are collected after approximately 10 additional min, they prove to be fairly pure **5c**. However, if the reaction is allowed to run longer, the product becomes a mixture of **5c** and **4c** in a ratio of ≈40:60.

Anal. Calcd for $C_{34}H_{38}N_4$: C, 81.23; H, 7.62; N, 11.15. Found: C, 80.92; H, 7.75; N, 11.15.

***trans*-1,4,5,8-Tetrabenzyl-1,4,5,8-tetraazadecalin (4c).** A solution of 40% aqueous glyoxal (1.45 g, 10 mmol) in 50 mL of ethanol is stirred while a solution of *N,N*-dibenzylethylenediamine (7.2 g, 30 mmol) in 50 mL of ethanol is added dropwise. After the addition is complete the mixture is refluxed for 3 h. The mixture is cooled, the product collected, and the product is then washed with ethanol. After drying, the product weighs 2.09 g (4.1 mmol, 41%) and melts at 190–192 °C.

Anal. Calcd for $C_{34}H_{38}N_4$: C, 81.23; H, 7.62; N, 11.15. Found: C, 81.11; H, 7.66; N, 11.13.

***cis*-1,4,5,8-Tetrabenzyl-1,4,5,8-tetraazadecalin (3c).** A solution of 1.0 g of pure **4c** in 5.0 mL of $CDCl_3$ is heated at 60 °C under nitrogen for 18 h. The solvent is removed at reduced pressure and the resulting semisolid triturated with 20 mL of pentane. The pentane is removed at reduced pressure to give 0.45 g of **3c** as a gummy oil.

Acknowledgment. This work was funded under the Naval Weapons Center Independent Research Task and the NAVSEA Explosive Research and Development Program Task SR02403. The authors are indebted to Ralph Hurd of General Electric NMR for the 300-MHz ^1H NMR spectra of **3c** and **4c**.

Registry No. **3c**, 96482-22-3; **4c**, 96444-73-4; **5c**, 96444-74-5; $PhCH_2NH(CH_2)_2NHCH_2Ph$, 140-28-3; glyoxal, 107-22-2.

New Chemistry from the Reaction of N,N′-Disubstituted Ethylenediamines with Glyoxal: Synthesis of 2-Imidazolidinecarboxaldehydes and 1,4,6,9-Tetraalkyl-1,4,6,9-tetraaza-5,10-dioxaperhydroanthracenes

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The reaction of *N,N′*-di-*tert*-butylethylenediamine with glyoxal in water gives initially *trans*-2,3-dihydroxy-1,4-di-*tert*-butylpiperazine, **6f**, which rearranges thermally to 1,3-di-*tert*-butyl-2-imidazolidinecarboxaldehyde, **8f**, and then to 1,4-di-*tert*-butyl-2-ketopiperazine, **5f**. The reaction of *N,N′*-diisopropylethylenediamine with glyoxal in water produces 1,4-diisoproyl-2-ketopiperazine, **5e**, as the only isolable product. The reaction of a series of N,N′-dialkyl-substituted ethylenediamines with glyoxal in ethanol at low temperature has been found to give a series of *cis-trans-cis*-1,4,6,9-tetraalkyl-1,4,6,9-tetraaza-5,10-dioxaperhydroanthracenes, **9b,c,e**, as minor products. The crystal structure of **9e** was determined confirming the stereochemistry of the ring junctures. *N,N′*-Diphenylethylenediamine reacts with glyoxal to give 1,3-diphenyl-2-imidazolidinecarboxaldehyde, **8d**. **8d** shows no tendency to rearrange to **5d**. A modified reaction scheme for the reaction of N,N′-disubstituted ethylenediamines with glyoxal is presented which accounts for the formation of these new types of products.

The reactions of ethylenediamine and N,N′-disubstituted ethylenediamines, **1a–d**, with glyoxal have been the subject of several investigations.[1-9] The reactions have been found to yield four different types of products, namely *trans*-1,4,5,8-tetraazadecalins, **2**, *cis*-1,4,5,8-tetraazadecalins, **3**, 2,2′-biimidazolidines, **4**, and lactams **5** (see Scheme III for structures). The product(s) obtained has been found to depend both on the amine substituent and the reaction conditions. When R is hydrogen, the product is the *trans*-tetraazadecalin **2a**.[1,2] When R is methyl, the product is a mixture of the *trans*- and *cis*-tetraazadecalins **2b** and **3b** when the reaction is run under mild conditions[3,4] and the lactam **5b** when the reaction is run under more vigorous conditions.[2] When R is benzyl, the product is a mixture of the *trans*-tetraazadecalin **2c** and biimidazolidine **4c**.[5] The *trans*-tetraazadecalin **2c** is in equilibrium with the cis isomer **3c** at elevated temperatures in chloroform. When R is phenyl, the product is the 2,2′-biimidazolidine **4d**.[6] Fuchs has proposed a reaction scheme to account for these products.[2]

As an outgrowth of our interest in diamine–glyoxal chemistry,[5,10] we have studied the reaction of *N,N′*-diisopropylethylenediamine, **1e**, and *N,N′*-di-*tert*-butylethylenediamine, **1f**, with glyoxal and reexamined the reaction of **1b**, **1c**, and **1d** with glyoxal under different conditions. In this paper we report our experimental results and show how they fit into an expanded reaction scheme.

Results

We first examined the reaction of *N,N′*-di-*tert*-butylethylenediamine (**1f**) with glyoxal. The addition of 1 mol equiv of **1f** to a well-stirred aqueous solution of glyoxal

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‡ 1982 American Society for Engineering Education Summer Faculty Research Participant at the Naval Weapons Center.

(1) Chitwood, H. C.; McNamee, R. W. U.S. Patent 2345237, 1944; *Chem. Abstr.* **1945**, *38*, 4274.
(2) Fuchs, B.; Ellencweig, A. *Recl. Trav. Chim. Pays-Bas.* **1979**, *98*, 326.
(3) Ferguson, I. J.; Katritzky, A. R.; Patel, R. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1564.
(4) Fuchs, B.; Weinman, S.; Shmucli, U.; Katritzky, A. R.; Patel, R. *Tetrahedron Lett.* **1981**, *22*, 3541.
(5) Willer, R. L.; Moore, D. W.; Vanderah, D. *J. Org. Chem.*, submitted for publication.
(6) Wanzlick, H. W.; Lichel, W. *Chem. Ber.* **1953**, *84*, 1463.
(7) Edwards, J. M.; Weiss, U.; Gilardi, R. D.; Karle I. L. *Chem. Commun.* **1968**, 1649.
(8) Baganz, H.; Domaschke, L.; Kirchner, G. *Chem. Ber.* **1964**, *94*, 2676.
(9) Cort, L. A.; Francis, N. R. *J. Chem. Soc.* **1964**, 2799.
(10) Willer, R. L. *Propellants, Explos., Pyrotech.* **1983**, *8*, 65.

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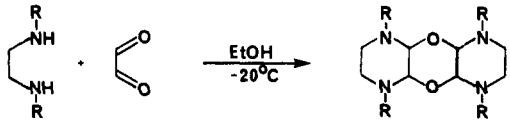
Table I. Yields of 9 from the Reaction of a N,N'-Disubstituted Ethylenediamine with Glyoxal at Low Temperature



1 9

R	yield[a]	mp, °C[b]
9b, CH_3	11	151–160
9c, CH_2Ph	3	207–209
9e, $CH(CH_3)_2$	5	179–182

[a] Not optimized. [b] All new compounds gave satisfactory C, H, and N analyses (±0.4%).

initially gives a gummy solid which eventually crystallizes to a $C_{12}H_{26}N_2O_2$ compound, mp 92–94 °C. We have assigned the *trans*-1,4-di-*tert*-butyl-2,3-dihydroxypiperazine structure **6f** to this compound on the basis of a moderately intense OH stretch in its IR spectrum and the ^1H NMR spectrum which showed four absorptions at δ 1.10, 2.75, 3.35, and 4.55 with a relative intensity ratio of 18:4:2:2. The stereochemical assignment was made on the basis of the coupling constants derived from a stimulation of the AA'BB' subspectrum of the ethylene moiety which showed a coupling constant typical of a staggered ethylene fragment.

If the 1:1 reaction mixture is briefly warmed to 60 °C, the initial solid product is converted to an isomeric liquid, bp 66–68 °C at 0.025 mm, which can be isolated in over 85% yield by extraction into ether followed by vacuum distillation. We have assigned to this compound the 1,3-di-*tert*-butyl-2-imidazolidinecarboxaldehyde structure **8f** on the basis of a 1729 cm^{-1} stretch in the IR for the aldehyde carbonyl and a pair of doublets (J = 6.0 Hz) for the aldehyde and aminal protons at 9.20 and 3.90 ppm in the ^1H NMR spectrum.

Interestingly, **8f** slowly rearranges to lactam **5f** upon standing at room temperature and more quickly upon heating. We believe that the aldehyde **8f** represents the kinetically controlled product from the rearrangement of carbocation **7f** while the lactam is the thermodynamically controlled product. Calculations of heats of formation support this belief.[11] The rearrangements of **6f** to **8f** and of **8f** to **5f** are akin to the familiar pinacol–pinacalone rearrangement.[12,13] All attempts to get aldehyde **8f** to react with an additional equivalent of **1f** to give biimidazolidine **4f** failed apparently because of the steric congestion present in the molecule.

We next turned our attention to the reaction of *N,N'*-diisopropylethylenediamine, **1e**, with glyoxal. The addition of 1 or 2 equiv of **1e** to an aqueous glyoxal solution at room temperature gave lactam **5e** as the only isolable product. However, the ^1H NMR spectrum of the crude product did show a weak doublet at 9.1 ppm which appeared to belong to aldehyde **8e** and the IR spectra showed a weak stretch at 1730 cm^{-1}.

We then examined the reaction at −20 °C diluting the glyoxal with ethanol instead of water. Under these conditions, a solid precipitated from the reaction mixture. Surprisingly, this minor product was neither dihydroxypiperazine **6e** nor aldehyde **8e**. Based upon the lack of

Scheme I. Possible Stereoisomers of 9

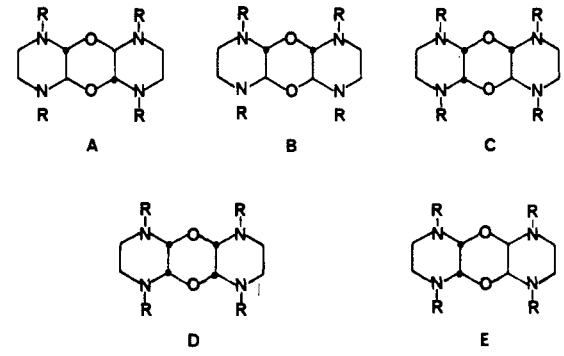


Table II. Coupling Constants and Chemical Shifts Derived from Computer Simulation of Ethylene Moiety in 9b,c,e

no.	ν_A	ν_B	$J_{AA'}$	$J_{BB'}$	$J_{AB(A'B')}$	$J_{AB'(A'B)}$
9b	473.3	583.1	2.92	3.10	−11.07	6.91
9c	449.9	562.3	2.82	3.00	−11.03	6.99
9e	477.6	573.0	3.18	3.18	−10.75	7.03

both hydroxyl and carbonyl absorptions in the IR spectrum, the appearance of a m/e 369 peak in the methane–CI mass spectrum, and on the ^1H NMR spectrum, we have assigned this product the 1,4,6,9-tetraisopropyl-1,4,6,9-tetraaza-5,10-dioxaperhydroanthracene structure **9e**. A more detailed discussion of the ^1H NMR spectrum of **9e** will be given below.

This result prompted us to try the low-temperature reaction conditions with the other N,N'-disubstituted ethylenediamines **1b–d** and **1f**. In each case except phenyl and *tert*-butyl, we isolated analogues of **9e** in low but reproducible yields. The yields and melting points are summarized in Table I. The major products from these reactions are the lactams **5b,c,e** except with the phenyl and *tert*-butyl compound where the aldehydes **8d** and **8f** were the major products.

The structural assignment of **8d** was based upon its parent mass, a strong carbonyl absorption at 1700 cm^{-1} in the IR spectrum, and the appearance of the aldehydic proton as a doublet (J = 6.0 Hz) at 9.10 ppm. Unlike the *tert*-butyl analogue **8f**, **8d** shows no tendency to undergo rearrangement to the lactam **5d**. In fact, **8d** survives prolonged heating at 120 °C with only minor amounts of disproportionation to the biimidazolidine **4d** and glyoxal. Even with 2 equiv of diamine **1d** the major product under these mild conditions was **8d**. However, when the reaction temperature was raised to 78 °C, the major product with 2 mol of **1d** became the biimidazolidine as reported.[2,6]

Stereochemistry of 9b,c,e. If one neglects isomers due to different arrangement of the *N*-alkyl substituents (i.e., axial vs. equatorial), there are five possible stereoisomers for the 1,4,6,9-tetraalkyl-1,4,6,9-tetraaza-5,10-dioxaperhydroanthracenes **9b,c,e**. They are the trans-transoid-trans, A, trans-cisoid-trans, B, cis-transoid-trans, C, cis-cisoid-cis, D, and cis-transoid-cis, E, as shown in Scheme I.

It proved to be surprisingly easy to assign stereochemistry to these compounds. In all three homologues (**b,c,e**), the ethylene moieties appear as AA'BB' spectra which can be simulated[14] with essentially identical coupling constants and slightly different chemical shifts. The coupling constants and chemical shifts derived for **9bc,e** are summarized in Table II.

(11) Benson, S. W.; Cruickshank, F. R.; Golden, D. M.; Haugen, G. R.; O'Neal, H. E.; Rodgers, A. S.; Shaw, R.; Walsh, R. *Chem. Rev.* **1969**, *69*, 279–324.

(12) (a) Ferruti, P.; Fere, A.; Zetta, L.; Bettelli, A. *J. Chem. Soc. C* **1971**, 2984. (b) Ferruti, P.; Segre, A.; Fere, A. *J. Chem. Soc. C* **1968**, 2721.

(13) Darko, L. L.; Karliner, J. *J. Org. Chem.* **1971**, *36*, *3810*.

(14) Castellano, S.; Bothner-By, A. A. *J. Chem. Phys.* **1964**, *41*, 3863–3869. The adaptation of this program known as ITRCAL written for the Nicolet 1280 computer was used.

Scheme II. Chair–Chair Interconversion in a *cis-anti-cis*-1,4,6,9-Tetraalkyl-1,4,6,9-tetraaza-9,10-dioxaperhydroanthracene

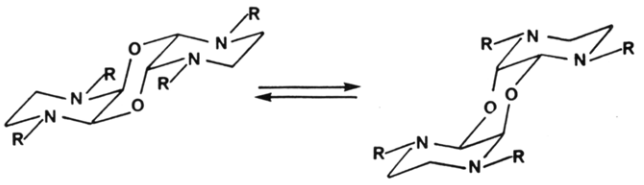


Table III. Ring Inversion Barriers in *cis-anti-cis*-1,4,6,9-Tetraalkyl-1,4,6,9-tetraaza-5,10-dioxaperhydroanthracene

R	δ_1, ppm	δ_2, ppm	$\Delta\nu$, Hz	Tc, °C	ΔG
CH_3	3.68	4.73	210	5	12.84
CH_2Ph	3.60	4.70	220	6	12.83
$CH(CH_3)_2$	4.11	5.02	182	−17	11.87

The fact that the $J_{AB'}$ and $J_{A'B}$ are the same and equal to the average of J_{aa} and J_{ee} coupling constants clearly means we are dealing with a time averaged system undergoing chair–chair interconversion. This eliminates both trans–trans stereoisomers (A and B, Scheme I) as possibilities. The trans-cisoid-cis isomer (C) can be eliminated on the basis that it would not show the symmetry we observe. Of the two remaining possibilities, the cis-transoid-cis seems the most reasonable since models of the cis-cisoid-cis indicate that it might prefer to exist in a chair-boat-chair conformation. Also consistent with this assignment is the fact that the methine protons are exchange broadened by chair–chair interconversion (see Scheme II). Inversion barriers in **9b,c,e** determined by the variable temperature ^{1}H NMR spectra are shown.[15] These are summarized in Table III.[15] These barriers are consistent with the cis-transoid-cis stereochemistry since in perhydroanthracene the barriers for ring reversal in the cis-transcoid-cis isomer is 14.0 kcal/mol[16] while in the cis-cisoid-cis isomer it is 10.4 kcal/mol.[17]

The crystal structure of the new compound 1,4,6,9-tetraisopropyl-1,4,6,9-tetraaza-5,10-dioxaperhydroanthracene, **9e**, was solved to confirm the ring juncture stereochemistry and determine the overall molecular conformation. Details regarding the data collection and structure solution and refinement are presented in the Experimental Section. The atomic coordinates and thermal parameters are given in the supplementary pages. A diagram of **9e** with the atom numbering and a plot of the rings are shown in Figure 1. The molecule sits on a site with $\bar{1}$ symmetry and, hence, itself contains an inversion center in the middle of the central ring. The primed atoms are symmetry related by inversion to the unprimed atoms. The four hydrogens at the ring junctures are plotted in Figure 1 to more clearly show the cis-transoid-cis configuration. All three rings have chair conformations. The angles of the plane of the isopropyl groups to the C–N–C plane are 70.4° and 69.8°. The dihedral angle between H(1) and H(4) is 52.6°.

We have also examined the effect of the mode of addition and solvent on the reactions of **1b** and **1c** with glyoxal. When an aqueous solution of glyoxal is added to an aqueous solution of 2 mol equiv of **1b** (normal addition) at 0 °C, the product is almost pure **2b** containing a small

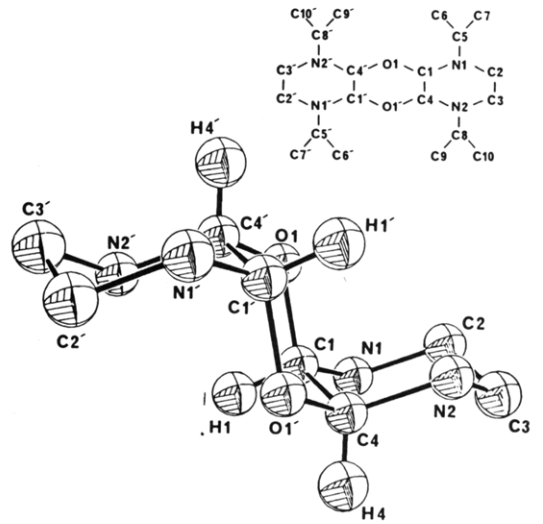
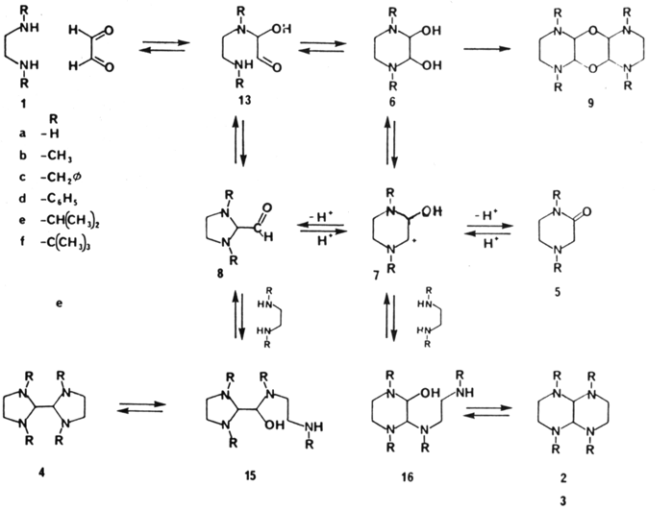


Figure 1. Diagram of **9e** with atom numbering and a plot of the rings of **9e** with 50% probability thermal ellipsoids.

Scheme III. Modified Reaction Scheme for the Reaction of an N,N′-Disubstituted Ethylenediamine and Glyoxal



amount of **3b** as reported by Katritzky et al.[3] The same result is obtained by adding the solution of **1b** to the glyoxal solution (inverse addition). Switching to ethanol solvent produces the same results with normal addition, but with the inverse addition, a third compound is present in the product. This third product seems to be the biimidazolidine **4b** based on its mass spectral behavior (strong M/2 peak), but we have been unable to isolate it pure. The approximate product ratio is 39% **4b**, 49% **2b**, and 12% **3b**. Similar results are obtained from the reaction of **1c** and glyoxal. Addition of an ethanol solution of **1c** gives a product which is ≈60% **2c** and 40% **4c** while reversing the mode of addition gives a product which is ≈80% **4c** and 20% **2c**.

Discussion

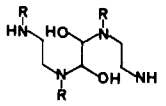
Our results indicate that Fuchs' reaction scheme needs to be expanded to account for the new products found here. A modified reaction scheme which accounts for all the observed products is presented in Scheme III.

One of the major differences between Scheme II and Fuchs' original reaction scheme is the inclusion of the 2-imidazolidinecarboxaldehydes 8 as both intermediates and products. Scheme III also points out that there are two ways to form the aldehydes, by 1,1-addition of the

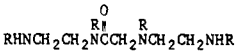
(15) Lambert, J. B., In "Organic Structural Analysis"; J. B. Lambert, Ed.; Macmillian: New York, 1976, p 117.
(16) Vanhee, P.; DePessemier, F.; Anteunis, M.; Tavernier, D. *Recl. Trav. Chim. Pays-Bas* **1979**, *98*, 294.
(17) Fawcett, A. H.; Heatley, F. *J. Chem. Res. Synop.* **1981**, 294.

ethylenediamine to glyoxal to generate the aldehyde directly or by initial 1,2-addition of the ethylenediamine to the glyoxal generating a 2,3-dihydroxypiperazine which subsequently undergoes a pinacol–pinacolone type rearrangement to the aldehyde.

Scheme III also differs from Fuchs in that we see no need to invoke intermediate **14**. No products of type **17** are seen in the 2:1 reactions of **1e** and **1f** with glyoxal. One would expect to see such products if **14** were an important intermediate.



14



17

Scheme III also includes the 1,4,6,9-tetraalkyl-1,4,6,9-tetraaza-5,10-dioxaperhydroanthracenes. Although minor products, these compounds can be isolated and, thus, need to be included in the reaction scheme.

We believe that all of the *N,N'*-dialkyl-substituted ethylenediamines (**1b,c,e,f**) react by the initial 1,2-addition pathway to generate the predominately *trans*-2,3-dihydroxypiperazines. This belief is based upon the fact that Ferrati et al. isolated, in good yield, an 88:12 mixture of *trans*- and *cis*-2,3-dimethoxy-1,4-dimethylpiperazines from the reaction of **1b** with glyoxal in methanol, while we obtained in equally good yield, *trans*-2,3-dihydroxy-1,4-di-*tert*-butylpiperazine from the reaction of **1f** and glyoxal. There is little reason to suspect that the diamines with intermediate size alkyl substituents (benzyl, isopropyl) should react differently. This means that the final products obtained from a particular reaction are due to the further transformations of this intermediate. This may explain the differences in the product distribution found in the reaction of **1b** and **1c** with glyoxal employing normal and inverse addition modes. When the dihydroxypiperazine is generated in the presence of an excess of diamine (normal addition), the predominant reaction is the generation of intermediate **16** which leads to the tetraazadecalin (TAD) products. However, if **6** is generated with little excess diamine present (inverse addition), more time exists for it to rearrange to **8** which eventually leads to the biimidazolidine products. This seems to occur to a larger extent in ethanol than in water which suggests that the rearrangement of **6** to **8** occurs faster in ethanol. It also occurs to a larger extent in the benzyl case, suggesting that the rate of the reaction of intermediate **6** via ion **7** with another molecule of **1** to generate **16** is very sensitive to the size of alkyl substituent on nitrogen. Since no TAD products are observed with **1e** and **1f** regardless of the mode of addition, the rate of reaction of **6e** and **6f** with **1e** and **1f** must be much slower than the rate of the rearrangement of **6e** and **6f** to **8e** and **8f**.

Two things are unusual about the reaction of *N,N'*-diphenylethylenediamine with glyoxal. First, the aldehyde **8d** appears to be the initial product of the reaction. This may well mean that it reacts by the 1,1-addition route to generate the aldehyde directly. Secondly, a 2:1 product (the biimidazolidine **4d**) can be isolated even though the phenyl group is larger (*A* value = 3.0 kcal/mol) than the isopropyl group (*A* value = 2.15 kcal/mol).[18] It appears the reason for this is the greater stability of **8d** as compared to **8e**. This allows sufficient time for **8d** to react with an additional molecule of **1d** to generate **4d** while **8e** apparently rearranges to lactam **5e** before it can react with another molecule of **1e** to give **4e**.

Experimental Section

Infrared spectra were determined as film (liquids) or as KBr pellets (solids) on a Nicolet 7000 FT-IR System. NMR spectra were recorded on a Nicolet WB200 Spectrometer. Mass spectra were recorded on a Hewlett-Packard 589A Mass Spectrometer. Elemental analyses were conducted by Galbraith Laboratories, Knoxville, TN.

***trans*-1,4-Di-*tert*-butyl-2,3-dihydroxypiperazine (6f).** To a stirred solution of 2.90 g of 40% aqueous glyoxal (20 mmol) dissolved in 10 mL of distilled water cooled to 0 °C (salt–ice bath) is added 3.44 g (20 mmol) of *N,N'*-di-*tert*-butylethylenediamine dissolved in 10 mL of H_2O dropwise over 5 min. The mixture is stirred for 10 min and then the product is collected by vacuum filtration, washed with water, and dried. The yield is 3.70 g (17 mmol, 85%) of **6f**: mp 92–94 °C; IR 3450 cm^{-1}; NMR ($CDCl_3$) δ 1.10 (s, 18 H *tert*-butyls), 2.75 (AA'BB', 4 H, CH_2), 3.35 (d, J = 8.0 Hz, 2 H, exchange with D_2O, OH), 4.55 (d, J = 8.0 Hz, 2 H, C*H*OH). Anal. Calcd for $C_{12}H_{26}N_2O_2$: C, 62.56; H, 11.37; N, 12.16. Found: C, 62.42; H, 11.22; N, 12.05.

1,3-Di-*tert*-butyl-2-imidazolidinecarboxaldehyde (8f). The reaction is run as described for the preparation of **6f** except the solution is then heated at 60 °C for 5 min after the addition. The solution is cooled and extracted with ether (3 × 50 mL), the combined ether extracts are dried (Na_2SO_4) and filtered, and the solvent is removed at reduced pressure to give the crude **8f**. The crude product is then Kugelrohr distilled to give pure **8f**: bp 66–68 °C (0.20 mm). The yield is 3.5–3.6 g (17 mmol, 85%): IR 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.05 (s, 18 H, *tert*-butyls), 3.00 (bs, 4 H, NCH_2), 3.90 (d, J = 6.0 Hz, 1 H NC*H*N), 9.15 (d, J = 6.0 Hz, 1 H, CHO); ^{13}C NMR ($CDCl_3$) δ 27.66 (q, 6 C, $C(CH_3)_3$), 46.26 (t, 2 C, CH_2), 54.05 (s, 2 C, $C(CH_3)_3$), 76.83 (d, 1 C, CHCHO), 198.02 (d, 1 C, CHO); MS (CH_4, CI), 213 (73), 157 (100). Anal. Calcd for $C_{12}H_{24}N_2O$: C, 67.92; H, 11.32; N, 13.21. Found: C, 67.68; H, 11.22; N, 13.20.

1,4-Di-*tert*-butyl-2-ketopiperazine (5f). A solution of crude **8f** in 100 mL of chloroform is refluxed overnight to give the crude product which is purified by vacuum distillation to give pure **5f**: bp 80–82 °C (0.20 mm); IR 1653 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.06 (s, 9 H, $NC(CH_3)$), 1.45 (s, 9 H, $C(=O)NC(CH_3)$, 2.72 (m, 2 H, CH_2), 3.32 (s, 2 H, CH_2CO), 3.36 (m, 2 H, CH_2); ^{13}C NMR ($CDCl_3$) δ 25.12 (q, 3 C, CCH_3), 27.91 (q, 3 C, $C(CH_3)_3$), 44.17 (t, 1 C, C_5), 44.45 (t, 1 C, C_6), 52.99 (t, 1 C, C_3), 52.05 (s, 1 C, $C(CH_3)_3$), 53.14 (s, 1 C, $C(CH_3)_3$) 168.80 (q, 1, CO). Anal. Calcd for $C_{12}H_{24}N_2O$: C, 67.92; H, 11.32; N, 13.21. Found: C, 67.88; H, 10.93; N, 13.23.

General Procedure for 1,4,6,9-Tetraalkyl-1,4,6,9-tetraaza-5,10-dioxaperhydroanthracenes (9b,c,e). To a magnetically stirred solution of 2.4 g (16.4 mmol) of 40% aqueous glyoxal in 5 mL of absolute alcohol maintained at −20 °C (dry ice–ethanol) is added dropwise a solution of 16.4 mmol of the *N,N'*-dialkylethylenediamine dissolved in 5 mL of absolute alcohol. After the solution is stirred for an additional 15 min, the solvent is removed at reduced pressure to yield a semicrystalline mass which is triturated with 4–5 mL of absolute ethanol and the products collected by vacuum filtration. The yields and melting point are summarized in Table II. The ^1H NMR for these compounds is summarized in the text (See Tables II and III).

1,3-Diphenyl-2-imidazolidinecarboxaldehyde (8d). A magnetically stirred solution of 2.4 g (16.4 mmol) of 40% aqueous glyoxal in 5 mL of absolute ethanol is maintained at −5 °C (salt–ice bath) while a solution of 3.45 g (16.4 mmol) of **1d** dissolved in 50 mL of absolute ethanol is added dropwise over 10 min. The cooling bath is removed and the mixture stirred for 15 min. The solvent is removed at reduced pressure to yield a gummy solid. This is triturated with 8 mL of absolute ethanol. A small amount of white solid forms which proves to be the biimidazolidine **4d**. The ethanol soluble material is largely **8d** which can be purified by recrystallization from ethanol: yield, 3.9–4.0 g; IR (KBr) 1725 (s), 1595 (s), 1501 (s), 1472 (m), 1358 (s), 1324 (s), 743 (s), 693 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.81 (m, 4 H, CH_2), 5.15 (d, J = 7.0 Hz, *H*CHO), 6.8–7.7 (m, 10 H, C_6H_5), 9.22 (d, J = 7.0 Hz, 1 H, CHO); precise mass calcd for $C_{16}H_{16}N_2O$ 252.207, found 252.208.

Crystallography of 1,4,6,9-Tetraisopropyl-1,4,6,9-tetraaza-5,10-dioxaperhydroanthracene, 9e. Precession and oscillation diffraction photographs of acicular crystals of **9e** indicated

(18) Hirsch, J. In "Topics in Stereochemistry", Eliel, E. L., Allinger, N. L., Eds.; Wiley Interscience: New York, 1967; Vol. I, pp 206–207.

triclinic symmetry. Unit cell parameters were determined from 25 computer-centered reflections with 2θ values ranging from 4 to 36° (Mo Kα). Based on the unit cell size there was one molecule per unit cell suggesting space group $P\bar{1}$. Intensity data for the octants were collected on a Nicolet XRD R3 four-circle diffractometer with monochromatized Mo Kα from 4° (2θ) to 60° (2θ) with $2\theta/\theta$ scans. The scan speed varied form 2° (2θ)/min to 6° (2θ)/min depending on the intensity of the reflection. Scan ranges were from 1° < K$\alpha_1(2\theta)$ to 1° > K$\alpha_2(2\theta)$. Backgrounds were measured at the beginning and end of each scan for a total background counting time equivalent to that of the scan time. Two check reflections, ($1\bar{4}\bar{2}$) and ($30\bar{3}$), were collected every 46 reflections. The check reflections were used for scaling and then deleted. The measured reflections were corrected for Lorentz and polarization effects. Reflections with $I < 0.5\sigma(I)$ were reset to $I = 0.25\sigma(I)$. The direct methods part of SHELXTL[19] was used to find four possible phase sets, one of which was correct and indicated the positions of the ring atoms and parts of the isopropyl groups. The rest of the carbon atoms of the isopropyl groups were found on a difference Fourier map. Refinement was done by using the least-squares blocked-matrix-cascading algorithm of SHELXTL.[19] The final model of 91 parameters used in the refinement included hydrogen atoms "riding" on carbon atoms with idealized geometry and with temperature factors fixed at 1.2 (secondary and tertiary H's) of 1.3 (primary H's) times the U_{eq} of the associated carbon atom. Carbon atoms of the isopropyl groups were refined with anisotropic temperature factors. All other C, N, O atoms were refined isotropically. H(1) and H(4), hydrogens at the ring junctures, were allowed to freely refine. Weights for the refinement were taken as $w = 1/[\sigma^2(F) + gF^2]$ with $g = 0.002$ (not refined). For 1653 reflections with $|F_o| > 4\sigma(F_o)$, $R = (\sum |F_o - F_c|/\sum F_o) = 0.080$ after convergence. Final atomic coordinates and temperature factors are given in supplementary material.

Crystal data for **9e**: formula, $C_{20}H_{40}N_4O_2$; M_r 368.57 g/mol. Cell: triclinic, $P\bar{1}$; $a = 5.981$ (1) Å, $b = 9.529$ (1) Å, $c = 10.021$ (2) Å; $\alpha = 97.53$ (1)° $\beta = 101.07$ (1)° $\gamma = 99.66$ (1)°. Density, $d_x = 1.12$ g/cm^3. Crystal size, 0.13 × 0.18 × 0.54 mm^3. Data collection: Mo Kα (monochromated); $\mu = 0.68$ cm^{-1} $F(000) = 203.96$; octants $h\bar{k}\bar{l}$, $hk\bar{l}$, $h\bar{k}l$, hkl; shell 4°(2θ) to 60°(2θ); 3513 data; 2515 unique reflections; 1653 reflections with $F_o > 4\theta(F_o)$. Refinement: over ΔF (blocked cascade); $R = 0.080$; GOF = 1.85.

Registry No. **1b**, 110-70-3; **1c**, 140-28-3; **1d**, 150-61-8; **1e**, 4013-94-9; **1f**, 4062-60-6; **2b**, 61736-90-1; **2c**, 96444-73-4; **3b**, 61736-89-8; **4b**, 96444-72-3; **4c**, 96444-74-5; **4d**, 56018-47-4; **5b**, 7556-57-2; **5c**, 32705-80-9; **5e**, 37791-60-9; **5f**, 96444-75-6; **6f**, 96444-67-6; **8d**, 96444-76-7; **8f**, 96444-68-7; **9b**, 96444-69-8; **9c**, 96444-70-1; **9e**, 96444-71-2; CHOCHO, 107-22-2.

Supplementary Material Available: Table of atom coordinates (2 pages). Ordering information is given on any current masthead page.

(19) SHELXTL, Version 3.0A (Nicolet XRD), July, 1981.

Alkynes from 5-Aminoisoxazoles

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Diazotization of 5-aminoisoxazoles that bear at least one electron-withdrawing group by reaction with sodium nitrite in AcOH–H_2O affords substituted acetylenes. A reaction path is proposed.

The nature of the products formed in the diazotization of 5-aminoisoxazoles is controversial,[1] and such reactions carried out at the same acidity have been reported to give different products.[2] Diazotization in dilute acid or under aprotic conditions leads to either triazene derivatives or 4-isoxazolyl-3,4-dialkylisoxazol-5-ones.[3] Thermal or photochemical reactions of 5-amino-3,4-dimethylisoxazole with an excess of an alkyl nitrite are reported to generate the corresponding isoxazol-5-yl radical.[4]

We wish to report that 5-aminoisoxazoles bearing at least one electron-withdrawing group react with sodium nitrite in AcOH–H_2O solution to give substituted acetylenes (Scheme I).

Good yields are obtained when the electron-withdrawing group is in the 4-position of the isoxazole (Table I). The effect of the group at the 4-position is illustrated by comparison of the yields of ethyl phenylpropiolate from **1b** and **1n**.

Isoxazoles **1h,i**, unsubstituted at the 3-position, gave acetylenes in very low yields (10%), and (arylsulfonyl)-

(1) Butler, R. N. *Chem. Rev.* **1951**, *75* 241.
(2) Saito, N.; Kurihara, T.; Yasuda, S.; Akagi, M. *Yakugaku Zasshi* **1970**, *90*, 32; *Chem. Abstr.* **1970**, *72*, 90353. Saito, N.; Kurihara, T. *Ibid.* **1970**, *90*, 20; *Chem. Abstr.* **1970**, *72*, 90352. Quilico, A.; Fusco, R.; Rosnati, V. *Gazz. Chim. Ital.* **1946**, *76*, 30, 87.
(3) (a) Kano, H.; Adachi, I.; Yamazaki, E. *Chem. Pharm. Bull.* **1964**, *12*, 1021. (b) Siv, C.; Vernin, G.; Metzger, J. *Helv. Chim. Acta* **1979**, *62*, 1570.
(4) Vernin, G.; Siv, C.; Treppendahl, S.; Metzger, J. *Helv. Chim. Acta* **1976**, *59*, 1705. Julliard, M.; Siv, C.; Vernin, G.; Metzger, J. *Ibid.* **1978**, *61*, 2941.
(5) Quilico, A.; Fusco, R. *Ist. Lomb. Accad. Sci. Lett.* **1936**, LXIX, 1.
(6) Dornov, A.; Teckenburg, H. *Chem. Ber.* **1960**, *93*, 1103.
(7) Present work.
(8) Heep, U. *Liebigs Ann. Chem.* **1973**, 578.
(9) Neplynev, V. M.; Sinenko, T. A. *Khim. Geterosikl, Soedin.* **1978**, 969. Neplynev, V. M.; Sinenko, T. A. *Zh. Org. Khim.* **1974**, 1953.
(10) Harsanyi, K.; Heya, G. *Chem. Ber.* **1974**, *107*, 2794.
(11) Renzi, G.; Dal Piaz, V. *Gazz. Chim. Ital.* **1965**, *95*, 1478.
(12) Abushanab, E.; Lee, D. Y.; Goodman, L. *J. Heterocycl. Chem.* **1973**, 181.
(13) Dal Piaz, V.; Pinazuti, S.; Lacrimini, P. *Synthesis* **1975**, 664.
(14) Graven, W. M. *Anal. Chem.* **1959**, *31*, 1197.
(15) Beccalli, E. M.; Gioia, B.; Marchesini, A. *J. Heterocycl. Chem.* **1980**, *17*, 763.

0022-3263/85/1950-2372$01.50/0