br, D_2O exch), 5.3–5.8 (2 H, CH=CH, m), 7.1–7.8 (3 H, Py H, m), 8.5 (1 H, Py α-H, d); IR (film) ν_{max} 3400 (OH), 1590, 960 cm^{-1}; MS, *m/e* 193 (M), 178, 177, 176, 160, 144, 123, 122 (base peak), 80, 79, 70.

2-(2-Pyridyl)-2,3-dihydroxy-5-phenyl-4-pentene (6j): threo and erythro mixture; oil; NMR ($CDCl_3$) δ 1.5 and 1.6 (3 H, CH_3, 2 s), 4.45 (1 H, CH, d, *J* = 6 Hz), 4.8 (2 H, 2 OH, br, D_2O exch), 6.25 (1 H, CH=C, 55, *J* = 6, 15 Hz), 6.6 (1 H, C=CH, d, *J* = 15 Hz), 7.2 (5 H, Ph H, m), 7.6 (3 H, Py H, m), 8.5 (1 H, Py α-H, m); IR (film) ν_{max} 3400 (OH), 1590, 690 cm^{-1}; MS,[27] *m/e* 255 (M), 237 (M – H_2O), 220, 208, 194, 132, 131, 122 (base peak), 104, 103, 80, 79, 78, 77.

2-(4-Pyridyl)-2,3-dihydroxy-4-pentene (6k): threo and erythro mixture; oil; NMR ($CDCl_3$) δ 1.42 and 1.55 (3 H, CH_3, 2 s), 4.2 (1 H, CH, d), 5.0–5.3 (2 H, CH_2=C, m), 5.2 (2 H, 2 OH, s, D_2O exch), 5.5–5.8 (1 H, C=CH, m), 7.4 (2 H, Py β-H, m), 8.5 (2 H, Py α-H, d); IR (film) ν_{max} 3500–3100 (OH, br), 1600, 1410, 1000, 920 cm^{-1}; MS, *m/e* 180 (M + 1),[28] 179, 164, 162, 146, 122 (base peak), 78, 77, 55.

2-(4-Pyridyl)-2,3-dihydroxy-4-hexene (6l). The threo and erythro isomers were separated by preparative chromatography (eluant hexane/ethyl acetate, 9/1). One isomer: oil; NMR ($CDCl_3$) δ 1.58 (3 H, CH_3, s), 1.60 (3 H, CH_3, d), 4.12 (1 H, CH, d), 4.4 (2 H, 2 OH, s, D_2O exch), 5.1–5.8 (2 H, CH=CH, m), 7.4 (2 H, Py β-H, m), 8.5 (2 H, Py α-H, d); IR (film) ν_{max} 3400–3100 (OH, br), 1600, 960 cm^{-1}; MS, *m/e* 193 (M), 178, 149, 123, 122 (base peak), 106, 80, 79, 78, 71. The other isomer: oil; NMR ($CDCl_3$) δ 1.44 (3 H, CH_3, s), 1.72 (3 H, CH_3, d), 3.45 (2 H, 2 OH, s, D_2O exch), 4.16 (1 H, CH, d), 5.5–5.7 (2 H, CH=CH, m), 7.4 (2 H, Py β-H, m), 8.5 (2 H, Py α-H, d).

2-(4-Pyridyl)-2,3-dihydroxy-5-phenyl-4-pentene (6m): threo and erythro mixture; oil; NMR ($CDCl_3$) δ 1.46 and 1.6 (3 H, CH_3, 2 s), 4.35 (1 H, CH, d), 5.15 (2 H, 2 OH, s, D_2O exch), 6.0–6.7 (2 H, CH=CH, m), 7.32 (7 H, 5 Ph H and 2 Py β-H, m), 8.43 (2 H, Py α-H, d); IR (film) ν_{max} 3400–3000 (OH, br), 1600, 960, 750 cm^{-1}; MS,[27] *m/e* 255 (M), 237 (M – H_2O), 220, 209, 208, 194, 132, 131, 122 (base peak), 104, 103, 80, 79, 78, 77.

(27) Primary loss of water (M – H_2O) leads to unusual formation of an epoxide structure. Clerici, A.; Traldi, P. *Org. Mass Spectrom.* **1983**, *18*, 114.

Registry No. 1 (R = Ph; X = CN), 613-90-1; 1 (R = Ph; X = $COOCH_3$), 15206-55-0; 1 (R = Ph; X = COOH), 611-73-4; 1 (R = CH_3; X = 2-Py), 1122-62-9; 1 (R = CH_3; X = 4-Py), 1122-54-9; **6a** (isomer 1), 85097-67-2; **6a** (isomer 2), 85097-68-3; **6b** (isomer 1), 85097-69-4; **6b** (isomer 2), 85097-70-7; **6c** (isomer 1), 85097-71-8; **6c** (isomer 2), 85097-72-9; **6d** (isomer 1), 85097-73-0; **6d** (isomer 2), 85097-74-1; **6e** (isomer 1), 85097-75-2; **6e** (isomer 2), 85097-76-3; **6f** (isomer 1), 85097-77-4; **6f** (isomer 2), 85097-78-5; **6g**, 85097-79-6; **6g**·Na, 85097-80-9; **6h** (isomer 1), 85115-78-2; **6h** (isomer 2), 85097-81-0; **6i** (isomer 1), 85097-82-1; **6i** (isomer 2), 85097-83-2; **6j** (isomer 1), 85097-84-3; **6j** (isomer 2), 85097-85-4; **6k** (isomer 1), 85097-86-5; **6k** (isomer 2), 85097-87-6; **6l** (isomer 1), 85097-88-7; **6l** (isomer 2), 85097-89-8; **6m** (isomer 1), 85097-90-1; **6m** (isomer 2), 85097-91-2; **7b**, 85097-92-3; **7d**, 85097-93-4; acrolein, 107-02-8; crotonaldehyde, 4170-30-3; cinnamaldehyde, 104-55-2; titanium trichloride, 7705-07-9.

Synthesis and Reactions of Cyclic Carbodiimides

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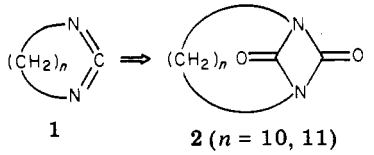
Modified Tiemann rearrangement on cyclic amidoxime *O*-methanesulfonates **4** has been used to synthesize cycloalkylene carbodiimides **1** and 4,5,6,7-tetrahydrobenzo-1,3-diazonine (**1g**). 1,3-Diazacycloocta-1,2-diene (**1b**, *n* = 5) was also prepared by dehydrosulfuration of pentamethylenethiourea. [2 + 2] cycloadducts of the type **20** and **21** are readily formed from **1** as well as **1g** with aryl isocyanates and *N,N'*-diphenylcarbodiimide. Hexafluoroacetone and **1d** (*n* = 7) give a dioxazane, **24b** (*n* = 7), while **1c** (*n* = 6) produces inseparable mixtures of **24a** (*n* = 6) and oxazetidine **23**. 1,3-Diazacyclohepta-1,2-diene (**1a**, *n* = 4) oligomerizes on preparation from tetramethylenethiourea, giving predominantly cyclodimer **7** and trimer **8** (not isolated); it can also be trapped with *N,N'*-diphenylcarbodiimide to give **20a** (*n* = 4, X = NC_6H_5).

We have recently reported about the synthesis of two novel intramolecular alkylene diisocyanate dimers with structure **2**, both of which were prepared from the corresponding cycloalkylene carbodimides in a three-step synthesis.[1]



1 **2** (*n* = 10, 11) (1)

Knowledge about compounds of type **1**, which contain the carbodiimide moiety as part of a ring system, was limited at the time we started our investigation,[2] although several recent publications are testimony to renewed interest in this area.[3-5] Especially lacking was an efficient synthetic method which would allow the preparation of larger quantities of cycloaliphatic carbodiimides for further studies. This need has consequently led us to (a) attempt to find an improved route to **1** and (b) study the chemistry of these carbodiimides as well as some of their precursors.

Synthesis of Cycloaliphatic Carbodiimides

The only method available for the preparation of alkylenecarbodiimides **1** with *n* ≥ 5 until 1979 consisted of dehydrosulfuration of the corresponding thioureas.[2] Cy-

(1) Richter, R.; Tucker, B.; Ulrich, H. *J. Org. Chem.* **1981**, *46*, 5226.
(2) Behringer, H.; Meier, H. *Justus Liebigs Ann. Chem.* **1957**, *607*, 67.
(3) Hiatt, R. R.; Shaio, M. J.; George, F. *J. Org. Chem.* **1979**, *44*, 3265.
(4) Recently, several very labile seven-membered-ring carbodiimides were prepared and spectroscopically identified by flash vacuum pyrolysis of heteroaromatic azides (which are generated from tetrazolopyridines or pyrimidines and other benzo-annealated systems) at elevated temperatures: Wentrup, C.; Winter, H. W.; *J. Am. Chem. Soc.* **1980**, *102*, 6159. Wentrup, C.; Thetaz, C.; Tagliaferri, E.; Lindner, H. J.; Kitschke, B.; Winter, H. W.; Reisenauer, H. P. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 566.
(5) Damrauer, R.; Soucy, D.; Winkler, P.; Eby, S. *J. Org. Chem.* **1980**, *45*, 1315.

0022-3263/83/1948-1694$01.50/0

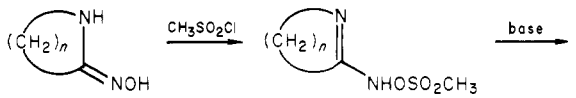
Table I. Cycloaliphatic Carbodiimides and Amidoxime Precursors

		amidoximes 3b-f		amidoxime O-mesylates 4b-f		carbodiimides 1b-f		
compd	n	yield, %	mp, °C	yield, %	mp, °C	base	yield, %	bp, °C (mmHg)
b	5	quant	169-170[a]	90	89-90[a]	$NaOH-H_2O$	>90	[b]
c	6	96	174-177[c]	80	99-100[d]	K-t-BuO	74	48-49 (0.5)[e]
d	7	93	118[d,f]	74	65-66[d]	K-t-BuO ($KOH-H_2O$)	84 (21)	60-63 (0.5)[g]
e	10	89	73-74	high[h]		$KOH-H_2O$	24	72 (0.1)[d]
f	11	77	124-125[d]	90	105-106[d]	K-t-BuO ($KOH-H_2O$)	87 (14)	85-86 (0.1)[d]

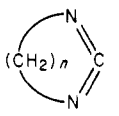
[a] Reference 8. [b] Not distillable. [c] Lit.[2] mp 170 °C. [d] Satisfactory combustion analytical data for C, H, and N were reported for these compounds. [e] Lit.[5] bp 48 °C (0.85 mm). [f] Lit.[2] mp 118 °C. [g] Lit.[2]: no exact boiling point reported. [h] Material decomposed on attempted purification.

clization of diamines with carbon disulfide in presence of hydrogen chloride or pyridine/I_2 to thioureas (by far the best method for their preparation) is limited because long-chain diamines tend to produce macrocyclic bis or oligo thioureas instead,[6,7] and yields are only moderate at best. Other methods of preparing cyclic thioureas are even more involved.[2]

The facile Tiemann rearrangement with ring enlargement of hexahydro-2H-azepin-2-one O-(methylsulfonyl)-oxime in presence of aqueous base (KOH) to perhydro-1,3-diazocin-2-one[8] was thought to be applicable to the synthesis of alkylenecarbodiimides provided care was taken to prevent their hydrolysis to alkyleneureas. Thus, several cycloalkylene amidoximes of type **3**, readily available from the corresponding lactim methyl ethers, were converted into mesylates **4** (eq 2) and the latter treated with potas-



3b-f 4b-f



(2)

1b-f

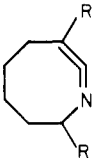
sium *tert*-butoxide in 1,2-dimethoxyethane solution at room temperature. This way we obtained good yields of the carbodiimides **1c,d,f** (with n = 6, 7, and 11; Table I). In contrast to other lower molecular weight N,N'-dialkylcarbodiimides, these compounds were found to be easily distillable, stable liquids which could be kept for several months at room temperature without signs of oligomerization or polymerization. IR spectra of the compounds show strong bands for the N=C=N group at 2120 cm^{-1}.

A variation of this method, using the O-tosylate for the synthesis of **1c**, has been published while this work was in progress.[5]

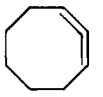
Although at first it seemded that potassium *tert*-butoxide was the base of choice for the modified Tiemann rearrangement of amidoxime O-mesylates into carbodiimides. However, this proved to be not the case as we were unable to prepare decamethylenecarbodiimide (**1e**, n = 10) by this method. While all the amidoxime O-mesylate precursor was consumed in the reaction, only traces of **1e** could be detected in the IR spectrum of the reaction mixture. In addition, the mesylate **4e** was found to be a very sensitive compound which tended to decompose even on storage at room temperature. **1e** could finally be prepared by treating a benzene solution of **4e** with aqueous potassium hydroxide at ambient temperature. The IR spectrum of the crude reaction product did not indicate the presence of significant amounts of byproducts, but extensive oligomerization during vacuum distillation reduced the yield of carbodiimide to 23% (best of several runs).

The unexpected stability of the cyclic alkylenecarbodiimides, especially of the nine-membered heterocycle **1c**, prompted us to attempt the synthesis of 1,3-diazacyclohepta-1,2-diene (**1a**) and 1,3-diazacycloocta-1,2-diene (**1b**). Dreiding models of these carbodiimides indicate that fairly unstrained arrangement of the heterocumulene N=C=N is still possible in the eight-membered ring.[9]

Behringer and Meier[2] reported that traces of **1b** were indeed formed (which readily polymerized) on treating pentamethylenethiourea with yellow mercury(II) oxide in methylene chloride. The synthesis of 3,8-disubstituted 1-azacycloocta-1,2-diene (**5**) has been described,[10] and the

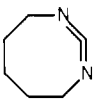


5



6

1a



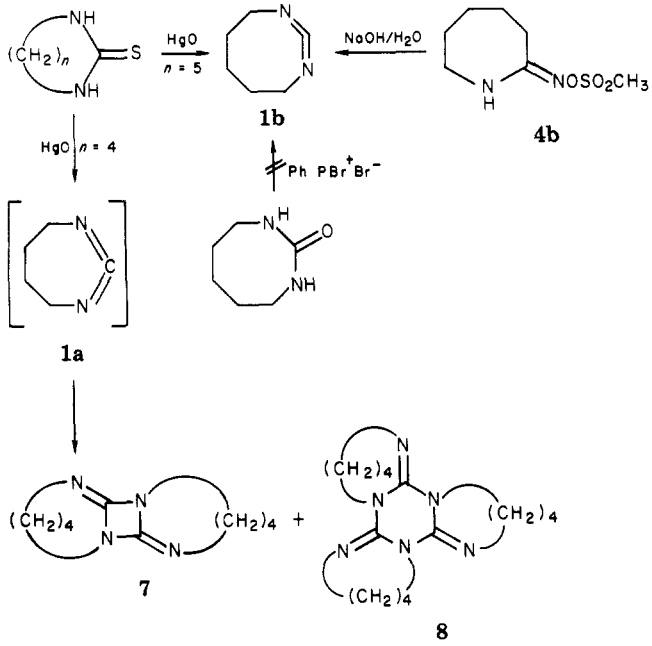
1b

cyclic allene **6** could be synthesized and trapped as well.[11] More recently, even the six- and seven-membered-ring allenes could be synthesized and characterized as cycloadducts.[12]

In an attempt to prepare **1b** by dehydration from pentamethylene urea with triphenylbromophosphonium bromide/triethylamine under rather mild conditions,[13,14] we obtained reaction products showing extremely weak infrared bands at 2100 cm^{-1} indicative of the presence of traces of carbodiimide. Dehydrosulfuration of pentamethylene thiourea with mercury(II) oxide in methylene chloride in the presence of sodium sulfate as a dehydrating agent gives the desired carbodiimide **1b** in high yield (>80%) and free of byproducts. The eight-membered-ring heteroallene is a mobile liquid with a characteristic odor. In solution it can be kept for several days with only minor changes; undiluted it will start to oligomerize gradually to

(6) Arya, V. P.; Honkan, V.; Shenoy, S. J. *Indian J. Chem., Sect. B* **1976**, *14B*, 773.
(7) Bogatskii, A. V.; Lukyanenko, N. G.; Kinichenko, T. I. *Zh. Org. Khim.* **1980**, *16*, 1301.
(8) Ulrich, H.; Tucker, B.; Richter, R. *J. Org. Chem.* **1978**, *43*, 1544.
(9) X-ray crystallographic studies have shown that the N=C=N group of aromatic and aromatic–aliphatic carbodiimides is not linear; the bond angle varies from 166° to 170°. A similar, if not even larger, bending has to be expected for cyclic aliphatic carbodiimides. (For references see: Williams, A.; Ibrahim, I. T. *Chem. Rev.* **1981**, *81*, 589.)
(10) Firl, J.; Schink, K.; Kosbahn, W. *Chem. Lett.* **1981**, 527.
(11) Marquis, E. T.; Gardner, P. D. *Tetrahedron Lett.* **1966**, 2793.
(12) Balci, M.; Jones, W. M. *J. Am. Chem. Soc.* **1980**, *102*, 7607.
(13) Bestmann, H. J.; Lienert, J.; Mott, L. *Justus Liebigs Ann. Chem.* **1968**, *718*, 24.
(14) Palomo, C.; Mestres, R. *Synthesis* **1981**, 373.

Scheme I

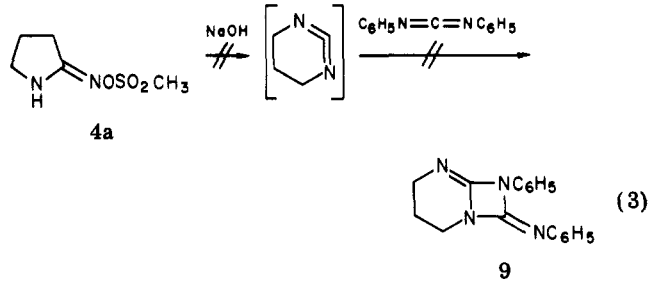


produce eventually a glassy colorless mass. This process takes several days to be complete and can be followed by IR spectroscopy by monitoring the disappearance of the carbodiimide band at 2100 cm^{-1} and the appearance of a broad band at 1630 cm^{-1}, indicative of formation of a polyguanidine. The ^{13}C NMR spectrum (in $CDCl_3$) of **1b** shows signals at 52.56 ppm for the carbon next to nitrogen and at 32.31 and 25.39 ppm for carbons 5/7 and 6; no signal appears for carbon 2. ^1H NMR spectra ($CDCl_3$) show an unsymmetric triplet centered at 3.5 ppm (four protons, CH_2–N) and a six-proton multiplet centered at ~1.85 ppm. The IR carbodiimide band at 2100 cm^{-1} is about 20 cm^{-1} lower than the bands for **1c,d,f**, which is likely due to a weakening of the heterocumulene bond as a result of an increased strain on the N=C=N moiety.

1,3-Diazacycloocta-1,2-diene reacts readily with other heterocumulenes (see the Reactions section), but the addition of water to form pentamethylene urea is relatively slow. In the light of this observation it was not surprising to find that **1b** can also be prepared by Tiemann rearrangement from the mesylate **3b** (dissolved in methylene chloride) on treatment with aqueous sodium hydroxide. This reaction, when carried out at room temperature, is very slow and not complete after 24 h. Addition of 5 wt % of Aliquat 336[29] as a phase-transfer agent reduces the reaction duration to several hours, with yields of **1b** being virtually quantitative.

On attempting to synthesize the next lower homologue, 1,3-diazacyclohepta-1,2-diene (**1a**), via dehydrosulfuration of tetramethylene thiourea, no monomeric product was obtained. The IR spectrum of the reaction solution showed the most intensive bands at 1630 and 1690 cm^{-1}, indicative of formation of oligomeric products. Gel-permeation analysis revealed the presence of predominantly two products which we assume to be the cyclic dimer and trimer of **1a**. It was further found that the ratio of these two oligomers can be influenced by variation of the reaction temperature: lower temperatures favor formation of the trimeric component while higher temperatures give more dimer. Workup of crude product mixtures with different solvents and solvent mixtures led to isolation of pure dimer **7** (mp 118–120 °C; Scheme I; identified by molecular weight determination and elemental analysis) which shows an infrared band at 1690 cm^{-1} for the C=N groups of the three ring system. The other oligomerization product, which we believe to be the trimer **8**, has not yet been isolated in pure form. The assumption that products like **7** and **8** are indeed formed via a very labile, monomeric carbodiimide, **1a**, could be ascertained by trapping **1a** with another heterocumulene (*N,N'*-diphenylcarbodiimide) during dehydrosulfuration of the thiourea (see the Reactions section).

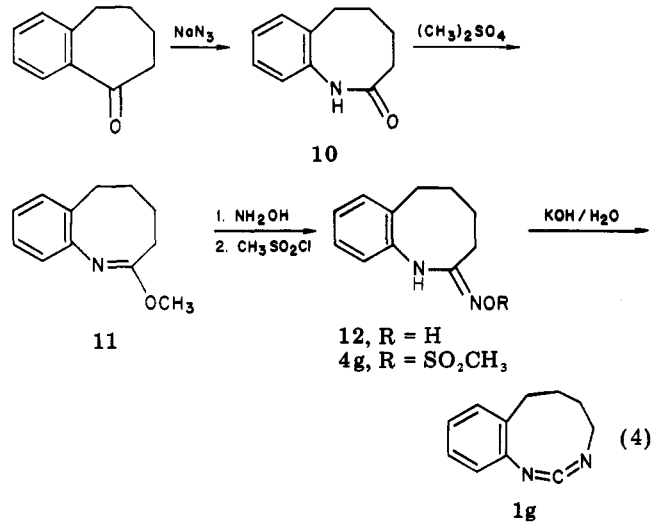
We have also tried to trap the six-membered-ring carbodiimide 1,3-diazacyclohexa-1,2-diene by treating a methylene chloride solution of 1-azacyclopentan-2-one *O*-(methylsulfonyl)oxime with aqueous sodium hydroxide in presence of *N,N'*-diphenylcarbodiimide, hoping to obtain the cycloadduct **9** (eq 3) which has been prepared



(3)

previously by a different route.[15] Although all the mesylate and *N,N'*-diphenylcarbodiimide were consumed on stirring the mixture for 24 h, none of the adduct was formed since the IR spectra did not show a C=N band for the 2,4-diimino-1,5-diazetidine at ~1680 cm^{-1}.

In an extension of the synthesis of cycloaliphatic carbodiimides from amidoxime precursors via Tiemann rearrangement, we have tried to prepare cyclic *N*-alkyl-*N'*-aryl- and *N,N'*-diarylcarbodiimides by this method. Problems were encountered while attempting to rearrange the mesylate **4g** of 7,8,9,10-tetrahydro-6-(hydroxyamino)benz[*b*]azoc-5-ene (synthesized from benzosuberone via the sequence shown in eq 4). Potassium *tert*-butoxide

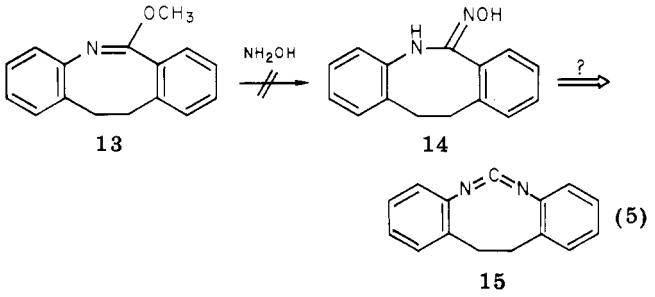


(4)

in DME failed completely, and aqueous potassium hydroxide gave only a 27% yield of 4,5,6,7-tetrahydrobenzo-1,3-diazonine (**1g**).

The synthesis of 6,7-dihydrodibenzo[*d,h*]-1,3-diazonine (**15**) via a similar sequence failed at an early stage, as we were not able to convert the iminomethyl ether **13**[16] into the amidoxime **14** by any known method (eq 5).

(15) Burkhardt, J.; Hamann, K. *Chem. Ber.* **1968**, *101*, 3428.
(16) Paquette, L. A.; Anderson, L. B.; Hansen, J. F.; Lang, S. A., Jr.; Berk, H. *J. Am. Chem. Soc.* **1972**, *94*, 4907.



Other attempts of using derivatives of amidoximes as carbodiimide precursors failed altogether. Thus the cyclic amidoxime **3f** was treated with phosgene to yield quantitatively the bicyclic 4*H*-1,2,4-oxadiazol-5-one **16** (Scheme II). It was hoped that thermal fragmentation of **16** would yield carbon dioxide and a nitrene intermediate capable of undergoing Tiemann rearrangement, reminiscent of the reported base-catalyzed fragmentation of *N*-alkyl salts of structurally similar compounds.[17] It was found, however, that **16** is thermally stable up to 235 °C and can be vacuum distilled at this temperature with negligible decomposition.

Similarly, certain 3,4-disubstituted 1,2,3,5-oxathiazole 2-oxides are known to lose sulfur dioxide on heating to yield carbodiimides.[18] Treatment of **3f** with thionyl chloride yields the oxathiadiazoline-2-oxide **17** which was heated to induce fragmentation both with and without solvents. A sample of **17** decomposed violently in an oil bath of 125 °C, producing a dark brown residue devoid of any carbodiimide **1f**. Similarly, heating of **17** in chlorobenzene at 125 °C failed to yield **1f**.

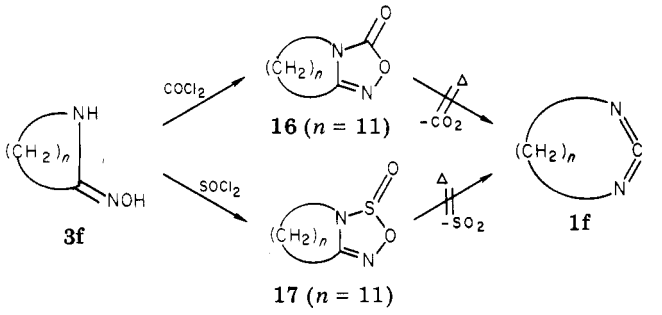
Reactions

Low molecular weight, straight-chain dialkylcarbodiimides are not very stable in the monomeric form and polymerize within days. Increasing steric crowding at the nitrogens, as in *N,N'*-dicyclohexyl, diisopropyl-, and di-*tert*-butylcarbodiimide enhances the stability. Interestingly, **1c–f** were found to be stable at room temperature for several months. Slow, partial hydrolysis of samples of **1c,e** on storage resulted in formation of small amounts of ureas. As expected, lowering the number of the chain links decreases the stability of the carbodiimides as seen in **1a** and **1b**, which form oligomeric (dimer, trimer) and polymeric products during or shortly after formation. In our attempts to oligomerize **1c,f**, we used a strong acid as a catalyst in analogy to reactions described by Hardtke et al.[19] Treatment of methylene chloride solutions of **1c,f** with catalytic amounts of tetrafluoroboric acid affords mixtures of dimers **18** (Scheme III) and higher oligomers which we believe to be long-chain (or cyclic) polyguanidines of type **19**. Crude reaction mixtures show IR bands at 1685 cm^{-1} for the dimers and at 1635 cm^{-1} for the oligomeric products.[20] In case of **1f** we were able to isolate, in fairly pure form, the dimer **18a** from the product mixtures. Higher oligomeric products could not be further characterized; they are initially soluble in the reaction medium but, once precipitated, are difficult to redissolve.

The addition of phosgene to the N=C=N bond of **1d–f** to product *N*-(chlorocarbonyl)chloroformamidines has been described in connection with the synthesis of intramolecular isocyanate dimers.[1]

Aliphatic carbodiimides are known to readily undergo cycloaddition reactions with other heterocumulenes such as isocyanates.[21] We also found that [2 + 2] cycloadducts of type **20** are formed quantitatively on mixing equimolar amounts of aryl isocyanates or *N,N'*-diphenylcarbodiimide with the cyclic carbodiimides. Formation of 2-imino-1,3-diazetidin-4-ones (X = O) from isocyanates is exothermic and complete within minutes; the nature of the cycloadducts is independent of the molar ratio of the two heterocumulenes. The corresponding adducts with *N,N'*-diphenylcarbodiimides are formed much more slowly, especially with the larger ring carbodiimides such as **1e,f**. The seven-membered-ring carbodiimide **1a**, which we were not able to identify as a stable monomer, could be trapped with *N,N'*-diphenylcarbodiimide during dehydrosulfuration of tetramethylenethiourea to produce **20a**. Benzo[*d*]-1,3-diazanona-1,2-diene (**1g**) reacts exothermically with phenyl isocyanate with addition across the "aliphatic" CN double bond of the carbodiimide to afford **21** (eq 6). Our structure assignment is based on a comparison of CH_2–N proton triplets in the ^1H NMR spectra of **1g** and **21** which

Scheme II



Scheme III

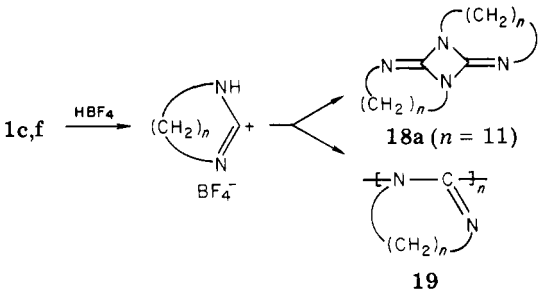


Table II. [2 + 2] Cycloadducts of Cyclic Carbodiimides with Aryl Isocyanates and *N,N'*-Diphenylcarbodiimide[a]

compd	*n*	R	X	mp, °C	IR (C=X), cm^{-1}
20a	4	C_6H_5	NC_6H_5	103-104	1680
20b	5	C_6H_5	O	oil	1725
20c	5	*p*-ClC_6H_4	O	65	1725
20d	6	C_6H_5	O	74-75	1715
20e	6	C_6H_5	NC_6H_5	107-108	1680
20f	7	C_6H_5	O	54-56	1715
20g	7	C_6H_5	NC_6H_5	135-136	1680
20h	11	C_6H_5	O	75	1715
20i	11	C_6H_5	NC_6H_5	90	1680
21				158-160	1715

[a] Satisfactory combustion analytical data were obtained for these compounds.

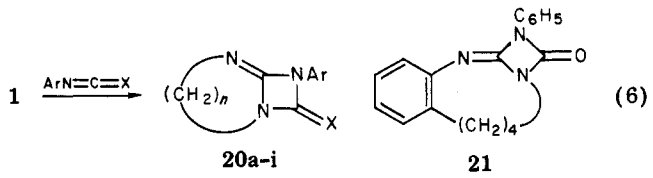
(17) Olofson, R. A.; Lotts, K. D. *Tetrahedron Lett.* **1979**, 3131.

(18) (a) Dondoni, A.; Barbaro, G.; Battaglia, A. *J. Org. Chem.* **1977**, *42*, 3372. (b) Rajagopalan, P.; Advani, B. G. *Ibid.* **1965**, *30*, 3369. (c) Beltrame, P.; Vitrani, C. *J. Chem. Soc. B* **1970**, 873. (d) Eloy, F. *Helv. Chim. Acta* **1965**, *48*, 380.

(19) Hardtke, K.; Rossbach, F.; Radau, M. *Justus Liebigs Ann. Chem.* **1972**, *762*, 167.

(20) The structurally related N^1,N^2,N^3,N^4,N^5-pentaarylbiguanides show bands at 1630 cm^{-1} for the C=N group.

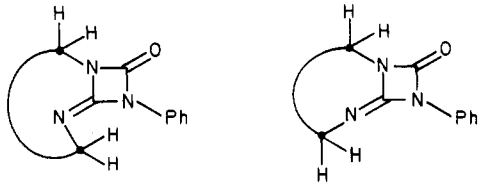
(21) Hofmann, R.; Schmidt, E.; Reichle, A.; Moosmüller, R. U.S. Patent 3 065 224, 1962 (to Farbenfabriken Bayer AG).



20a-i 21 (6)

show an upfield shift of ~0.5 ppm from 3.53 to 3.03 ppm in the adduct. Shifts similar in magnitude were also observed for adducts **20d,f**. In addition, a 0.4-ppm upfield shift of the *N*-methyl signal (from 3.00 to 2.60 ppm) is also found in the pair *N*-methyl-*N'*-phenylcarbodiimide and 1-methyl-3-phenyl-2-(phenylimino)-1,3-diazetidinone.[28] Melting points and analytical data for all the [2 + 2] cycloadducts **20** and **21** are summarized in Table II.

^{13}C NMR spectra (in $CDCl_3/Me_4Si$) of the isocyanate adducts **20c,d** show a pair of carbon signals at 42.22/47.10 and 43.61/45.36 ppm, respectively, for the two methylene carbons adjacent to the nitrogens of the eight- and nine-membered heterocycles. The adduct **20h**, derived from the 14-membered-ring carbodiimide **1f** and phenyl isocyanate, however, shows four broad, partly resolved resonances at 40.42/42.70 and 47.20/48.01 ppm for these carbons on recording the spectra at ambient temperature (35–40 °C). This signal splitting is undoubtedly caused by a syn–anti isomerism of the two forms of **20h** as shown below. On heating the sample to 75 °C during recording,



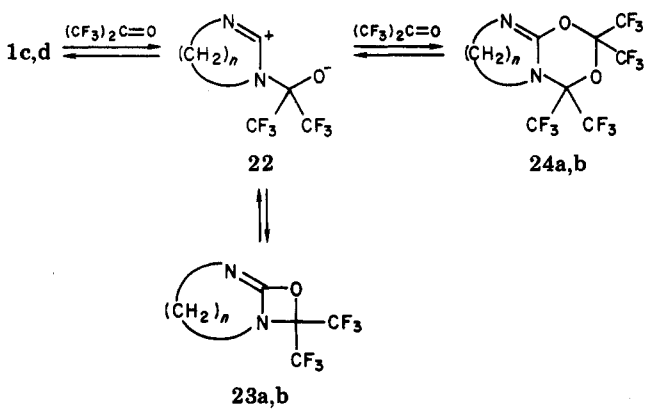
20h, "syn" (*Z*) 20h, "anti" (*E*)

collapse of the four signals to two (at 41.84 and 47.80 ppm) is observed which is indicative of the presence of only one isomer. At this temperature, however, partial dissociation of the adduct takes place also as the spectra show an additional N–CH_2 signal at 46.29 ppm for the carbodiimide **1f**. On cooling of the sample, reappearance of the four signals is observed, although the recombination of **1f** with phenyl isocyanate is not complete, and the band at 46.29 ppm is still present. This type of stereoisomerism is, of course, not possible for adducts **20c,d** because of the restricted flexibility in the eight- and nine-membered rings. A similar syn–anti isomerism dependent upon ring size in hetereocycles has been shown to exist in cyclic thioamides, imidates, and thioimidates.[22]

The capability of the cycloaliphatic carbodiimides to undergo cycloaddition reactions is not limited to heterocumulenes. Hexafluoroacetone was found to react with **1d** (n = 7) in chloroform to give a thermostable liquid adduct with a molar ratio of hexafluoroacetone to **1d** of 2:1 which we believe to have structure **24b**. The IR spectrum of the imino-1,3,5-dioxazane shows an intense band at 1740 cm^{-1} for the C=N group. This is rather high for a C=N absorption on six-membered rings and difficult to explain when compared with the [2 + 2] cycloadducts of type **20**.

The next lower homologue, **1c**, reacts also with hexafluoroacetone to yield an inseparable mixture of 1:1 and 1:2 cycloadducts. On introduction of gaseous $(CF_3)_2CO$ into neat carbodiimide **1c** at room temperature the product initially formed shows a strong IR band at 1790 cm^{-1} which we believe to belong to a oxazetidine **23**. Increasing amounts of a second product, with a band at 1735 cm^{-1} and believed to be **24a**, start to appear on continued ketone introduction, with an equilibrium state being reached after several hours. On attempting to separate the products by distillation, dissociation takes place, as only unchanged **1c** mixed with **24a** is obtained. In repeated experiments under a variety of conditions we were not able to obtain either of the products in pure form. It is likely that the formation of both cycloadducts proceeds via a dipolar intermediate, **22** (Scheme IV).

Scheme IV



Experimental Section

Infrared spectra were recorded on a Beckman Acculab 4 spectrophotometer with chloroform and potassium bromide as media; ^1H NMR spectra were determined on a Varian T-60 spectrometer and ^{13}C NMR spectra on a Varian CFT-20 spectrometer with $CDCl_3$ as the solvent and Me_4Si as an internal standard. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN; melting points are uncorrected.

Starting Materials. 2-Azacyclododecanone was prepared by the following route. Ring contraction of cyclododecanone as described by Schank and Eisert[23] and by Ziegenbein[24] gave cycloundecanone which was treated with sodium azide/HCl in DME to afford the desired lactam in 98% yield. This modified Schmidt reaction gave considerably better results than the route via Beckmann rearrangement of the cycloundecanone oxime.[25,26] Methylation of 2-azacyclododecanone with dimethyl sulfate at 90–92 °C gave a 77% yield of **1-aza-2-methoxycyclododec-1-ene**, bp 75–76 °C (0.05 mm). Anal. Calcd for $C_{12}H_{23}NO$: C, 73.04; H, 11.75; N, 7.10. Found: C, 72.89; H, 12.02; N, 7.39.

7,8,9,10-Tetrahydrobenz[*b*]azocin-6-one (10) was prepared in 82% yield from benzosuberone with sodium azide/HCl in DME at room temperature. These conditions are milder and eliminate the use of trichloroacetic acid as suggested by Smith and Berry.[27] Methylation of **10** to give **11** was tried both with dimethyl sulfate at 90–95 °C (38% yield) and trimethyloxonium fluoroborate (84%) in analogy to a literature procedure:[16] bp 81–84 °C (0.1 mm); IR ($CHCl_3$) 1660 cm^{-1} (C=N). Anal. Calcd for $C_{12}H_{15}NO$: C, 76.15; H, 7.99; N, 7.40. Found: C, 76.27; H, 8.19; N, 7.61.

Lactamoximes (cyclic amidoximes) 3b–f and 12 were prepared from the corresponding *O*-lactim methyl ethers with hydroxylamine hydrochloride/$NaHCO_3$ in refluxing methanol according to literature procedures[2,8] (yields nearly quantitative).

Lactam oxime *O*-mesylates 4b–g are obtained on treating an ice-cooled suspension of the lactam oximes in pyridine with

(22) (a) Moriarty, R. M.; Yeh, C. L.; Curtis, V. A.; Ramey, K. C. *Tetrahedron Lett.* **1971**, 4843. (b) Moriarty, R. J.; Yeh, C. L.; Ramey, K. C.; Whitehurst, P. W. *J. Am. Chem. Soc.* **1970**, *92*, 6360. (c) Yeh, E. L.; Moriarty, R. M.; Yeh, C. L.; Ramey, K. C. *Tetrahedron Lett.* **1972**, 2655.

(23) Schank, K.; Eistert, B. *Chem. Ber.* **1965**, *98*, 650.
(24) Ziegenbein, W. *Chem. Ber.* **1961**, *94*, 2989.
(25) Ruzicka, L.; Kobelt, M.; Häfliger, O.; Prelog, V. *Helv. Chim. Acta* **1949**, *32*, 544.
(26) Huisgen, R.; Brade, H.; Walz, H.; Glogger, I. *Chem. Ber.* **1957**, *90*, 1437.
(27) Smith, P. A. S.; Berry, W. L. *J. Org. Chem.* **1961**, *26*, 27.
(28) D. S. Gilmore Research Laboratories, unpublished data.

molar amounts of methanesulfonyl chloride in analogy to a literature procedure.[8] Pyridine removal in vacuo at a bath temperature of 40–60 °C and trituration of the semisolid residues with water generally leads to separation of the mesylates as colorless solids which are filtered, washed with water, and dried at ambient temperature.

1-Azacyclodecan-2-one *O*-(methylsulfonyl)oxime (4e) separated as an oil on workup with water and was not further purified. It was used in a CH_2Cl_2 solution in the Tiemann rearrangement.

1-Azacyclopentan-2-one *O*-(methylsulfonyl)oxime (4a) is soluble in water and was extracted with methylene chloride from the aqueous phase; mp 70–72 °C (colorless crystals from benzene/hexane). Anal. Calcd for $C_5H_{10}N_2O_3S$: C, 33.71; H, 5.66; N, 15.73. Found: C, 33.49; H, 5.78; N, 15.51.

General Procedures for the Preparation of Cyclic Carbodiimides 1b–g. (A) From Lactam Oxime *O*-Methanesulfonates with Potassium *tert*-Butoxide. To a suspension of 42.0 g (0.375 mol) of potassium *tert*-butoxide in 200 mL of dimethoxyethane (DME) is added dropwise with vigorous stirring and ice cooling a slurry of 0.3 mol of mesylates **4c,d,f** over a period of 30 min. The reaction mixture is stirred at ambient temperature for another 60–90 min, after which the inorganic salts are filtered off and washed thoroughly with DME. The filtrate is concentrated under aspirator vacuum. The pale yellow oil left behind is dissolved in ~200 mL of CH_2Cl_2 and the solution extracted 3 or 4 times with 20-mL portions of water to remove traced of potassium hydroxide and *tert*-butoxide. The resulting solution is dried over Na_2SO_4, concentrated, and vacuum distilled, giving the carbodiimides as mobile, characteristically smelling liquids; yields, boiling points, and elemental analysis are given in Table I.

With Potassium or Sodium Hydroxide. (1) The Tiemann rearrangement of **4e** is carried out in methylene chloride with a crude sample obtained by reacting 0.1 mol of **3e** with 0.1 mol of methanesulfonyl chloride in 25 mL of pyridine. Removal of pyridine after 1 h and dilution of the residue with water and ice left a yellow oil which was twice washed with ice–water before being taken up in 50 mL of CH_2Cl_2. This solution is treated with aqueous potassium hydroxide (10 g in 30 mL of water) at room temperature for 20–30 min, after which the organic phase is dried over Na_2SO_4 and concentrated in vacuo, and the yellow-orange residue is taken up in 50 mL of *n*-hexane, leaving some orange material undissolved. Filtration and concentration leaves an oil which is vacuum distilled to yield **1e**.

(2) The carbodiimide **1g** is prepared from 0.1 mol of the mesylate precursor **4g**, dissolved in 120 mL of CH_2Cl_2, on treatment with aqueous potassium hydroxide (20 g in 60 mL of H_2O) at room temperature. The rearrangement is complete after 10–15 min, as indicated by monitoring the disappearance of **4g** by infrared spectroscopy. Distillation yields 27% of **1g**, bp 90 °C (0.1 mm); large amounts of a viscous (polymeric) residue are left behind; IR ($CHCl_3$) 2120 cm^{-1} (N=C=N). Anal. Calcd for $C_{11}H_{12}N_2$: C, 76.71; H, 7.02; N, 16.27. Found: C, 76.64; H, 7.24; N, 16.36.

(3) Treatment of a solution of 0.01 mol of **4b** in 20 mL of CH_2Cl_2 with 10 mL of 10 N NaOH containing 100 mg of Aliquat 336[29] (the progress of the reaction is monitored by infrared spectroscopy) results in formation of **1b** within 2.5–3 h. The organic phase is washed several times with small portions of water, dried over Na_2SO_4, and concentrated in vacuo, leaving a mobile, colorless, strongly smelling liquid: the IR spectrum of **1b** ($CHCl_3$) is devoid of any bands in the 1600–1800-cm^{-1} region but shows a strong band at 2100 cm^{-1} for the N=C=N group; ^{13}C NMR ($CDCl_3$/Me_4Si) 26.39 (C-6), 32.31 (C-5 and -7), 52.56 ppm (C-4 and -8); ^1H NMR ($CDCl_3$/Me_4Si) 1.85 (m, 6 H), 3.50 ppm (distorted triplets of 4 H).

(B) From Alkylene Thioureas. (1) A solution of pentamethylenethiourea (0.01 mol) in 20 mL methylene chloride is treated with 5.0 g of powdered sodium sulfate (anhydrous) and excess yellow mercury(II) oxide (8.0 g). The resulting suspension is stirred at room temperature for 2–3 h. Removal of the black mercury(II) sulfide/Na_2SO_4 mixture by filtration leaves a colorless filtrate which on concentration in vacuo yields **1b** as a colorless liquid, identical on IR comparison with a sample obtained according to the procedure given above. The yield of product is determined by cycloadduct formation with a weighed amount of aryl isocyanate.

(2) Treatment of a solution of tetramethylenethiourea (0.01 mol) in 30 mL of methylene chloride with yellow mercury(II) oxide (8.0 g) and Na_2SO_4 (5.0 g) at room temperature results in a very fast formation of black mercury(II) sulfide (10–20 min) accompanied by a weak exotherm. The workup of the reaction mixture after 1 h gives a colorless filtrate containing **7** and **8**. Solvent removal in vacuo leaves a semisolid (0.95 g; quantitative yield) which, according to gel-permeation analysis contains the oligomers **7**/**8** in a ratio of 36:62. Repeated recrystallization of the residue from *n*-hexane yields pure **7**: mp 118–120 °C; IR ($CHCl_3$) 1695 cm^{-1} (C=N). Anal. Calcd for $C_{10}H_{16}N_4$: C, 62.47; H, 8.39; N, 29.14. Found: C, 62.45; H, 8.57; N, 29.18; mol wt 190 (vapor pressure osmometry in $CHCl_3$).

Substitution of methylene chloride with chloroform as the reaction medium and carrying out the dehydrosulfuration at reflux temperature affords a mixture of **7** and **8** in a ratio of approximately 61:34 and 5% of higher oligomers.

Attempts To Synthesize 1f from 16 and 17. (1) The oxadiazolo[3,4-*a*]azacyclotridecan-2-one **16** is prepared in virtually quantitative yield on treating a chloroform solution of **3f** with phosgene, initially at room temperature and later at reflux temperature, for a total of 2.5 h. An intermediate is formed in this reaction which slowly converts to **16** as indicated by the appearance and disappearance of an IR band at 1670 cm^{-1} and final appearance of the product carbonyl band at 1765 cm^{-1}. Solvent and phosgene removal leave a tan oil, bp 192–195 °C (0.1 mm). Anal. Calcd for $C_{13}H_{22}N_2O_2$: C, 65.51; H, 9.31; N, 11.76. Found: C, 65.67; H, 9.18; N, 11.70.

Heating samples of **16** to 230–235 °C for 1 h does not result in gas evolution or changes in the IR spectrum of the material despite darkening.

(2) The oxathiadiazolo[3,4-*a*]azacyclotridecane 2-oxide **17** is prepared from **3f** with excess thionyl chloride in refluxing chloroform solution (2 h). The resulting orange resin which is obtained after removal of chloroform and excess thionyl chloride is redissolved in methylene chloride and treated with a saturated sodium bicarbonate solution to remove acidic impurities. Drying of the organic phase (Na_2SO_4) and solvent removal leaves a thick liquid which shows a strong IR band at 1180 cm^{-1} (S=O) in $CHCl_3$.

A sample of **17** heated to 125 °C decomposed violently with gas evolution and charring of the residue. No carbodiimide **1f** could be detected by IR spectroscopy. Similarly, attempted thermolysis of **17** in chlorobenzene solution at 125 °C (3 h) did not result in formation of **1f** although the starting material was slowly consumed.

Oligomerization of 1c,f. Samples (0.01 mol) of 1,3-diazacyclonona-1,2-diene (**1c**) and 1,3-diazacyclotetradeca-1,2-diene (**1f**), dissolved in methylene chloride, are treated with several drops each of a solution of tetrafluoroboric acid in diethyl ether which causes the separation of polymeric guanidines of type **19** while lower oligomers and dimer stay in solution. In case of **1c**, polymerization is the dominating reaction. Filtration of reaction mixtures after complete disappearance of carbodiimide (~10–20 min) yields gelatinous polymers **19a,b**, IR (KBr) 1635 cm^{-1} (C=N). On slow concentration of the filtrates more oligomeric and polymeric product precipitates and is removed by filtration. Amorphous residues consisting predominantly of dimers **18a,b** each are obtained on completely removing the solvent. Purification of **18b** by repeatedly dissolving it in CH_2Cl_2 and precipitating traces of oligomers by gradual addition of acetone followed by solvent removal afforded a waxy solid: mp 115–122 °C; IR ($CHCl_3$) 1685 cm^{-1} (C=N). Anal. Calcd for $C_{24}H_{44}N_4$: C, 74.17; H, 11.41; N, 14.42. Found: C, 73.79; H, 11.57; N, 14.25.

Cycloadducts 20a–i and 21. The cycloadducts of alkylenecarbodiimides and aryl isocyanates are obtained in quantitative yield on mixing equimolar quantities (generally 0.01 mol each) without solvent. Adduct formation with aryl isocyanate is exothermic and complete within minutes (IR); **1b** is reacted in methylene chloride solution with the isocyanates to avoid side reactions (oligomerization). Cycloadditions with *N,N'*-diphenylcarbodiimide are generally slower and require several hours for completion if carried out at ambient temperature but are considerably faster at 90–95 °C.

(29) Aliquat 336 is tricaprylylmethylammonium chloride.

The adduct **20a** is obtained in only 74% yield on dehydrosulfurating tetramethylenethiourea solutions (CH_2Cl_2) with HgO (yellow) in presence of equimolar quantities of *N,N'*-diphenylcarbodiimide; small amounts of unidentified sulfur-containing byproduct were also formed in this reaction. Analytical data of recrystallized samples (hexane or methanol) are given in Table II.

Reactions of Carbodiimides 1c,d with Hexafluoroacetone. (1) Introduction of gaseous hexafluoroacetone into a solution of 1.38 g (0.01 mol) of 1,3-diazacyclodeca-1,2-diene (**1d**) in 30 mL of chloroform leads to slow formation of cycloadduct **24b** (n = 7). Progress of the reaction can be followed by IR spectroscopy by monitoring disappearance of the carbodiimide band at 2120 cm^{-1} and the appearance of a new C=N band at 1740 cm^{-1}. The resulting reaction solution is concentrated in vacuo, leaving a colorless liquid (contaminated by trace amounts of heptamethyleneurea): bp 46–47 °C (0.1 mm); 3.90 g (83%). Anal. Calcd for $C_{14}H_{14}N_2O_2F_{12}$: C, 35.76; H, 3.00; N, 5.95. Found: C, 35.71; N, 2.96; N, 5.84.

(2) A reaction similar to the one described above is carried out with 1,3-diazacyclonona-1,2-diene (**1c**) and hexafluoroacetone. After approximately a 1-h reaction duration, IR spectra of the reaction mixture show a strong band at 1790 cm^{-1} and a small band at 1740 cm^{-1} aside from those of unchanged **1c**. Continued hexafluoroacetone introduction leads slowly to a nearly complete disappearance of the carbodiimide band at 2120 cm^{-1} and a significant decrease in the band at 1790 cm^{-1}. During distillation of the crude product in vacuo, a pressure drop is noticed as the bath temperature reaches 40–50 °C. A liquid, distilling at 53–55 °C (0.1 mm) at a bath temperature of 75–80 °C, is collected which consists according to its IR spectrum of a mixture of **1c** and **24a** (C=N at 1740 cm^{-1}); small amounts of a semisolid, consisting of oligomeric **1c**, are left behind.

Registry No. 1b, 85237-12-3; **1c**, 6248-74-4; **1d**, 6543-91-5; **1e**, 79568-35-7; **1f**, 72995-04-1; **1g**, 85237-13-4; **3b**, 19214-08-5; **3c**, 55040-59-0; **3d**, 55040-57-8; **3e**, 83594-28-9; **3f**, 55040-58-9; **4a**, 85237-14-5; **4b**, 65252-84-8; **4c**, 85237-15-6; **4d**, 85237-16-7; **4e**, 83594-29-0; **4f**, 83594-27-8; **4g**, 85237-17-8; **7**, 85237-18-9; **8**, 85237-19-0; **10**, 22246-75-9; **11**, 85237-20-3; **12**, 85237-21-4; **16**, 85237-22-5; **17**, 85237-23-6; **18** (n = 11), 85237-24-7; **18** (n = 6), 85237-25-8; **19** (n = 11), 85237-11-2; **19** (n = 6), 85237-10-1; **20a**, 20991-09-7; **20b**, 85237-26-9; **20c**, 85237-27-0; **20d**, 85237-28-1; **20e**, 85237-29-2; **20f**, 85237-30-5; **20g**, 85237-31-6; (*Z*)-**20h**, 85237-32-7; (*E*)-**20h**, 85237-33-8; **20i**, 85237-34-9; **21**, 85237-35-0; **23** (n = 6), 85237-36-1; **24a**, 85237-37-2; **24b**, 85237-38-3; 1-aza-2-methoxycyclohex-1-ene, 5693-62-9; 1-aza-2-methoxycyclohept-1-ene, 2525-16-8; 1-aza-2-methoxycyclooct-1-ene, 1889-06-1; 1-aza-2-methoxycyclododec-1-ene, 41471-03-8; 1-aza-2-methoxycyclotridec-1-ene, 29376-34-9; 2-azacyclododecanone, 1202-71-7; cycloundecanone, 878-13-7; benzosuberone, 826-73-3; hydroxylamine hydrochloride, 5470-11-1; pentamethylenethiourea, 5269-85-2; tetramethylenethiourea, 5700-04-9; phosgene, 75-44-5; thionyl chloride, 7719-09-7; *N,N'*-diphenylcarbodiimide, 622-16-2; hexafluoroacetone, 684-16-2; phenyl isocyanate, 103-71-9; *p*-chlorophenyl isocyanate, 104-12-1.

Reaction of (Arylmethyl)amines with Superoxide Anion Radical in Aprotic Media. Insights into Cytokinin Senescence Inhibition

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The cytokinins are a group of plant senescence retarding phytohormones, usually *N*-arylmethyl derivatives of adenine. Purine, adenine, and the cytokinins kinetin [6-(furfurylamino)purine] and 6-(benzylamino)purine were reacted with $O_2^{-}\cdot$ generated from KO_2 solubilized in diethylamine by 18-crown-6 polyether. The only reaction observed was simple deprotonation of the N-7 hydrogen, yielding an air-stable salt. In order to uncover other modes that might be available in the absence of this simple acid–base reaction, we reacted various (arylmethyl)amines (i.e., furfurylamine and benzylamine) and (arylmethyl)anilines (**2a–c**) with $O_2^{-}\cdot$ in benzene. The products in the case of (arylmethyl)amines were the corresponding aroylamines isolated in greater than 60% yield. Compounds **2a–c** yielded the corresponding amides (**3**), benzoic acids (**4**), nitrobenzenes (**5**), and arenes. Similar results were obtained when *tert*-butoxide or hydroxide replaced superoxide, with the rate of reaction decreasing in the order t-$BuO^- > O_2^{-}\cdot > HO^-$, the apparent order of decreasing basicity. The results suggest that the process observed involves a base-catalyzed autoxidation of the benzylic carbon of the benzylamines. The resulting hydroperoxide rearranges and/or undergoes oxidative cleavage, ultimately yielding the observed products. Aniline itself reacts with $O_2^{-}\cdot$, yielding azobenzene, nitrobenzene, and (4-nitrophenyl)phenylamine. The latter presumably results from the nitrobenzene trapping of the anilinyl radical.

The cytokinins are a group of plant senescence retarding phytohormones which are generally derivatives of the nucleic purine base adenine (**1b**), examples of which are kinetin [6-(furfurylamino)purine, **1c**] and N^6-benzyladenine [6-(benzylamino)purine, **1d**].[1] Various cytokinins have also displayed antiviral action,[2] while kinetin ribofuranoside has been shown to be an anticancer agent.[3]

Recently, Leshem et al. reported[4] in vivo experiments with intact pea plants which indicated that enzymatically generated (using xanthine–xanthine oxidase) superoxide anion radical ($O_2^{-}\cdot$) induced senescence in plant tissue which was inhibited by kinetin (**1c**). These experiments

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