation of azo dioxides could be hastened by utilization of a similar procedure. Accordingly compounds 3 (n = 1-4), 4b, and 5b are conveniently prepared by peroxide oxidation of azo alkane precursors¹² (Table I). Substance 6b is similarly derived from the azoxy precursor 6a. In the case of dioxides 3 (n = 1, 2), 4b, and 6b the low yields simply reflect incomplete conversion under the conditions used. The corresponding monoxides 2 (n = 1, 2)and 4a are obtained in 70, 17, and 70% yields, respectively, from the same reaction. Likewise for the quadricycle 6b, 59% of the starting azoxy is recovered unchanged. The oxide mixtures are easily separated (see Experimental Section).

An unusual transformation occurred in an effort to prepare dioxide 9 by Na_2WO_4 -catalyzed peroxide oxidation of 2,5-diamino-2,5-dimethylhexane (7). This reagent mixture has been utilized for the conversion of *tert*-butylamine to the nitroso derivative in 24% yield.^{3b} Diamine 7 delivers only the monocyclic tetramethyl azoxy 8 (64%) and the corresponding azo alkane (21%). It appears that ring closure occurs after oxidation of only one of the amino groups either to the nitroso or the nitro function. Subsequent oxidation of monoxide 8 with MCPBA produces the desired azo dioxide 9.



The structures of the dioxides follow from their microanalyses, physical properties, and reaction with hexachlorodisilane. Each exhibits bands in the infrared between 1290 and 1500 cm⁻¹ characteristic of aliphatic cis nitroso dimers.^{2a,15,16} In the ultraviolet, series 3 shows the expected $\pi - \pi^*$ absorption between 265 and 271 nm (96% EtOH) with a slightly increasing λ_{\max} as *n* increases from 1 to 4. The proton NMR spectra are interpreted in a straightforward manner. Diagnostic are the broad α -nitrogen bridgehead resonances falling in the range τ 5.1–5.45. Not surprisingly, the dioxide values appear at slightly lower field than those of the corresponding monoxides $(\tau.5.3-5.45)$.^{9a,b} The natural abundance ¹³C spectrum of 3 $[n = 2, \delta (CH_2Cl_2, Me_4Si)$ 25.8 and 70.3 ppm] confirms that oxidation of 2 [$n = 2, \delta$ (CHCl₃, Me₄Si)^{9a} 23.9, 25.6, 57.7, and 71.7 ppm] introduces a molecular symmetry plane. The mass spectra of azo dioxides 3 (n = 1, 2) have already been discussed.¹⁷ The spectroscopic data are assembled in Table I. Finally, treatment of 3 (n = 2) with the effective deoxygenating agent hexachlorodisilane^{9a} leads cleanly to azo compound 1 (n =2) at room temperature.

In addition to compound 10^{10} and the pyridazine 1,2dioxides,¹¹ a number of cis 1,2-*N*,*N'*-dioxides have been previously described. In the acyclic series both thermally stable aromatic¹ and thermally unstable aliphatic^{15,16} examples have been generated from nitroso precursors. The cyclic aliphatic dioxide 11 is prepared similarly.¹⁸ Finally,



several unsaturated cases arise by cyclization, possibly by means of the intermediacy of the N-nitrosonitrone moietv.¹⁹

Dioxime Chlorination. The bridgehead halogen substituted bicycle 11 is prepared via the bis(nitrosocyclohexane) c-13 by chlorination of the corresponding dioxime.¹⁸



In order to comparatively evaluate the 11/13 equilibrium, we have attempted to exploit the dioxime halogenation route for the preparation of similar systems. Whereas the reaction of dioxime 12 proceeds cleanly in concentrated HCl to give an easily separated mixture of the cis and trans dichlorodinitroso compounds c-13/11 and t-13, respectively,¹⁸ it is not generally applicable to other cyclic dioximes. Dichloro N,N'-dioxides 15 (n = 1) and 16 (n = 1) are, however, accessible in 23 and 42% yields from the latter precursors.

For azodioxy 15, the transformations are outlined in Scheme I. Dioxime 17 suspended in ethyl acetate leads to two substances when treated with chlorine gas. The first is a thermally labile blue solid. All attempts at further purification led only to the recovery of tarry material. The substance exhibits several characteristic bands in the infrared: λ_{max} (KBr) 3160 (broad, OH, intramolecular H-bonded),



a n = 1.



1545 (N=O), 935 cm⁻¹ (N-O, oxime). Elemental analysis is in accord with the oxime chloro nitroso structure 18. The observed lability of the latter was encountered in several other instances to be mentioned below.

A second high-melting material (238° dec) is assigned the azo dioxide structure 15 and is presumed to arise via the intermediacy of dinitroso 19. Its physical properties conform to those of the cis dioxides described in the previous section (cf. Table I). In addition N-oxide 20 is derived by deoxygenation with hexachlorodisilane. Dioxide 11 (X = Cl) is similarly reduced with this reagent to the corresponding monoxide.

The stereochemistry of dioxide 15 has not been unambiguously established. However, molecular models suggest that approach by chlorine on dioxime 17 is least hindered outside the molecular cusp. The resulting bis nitroso species 19 would consequently lead to compound 15. Conversely, the formation of epimer 21 can in principle deliver azo dioxide 22, a system which can be anticipated to experience serious nonbonded hydrogen interaction. A van der Waals radius of 1.5 Å implies that a nonrepulsive hydrogen-hydrogen distance as measured from the center of electronic charge would be ≥ 3.0 Å. The distance estimated for the circled hydrogens of 22 from Dreiding models is 0.4-0.6 Å. Analogous steric congestion is completely absent in structure 15.²⁰ We consequently prefer formulation 15 over 22.

The proton NMR spectra of dioxide 15 and that of azoxy 20 are consistent with the assignment. Consider first the spectra of series 1-3 (n = 2).

While it is known that the azo function in a diazirine ring exerts a considerable shielding effect on a proton above the N=N plane,²² no comparative correlations have been tabulated for the related oxides. It is, however, evident that N-



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oxidation leads to a clear-cut downfield shift for protons lying above the heavy atom plane.²³ Azo dioxide 15 (n = 1)exhibits its highest field absorption as a multiplet centered at τ 8.67 (DMSO-d₆, Me₄Si), while the corresponding value for N-oxide 20 is τ 8.56 (CDCl₃, Me₄Si). The endo hydrogens for norbornane fall at τ 8.82.²⁴ Structures 15 and 20 consequently suggest a deshielding of the latter by about 0.2 ppm in accord with the pattern observed for 1–3.

Alternatively, the downfield shifts might be attributed to van der Waals effects in dioxide 22. However for two bound hydrogens separated by 1.7 Å the deshielding effect is calculated to be >0.5 ppm,²⁵ a factor which might well be enhanced in the latter considering the H–H separation estimated above.

The polycyclic dioxide 16 can be obtained as outlined in Scheme II. The dihydrochloride of hydrate 25 (Z = O, mp 50°) has been reported as the single product (100% yield) from the reaction of hydroxylamine hydrochloride with diketone 23 in the presence of hydroxide.²⁶ In our hands the same conditions led to a high-melting, insoluble product (310-320° dec) which contains no chlorine but analyzes for structure 24. Substitution of pyridine for OH⁻ caused no change in the product composition. Acetylation results in diacetate 26 in essentially quantitative yield. There is no doubt that oxime 24 has indeed been isolated.

The oxime product suspended in CH_2Cl_2 was treated with chlorine. The resulting blue solution delivers the colorless, crystalline dioxide 16. The infrared and ultraviolet spectra (Table I) confirm the structure. Accordingly, disilane reduction leads to azoxy 27.

Several other unsuccessful attempts to generate α, α' -dichloro cis azo dioxides were made. For example, with cyclo-



Polycyclic Cis Azo N,N'-Dioxide Synthesis

		-				-	•	
	R	ΔE_{strain}^{b}	∆ <i>H</i> , kcal/mol	∆S,eu	$T\Delta S$, kcal/mol	∆G,kcal/mol	$K_{eq} \times 10^7$, mol/1.	$K_{eq} \times 10^7$
i	tert-Butyl	9-10	11.8°	41.5	12.2	-0.38	1.92×10^7	
ii	$CH_3CO(CH_3)_2C$	2-3	18.9^{d}	40.9^{f}	12.0	6.9	68.6	
iii	$c - C_{e}H_{11}$	<u> </u>	20.6^{d}	39.2^{f}	11.5	9.1	1.55	
	0 11	0.0	24.8^{e}	52.5	15.4	9.4	0.96	
	$C_{e}H_{5}CH_{2}$	0.0	20.4^{d}	34.3^{f}	10.1	10.4	0.187	
iv	3 : bicycle a	0.0	22.0	7.5	2.2	19.8		$1.6 imes10^{-8}$
	n = 1	16.1	5.9	7.5	2.2	3.7		$1.7 imes 10^4$
	n = 2	14.3	7.7	7.5	2.2	5.5		$7.8 imes10^2$
	n = 3	12.3	9.7	7.5	2.2	7.5		$2.5 imes 10^1$
	n = 4	22.1	-0.1	7.5	2.2	-2.3		$5.2 imes10^8$
	9	6.0	16.0	15.0	4.4	11.6		2.2 $ imes$ 10 ⁻²
	10	30.0	-8.0	5.0	1.4	-9.4		$1.1 imes 10^{14}$
	10'	19.3	2.7	5.0	1.4	1.3		$1.0 imes 10^6$

 Table II

 Thermodynamic Quantities for the Azo Dioxide–Nitroso Equilibrium, 20° a

^a Categories i, ii, and iii list experimental values; category iv includes only estimated values (see text). ^b E_{strain} (azo dioxide) – E_{strain} (nitroso). ^c Reference 3b, solvent CCl₄. ^d Reference 3a, solvent benzene. ^e Reference 4e, solvent decane. ^f Recalculated for dilute solution³⁶ using the expression $\Delta S = \Delta U/T + R \ln K_c$. ^g Corrected by a factor of 0.1; cf. ref 3a.

hexadiene as ultimate precursor, dioxime 17 (n = 2) was prepared. Excess chlorine delivers only the half-converted nitroso oxime 18 (n = 2). In the case of the polycyclic diketone 23 (n = 2) oximation leads to a high-melting solid which analyzes for 25 (n = 2, Z = NOH). Given the propensity for 23 (n = 2) to form a hydrate,²⁰ this result is not surprising. Chlorination of 25 in concentrated HCl as well as in organic solvents results in blue products, none of which provided the desired dioxide. The same conditions were applied to 1,3-cyclohexanedione dioxime 28. Evidence for the formation of nitroso oxime 29 and its conversion to 30 was gathered. Again no N,N'-dioxide could be isolated.



Nitroso Dimerization and Azo Dioxide Dedimerization. The existence of a facile equilibrium between nitroso monomers and the corresponding dimer is well documented. While unhindered aromatic derivatives are monomeric in solution, appropriate ring substitution promotes an ambient equilibrium mixture containing significant quantities of both monomer and dimer.³ Dissolved alkylsubstituted nitroso compounds, RNO, are generally dimeric at room temperature unless R is either bulky [t-BuNO,^{3b} (CH₃)₃CH₂(CH₃)₂CNO,^{3b} Et(CH₃)₂CNO^{4a}] and/or contains an electronegative substituent $[Cl(CH_3)_2CNO, {}^{18,27}]$ F(CF₃)₂CNO²⁸]. Several studies demonstrate nonetheless that simple aliphatic dimers are readily equilibrated with the nitroso monomer. In particular acyclic cis-nitroso dimers are rapidly converted into the trans isomers in solution at room temperature or below.4g,16,29 The characteristic blue nitroso color is obtained by refluxing organic solutions of either isomer.^{4c,f,29} Finally, spectrophotometry in the visible region has been utilized for collection of thermodynamic quantities for the nitrosocyclohexane and related equilibria.3a,4f

Attempts to obtain equilibrium data for series 3, 4b, 5b, and 6b have been frustrated by the complete absence of evidence for the systems' nitroso component. The azo dioxides in boiling organic solvents, be they polar or nonpolar, hydroxylic or aprotic, remain colorless up to the decomposition point ($\leq 250^\circ$). Similarly, in the solid state, slow warming leads only to charring in every case without the intermediate development of color.³⁰

These observations stimulated our preparation of the dichloro-bridgehead cases 15 and 16. Azo dioxide 11 on warming in a variety of solvents reversibly develops a deep blue color indicative of ring opening to give dinitroso $31.^{18}$



The preparation of both 15 and 16 involves preformation of either blue solutions or blue solids which give way upon warming or dissolution to colorless dioxides (see Experimental Section). However, as found for the unchlorinated azo dioxides, once formed neither 15 nor 16 can be coaxed to color either in the solid state or in solution prior to decomposition.³⁰

Clues to an understanding of the failure to observe monomer from the polycyclic cis dioxides described above may be gained by inspection of the thermodynamic quantities gathered in Tables II and III. Consider first the equilibrium data of Table II. Of greatest significance is the fact that the first four experimental cases all involve a very large entropy term which contributes 10-16 kcal/mol (i.e., $T\Delta S$) to the free energy of the monomeric equilibrium partner. Since the measurements were taken in nonpolar media (C_6H_6 , CCl_4 , decane), the bulk of the entropy value is not attributable to solvent orientation effects and must be assigned to substrate reorganization.³¹ In spite of this only the tert-butyl case exists predominantly as the monomer in solution. Since ΔS is nearly constant for the experimental series, the ΔH contribution to ΔG is the factor responsible for the relative K_{eq} values. Its variation may be rationalized by considering the effect of substituents on the nitroso dimer. The alkyl functions can be classified into three groups according to relative size. Conformation 32 is illustrative.³² \mathbb{R}^2 : i > ii > iii. Along this series the dimin-

Table III Activation Parameters for the Nitroso Dimer $[(RNO)_2]$ Dissociation: Dimer $\rightarrow 2$ Monomer 20°

	Dissociut	Jon. Dimer	2 IVI01	iomer	, 20	
	R	∆H [‡] ,kcal/mol	∆ S [‡] , eu	<i>T∆S</i> ‡, kcal/ mol	Δ G[‡], kcal/ mol	Solvent
i	$CH_3CH_2(CH_3)_2C$	24.3 ^a 21.9-23.2 ^b	9.4	2.8	21.5	Benzene
	$\begin{array}{c} AcOCH_2(CH_3)_2C \\ (CH_3)_3C \\ AcCH_2(CH_3)_2C \end{array}$	25.8^a 21.5^b 23.4^c	16.0	4.7	21.1	Benzene Benzene Benzene
ii	$Ac(CH_3)_2C$	29.6^d 27.7	$\begin{array}{c}18.6\\13.2\end{array}$	5.5 3.9	24.1 23.8	$CC1_4$ c-C ₆ H ₁₂
iii	$C_6H_5CH_2$	35.8 ^e 27.7	$\begin{array}{c} 27.8 \\ 11.8 \end{array}$	8.1 3.5	$\begin{array}{c} 27.7 \\ 24.2 \end{array}$	$CC1_4$ c-C ₆ H ₁₂
	$c-C_6H_{11}$ $(CH_3)_2CHCH_2$ CH_3	33.1^r 26.0 ^s 21.8 ^s				Decane Gas phase Gas phase

^a Reference 4b. ^b E. Bamberger and R. Seligman, *Chem. Ber.*, **36**, 685 (1903), computed in ref 4c. ^c Reference 4a. ^d Reference 4d. ^e Reference 4e. ^f Reference 4f. ^g Reference 4c.

ishing dissociation tendency parallels the increase in ΔH . If grouping iii is taken as "unstrained", the *tert*-butyl derivative is seen to incorporate 9–10 kcal/mol of strain energy.³³



The influence of molecular crowding is felt in the dissociation rates for the nitroso dimer as well (Table III). The cases tabulated are ones studied either in the gas phase or in nonpolar solvents. Activation energies are somewhat less in polar media^{4d} and anomalously high in water.^{4e} For groups i, ii, and iii, the ΔG^{\ddagger} ranges are 21.1–21.5, 23.8–24.1, and 24.2–27.7 kcal/mol, respectively. The entropy contribution is relatively constant, ΔH^{\ddagger} controlling relative rates.

No thermodynamic values have yet been recorded for polycyclic cis azo dioxides such as 3. In the discussion to follow both entropy and strain energy values are estimated from literature data. The resulting K_{eq} and k trends are analyzed in terms of the observed cyclic N,N'-dioxide behavior. The nitroso azo dioxide equilibrium will be considered first.



Difference method estimates³⁵ suggest that ring opening exemplified by $3 \rightarrow 33$ can be associated with $\Delta S = 5-10$

eu. An intermediate value of 7.5 eu will be employed here. Thus for a "strainless" system, bicycle a (3, $\Delta H = 22.0$ kcal/mol, the average value of entries 3-5, column 2, Table II), a free-energy difference of 19.8 kcal/mol is calculated. The corresponding equilibrium constant indicates that for a 0.01 M solution there would be approximately 10^{12} fewer moles of cyclic dinitrosoalkane in equilibrium with bicycle a at 20° than moles of nitrosocyclohexane in equilibrium with its dimer at the same temperature³⁷ (cf. Table II). Increased temperature will not ameliorate the situation. Figure 1 exhibits a plot of the decrease in ΔG as a function of temperature for both bicycle a and the cyclohexane derivative.³⁸ For the latter the free-energy difference drops steadily with temperature until it becomes zero around 200°. Indeed the cyclohexylnitroso dimer has been found to be 42% dissociated at 130°.^{4f} On the contrary, ΔG for bicycle a decreases at a much slower rate over the same temperature range.³⁹ This difference is due almost entirely to the effect of temperature on the $T\Delta S$ term: cyclohexyl, $T\Delta S$ (0 \rightarrow 300°) = 14.1-30.1 kcal/mol; bicycle a, $T\Delta S$ (0 \rightarrow 300°) = 2.1-4.3 kcal/mol. It should be noted that the slope of the lines plotted in Figure 1 is a direct measure of ΔS . Figure 2 depicts the situation in another way by illustrating the behavior of $\ln K_{eq}$ as a function of the reciprocal of the temperature. Thus for a "strain-free" bicycle 3, the absence of a considerable equilibrium entropy contribution can be expected to prevent observable nitroso formation even at elevated temperatures.

For most of the substances listed in Table I the strainfree model is not directly applicable. Since the dissociation of trans *tert*-butyl azo dioxide is strongly affected by steric congestion, angle strain in 3 should in principle exert a similar influence on the cyclic azo dioxide-nitroso equilibrium partition. Accordingly, two mechanistically different interpretations, one kinetic and one thermodynamic (i.e., entropy control as outlined above), will accommodate the experimental observations. In order to assess them it is necessary to derive strain energy values for the cyclic and bicyclic azo dioxides.

Strain Energies. For the purpose of estimating the relief of strain in the 3/33 system, we assume a qualitative parallel between the strain energies of azo dioxides 3 (n =1-4) and those of the corresponding unsaturated hydrocarbons. In order for this assumption to be valid, a knowledge of the force constants associated with the bending of the CNN angle of 3 relative to a corresponding CCC angle would be useful. While azo oxides have yet to be evaluated, several comparisons between trans azo compounds and their isoelectronic carbon counterparts have been made using a common force field. In every case the CNN bond is tighter than the corresponding CCC bond.⁴⁰ The consequence of N-oxidation is suggested by a comparative study of acetonitrile ($F_{\rm CCN} = 0.265$ mdyn-Å/rad²) and acetonitrile N-oxide ($F_{\rm CCN}$ = 0.397 mdyn-Å/rad²).⁴¹ To a first approximation hydrocarbon strain energies would thus seem to represent at least lower strain limits for the cyclic and bicyclic azo dioxides.

Recent force-field calculations estimate strain energies for norbornene and bicyclo[2.2.2]octene to be 23.6 and 16.0 kcal/mol, respectively.³⁴ By utilizing data from the tables of Engler et al.⁴² and applying Allinger and Sprague's E_{strain} (alkane – alkene) values,³⁴ 20.3 and 33.6 kcal/mol can be derived for the strain energy content of bicyclo-[3.2.2]nonene-2 and bicyclo[4.2.2]decene-2, respectively. Subtracting the strain associated with the simple cycles^{34,43} **33**, bicycle **3** is estimated to contain the residual strain energies, ΔE_{strain} , listed in Table II affecting the position of the **3/33** equilibrium. Similarly, dioxide 9 is estimated to contain 6 kcal/mol strain based on the values for cyclohexene and 3-methylcyclohexene.³⁴ Finally, the thermally stable four-membered ring azo dioxide 10 must be considered. The strain energy of cyclobutene has recently been placed at 30.6 kcal/mol.⁴⁴ However, in addition to the four ring, 10 incorporates two eclipsing interactions between vicinal methyl groups.⁴⁵ A reasonable strain estimate might be 30–35 kcal/mol. In view of the congestion in the ring-opened isomer, 2,3-dimethyl-2,3-dinitrosobutane, a $\Delta S = 5$ eu is assigned to the ring opening.

If the strain energy appraisals derived above are meaningful and 22.0 kcal/mol represents a near-strain-free ΔH for the azo dioxide-nitroso equilibrium, then ΔH for the latter can be set from -8.0 to 16.0 kcal/mol for **3**, **9**, and **10** as indicated in category iv in Table II. The corresponding ΔG 's and $\ln K_{eq}$'s are plotted as a function of temperature in Figures 1 and 2.

Least-Motion vs. Non-Least-Motion Azo Dioxide Fragmentation. Taking the results of Figures 1 and 2 at face value, the incorporation of ring strain in the azo dioxides, a minimal entropy contribution notwithstanding, is predicted to lead to favorable equilibrium constants ($K_{eq} \geq$ $(10^{-3})^{30}$ for n = 1, 2 above 100°. Dioxide 3 (n = 4) ought to mimic the room-temperature behavior of the colorless tertbutyl nitroso dimer. As mentioned above, dissolving the latter in organic solvents leads to a spontaneous production of the blue monomer ($\Delta G = -0.38$ kcal/mol). The situation for four-ring 10 ($\Delta G = -9.4$ kcal/mol) should be further exaggerated in K_{eq} by nearly 10⁶. Furthermore, if the above generalization concerning strain and dissociation rates (Table III) likewise holds in the bicyclic series, activation energies for dedimerization should diminish progressively from bicycle a to compound 10.

To recapitulate, with the exception of dioxide 11 none of the cis cyclic azo dioxides described in this report,⁴⁶ including the bridgehead chlorinated ones, yield nitroso monomer in solution at accessible temperatures ($\leq 250^{\circ}$).⁴⁷ The fact that predicted equilibrium properties of cyclic azo dioxides are in conflict with observation suggests a kinetic origin for the lack of ring opening. Unlike the acyclic nitroso dimers the behavior of substances 3 and 10 seems to reflect *enhanced* activation barriers to fragmentation with increased ring strain. A nonlinear decomposition pathway⁵ can be anticipated to introduce considerable geometric constraint in the transition state for a rigid system. Were the dissociation to proceed by a linear motion, there is little doubt that ring opening would parallel strain energy.

Inspection of molecular models indicates that for 3 and 16 [and possibly 3 (n = 2) and 15 as well] the computed low-energy pathway is difficult to achieve. On the contrary, models suggest no unambiguous reason why the twisted transition state cannot be attained by 3 (n = 3, 4) and 10. The chloro-substituted case 11 is interesting and argues that for 3 $(n \ge 2)$, if the non-least-motion mechanism is operating, the required transition state can indeed be reached. Alternatively, the introduction of strongly electronegative substituents may in fact alter the stereochemical requirements of the activated complex.

Entropy Control. In view of the above strain estimates, the existence of the four-ring azo dioxide 10 is surprising. It signals that a positive contribution by the N-N bond energy is suppressing ring destruction. Assuming for this compound $K_{eq} = 1$ and $\Delta S = 5$ eu, a $\Delta H = 2.7$ kcal/mol for ring opening is derived (10', Table II). The latter implies a strain energy of about 20 kcal/mol, 10-15 kcal/mol less than that obtained from the hydrocarbon estimate. If this result were to carry over to all the models listed in Table II



Figure 1. The influence of temperature on the free energy of dissociation for the nitrosocyclohexane and the 2-methyl-2-nitrosopropane dimers and several cyclic azo dioxides (cf. Table II).



Figure 2. Variation of the equilibrium constant for the azo dioxide-nitroso equilibrium as a function of temperature (K) (cf. Table II).

(category iv), the conclusion that ring opening is prevented primarily by the absence of an appreciable ΔS is inescapable.

Conclusion

Entropy plays an important and in some cases a decisive role in suppressing the cleavage of nitroso dimers in the cyclic series. For substances normally considered to be highly strained, entropy effects can in principle be overridden by strain effects. The apparent absence of the influence of the

Table IV

Compd	Mp, [°] C (recrystn solvent)	Yield, %
2(n = 2)	158–159 (EtOH)	89
2(n = 3)	175—176 (hexane)	94
2 $(n = 4)$	133–134 (hexane)	98
4 a	48–49 (Et ₂ O)	87
5a	$131 - 137 (CCl_4)$	70
6a	137–138 (EtOH)	86

latter may be rationalized in kinetic or thermodynamic terms. Either the transition state for azo dioxide dedimerization is even more congested than the ground state (via a non-least-motion pathway) or cyclic cis azo dioxides are far less strained than their unsaturated hydrocarbon counterparts in spite of force constant data to the contrary. The present analysis provides no unambiguous choice between the alternatives but does suggest certain illuminating experiments. Further work is in progress.

Experimental Section

General. Microanalyses were performed by Scandinavian Microanalytical Laboratory, Herlev, Denmark, and The Microanalytical Laboratory, Kemisk Laboratorium II, The H. C. Ørsted Institute, University of Copenhagen. Melting points were measured on a Thomas-Hoover apparatus and a Büchi instrument and are corrected. Infrared (ir) spectra were recorded on Perkin-Elmer Models 257 and 337 grating spectrophotometers. The nuclear magnetic resonance (NMR) spectra were obtained with Varian A-60 and Bruker HX-90E (¹³C) spectrometers. Ultraviolet spectra were taken on Cary 15 and Unicam SP-1800 recording spectrophotometers. Except where noted solvents were reagent grade and were used as received.

The following is a general procedure for stable azoxy alkanes.

Phosphate Buffer. Stock solutions of 0.2 M NaHPO₄ and 0.2 M Na₂HPO₄ were prepared. The phosphate buffer of pH 7.5 was prepared using 31 ml of 0.2 M NaH₂PO₄ and 69 ml of Na₂HPO₄, then diluting to a final volume of 200 ml.

2,3-Diazabicyclo[2.2.2]oct-2-ene N-Oxide, 2 (n = 2). A stirred solution of 2,3-diazabicyclo[2.2.2]oct-2-ene⁶ (4.3 g, 39 mmol), mp 139–140°, in CH₂Cl₂ (75 ml) cooled to 10° was treated dropwise with MCPBA (98%, 7.6 g, 55 mmol) dissolved in CH₂Cl₂ (175 ml). After one-half of the addition was complete, a white percipitate formed which persisted throughout the reaction. At the end of the addition, which consumed 1.5 hr, 100 ml of a phosphate buffer solution, pH 7.5, was added in one portion and the reaction mixture was stirred for an additional 1.0 hr. The excess oxidant was destroyed with the dropwise addition of 2 M sodium bisulfite solution, and then the pH was adjusted to 9.0 with 2 M Na₂CO₃. The organic layer was separated, washed with 2 × 75 ml of NaCl solution, dried (MgSO₄), and the solvent removed in vacuo to yield a white solid (4.6 g). Recrystallization from EtOH afforded white crystals, 2 (n = 2) (4.1 g), mp 158–159°. A second crop was obtained from the mother liquor (0.3 g, total 4.4 g, 35 mmol, 89%).

6,7-Diazatricyclo[3.2.2.0^{2.4}]non-6-ene N-Oxide, 6b. All operations were carried out below 0°.

The following solutions were prepared and cooled to -10° with a NaCl-ice bath: 500 ml of NaCl solution, 500 ml of CH₂Cl₂, and 150 ml of concentrated NH4OH. To concentrated NH4OH (150 ml) at was added 6,7-diazatricyclo[3.2.2.0^{2.4}]non-6-ene-cuprous -10° bromide complex⁶ (17.4 g, 50.0 mmol) with stirring. The solution became blue, then blue-green, and agitation was required to effect complete solution. The reaction mixture was extracted in a precooled separatory funnel with cold CH_2Cl_2 (2 × 200 ml), and the organic extract was washed with cold NaCl solution (4 \times 100 ml), dried (MgSO₄), filtered, and added to a 1-l. three-neck flask fitted with an overhead stirrer, a low-temperature thermometer, a dropping funnel, and an external cooling bath (Dry Ice-acetone). Stirring was initiated as the solution was cooled to -30° , and a solution of MCPBA (95%, 10.0 g, 55 mmol) dissolved in CH₂Cl₂ (175 ml) was added dropwise. Addition consumed 1.0 hr and the reaction mixture, which was stirred for an additional 1 hr at 0°, contained excess MCPBA (starch-iodide probe).

Work-up as above afforded an off-white solid (6.25 g), mp 132-133°. Recrystallization from EtOH deposited white needles of 6b

(4.16 g) and a second crop (1.78 g, total 5.94 g, 43.0 mmol, 86%), mp 137–138°.

Compounds 2 (n = 1, 2) and 4a are likewise obtained from the azo dioxide forming reaction described below (Table IV).

The N-oxides are identical in all respects with those previously reported.^{9b}

Synthesis of Azo Dioxides with Peracetic Acid. The following is a general procedure.

2,3-Diazabicyclo[2.2.2]oct-2-ene 2,3-N,N'-Dioxide. To a 250-ml flask, fitted with a reflux condenser and an external oil bath, was added 2,3-diazabicyclo[2.2.2]oct-2-ene [1 (n = 2)], 5.5 g, (50 mmol), mp 139-140°, dissolved in reagent grade glacial acetic acid (50 ml), 50% H_2O_2 (50 ml), and concentrated H_3PO_4 (2 drops). The water-white solution was heated at 100° for 6.0 hr, and to ensure an excess of peroxide the solution was periodically tested with starch-iodide paper. If the solution darkened, which was normally a sign of insufficient peroxide, or tested weakly positive to starchiodide paper, an additional 100 ml of 50% H₂O₂ was added, and the solution was heated until a light yellow color was maintained. At the end of the reaction, the solution was cooled to 35° and the excess oxidant was destroyed with small additions of 1 M sodium bisulfite solution. The acetic acid and the water were removed at low pressure, leaving a white slurry which was dissolved in H₂O (20 ml), and the pH adjusted to 10.0 with $2 M \text{ Na}_2\text{CO}_3$. The aqueous phase was extracted with methylene chloride $(3 \times 75 \text{ ml})$. The organic phase was washed with saturated NaCl (3 \times 50 ml), dried (MgSO₄), and filtered, and the solvent was removed in vacuo, leaving an off-white solid, whose NMR showed two peaks at τ 5.50 (azoxy) and 5.28 (dioxide) in the ratio of 1:3. The crude solid was triturated with ether $(3 \times 50 \text{ ml})$, removing the azoxy (1.08 g, 8.6 s)mmol, 17%) and leaving a powdery, white solid. Recrystallization from ethanol, after treatment with charcoal, afforded a white, crystalline solid, 2.1 g, and a second crop, 0.8 g (20 mmol total, 41%: based on recovered azoxy, 85%), mp 221-222° dec.

Procedural changes where they are necessary for the other azo dioxides are as follows.

Azoxy Alkane 2 (n = 1) and Azo Dioxide 3 (n = 1). After the reaction solution was heated at 100° for 12 hr an additional 35 ml of 50% H₂O₂ was added and the reaction continued for 8 hr. Workup as above furnished a white solid, the NMR of which showed two peaks at τ 5.40 (azoxy) and 5.23 (dioxide) in the ratio of 5:1. Trituration of the crude product with ether (8 × 50 ml) left a chalky, white solid. The ether was dried (MgSO₄), filtered, and stripped in vacuo to yield a hygroscopic solid. Recrystallization (dry ether) with rapid filtration of the crystalline product under dry nitrogen afforded a white solid 2 (n = 1), mp 96–97° (70%). The material is hygroscopic and volatile. Drying under vacuum will lead to substantial, if not complete, loss. The N-oxide can be stored at atmospheric pressure under nitrogen.

The ether-insoluble white solid was recrystallized from EtOH, 3 (n = 1) (16%; based on recovered azoxy, 60%).

Azo Dioxide 3 (n = 3, 4). Work-up as above led to crude products which by NMR were completely free of the azoxy intermediate. The ether trituration step can thus be eliminated.

Azo Dioxide 6b. Azoxy 6a (1.0 g, 7.2 mmol), mp 136–137°, and MCPBA (98%, 2.5 g, 14 mmol) were dissolved in CHCl₃ (75 ml) and stirred magnetically at 85° for 5.0 hr. Work-up of the yellow solution proceeded as above, yielding a pale white solid (0.84 g), the NMR of which showed two bands at τ 5.50 (dioxide) and 5.30 (azoxy) in the ratio of 1:3. Trituration of the solid with ether (4 × 50 ml), then warm hexane (4 × 50 ml) led to the soluble azoxy alkane (0.52 g, 57%) and an insoluble white solid. Recrystallization from a minimum amount of ethanol yielded a white solid 6b (0.32 g, 2.1 mmol, 30%; based on recovered azoxy, 64%). Azo dioxide 6b may also be obtained in somewhat better yield (51%) by allowing the oxidation to proceed at room temperature for 5 days [MCPBA: azoxy alkane (3:1), CHCl₃].

The physical properties of the azo dioxides are tabulated in Table I.

Preparation of 3,3,6,6-Tetramethyl-1,2-diazacyclohexene N-Oxide (8). A solution of 2,5-diamino-2,5-dimethylhexane (14.4 g, 100 mmol) and Na₂WO₄·2H₂O (0.987 g, 3.0 mmol) in water (20 ml) was cooled in an ice bath to 0°. Initial dropwise addition of H_2O_2 (30%, 45.3 g, 400 mmol) gave a highly exothermic reaction after a 5–10-min induction period. The temperature of the reaction mixture was maintained between 15 and 25° by ice cooling and slow addition. After final addition and stirring at 25° for an additional 1 hr, the reaction mixture was extracted with methylene chloride (2 × 150 ml), and the organic phase was washed with 1 N HCl (2 × 50 ml) and saturated NaCl solution (2 × 50 ml), dried

PLC chromatography of 1.0 g of the crude product on 20×100 mm, 2.5 mm silica gel and elution with ether (once) effected separation of the mixture. The more polar component $(R_f 0.3, \text{ ether})$ yielded a white solid, 8 (0.720 g, 64 mmol, 64%): mp 120-121 (ether); NMR (CDCl₃, Me₄Si) τ 7.8-8.4 [4 H, complex, -(CH₂)₂-], 8.40 (6 H, singlet, CH₃), 8.65 (6 H, CH₃); ir v_{max} (KBr) 1450, 1470 cm⁻¹; uv λ_{max} (96% EtOH) 233 nm (ϵ 6200).

Anal. Calcd for C₈H₁₆N₂O: C, 61.5; H, 10.3; N, 17.9. Found: C, 61.5: H. 10.5: N. 18.4.

The less polar component from 0.7 g of crude product (PLC, ether) yielded a light yellow-green oil with a camphorous odor, 3,3,6,6-tetramethylazocyclohexane (0.15 g, 21 mmol, 21%): NMR (CDCl₃, Me₄Si) 7 8.50 [4 H, singlet, -(CH₂)₂-], 8.68 (12 H, singlet, CH₃); ir ν_{max} (thin film, NaCl) 1560 cm⁻¹; uv λ_{max} (hexane) 379 nm $(\epsilon 150).$

Anal. Calcd for C₈H₁₆N₂: C, 68.5; H, 11.5; N, 20.0. Found: C, 68.0; H, 11.3; N, 19.7.

Preparation of 3,3,6,6-Tetramethylazocyclohexane 1.2-N,N'-Dioxide (9). To a stirred solution of azoxy 8 (0.468 g, 3.0 mmol) in methylene chloride (150 ml) cooled to 10° was added dropwise a solution of MCPBA (85%, 1.18 g, 6.0 mmol) in methylene chloride (25 ml). A slight exothermic reaction was noted during addition, and the mixture was stirred for 9.0 hr. The excess peracid was destroyed with careful addition of 1.0 M sodium thiosulfate, the pH was adjusted to 7.0 with 2 M NaHCO₃, and the organic phase was washed with saturated NaCl (3×100 ml), dried $(MgSO_4)$, filtered, and the solvent removed in vacuo to yield a white, crystalline solid, 9 (0.470 g, 2.7 mmol, 91%). TLC indicated only one spot, R_i 0.0 (Et₂O). See Table I for the physical constants.

Hexachlorodisilane Reduction of Azo Dioxide 3 (n = 2). Azo dioxide 3 (n = 2) (43 mg) dissolved in CDCl₃ (400 mg) was treated at intervals with a drop of Si₂Cl₆. Each addition led to an exothermic reaction at room temperature. The mixture was monitored by proton NMR. Characteristic is the change in the bridgehead region. Initially only the dioxide peak at τ 5.25 was present. The first addition of disilane caused an instantaneous appearance of the monoxide at τ 5.50 (2, n = 2). With additional reagent the dioxide band disappeared, the monoxide peak grew in intensity, and the azo alkane resonance at τ 4.91 became evident (1, n = 2). The changes continued until only azo alkane absorption remained. Corresponding changes in the spectrum between τ 7.5 and 8.9 were likewise observed.

Dichloro Azo Dioxide 15 and Chloro Nitroso Oxime 18 (n =1). Dry chlorine gas was bubbled into an ethyl acetate (20 ml) suspension of dioxime 17 $(n = 1)^{49}$ (1.0 g, 4.8 mmol) at 0° for 30 min. The mixture turned blue within a few minutes as the dioxime dissolved. A blue solid formed gradually during the chlorine treatment. The mixture was filtered and the blue solid (18) was washed with a NaHCO₃ buffer (pH 7) and water and then dried on a porous plate (200 mg, 0.82 mmol, 17%), mp 127-128°. Attempted recrystallization and chromatography led to decomposition; ir, see text.

Anal. Calcd for C11H15N2O2Cl: C, 54.4; H, 6.2; N, 11.5. Found: C, 54.7; H, 6.3; N, 11.6.

The blue-green filtrate was washed with 2 N NaOH (2×20 ml), then water, dried (MgSO₄), and stripped of solvent in vacuo to white crystals (15, 300 mg, 1.1 mmol, 23%): mp 237-238° dec; physical data, see Table I. Anal. Calcd for C₁₁H₁₄N₂O₂Cl₂: Cl, 25.2. Found: Cl. 25.6.

Dichloroazoxy Alkane 20 (n = 1). Dioxide 15 (100 mg, 0.36 mmol) suspended in CH₂Cl₂ (25 ml) was treated with hexachlorodisilane at 25° (excess), whereupon starting material dissolved completely. After 10 min the mixture was quenched with water, extracted with CH_2Cl_2 (3 × 20 ml), dried (MgSO₄), and stripped in vacuo to pale yellow crystals, which were recrystallized twice from methanol and washed once with a small amount of dry ether to obtain white crystals (20): mp 165-166° (108 mg, 0.41 mmol, 57%); ir λ_{max} (KBr) 1460 (N–O), 1425, 1286 cm⁻¹ (N–O); NMR (CDCl₃, Me₄Si) τ 6.9–7.6 (4.5 H, m), 7.7 (3.5 H, broad s), 8.1–9.0 (6 H, m); uv λ_{max} (96% EtOH) 237 nm (ϵ 6300); NMR (CDCl₃, Me₄Si) τ 7.29 (4 H, m), 7.67 (4 H, s), 8.56 (6 H, m).

Anal. Calcd for C₁₁H₁₄N₂OCl₂: C, 50.6; H, 5.4; N, 10.7. Found: C, 50.4; H, 5.5; N, 10.9.

Deoxygenation of Chloro Dioxide 11. Dioxide 11¹⁸ (ca. 50 mg) in $CDCl_3$ in an NMR tube was treated with Si_2C_6 (3-4 drops) at room temperature. A multiplet at τ 7.6 characteristic for the N $oxide^{50}$ appeared immediately. Additional Si_2Cl_6 caused no further change. The CDCl₃ solution was washed with water, extracted with

CH₂Cl₂, dried (MgSO₄, and stripped in vacuo to white crystals: mp 185-186° (lit.⁵⁰ mp 186°); NMR (CDCl₃, Me₄Si) 7 7.6 (m) [lit.⁵⁰ 7 7.9 (m)]

Dioxime 24 (n = 1). Diketone 23²⁶ (3.7 g, 2.1 mmol), hydroxylamine hydrochloride (2.8 g, 40 mmol), and 1 N NaOH (40 ml) in absolute ethanol (200 ml) were refluxed for 1 hr. The cooled solution was concentrated to a small volume in vacuo. The resulting white solid was filtered and recrystallized from H₂O-EtOH as white crystals: mp 310-320° dec (3.3 g, 1.6 mmol, 77%); no chlorine (Beilstein test); ir v_{max} (KBr) 3150 (broad, OH), 1705, 1660, 1425. 900 cm⁻¹ (N-O, oxime).

Anal. Calcd for C11H12N2O2: C, 64.7; H, 5.9; N, 13.7. Found: C, 64.8; H, 6.0; N, 13.9.

Substitution of pyridine for 1 N NaOH (4 M excess of NH₂OH. HCl, 2 hr reflux) led to a white solid, mp 304° dec (79%), with the same elemental composition.

Diacetate 26. Dioxime 24 (1.0 g, 4.9 mmol) was suspended in acetic anhydride (20 ml). After several minutes all solid dissolved. The solution was heated on a steam bath (1 hr). Solvent removal in vacuo afforded a white solid (26), mp 150° (1.3 g, 4.6 mmol, 94%). Recrystallization from hexane-acetone provided white crystals: mp 159-160° (750 mg); ir v_{max} (KBr) 1727, 1628, 1339, 1190, 910 cm^{-1} ; NMR (CDCl₃, Me₄Si) τ 6.0–7.4 (8 H, m), 7.7–8.3 (8 H, m).

Anal. Calcd for C₁₅H₁₆N₂O₄: C, 62.5; H, 5.6; N, 9.7. Found: C, 62.2; H, 5.7; N, 9.4.

Dichloro Azo Dioxide 16. Chlorine gas was bubbled into a CH₂Cl₂ (20 ml) suspension of dioxime 24 (450 mg, 2.2 mmol) cooled to 0°. A deep blue color developed over a 5-7 min period as the starting solid dissolved. The reaction was filtered from traces of solid and stripped in vacuo at room temperature. A blue solid (600 mg) was obtained, mp 150°. Washing with ether led to pale blue crystals; recrystallization from acetone delivered white crystals (16), mp 241-242° dec (250 mg, 0.92 mmol, 42%). Likewise, suspending the pale blue solid in ethanol caused an immediate disappearance of the blue color: mp 245° dec; physical data, see Table I; chlorine present (Beilstein test).

Dichloroazoxy Alkane 27. Dioxide 16 (200 mg, 0.78 mmol) was treated with Si₂Cl₆ as above to obtain pale yellow crystals, mp 85°, which were recrystallized twice from CH₃OH and washed once with ether to obtain white crystals (27): mp 185–186° (159 mg, 0.62 mmol, 79%); ir v_{max} (KBr) 1459 (N-O), 1275 (N-O), 995 cm⁻¹; uv λ_{max} (96% EtOH) 236 nm (ϵ 6900).

Anal. Calcd for C11H10N2OCl2: C, 51.4; H, 3.9; N, 10.9. Found: C, 51.5; H. 4.0; N. 10.9.

Dioxime 17 (n = 2**).** The requisite diketone⁵¹ (Scheme I, n = 2, 1.8 g, 9.4 mmol), hydroxylamine hydrochloride (2.6 g, 37 mmol), pyridine (20 ml), and absolute ethanol (20 ml) were refluxed for 2 hr. The cooled solution was treated with charcoal, filtered, and stripped in vacuo to a white solid. The latter was taken up with water (20 ml), cooled, filtered, and the insoluble white solid (17) washed with cold water, mp 240° (1.8 g, 8.1 mmol, 86%). Double recrystallization from H₂O-EtOH afforded a white solid: mp 255° dec; ir ν_{max} (KBr) 3150 (broad, OH, intramolecular H bond), 1422, 928 cm⁻¹ (N-O, oxime).

Anal. Calcd for C12H18N2O2: C, 64.8; H, 8.2; N, 12.6. Found: C, 65.0; H, 7.9; N, 12.6.

Chlorination of Dioxime 17 (n = 2). Chlorine gas was bubbled through a CH_2Cl_2 (15 ml) suspension of dioxime 17 (n = 2) (1.0 g, 4.5 mmol) cooled to 0°. A blue-green solution appeared within a few minutes as the solid dissolved almost completely. The solution was filtered and the blue-green filtrate stripped in vacuo at room temperature. The resulting blue-green solid was washed with ether several times and dried on a porous plate, mp 110° dec (300 mg). Double recrystallization from MeOH (below 50°) led to blue crystals: mp 116-117° dec; ir v_{max} (KBr) 3175 (broæd, OH, intramolecular H bond), 1548 (N=O), 925 cm⁻¹ (N=O, oxime). Anal. Calcd for $C_{12}H_{17}N_2O_2Cl: C, 56.1; H, 6.7; N, 10.9.$ Found: C,

55.4; H, 6.6; N, 10.7.

The blue compound is assigned structure 18 (n = 2). Further chlorination under the above conditions does not lead to dioxide 15 (n = 2). As in the case of nitroso 18 (n = 1) the blue material here is thermally sensitive, particularly in solution (CH₂Cl₂). Standing overnight results in tarring. The material may, however, be stored for longer periods as a solid at room temperature or below. In MeOH overnight the blue color gives way to yellow. Evaporation of solvent led to a yellow solid: mp 160° dec; ir ν_{max} (KBr) 3150 (broad, OH), 1535, 1358, 920 cm⁻¹. This material was not investigated further.

Following some runs a chlorine-free white solid, mp 285° dec, with an infrared spectrum nearly superimposable with that of dioxime 17 (n = 2) was isolated. The latter substance was likewise not characterized further.

Dioxime-Hydroxylamine Adduct 25 (n = 2, Z = NOH). Diketone 23 (n = 2) (2.0 g, 11 mmol), hydroxylamine hydrochloride (4.4 g, 63 mmol), pyridine (20 ml), and absolute ethanol (20 ml) were refluxed for 2 hr. The cooled solution delivered a white solid (25) which was washed successively with water, MeOH, and ether: mp 249–250° (2.1 g, 8.4 mmol, 76%); ir ν_{max} (KBr) 3425, 3180, 1309, 1120, 1045, 858, 780 cm⁻¹.

Anal. Calcd for C₁₂H₁₇N₃O₃: C, 57.4; H, 6.8; N, 16.7. Found: C, 57.4: H. 6.7: N. 16.7.

Dioxime 28. 5,5-Dimethylcyclohexane-1,3-dione was converted to dioxime as reported⁵² and recrystallized from water, giving a white solid (28): mp 169–170° (lit.⁵² mp 171–173°); ir ν_{max} (KBr) 3150 (broad, OH), 1405, 1250, 945 (N-O, oxime).

Anal. Calcd for C₈H₁₄N₂O₂: C, 56.3; H, 8.2; N, 16.3. Found: C, 56.5; H, 8.3; N, 16.5.

Chlorination of Dioxime 28. A. Chlorine, Concentrated HCl. Chlorine gas was bubbled into a suspension of dioxime 28 (1.0 g, 5.9 mmol) in concentrated HCl (10 ml) at 0°. A yellow solid formed and was recrystallized from H₂O-EtOH to give a pale yellow solid (30): mp 224–225°; ir ν_{max} (KBr) 3150 (broad, OH), 1680 (C=O), 1560, 1385, 1250, 1075, 940 (N-O, oxime), 870 cm⁻¹; NMR (CDCl₃-DMSO- d_6 , Me₄Si) τ 6.2-6.6 (2 H, broad, OH, D₂O exchange), 7.42 (4 H, broad s), 8.98 (6 H, s); no chlorine (Beilstein test).

Anal. Calcd for C₈H₁₂N₂O₃: C, 52.2; H, 6.6; N, 15.2. Found: C, 52.1; H, 6.6; N, 15.1.

B. Chlorine, Ethyl Acetate. Chlorine was introduced into an EtOAc (20 ml) suspension of dioxime 28 (500 mg) at 0°. Within 5 min the suspension turned dark blue and the dioxime dissolved. The solvent was stripped in vacuo at room temperature, depositing blue crystals, mp 95°. Attempted chromatography (TLC) on alumina (hexane-EtOAc) led to an immediate loss of blue color. Elution from a silica gel column (hexane), on the other hand, gave blue crystals showing three spots on tlc (silica gel-hexane-EtOAc), ir ν_{max} (KBr) 3180 (broad, OH), 1560 (N=O), 970 cm⁻¹ (N-O, oxime), Recrystallization of the blue crystals from hexane afforded an insoluble, pale yellow solid. The latter was recrystallized from H₂O-EtOH to obtain pale yellow crystals (30), mp 220° dec, ir (KBr) superimposable on that of the solid obtained from method Α

The labile blue crystals are assigned the oxime chloro nitroso structure 29. Further chlorination was ineffective in providing the desired dioxide. Chlorination in CH₂Cl₂ or hexane solutions did not cause development of the characteristic nitroso color.

Attempts to Induce Cyclic Azo Dioxides to Ring Open Thermally. All of the new cis azo N,N'-dioxides listed in Table I were melted slowly. Decomposition set in without the development of blue color. For qualitative solution behavior dichloro dioxide 11^{18} was used as a comparative standard. Compound 11 (1-3 mg) was dissolved in the following solvents $(1-3 \text{ ml}, 10^{-2}-10^{-3} M)^{30}$ and the solution was brought to reflux (boiling point indicated): EtOH (78°), acetic acid (118°), ethylene glycol (197°), acetophenone (202°), benzoic acid (249°), and benzophenone (306°). In every case a blue color developed immediately. The process was reversible for all but the latter three high-boiling solvents, for which decomposition occurred following dinitroso formation. Similarly azo dioxides 3 (n = 1-4), 9, 15 (benzophenone only), and 16 were heated in the indicated solvents. Either no color change took place on prolonged heating or the initially colorless solutions turned velow and brown.⁴⁷ Not unexpectedly, the bicycloheptene system 3 (n = 1) proved to be most labile. It rapidly produced yellow-brown solutions in boiling acetic acid and ethylene glycol, solvents in which the other azo dioxides were inert.

Acknowledgments. We are appreciative of the financial assistance provided by the National Institutes of Health (GM15927) and stimulating discussions with colleagues Martin Ettlinger, Steen Hammerum, and Per Halfdan Nielsen (University of Copenhagen). Henrik Olsen generously offered technical aid.

Registry No.—1 (n = 1), 2721-32-6; 1 (n = 2), 3310-62-1; 1 (n = 2)3), 43195-77-3; 1 (n = 4), 32634-64-3; 2 (n = 1), 22509-00-8; 2 (n = 2), 25926-96-9; 2 (n = 3), 26081-83-4; 2 (n = 4), 25926-97-0; 3 (n = 4)1), 36335-10-1; 3 (n = 2), 36479-80-8; 3 (n = 3), 54143-30-5; 3 (n = 3)4), 54143-31-6; 4a, 25927-00-8; 4a corresponding azo alkene,

16104-45-3: 4b. 54142-91-5; 5a, 34098-80-1; 5a corresponding azo alkene, 24046-80-8; 5b, 54143-32-7; 6a, 25926-99-2; 6b, 54143-33-8; 8, 54143-34-9; 9, 54143-35-0; 11 (X = Cl), 54143-36-1; 15 (n = 1), 54142-97-1; 16 (n = 1), 54142-93-7; 17 (n = 1), 54142-96-0; 17 (n = 2), 54143-37-2; 17 (n = 2) diketone analog, 54143-38-3; 18 (n = 1), 54143-39-4; 18 (n = 2), 54143-40-7; 20 (n = 1), 54143-41-8; 23 (n = 1)2), 712-25-4; 23 (n = 1), 2958-72-7; 24 (n = 1), 54142-92-6; 25 (n = 1)2, Z = NOH), 54182-33-1; 26, 54143-42-9; 27, 54143-43-0; 28, 37110-24-0; 29, 54143-44-1; 30, 54143-45-2; 6,7-diazatricyclo-[3.2.2.0^{2.4}]non-6-ene, 25368-34-7; 2.5-diamino-2.5-dimethylhexane, 23578-35-0; 3,3,6,6-tetramethylazocyclohexane, 19403-24-8; 5,5dimethylcyclohexane-1,3-dione, 126-81-8.

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Convenient Synthesis of Bicyclic and Polycyclic Cis Azo N.N'-Dioxides

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Received August 13, 1974

Two methods for the synthesis of bicyclic and polycyclic cis azo N,N'-dioxides are described. Oxidation of azo alkanes with trifluoroperacetic acid afford their corresponding azo N, N'-dioxides, while chlorination of 1,4-dioximes give the α, α' -dichloro azo N,N'-dioxides. Structures of all new compounds are supported by spectral data and elemental analysis.

One of the distinct properties of C-nitroso compounds is their tendency to dimerize to form azo N, N'-dioxides. The acyclic dimers can exhibit cis-trans configurational isomerism with the trans isomer generally being more stable than the cis isomer. Although many examples of trans azo dioxides are known, there are very few examples reported of cis azo dioxides. Certain cyclic azo N,N'-dioxides can only exist in their cis form, e.g., the azo dioxides 1-3,^{1,2} and are



obtained by the ring closure of their corresponding bis nitroso precursors. In connection with other work we needed bicyclic and polycyclic cis azo N, N'-dioxides and would like to report convenient synthetic routes to these compounds.³

The key intermediate to the synthesis of the azo dioxide 8 is 2,3-diazabicyclo[2.2.1]hept-2-ene (6), which was prepared in high yield according to Scheme I. The Diels-Alder adduct of cyclopentadiene and ethyl azodicarboxylate was hydrogenated and the product 4 was hydrolyzed with strong base in ethylene glycol.⁴ Oxidation of the crude reaction mixture with 30% hydrogen peroxide gave the bicyclic



azo compound 6 in overall 97% yield from 4. This observation is in contrast to Snyder's report of the formation of the cis azoxy compound 7 in 73% yield⁵ from 5 under similar conditions. The monoxide could, however, be easily obtained in 80% yield by *m*-chloroperbenzoic acid oxidation of the azo compound 6.6 The use of hydrogen peroxide for oxidation of hydrazines, such as 5, has a distinct advantage