Anal. Calcd for $C_{14}H_{11}NO$: C, 80.36; H, 5.30; N, 6.69. Found: c, 80.62; H, 5.24; N, 6.40.

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Registry No.—**1**, 230-27-3; **2**, 605-88-9; **2** picrate, 63783-90-4; **3**, 40174-37-6; **4**, 31485-96-8; **4** picrate, 63783-91-5; **5**, 59181-25-8; **6**, 17104-70-0; **7**, 85-01-8; **11**, 17104-69-7; **12**, 50697-49-9; **13**, 85-06-3; **14**, 3900-23-0; **15**, 59181-26-9; **16**, 832-69-9; **16** picrate, 63783-92-6; **17**, 62163-01-3; glycerol, 56-81-5; 1-naphthylamine, 134-32-7; crotonaldehyde, 4170-30-3; methyl vinyl ketone, 78-94-4; 4-methyl-1-naphthylamine, 4523-45-9; methylsulfinyl carbanion, 13810-16-7; dimethyl sulfoxide, 67-68-5; 4-methyl-2-naphthylamine, 4523-46-0.

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Synthesis with 1,2-Oxazines. 3.[1] Reactions of α-Chloro Aldonitrones with Enol Ethers: a Synthetic Route to Medium-Ring Lactones

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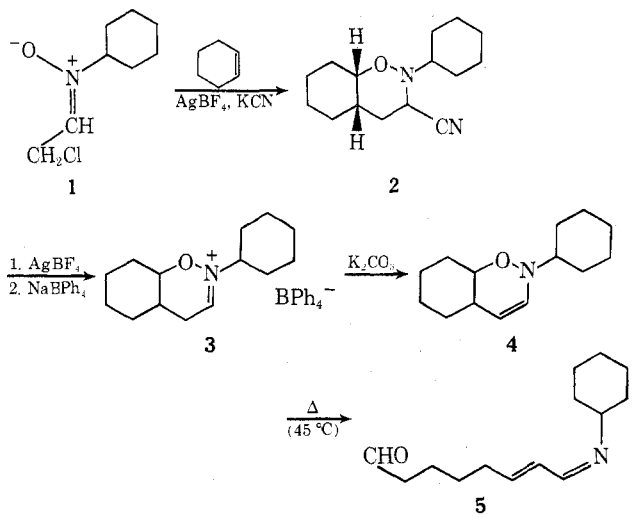
Cyclic enol ethers can undergo a Ag^+-induced cycloaddition with α-chloro nitrones. The corresponding polycyclic adducts were converted to enamoid structures of type **17b** via the immonium tetraphenylborate salts. The existence of an intramolecular ketal and the *N*-alkyl-5,6-dihydro-2*H*-1,2-oxazine ring as moieties in **17b** and **21a–c** allowed a thermolysis to the 10–12-membered lactones through cleavage of a central C–C bond in the polycyclic system. Structural effects on the thermolysis have been noted.

The usefulness of 1,4 dipolar cycloaddition for the construction of heterocyclic systems using positively charged heterodienes has been noted by some research groups.[2,3] α-Chloro nitrones were introduced by Eschenmoser as a new class of potent reagents of broad synthetic capability.[4–9] One major synthetic application of α-chloro nitrone chemistry was a new general way to construct the *N*-alkyl-5,6-dihydro-4*H*-oxazinium ion **3** in a Ag^+-induced cycloaddition reaction with isolated olefinic double bonds.[4] Imminium salts like **3** lead to a "carboxolytic" bond cleavage, occurring as a result of a retro-Diels–Alder reaction of the deprotonated enamoid derivative **4**, and end with the open-chain aldehyde **5**.



1 2 3 4 5

The object of this work was to examine if an analogous series of reactions could be applied to simple bicyclic enol ether **6** and **10a–c** (Scheme I). These were chosen as models for a possible synthesis of medium- and large-ring lactones in the α-chloro nitrone method. This involved (a) determining the generality of the cycloaddition reaction with enol ethers, (b) looking for "side" reactions and examining their influence on the cycloaddition, and (c) checking whether the carboxolytic bond cleavage procedure could also be applied in this case.

Starting enol ethers were prepared according to Obara (compound **6**)[10] and Immer (compounds **10a–c**).[11] Work on enol ethers was carried out in parallel with similar experiments on octalin (**13**) for possible special behavior in propellanes.[12] The reaction products obtained as a result of reaction with α-chloro nitrone **1** and the olefin were analyzed quantitatively and isolated by column chromatography. Results and yields are given in Table I.

The reaction products from enol ethers were mixtures of three main components: (1) cycloaddition products, (2) hydroxy ketones, and (3) a by-product having the structure **9**. Cycloaddition products were propellanes **7** and **11a–c**. It was

Table I. Products and Yields in the Ag^+-Induced Reaction of 1 with Enol Ethers

Registry no.	Enol ether (equiv)	1, equiv	Cycloaddition product (equiv)	Keto alcohol (equiv)	9, equiv	Enol ether recovered, equiv: From reaction	Enol ether recovered, equiv: Recycled keto alcohol	Net yield of cycloaddition based on enol ether consumed, %
7106-07-2	**6** (2.72)	1.0	**7** (0.26)	**8** (0.30)	0.02	1.12	0.28	26
63689-21-4	**10a** (1.20)	1.0	**11a** (0.19)	**11a** (0.52)	0.21	0.02	0.42	25
16425-91-5	**10b** (1.0)	1.02	**11b** (0.14)	**12b** (0.77)	0.22	0.01	0.52	29
	10b (1.0)	1.58	**11b** (0.21)	**12b** (0.68)	0.08		0.50	42
63689-22-5	**10c** (1.16)	1.0	**11c** (0.11)	**12c** (0.86)	0.20	0.30	0.69	64

Scheme I

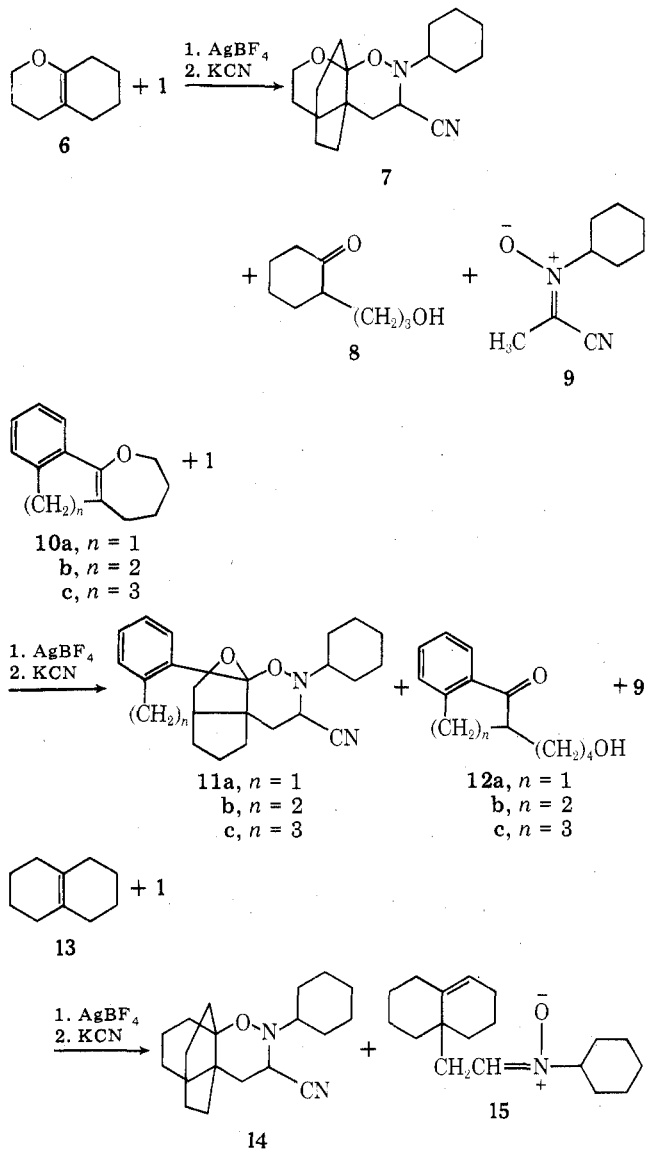
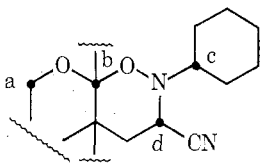


Table II. ^{13}C NMR Signals in Cycloadducts 7 and 11a–c[a]



Registry no.	Cycloadduct	^{13}C resonance (ppm): a	b	c	d	e
63689-23-6	7	61.9	101.7	47.7	61.2	118.4
63714-00-1	11a	65.2	112.5	47.8	61.1	118.4
63689-24-7	11b	64.9	103.8	48.0	61.9	118.2
63689-25-8	11c	66.3	108.4	48.7	62.5	118.6

[a] In $CDCl_3$. Compare Scheme II.

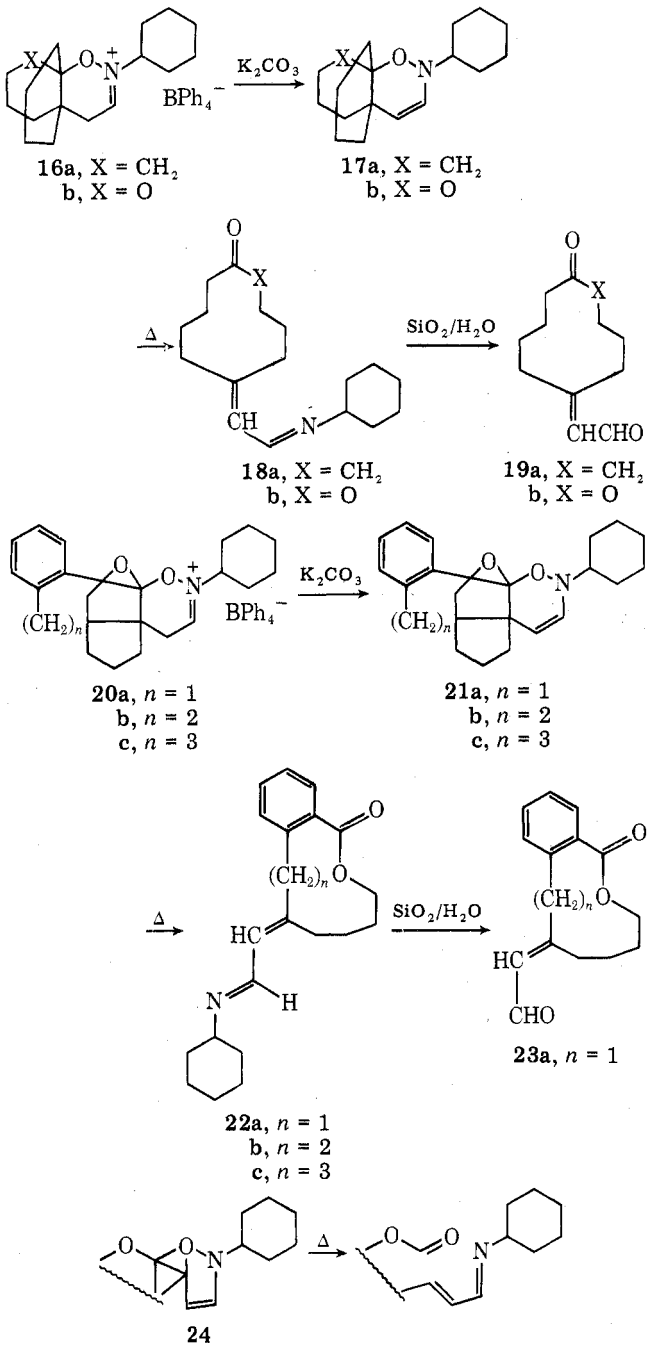
assumed that these CN^- addition products are a quantitative representation of the actual cycloaddition products, taking into account a very efficient CN^- addition reaction.[4] It was clear at that stage that cycloaddition to enol ethers **6** and **10a–c** is *regioselective*. However, the *direction* of α-chloro nitrone addition had to be determined. Structure assignment and proof for the existence of an intramolecular ketal in compounds **7** and **11a–c** were done mainly by ^{13}C NMR spectroscopy (see Table II). Signals at 101.7, 112.5, 103.8 and 108.4 ppm (remain as singlets in the "off-resonance" technique) gave proof for the structures in Scheme II, although these compounds were resistant to dilute HCl.[13]

The hydroxy ketones **8** and **12a–c** could be recycled to increase the yields of cycloaddition products. They could result from a relatively stable oxonium intermediate formed during the reaction to give the hydroxy ketones under the hydrolytic conditions present in the workup of the reaction.

Nitrone **9** was isolated also in the reaction with **13** and other olefins and was presumably overlooked in previous work. Its yield varies, however, and the mechanism by which it is formed is still obscure.

After achieving the first objectives—construction of propellanes **14**,[12] **7**, and **11a–c**—we came to the last aspect of this work: synthesis and thermal cycloreversion of enamines **17a,b** and **21a–c** applying reaction conditions already worked out by Eschenmoser et al.[5] to the solid tetraphenylborate immonium salts **16a,b** and **20a–c**, respectively. On treating these salts with solid K_2CO_3 in dichloromethane at 0 °C, deprotonation to the corresponding enamines took place. Differences in thermal stability of the enamines were observed as follows: compounds **17b** and **21a** were extremely unstable and could not be isolated even in solution at 0 °C. Instead, they were converted in good (76 and 81% overall) yields to the ten-membered lactones **18b** and **22a**, respectively. It was possible to trap **20b** at 0 °C and to take the IR and ^1H NMR spectra and determine thereby its structure. However, rapid decomposition ($t_{1/2}$ at 45 °C ~ 10 min) gave the corresponding lactone **22b** in 82% yield. **20c** was converted at **21c** in 78% yield. This material was far more stable ($t_{1/2}$ at 80 °C ~ 1.5 h) than the analogous compounds **21a** and **21b** and decomposed to the 12-membered lactone **22c** in only 56% yield. In comparison, the carbocyclic analogue **16a** gave an extraordinarily stable enamine **17a** in 87% yield. This was stable enough to allow recrystallization (mp 128–135 °C dec), making this material one of the most unusual members of the *N*-alkyl-6,6-dihydro-2*H*-1,2-oxazine series. Fortunately, this material still underwent thermolysis to the ten-membered ketone in 35% ($t_{1/2}$ at 80 °C ~ 3.5 h) yield. The differences in stability are evidently dependent on ring size (compare **21a** and **21c**) and the presence of the oxygen ring B as a part of the internal ketal. Comparison of **17a** and **17b** brought us to consider a possible anomeric effect leading to a higher energy content of the fragmenting system[14] **24** which is released by cleaving the long and relatively weak neopentyl bond. The effect re-

Scheme II



16a, X = CH_2
b, X = O

17a, X = CH_2
b, X = O

18a, X = CH_2
b, X = O

19a, X = CH_2
b, X = O

20a, n = 1
b, n = 2
c, n = 3

21a, n = 1
b, n = 2
c, n = 3

22a, n = 1
b, n = 2
c, n = 3

23a, n = 1

24

sulting from lone-pair interactions existing in **17a** and **21a–c** does not exist in **17b.** Steric hindrance in achieving a suitable conformation for cycloreversion was considered here as a possible reason for a thermal stability of **17a.** Different conformations of the cycloreverting intermediates can explain the appearance of 1:1 *E*/*Z* aldimines in **18b** and **22a–c.**[5] The aldimines were converted to the unsaturated aldehydo lactones in 76% (**18b** → **19b**) and 65% (**22a** → **23**) yield using the SiO_2/H_2O hydrolysis used previously.[5] Similarly, **18a** was converted to **19a** in 70% yield.

Enol ethers are very susceptible to cleavage under the reaction conditions and yield cycloaddition in low yields (18–25%). The resulting intramolecular ketals formed in the cycloaddition reaction serve as good models for a synthesis of medium- and large-ring lactones. The cleavage of the central bond in a polycyclic system, having an internal ketal and the *N*-alkyl-5,6-dihydro-2*H*-1,2-oxazine ring as moieties, allow such a thermolytic process. In this process, formation of the lactone ring and lactone carbonyl grouping is achieved simultaneously using as a tool the special properties of the 1,2-oxazine derivative. It looks, however, as if electronegative atoms could cause difficulties in the α-chloro nitrone cycloaddition to double bonds. Ring size was added to the list of steric effects governing the delicate cycloreversion process.[2] The anomeric effect resulting from the oxygen function on C-6 in **17a** and **21a–c** is still under investigation.

Experimental Section[15]

Ag^+-Induced Reaction of *N*-Cyclohexyl-2-chloroacetaldehyde Nitrone 1 with Enol Ethers. A solution of the α-chloro nitrone **1** in dry 1,2-dichloroethane (20 mL) was added under dry nitrogen with stirring to a solution of $AgBF_4$ in dry 1,2-dichloroethane (40 mL) and the enol ether at 0 °C during 2 h. After an additional 1 h at 0 °C, the mixture was shaken with 5 g of KCN in 20 mL of water during 5 min. The aqueous solution was then extracted twice with dichloromethane, and the combined organic layers were dried over Na_2SO_4. The residue obtained after removal of the solvents in vacuo was chromatographed over Al_2O_3[16] (using ligroine–benzene mixtures).

Products were obtained after reactions involving the following compounds.

(1) 3,4,5,6,7,8-Hexahydrobenzopyran (6)[10]. The enol ether **6** (1.5 g, 10.85 mmol), $AgBF_4$ (700 mg, 3.60 mmol), and **1** (700 mg, 3.98 mmol) gave 1.2 g of crude product. After chromatography, the following were obtained. (a) Propellane **7** (316 mg, 1.04 mmol): mp 138 °C (from hexane); 28% yield; IR 2225 and 1180 cm^{-1}; ^1H NMR δ 0.9–2.0 and 2.0–3.0 (two m, 25 H), 3.5–4.2 (m, 2 H); MS *m/e* (304.435) 304 (12%), 148 (100%), 136 (12%). Anal. Calcd for $C_{18}H_{28}N_2O_2$: C, 70.72; H, 9.25; N, 9.36. (b) **9** (47 mg) obtained from the mother liquor of **7** (0.28 mmol, 7.86%): mp 113–114 °C; IR 2210 and 1530 cm^{-1}; UV λ_{max} 254 nm (ε 9500); ^1H NMR 1.9 (m, 10 H), 2.12 (s, 3 H), and 4.75 (m, 1 H); MS *m/e* (166.223) 166 (3%). Anal. Calcd for $C_9H_{14}N_2O$: C, 65.00; H, 8.71; N, 16.51. (c) Hydroxy ketone **8** (190 mg, 1.2 mmol). This was recycled to give 152 mg of **6.**

(2) 2,3,4,5,6-Pentahydroindano[1,2-*b*]oxepin (10a).[11] The enol ether **10a** (2.3 g, 12.35 mmol), α-chloro nitrone (1.8 g, 10.24 mmol), and $AgBF_4$ (2.0 g, 10.27 mmol) gave 4.0 g of crude product. After chromatography the following were obtained. (a) Starting ether **10a** (50 mg, 0.27 mmol). (b) Cycloaddition product **11a** (703 mg): mp 112 °C (from hexane); 19.35% yield; IR 3080, 3040, 2240, 1620 and 1100 cm^{-1}; ^1H NMR δ 0.9–3.0 (m, 21 H), 3.7–4.5 (m, 3 H), and 7.0–7.5 (m, 4 H); MS *m/e* (352.431) 352 (9%), 186 (100%). Anal. Calcd for $C_{22}H_{28}N_2O_2$: C, 74.71; H, 7.97; N, 7.95. (c) **9** (410 mg, 2.27 mmol), mp 113 °C, obtained from the mother liquor of **10a.** (d) Keto alcohol **12a** (1.09 g, 5.3 mmol). This was recycled to give 0.84 g of **10a.**

(3) 2,3,4,5,6,7-Hexahydronaphth[1,2-*b*]oxepin (10b).[11] The enol ether (4.0 g, 19.97 mmol), α-chloro nitrone (3.6 g, 20.49 mmol), and $AgBF_4$ (3.40 g, 20.55 mmol) gave 7.3 g of crude product. After chromatography the following were obtained. (a) Starting ether **10b** (50 mg). (b) Propellane **11b** (1 g, 2.720 mmol): mp 141 °C; 13.62% yield; IR 2240, 1600 and 1080 cm^{-1}; ^1H NMR δ 0.9–1.9 (m, 18 H), 2.80 (d, J = 2 Hz, 4 H), 2.6–2.8 (m, 4 H), 3.90 (t, J = 2 Hz, 1 H), 4.20 (t, J = 5 Hz, 2 H), and 7.30–7.60 (m, 4 H). Anal. Calcd for $C_{23}H_{30}N_2O_2$: C, 75.37; N, 7.64. (c) **9** (100 mg), mp 113 °C, obtained from the mother liquor of the **11b** cycloaddition product (22.01% yield). (d) Keto alcohol **12b** (2.7 g, 12.37 mmol). This was recycled to give 2.1 g of **10b.**

(4) 2,3,4,5,6,7,8-Heptahydrobenzo[6,7]cyclohept[1,2-*b*]oxepin (10c).[11] The enol ether **10c** (5.4 g, 25.19 mmol), chloro nitrone (3.7 g, 20.06 mmol), and $AgBF_4$ (4.0 g, 20.54 mmol) gave 8.5 g of crude product. After chromatography the following were obtained. (a) Starting enol ether **10c** (1.4 g). (b) Cycloaddition product **11c** (980 mg): mp 161–162 °C (from hexane–dichloromethane); 11.86% yield; IR (KBr) 2230 and 1070 cm^{-1}; ^1H NMR δ 0.9–3.5 (m, 23 H), 4.0–4.5 (m, 2 H), 4.8 (t, J = 7 Hz, 1 H), and 7.0–7.8 (m, 4 H); MS *m/e* (380.533) 380 (18%), 353 (18%), 214 (100%). Anal. Calcd for $C_{24}H_{32}N_2O_2$: C, 75.53; H, 8.34; N, 6.98. (c) **9** (750 mg), mp 112–113 °C, isolated from the mother liquor of **11c** (4.51 mmol, 20.83% yield from **1**). (d) Hydroxy ketone **12c** (3.7 g, 18.7 mmol). This was recycled to give 3.2 g of starting ether **10c.**

(5) 1,2,3,4,5,6,7,8-Octahydronaphthalene (13).[12] The olefin (500 mg, 3.67 mmol), α-chloro nitrone (800 mg, 4.5 mmol), and $AgBF_4$ (800 mg) gave 1.2 g of crude product. After chromatography the following were obtained: (a) Propellane **14** (475 mg, 1.58 mmol; 43% yield): mp 93–94 °C (lit.[12] 95–96 °C); from dichloromethane–hexane. (b) **9** (20 mg), mp 111–113 °C isolated from the mother liquor. (c) Nitrone **15** (200 mg, 0.98 mmol; 26% yield): mp 137 °C; IR 1600 and 1530 cm^{-1}; ^1H NMR δ 1.0–2.8 (m, 24 H), 2.6 (d, J = 6 Hz, 2 H), 3.5 (m, 1 H), 5.38 (m, 1 H), and 6.46 (t, J = 6 Hz, 1 H); MS *m/e* (275.436) 275 (4%). Anal. Calcd for $C_{18}H_{29}NO$: C, 78.90; H, 11.61; N, 5.08.

Preparation of the Imminium Tetraphenylborate Salts. Note: All operations were carried out under dry nitrogen. A solution of 1 mmol of nitrile in 1,2-dichloromethane (15 mL) was added dropwise with stirring to a solution of $AgBF_4$ (1.08 mmol) in 1,2-dichloroethane (30 mL) at room temperature during 5 min. After an additional 15 min at room temperature, the mixture was filtered to a solution of 2.5 g of $NaBPh_4$ in 20 mL of water. After shaking for 20 min, the resulting emulsion was filtered. The aqueous layer was extracted with dichloromethane, and the combined organic layers were dried (Na_2SO_4). Removal of the solvents in vacuo left a residue which was treated with ether and solidified. This was crystallized from ether–dichloromethane. The following were thus obtained.

(1) *N*-Cyclohexyl-7-oxa-8-ammonium[4.4.4]propell-8-ene Tetraphenylborate (16a): from **14** in 93% yield; mp 135–157 °C (dec); IR 1660 and 1590 cm^{-1}; ^1H NMR δ 0.9–2.0 (m, 26 H), 3.0 (m, 1 H), 3.8 (s, 1 H), 5.12 (t, J = 2 Hz, 1 H), 6.8–7.8 (m, 20 H). Anal. Calcd for $C_{42}H_{50}NOB$: C, 84.68; H, 8.46; N, 2.35.

(2) *N*-Cyclohexyl-7,11-dioxa-12-ammonium[4.4.4]propell-12-ene Tetraphenylborate (16b): from **7** in 97% yield; mp 141–163 °C (dec); IR 1665 cm^{-1}; ^1H NMR δ 0.9–2.0 (m, 22 H), 3.2 (m, 1 H), 5.05 (t, 1 H), and 6.9–8.0 (m, 20 H). Anal. Calcd for $C_{41}H_{48}NO_2B$: C, 82.40; H, 8.03; N, 2.34.

(3) *N*-Cyclohexyl-2,3-benz-6,11-dioxa-12-ammonium[5.4.3]propellene Tetraphenylborate (20a): from **11a** in 97% yield; mp 138–162 °C (dec); IR 1643 and 1600 cm^{-1}; ^1H NMR δ 0.9–2.3 (m, 17 H), 2.8 (m, 2 H), 3.4 (m, 4 H), 5.25 (t, 1 H), 7.2–7.8 (m, 24 H). Anal. Calcd for $C_{45}H_{48}NO_2B$: C, 83.39; H, 7.63; N, 2.21.

(4) *N*-Cyclohexyl-2,3-benz-7,12-dioxa-13-ammonium[5.4.4]propell-13-ene Tetraphenylborate (20b): from **11b** in 92% yield; mp 145–170 °C (dec); IR 1670 and 1600 cm^{-1}; ^1H NMR δ 0.9–2.0 (m, 20 H), 3.0 (m, 3 H), 3.75 (m, 2 H), 5.30 (t, J = 1 Hz, 1 H), 6.7–7.8 (m, 24 H). Anal. Calcd for $C_{46}H_{50}NO_2B$: C, 83.45; H, 7.78; N, 2.16.

(5) *N*-Cyclohexyl-2,3-benz-8,13-dioxa-14-ammonium[5.5.4]propell-14-ene Tetraphenylborate (20c): from **11c** in 81% yield; mp 143–182 °C (dec); IR 1665 and 1600 cm^{-1}; ^1H NMR δ 0.9–2.0 (m, 22 H), 2.5–2.8 (m, 3 H), 3.6 (m, 2 H), 6.4 (m, 1 H), 6.8–7.5 (m, 24 H). Anal. Calcd for $C_{47}H_{52}NO_2B$: C, 83.49; H, 7.92; N, 2.11.

Deprotonation of the Tetraphenylborate Salts. The tetraphenylborate imminium salt (1 mmol) was dissolved in dichloromethane (20 mL) and stirred vigorously under nitrogen with K_2CO_3 (Merck analyzed, powdered) at 0 °C during 1 h. After removal of the solvent, in vacuo at 0 °C, the following were obtained.

(1) *N*-Cyclohexyl-7-oxa-8-aza [4.4.4] propell-9-ene (17a): from **16a** in 71% yield; mp 128–135 °C (dec); IR 1640 cm^{-1}; ^1H NMR δ 0.9–2.2 (m, 26 H), 2.9 (m 1 H), 4.40 and 5.90 (two d, J = 8 Hz, each 1 H); MS m/e (275.436) 275 (2%). Anal. Calcd for $C_{18}H_{29}NO$: C, 78.41; H, 10.32; N, 5.90. This was refluxed in chloroform (5 mL) under dry nitrogen. Samples were taken at 10-min intervals and IR and ^1H NMR spectra were taken to follow the reaction. After 1.5 h, signals at δ 6.10 and 8.15 were of equal intensity as those at 4.40 and 5.90. An absorption at 1720 cm^{-1} indicated formation of a carbonyl function. The thermolysis proceeded for 5 h more, and solvents were removed in vacuo. Chromatography of the resulting oil yields 72 mg (0.26 mmol; 36% yield) of **18a:** mp 137–139 °C; IR 1720 and 1670 cm^{-1}; ^1H NMR δ 0.9–2.2 (m, 28 H), 3.0 (m, 1 H), 6.10 (d, J = 8 Hz, 1 H), and 8.15 (d, J = 8 Hz, 1 H); MS m/e (275.436) 275 (3%). Anal. Calcd for $C_{18}H_{29}NO$: C, 78.24; H, 10.30; N, 5.10.

(2) *N*-Cyclohexylimino-$\Delta^{6,\beta}$-ethano-2-oxocyclodecan-1-one (18b): from **16b;** after workup, no enamine was detected. Instead, lactone **18b** was isolated in 78% yield as an oil: IR (neat) 1730, 1640, and 1605 cm^{-1}; ^1H NMR δ 0.9–2.5 (m, 22 H), 3.0 (m, 1 H), 4.12 and 4.20 (two t, J = 7 and 6 Hz, together 2 H), 5.80 and 5.86 (two d, J = 9 Hz, together 1 H, 1:1), and 8.21 (d, J = 9 Hz, 1 H); MS m/e (277.408) 277 (4%). Anal. Calcd for $C_{17}H_{27}NO_2$: C, 73.54; H, 9.45; N, 4.73.

(3) *N*-Cyclohexylimino-$\Delta^{7,\beta}$-ethano-3,4,5,6-tetrahydro-8*H*-2-benzoxacin-1-one (22a): from **20a** in 81% yield. After removal of the solvent, no enamine was detected. Instead, lactone **22a** was isolated as an oil and was distilled at 150 °C (0.03 mmHg): IR 1720, 1645, and 1605 cm^{-1}; ^1H NMR δ 0.9–2.5 (m, 14 H), 3.0 (m, 1 H), 3.65 and 3.78 (two s, 1:1, together 2 H), 4.32 (m, 2 H), 5.88 (d, J = 9 Hz, 1 H), 6.8–7.5 (m, 3 H), 7.82 (m, 1 H), and 8.16 (d, J = 9 Hz, 1 H); signals at δ 3.65 and 3.78 indicated a E:Z = 1:1 in **22a;** MS m/e (340.488) 340 (4%). Anal. Calcd for $C_{22}H_{30}NO_2$: C, 77.62; H, 8.84; N, 4.10.

(4) *N*-Cyclohexylimino-$\Delta^{7,\beta}$-ethano-3,4,5,6,8,9-hexahydro-2-benzoxacycloundecan-1-one (22b): from **20b.** Propellane **21b** (290 mg) was isolated as an oil at 0 °C: IR (neat) 1660 and 1600 cm^{-1}; ^1H NMR δ 0.9–2.2 (m, 18 H), 2.80 (t, J = 7 Hz, 2 H), 2.0 (m, 1 H), 4.18 (m, 2 H), 4.50 and 6.10 (two d, each 1 H), 6.6–7.8 (m, 4 H). On taking the ^1H NMR spectrum at 45 °C cycloreversion took place. After 10 min, a new signal at 8.10 and the old at δ 4.10 were of the same intensity. The reaction continued for another 30 min at 45 °C, and the solvent was evaporated in vacuo. **22b** was obtained in this way in quantitative yield: IR (neat) 1710, 1640, and 1600 cm^{-1}; ^1H NMR δ 0.9–3.5 (m, 21 H), 4.42 (m, 2 H), 5.9 and 6.08 (two d, J = 9 Hz, together 1 H), 7.0–7.65 (m, 3 H), and 8.10 (d, J = 9 Hz, 1 H); signals at 5.9 and 6.08 refer to E and Z isomers of **22b;** MS m/e (354.514) 354 (4%). Anal. Calcd for $C_{23}H_{32}NO_2$: C, 77.80; H, 9.22; N, 8.87.

(5) *N*-Cyclohexylimino-$\Delta^{7,\beta}$-ethano-3,4,5,6,7,9,10-hexahydro-8*H*-2-benzoxacyclododecan-1-one (22c): from **20c.** Propellane **21c** (290 mg) (0.78 mmol; 78% yield) was isolated: IR (neat) 1670 and 1590 cm^{-1}. On boiling the material in chloroform for 5 h, decomposition to the lactone **22c** took place. The ^1H NMR experiment indicated that the signals at δ 8.25 and 6.10 were of same intensity after ca. 1.5 h. Heating was stopped after 5 h, since products other than the lactone were formed. After distillation (0.02 mmHg) at 160 °C, 152 mg of **22c** was isolated as a 1:1 E:Z isomer mixture: IR 1710 and 1600 cm^{-1}; ^1H NMR δ 0.9–3.5 (m, 23 H) 4.50 (m, 2 H), 6.0 and 6.10 (two d, J = 8 Hz, together 1 H, 1:1), 7.0–7.5 (m, 3 H), 8.0 (m, 1 h), and 8.25 (d, J = 8 Hz, 1 H); MS m/e 368 (368.540).

Procedure for Hydrolysis of Aldimino Lactones to Aldehydo Lactones. Aldimino lactone was filtered on a 100-fold SiO_2 + 10% water column at 0 °C using a 1:1 chloroform–benzene mixture as eluent. Filtration was done in a rate of 3 mL/min and fractions of 3 mL were collected and analyzed on TLC. Those having product were evaporated to give the following compounds.

$\Delta^{6,\alpha}$-Cyclodecanoneacetaldehyde (19a). 18a (32 mg, 0.11 mmol) yielded 15 mg of **19a** (0.07 mmol; 70%), mp 167–169 °C, which was collected: IR (KBr) 2850, 1725 1670, and 1620 cm^{-1}; ^1H NMR δ 0.9–3 (m, 10 H), 4.05 and 6.05 (two d, J = 9 Hz, each 1 H), and 10.0 (d, J = 1 Hz, 1 H); MS m/e (104.274). Anal. Calcd for $C_{12}H_{18}O_2$: C, 73.97; H, 5.10.

$\Delta^{6,\alpha}$-Oxacyclodecanoneacetaldehyde (19b). 18b (100 mg) distilled (0.05 mm, 120 °C) lactone **19b** (0.27 mmol; 76% yield): IR (neat) 1725, 1670, and 1620 cm^{-1}; ^1H NMR 0.93–3 (m, 8 H), 4.18 (t, J = 6 Hz, 2 H), 5.90 (d, J = 8 Hz, 1 H), and 10.1 (d, J = 8 Hz, 1 H); MS m/e 106 (196.247). Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.57; H, 8.04.

$\Delta^{7,\alpha}$-3,4,5,6-Tetrahydro-8*H*-benzoxacin-1-oneacetaldehyde (23a). 22a (E + Z) (150 mg, 0.44 mmol) was hydrolyzed to give 68 mg (0.28 mmol; 65% yield) of **23a** (E + Z): IR (neat) 2850, 1710, 1670 and 1595 cm^{-1}; ^1H NMR δ 0.9–2.0 (m, 6 H), 2.60 and 2.92 (two, each 2 H), 3.72 and 4.00 (two, together 2 H in 1:1 ratio), 4.46 (q, J = 5 Hz, 2 H), 5.30 and 5.70 (two d, J = 9 and 7 Hz, respectively, together 1 H); this is a 1:1 mixture of (E + Z)-**23a;** MS m/e 196 (196.247). Anal. Calcd for $C_{15}H_{16}O_3$: C, 67.54; H, 8.24.

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Registry No.—**1,** 37898-41-2; **8,** 62456-11-5; **9,** 63689-26-9; **12a,** 63689-27-0; **12b,** 16425-84-6; **12c,** 63689-28-1; **13,** 493-03-8; **14,** 58598-27-9; **15,** 63689-29-2; **16a,** 63689-31-6; **16b,** 63689-33-8; **17a,** 63689-34-9; **18a,** 63689-35-0; *E*-**18b,** 63689-36-1; *Z*-**18b,** 63689-37-2; **19a,** 63689-38-3; **19a,** 63689-39-4; **20a,** 63689-41-8; **20b,** 63689-43-0; **20c,** 63689-45-2; **21b,** 63689-46-3; **21c,** 63689-47-4; *E*-**22a,** 63689-48-5; *Z*-**22a,** 63689-49-6; *E*-**22b,** 63689-50-9; *Z*-**22b,** 63689-51-0; *E*-**22c,** 63689-52-1; *Z*-**22c,** 63689-53-2; *E*-**23a,** 63689-54-3; *Z*-**23a,** 63689-55-4.

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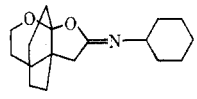
(13) Reaction with *t*-BuOK in *t*-BuOH gave imino lactone I in 76% yield. Compare ref 12.



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(15) Melting points are uncorrected. Ultraviolet spectra were measured on a Cary 14 instrument. Infrared spectra were taken on Perkin-Elmer 251 instrument. ^{1}H NMR spectra were taken in CCl_4 solutions for neutral materials or in deuteriochloroform for salts and are in δ values.

(16) Olefins and ethers are purified on distillation over Na. Merck Art 1097 activity II–III Al_2O_3 was used for the column chromotography. Dry solvent was obtained by distillation over P_2O_5 and filtration over a 100-fold amount of basic Al_2O_3 (activity I, Merck).

(17) The formation of a mass M − 166 as base peak in propellanes **42** and **48–50** was noted.

Reactions of Phthalaldehyde with Ammonia and Amines

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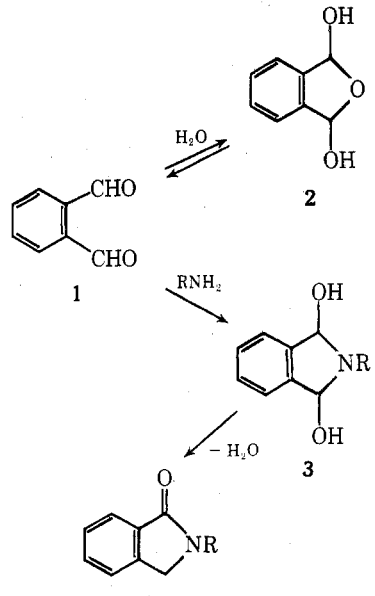
Reactions of phthalaldehyde with ammonia and amines are described. Major products from ammonia were phthalimidine and 3-(2-cyanophenyl)isoquinoline. Primary amines reacted with 2 mol of aldehyde to produce N-substituted adducts whose steric requirements lead to unusual NMR spectra. At elevated temperatures unidentified colored materials were formed. 1-Hydroxyisoindoles are proposed intermediates.

The reaction between phthalaldehyde and ammonia produces colored polymeric[1-3] products. These reactions have served as a basis for polarographic methods for the determination of ammonia[3] and for the location of sweat pores in the skin.[4] Similar reactions of phthalaldehyde with various primary amines, amino acids, and indoles also produce dark-colored products. Qualitative and semiquantitative methods for the detection of these nitrogen-containing materials depend on the fluorescence of their condensation products with phthalaldehyde.[5-7]

Preliminary to an investigation of the colored products, a study of these reactions under carefully controlled conditions was made.

Results

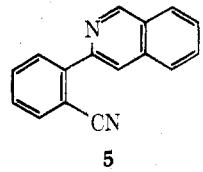
At room temperature water reacts reversibly with phthalaldehyde (1) to produce a hydrate[8] which was shown by NMR to have the structure **2**; phthalaldehyde was recovered unchanged by evaporating the solution to dryness. By contrast, the reaction with ammonia is not reversible. In cold dilute dimethyl sulfoxide (Me_2SO) an adduct formed which had an NMR spectrum consistent with **3a**. The initially formed product dehydrated and rearranged to phthalimidine (**4a**), identified by comparison to an authentic sample.[9] The diol **3a**, precipitated from dry ether at −70 °C, was very unstable and resinified rapidly when warmed to room temperature.



1 2 3 4

a, R = H
b, R = Me
c, R = Ph
d, R = 2,6-Me_2Ph

The products from the reaction of phthalaldehyde and ammonia in Me_2SO depended on the initial concentration of aldehyde. While phthalimidine (**4a**) was produced in high yield in dilute Me_2SO solutions, more concentrated solutions yielded 3-(2-cyanophenyl)isoquinoline (**5**) and a dark polymer



5

with a consequent decrease in the yield of **4a**. The structure of **5** was inferred from the following considerations: (1) IR showed a –CN; (2) NMR showed nine aromatic protons and a tenth at 9.29 ppm, characteristic of the proton in the 1 position of isoquinoline; and (3) its mass spectrum.

The reaction between phthalaldehyde and ammonia is strongly exothermic. The rate of ammonia addition had to be controlled carefully to maintain a low reaction temperature. Warming after the reaction had been completed did not affect the product composition, but at higher reaction temperatures greater amounts of polymer were formed at the expense of **4a** and **5**.

Reactions of excess aldehyde with primary amines in cold solutions (ether, acetone, benzene) produced **6** and N-substituted phthalimidines **4** as the major isolable products.

Elemental analyses of the products (**6**) from the primary amines showed that they were made up of 2 mol of aldehyde and 1 mol of amine with the loss of 1 mol of water. Mass spectra established their molecular weights and IR showed the presence of amide and hydroxyl groups, the latter of which was proved to be secondary by oxidation. In addition, the mass spectra indicated cleavage into two major fragments, each