Anal. Calcd. for $C_{17}H_{23}NO_4$: C, 66.4; H, 8.2. Found: C, 66.7; H, 8.4.

Diethyl 3-Piperidino-2,10-cyclodecadiene-1,2-dicarboxylate.—1-(1-Cyclooctenyl)piperidine (3.86 g., 0.02 mole) and diethyl acetylenedicarboxylate (3.40 g., 0.02 mole) were allowed to react in ether as described in the preceding example. There was obtained 4.4 g. (60%) of diethyl 3-piperidino-2,10-cyclodecadiene-1,2-dicarboxylate, m.p. 91–92°.

Anal. Calcd. for $C_{21}H_{33}NO_4$: C, 69.4; H, 9.2. Found: C, 69.5; H, 9.2.

Dimethyl 3-Pyrrolidinyl-2,14-cyclotetradecadiene-1,2-dicarboxylate.—To 1-(1-cyclododecenyl)pyrrolidine (8.5 g., 0.036 mole) in 25 ml. of ether was added, portionwise, dimethyl acetylenedicarboxylate (5.15 g., 0.036 mole) with cooling to keep the temperature at 30–35°. The ether was removed on a steam bath and the residue was crystallized from pentane to give 12.35 g. (90.5%) of crude dimethyl 3-pyrrolidinyl-2,14-cyclotetradecadiene-1,2-dicarboxylate. A sample for analysis, recrystallized from ether, melted at 94–95°.

Anal. Calcd. for $C_{22}H_{35}NO_4$: D, 70.0; H, 9.3. Found: C, 69.9; H, 9.1.

Hydrolysis of dimethyl 3-pyrrolidinyl-2,14-cyclotetradecadiene-1,2-dicarboxylate with dilute hydrochloric acid gave dimethyl 14-oxo-2-cyclotetradecene-1,2-dicarboxylate, m.p. 73–74° (recrystallized from ether), in 83% yield.

Anal. Calcd. for $C_{18}H_{28}O_5$: C, 66.6; H, 8.7. Found: C, 66.6; H, 8.8.

Hydrogenation of dimethyl 14-oxo-2-cyclotetradecene-1,2-dicarboxylate in methanol over 5% palladium on alumina at room temperature and 3 atm. gave dimethyl 3-oxocyclotetradecane-1,2-dicarboxylate, m.p. 93° (recrystallized from methanol), in 84% yield.

Anal. Calcd. for $C_{18}H_{30}O_5$: C, 66.2; H, 9.3. Found: C, 66.3; H, 9.3.

Treatment of dimethyl 3-oxocyclotetradecane-1,2-dicarboxylate (32.6 g., 0.1 mole) with a solution of 15 g. of sodium hydroxide in 250 ml. of methanol and 250 ml. of water at reflux for 5 hr., followed by acidification with concentrated hydrochloric acid, gave 21.5 g. (85%) of 3-oxocyclotetradecanecarboxylic acid, m.p. 142.5–143.5° (recrystallized from toluene).

Anal. Calcd. for $C_{15}H_{26}O_3$: C, 70.8; H, 10.3. Found: C, 70.6; H, 10.5.

Dimethyl 2,7-Dihydro-3-pyrrolidinyl-4,5-oxepindicarboxylate.—Dimethyl acetylenedicarboxylate (15.2 g., 0.107 mole) was added portionwise to 1-(2,5-dihydro-3-furyl)pyrrolidine (14.9 g., 0.107 mole) in 75 ml. of ether with cooling to maintain the temperature at 25–30°. The mixture was allowed to stand overnight and the ether was removed on a steam bath. After addition of more ether and chilling, 5 g. (17%) of dimethyl 2,7-dihydro-3-pyrrolidinyl-4,5-oxepindicarboxylate was obtained. A sample for analysis, recrystallized from a benzene–hexane mixture, melted at 162–163°.

Anal. Calcd. for $C_{14}H_{19}NO_5$: C, 59.8; H, 6.6. Found: C, 59.9; H, 6.7.

Ketenes I. Cycloaddition of Ketene and Dialkylketenes to Enamines

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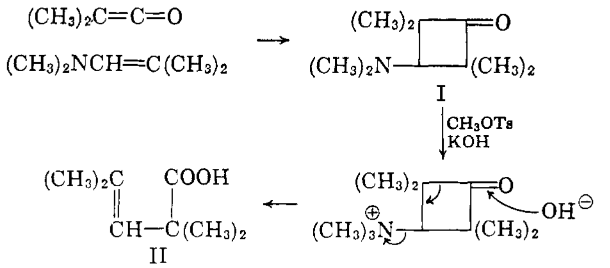
Received January 11, 1963

The cycloaddition of dialkylketenes to enamines derived from secondary aldehydes takes place readily to form 3-dialkylamino-2,2,4,4-tetraalkylcyclobutanones. When the cycloaddition involves enamines containing a β-hydrogen and/or ketene, the enolizable cyclobutanones are unstable and are isomerized thermally to dialkylaminovinyl ketones. A number of cyclobutanones and their rearrangement and reduction products are described.

Ketenes add to a number of olefinic compounds to form cyclobutane derivatives.[1] Ketene[2] and diphenylketene[3] have been studied more than any other member of the series; cycloadditions of dialkylketenes with olefinic compounds have been reported only for dimethylketene with ethyl vinyl ether[4] and cyclopentadiene.[4,5] In a study of the scope of the cycloaddition reactions of dialkylketenes, we observed the particularly facile addition of dimethylketene to enamines. This reaction, noted independently by other workers,[6,7] was reported briefly in a Communication.[8] The present paper is a more detailed account of our work.

Stable cyclobutanone derivatives were obtained by addition of dialkylketenes to enamines lacking any β-hydrogen atoms. Dimethylketene and N,N-dimethylisobutenylamine, mixed in isopropyl acetate at room temperature, reacted to give 3-dimethylamino-2,2,4,4-tetramethylcyclobutanone (I) in 64% yield. The structure of I was consistent with infrared and n.m.r. spectral data, and was confirmed by quaternization with methyl tosylate and alkaline degradation to 2,2,4-trimethyl-3-pentenoic acid (II).

The cycloaddition reaction was carried out with several dialkylketenes and a variety of enamines derived



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[1] J. D. Roberts and C. M. Sharts, *Org. Reactions*, **12**, (1962).

[2] (a) B. T. Brooks and G. Wilbert, *J. Am. Chem. Soc.*, **63**, 870 (1941); (b) A. T. Blomquist and J. Kwiatek, *ibid.*, **73**, 2098 (1951); (c) H. L. Dryden and B. E. Burgert, *ibid.*, **77**, 5633 (1955); (d) E. Vögel and K. Miller, *Ann.*, **615**, 29 (1958).

[3] (a) H. Staudinger and E. Suter, *Ber.*, **53**, 1092 (1920); (b) H. Staudinger and A. Rheiner, *Helv. Chim. Acta*, **7**, (1924); (c) J. R. Lewis, G. R. Ramage, J. L. Simonsen, and W. G. Wainwright, *J. Chem. Soc.*, 1837 (1937); (d) E. H. Farmer and M. O. Farooq, *Chem. Ind.* (London), **56**, 1079 (1937); (e) L. I. Smith, C. L. Agre, R. M. Leekley, and W. W. Prichard, *J. Am. Chem. Soc.*, **61**, 7 (1938); (f) E. Bergmann and O. Blum-Bergmann, *J. Chem. Soc.*, 727 (1938); (g) E. H. Farmer and M. O. Farooq, *ibid.*, 1925 (1938); (h) G. Spengler, *Angew. Chem.*, **61**, 308 (1949); (i) C. S. Marvel and M. I. Kohan, *J. Org. Chem.*, **16**, 741 (1951); (j) J. R. von der Bij and E. C. Kooyman, *Rec. trav. chim.*, **71**, 837 (1952); (k) K. Ziegler, H. Sauer, L. Bruns, H. Froitzheim-Kühlhorn, and J. Schneider, *Ann.*, **589**, 123 (1954); (l) M. O. Farooq, T. A. Vahidy, and S. M. Husain, *Bull. soc. chim. France*, 830 (1958); (m) M. O. Farooq and N. A. Abraham, *ibid.*, 832 (1958); (b) C. D. Hurd and R. D. Kimbrough, *J. Am. Chem. Soc.*, **82**, 1373 (1960).

[4] H. Staudinger and P. J. Meyer, *Helv. Chim. Acta*, **7**, 19 (1924).

[5] (a) J. M. Witzel, "Dimethylketene and Its Reaction with Cyclopentadiene," thesis, Cornell University, 1941; (b) M. D. Owen, *J. Indian Chem. Soc.*, **20**, 343 (1943); (c) T. L. Dawson and G. R. Ramage, *J. Chem. Soc.*, 3523 (1950).

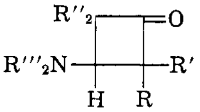
[6] (a) G. Opitz, H. Adolph, M. Kleemann, and F. Zimmermann, *Angew. Chem.*, **73**, 654 (1961); (b) G. Opitz, M. Kleeman, and F. Zimmermann, *ibid.*, **74**, 32 (1962).

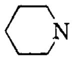
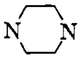
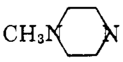
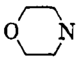
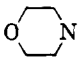
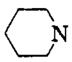
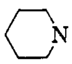
[7] G. A. Berchtold, G. R. Harvey, and G. E. Wilson, *J. Org. Chem.*, **26**, 4776 (1961).

[8] R. H. Hasek and J. C. Martin, *ibid.*, **26**, 4775 (1961).

TABLE I

DIALKYLAMINOCYCLOBUTANONES



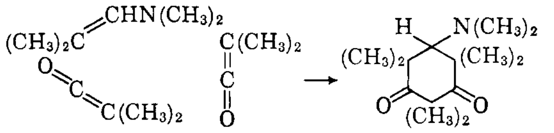
R[a]	R′[a]	R″	R‴₂N	B.p., °C. (mm.)	$n^{20}D$	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
CH_3	CH_3	CH_3	$(CH_3)_2N$	83–85 (24)	1.4439	71.1	71.3	11.2	11.2	8.3	8.1
CH_3	CH_3	CH_3		95–97 (4.2)	1.4705	74.5	74.3	11.0	11.2	6.7	6.5
CH_3	CH_3	CH_3		58–59.5[b]		68.3	68.3	10.0	10.0	6.6	6.6
CH_3	CH_3	CH_3		256 dec.[c]		72.0	72.1	10.2	10.2	8.4	8.3
CH_3	CH_3	CH_3		105–107 (3)[d]		69.7	70.2	10.7	10.8	12.5	12.4
CH_3	C_2H_5	CH_3		101–103 (1.3)	1.4736	69.4	69.6	10.2	10.4	6.2	6.3
C_2H_5	C_2H_5	CH_3	$(CH_3)_2N$	95–98 (8)	1.4585	73.1	72.9	11.7	11.8	7.1	7.0
C_2H_5	C_2H_5	CH_3		101–104 (0.7)[d]	1.4794	70.3	69.9	10.5	10.5	5.9	5.9
C_2H_5	C_2H_5	C_2H_5	$(CH_3)_2N$	112 (5)	1.4662	74.7	74.1	12.0	11.6	6.2	5.9
C_2H_5	C_2H_5	C_2H_5		130–132 (1.5)[d]		77.0	76.7	11.7	11.7	5.3	5.0
C_2H_5	C_4H_9	CH_3	$(CH_3)_2N$	94 (2)	1.4592	74.7	74.9	12.0	12.5	6.2	6.1
$-(CH_2)_5-$		CH_3		81–82.5[e]		77.1	77.1	10.8	11.0	5.6	5.4

[a] Substituents on original dialkylketene. [b] Melting point (from pentane). [c] Bis adduct, melting point (from toluene). [d] Solidified on standing. [e] Melting point (from ethyl alcohol).

from secondary aldehydes and secondary amines; the products are listed in Table I. In general, the reaction was more sluggish with enamines from higher aldehydes, and higher dialkylketenes also exhibited less reactivity. The effect of substituents on the nitrogen atom of the enamine was less obvious. *N*-Isobutenyl derivatives of dimethylamine, piperidine, and morpholine all reacted rapidly, but the corresponding derivative of *N*-methylaniline was relatively inert.

The order of addition of the reactants was important to obtain optimum yields. Best results were obtained by addition of the dialkylketene to a solution of the enamine. In the cycloaddition of dimethylketene and *N*,*N*-dimethylisobutenylamine, either simultaneous or inverse addition led to large amounts of dimethylketene polymer. This polymer had the poly(enol ester) structure described by Natta[9] and by Hasek.[10]

When highly polar solvents were used, the rate of the cycloaddition reaction was increased, as evidenced by a more exothermic reaction. In addition to the 1:1 adduct, appreciable quantities of 2:1 and 3:1 dialkylketene–enamine adducts were formed. Cycloaddition of equimolar quantities of dimethylketene and *N*,*N*-dimethylisobutenylamine in acetonitrile gave 24% of I, 32% of a 2:1 adduct, and 9% of a 3:1 adduct. The 2:1 adduct was identified as 5-dimethylamino-2,2,4,4,6,6-hexamethyl-1,3-cyclohexanedione (III); the assignment was based on infrared and n.m.r. spectra, and on the reduction of III with lithium aluminum hydride to a glycol. Some 2:1 adducts are listed in Table II; work on the 3:1 adducts is incomplete.



III

The 3-dialkylamino-2,2,4,4-tetraalkylcyclobutanones were reduced to the corresponding carbinols by metal hydrides and by catalytic hydrogenation. Sodium borohydride served adequately when the ring substituents were methyl groups, but lithium aluminum hydride gave better yields when the cyclobutanone contained larger alkyl groups. The reduction of I by sodium borohydride gave one isomer of 3-dimethylamino-2,2,4,4-tetramethylcyclobutanol (IV), m.p. 70–72°, in 92% yield, but catalytic hydrogenation over a ruthenium catalyst gave a mixture of this isomer and a higher melting one, m.p. 129–130°. The n.m.r. spectrum of the lower melting isomer contained a single peak for the ring methyl groups, whereas the spectrum of the higher melting isomer contained two such peaks. Apparently the magnetic anisotropies of the hydroxy and dimethylamino groups in IV are equivalent, and the chemical shifts of the methyl groups on the cyclo-

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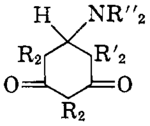
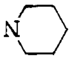
(9) (a) G. Natta, G. Mazzanti, G. Pregaglia, M. Binaghi, and M. Peraldo, *J. Am. Chem. Soc.*, **82**, 4743 (1960); (b) G. Natta, G. Mazzanti, G. Pregaglia, and M. Binaghi, *Makromol. Chem.*, **44**, 537 (1961).

(10) R. H. Hasek, R. D. Clark, E. U. Elam, and J. C. Martin, *J. Org. Chem.*, **27**, 60 (1962).

TABLE II

DIALKYLAMINOCYCLOHEXANEDIONES

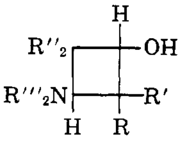


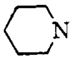
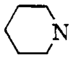
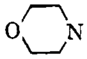
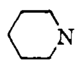
R[a]	R'	R''2N	B.p., °C. (mm.)	$n^{20}D$	Carbon, %		Hydrogen, %		Nitrogen, %	
					Calcd.	Found	Calcd.	Found	Calcd.	Found
CH_3	CH_3	$(CH_3)_2N$	132–134 (4)	1.4948	70.4	70.7	10.5	10.8	5.8	5.8
CH_3	CH_3		134–136 (1.2)	1.5090	73.2	73.0	10.4	10.4	5.0	4.9
C_2H_5	CH_3	$(CH_3)_2N$	130–133 (0.8)	1.4950	73.2	72.7	11.2	11.0	4.8	4.9

[a] Substituents on original dialkylketene.

TABLE III

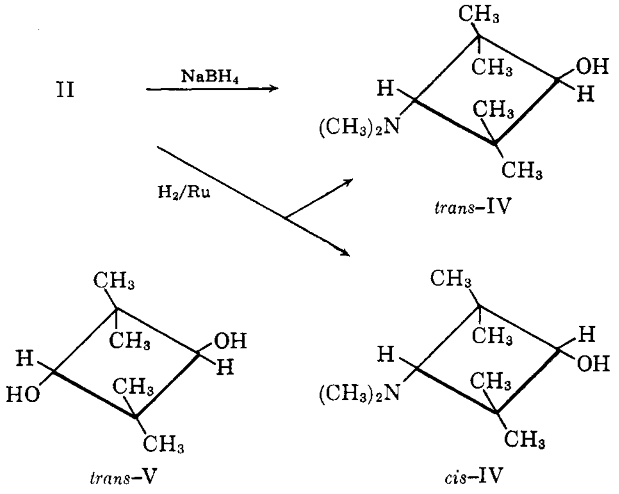
DIALKYLAMINOCYCLOBUTANOLS



R	R'	R''	R'''2N	Reducing agent[a]	M.p., °C.[b]	Carbon, %		Hydrogen, %		Nitrogen, %	
						Calcd.	Found	Calcd.	Found	Calcd.	Found
H	H	CH_3	$(CH_3)_2N$	A[c]	58–60	67.1	66.8	11.9	12.1	9.8	9.7
H	C_2H_5	H		A[c]	98[d]	72.1	72.2	11.5	11.7	7.7	7.6
H	C_2H_5	CH_3	$(CH_3)_2N$	A[c]	87–89[e]	74.0	74.2	11.8	11.8	6.6	6.8
CH_3	CH_3	CH_3	$(CH_3)_2N$	B, C	70–72[f]	70.3	70.3	12.3	12.5	8.2	8.1
CH_3	CH_3	CH_3	$(CH_3)_2N$	C	129–130[g]	70.3	70.4	12.3	12.7	8.2	8.1
CH_3	CH_3	CH_3		B	92–94	74.0	73.8	11.8	11.6	6.6	6.5
CH_3	CH_3	CH_3		A	100.5–103	67.7	67.7	10.8	10.8	6.6	6.5
C_2H_5	C_2H_5	CH_3	$(CH_3)_2N$	B	74–75	72.4	72.3	12.6	12.6	7.0	6.8
C_2H_5	C_2H_5	C_2H_5	$(CH_3)_2N$	A	75–78	74.0	74.2	12.8	13.0	6.2	6.4
C_2H_5	C_4H_9	CH_3	$(CH_3)_2N$	A	100–101[h]	74.3	73.9	12.4	12.7	6.2	6.1
$-(CH_2)_5-$		CH_3		B	141–142[i]	76.6	76.5	11.5	11.3	5.6	5.2

[a] A = $LiAlH_4$; B = $NaBH_4$; C = catalytic hydrogenation. [b] Recrystallized from hexane. [c] From unstable cycloadduct, which was not isolated. [d] Boiling point (0.8 mm.). [e] Boiling point (0.5 mm.). [f] *trans* Isomer. [g] *cis* Isomer. [h] Boiling point (1.3 mm.). [i] Recrystallized from benzene–hexane mixture.

butane nucleus are the same as those measured for the *cis* and *trans* isomers of 2,2,4,4-tetramethyl-1,3-cyclobutanediol (V).[11] The configurations of the isomers of IV thus correspond to those of the glycol V; the lower melting isomer is *trans* and the higher melting one is *cis*.



trans-IV

trans-V

cis-IV

A number of 3-dialkylaminocyclobutanols prepared by hydride reduction are listed in Table III. Many were obtained as crystalline compounds with fairly sharp melting points. Each solid product probably was a single isomer, but data were insufficient for assignment of configuration.

The cycloaddition reaction was extended to ketene and to enamines containing β-hydrogen atoms. The enolizable cyclobutanones obtained from these reactants were unstable and underwent ring opening to form aminovinyl ketones. Ketene and *N*,*N*-dimethylisobutenylamine, for example, reacted readily at 0° and a 93% yield of distilled product was obtained. This 1:1 adduct was not a cyclobutanone but the acyclic compound, 1-dimethylamino-4-methyl-1-penten-3-one (VI). The structure was assigned from infrared and n.m.r. spectra, and confirmed by an alternate synthesis;

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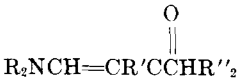
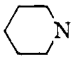
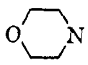
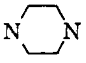
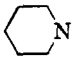
(11) R. H. Hasek, E. U. Elam, J. C. Martin, and R. G. Nations, *J. Org. Chem.*, **26**, 700 (1961).

TABLE IV

AMINOVINYL KETONES

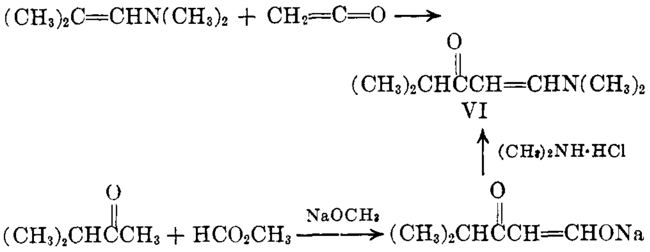


$R_2NCH{=}CR'\overset{\overset{O}{\|}}{C}CHR''_2$

R_2N	R′	R″	B.p., °C. (mm.)	$n^{20}D$	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, %[a] Calcd.	Nitrogen, %[a] Found
$(CH_3)_2N$	H	CH_3	105–107 (2)	1.5301	68.0	68.0	10.6	10.9	9.9	9.7
	H	CH_3	133 (1.7)	1.5485	72.9	72.9	10.5	10.2	7.7	7.9
	H	CH_3	137 (1.3)	1.5518	65.6	66.1	9.3	9.4	7.7	7.6
$C_6H_5NCH_3$	H	CH_3	121–127 (0.6)	1.6074	76.9	76.7	8.4	8.2	6.8	6.7
$(CNCH_2CH_2)_2N$	H	CH_3	158–159[b]		65.7	65.4	7.8	7.9	19.2	18.9
$(C_6H_5CH_2)_2N$	H	CH_3	100–105 (0.002)[c]		82.0	81.9	7.9	7.9	4.8	4.7
	H	CH_3	253–254[d]		69.0	68.8	9.4	9.3	10.1	10.3
$(CH_3)_2N$	H	C_2H_5	100–103 (0.7)	1.5235	71.0	70.8	11.2	11.4	8.3	8.0
	C_2H_5	CH_3	119–121 (0.6)	1.5424	74.6	74.3	11.0	10.9	6.7	6.6

[a] Spurious values for nitrogen were obtained by the Kjeldahl procedure; recorded values are by Dumas method. [b] Melting point (from ethyl alcohol). [c] Solidified on standing. [d] Bis adduct, melting point (from aqueous ethyl alcohol).

3-methyl-2-butanone and methyl formate were condensed to the sodium salt of 1-hydroxy-4-methyl-1-penten-3-one, which reacted with dimethylamine hydrochloride to give VI.[12]

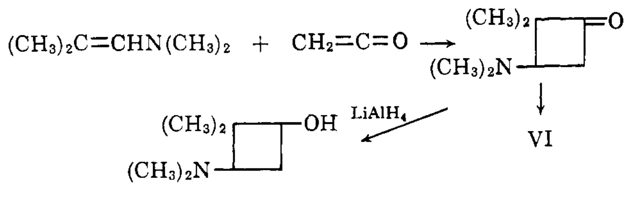


$$(CH_3)_2C{=}CHN(CH_3)_2 + CH_2{=}C{=}O \longrightarrow (CH_3)_2CH\overset{\overset{O}{\|}}{C}CH{=}CHN(CH_3)_2$$

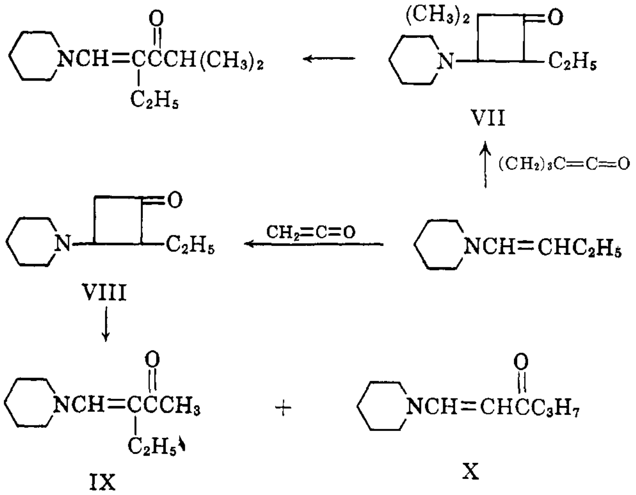
VI

$$(CH_3)_2CH\overset{\overset{O}{\|}}{C}CH_3 + HCO_2CH_3 \xrightarrow{NaOCH_3} (CH_3)_2CH\overset{\overset{O}{\|}}{C}CH{=}CHONa \xrightarrow{(CH_3)_2NH\cdot HCl} VI$$

The structure of VI, with the ketene moiety in the center of the molecule, indicated a cycloaddition mechanism followed by a ring cleavage. Infrared spectra confirmed this view, for the cold reaction product exhibited an absorption at 5.63 μ characteristic of cyclobutanones, which disappeared as the product was warmed.[13] Addition of lithium aluminum hydride to the cold reaction product converted the unstable cycloadduct to 3-dimethylamino-2,2-dimethylcyclobutanol.



All enolizable cyclobutanones prepared by other combinations of ketenes and enamines rearranged during distillation to aminovinyl ketones. The cycloadducts of dialkylketenes with enamines containing a β-hydrogen atom behaved in this manner. Dimethylketene and 1-(1-butenyl)piperidine in hexane solution at −20° gave 2-ethyl-4,4-dimethyl-3-piperidinocyclobutanone (VII), which rearranged during distillation to 2-ethyl-4-methyl-1-piperidino-1-penten-3-one. The cycloaddition and ketene and 1-(1-butenyl)piperidine gave 2-ethyl-3-piperidinocyclobutanone (VIII), which could undergo two modes of rearrangement to give a mixture of 2-ethyl-1-piperidino-1-buten-3-one (IX) and 1-piperidino-1-hexen-3-one (X). This mixture was not resolved by distillation, but the n.m.r. spectrum indicated a 1:2 ratio of IX to X.



The aminovinyl ketones prepared through the cycloaddition and rearrangement reactions are listed in Table IV. It is noteworthy that *N*-isobutenyl-*N*-methylaniline, which failed to react with dimethylketene, added to ketene. No 2:1 adducts of ketene and enamines were isolated from reactions carried out in polar solvents.

The mechanism of cyclobutanone formation from ketenes and olefins has not been ascertained; structures are compatible with a diradical mechanism or with an ionic process involving nucleophilic attack by the olefin. The ease of cycloaddition of ketenes to the strongly nucleophilic enamines supports the latter ionic mechanism. This is bolstered by the effect of polarity of

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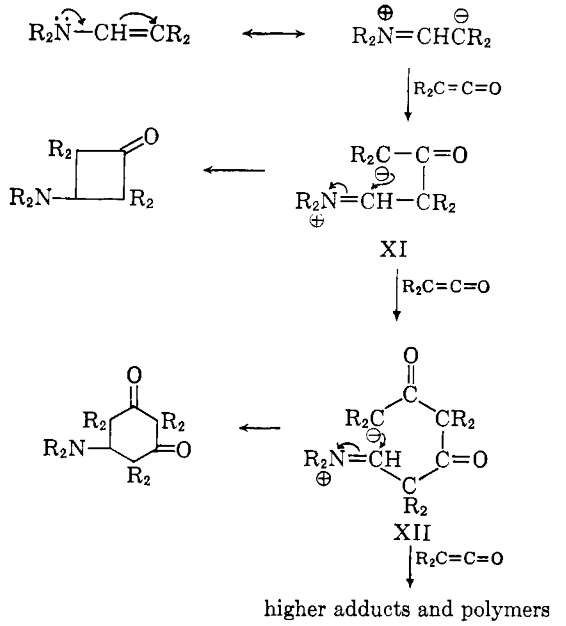
[12] E. Benary, *Ber.*, **63**, 1573 (1930).

[13] Other workers isolated some unstable ketene–enamine adducts and noted their rearrangement to the aminovinyl ketones.[6,7]

the solvent on the rate of reaction, and by the formation of by-products ranging from 2:1 adducts to ketene polymers. Stabilization of the charge separation in the ionic intermediates (XI and XII) might be expected to facilitate further addition of the ketene and the subsequent formation of the higher adducts.



Experimental

The enamines used in these experiments were prepared from aldehydes and secondary amines.[14–16] Two enamines not previously reported were prepared: 1-methyl-4-isobutenylpiperazine, b.p. 38–40° (1 mm.), $n^{20}\mathrm{D}$ 1.4718, and *N*,*N*-dibenzylisobutenylamine, b.p. 110–114° (0.8 mm.), $n^{20}\mathrm{D}$ 1.5591. Ketene was obtained from an industrial production unit, and dialkylketenes were prepared by pyrolysis of corresponding anhydrides.[17]

3-Dimethylamino-2,2,4,4-tetramethylcyclobutanone (I).—Over a period of 15 min., 70 g. (1.0 mole) of dimethylketene was added to a stirred solution of 99 g. (1.0 mole) of *N*,*N*-dimethylisobutenylamine in 400 ml. of isopropyl acetate under a nitrogen atmosphere. The reaction temperature slowly rose to 45°, but was then held at 25–30° by a water bath. The reaction solution was stirred for 6 hr. and then distilled through a 12-in. packed column to give some unchanged enamine, tetramethyl-1,3-cyclobutanedione, and 108 g. (64%) of 3-dimethylamino-2,2,4,4-tetramethylcyclobutanone, b.p. 83–85° (24 mm.), $n^{20}\mathrm{D}$ 1.4439.

Anal. Calcd. for $C_{10}H_{19}NO$: C, 71.1; H, 11.2; N, 8.2. Found: C, 71.3; H, 11.2; N, 8.1. Infrared maxima (smear[18]: 3.6 [$N(CH_3)_2$], 5.62 μ (cyclobutanone). N.m.r. spectrum (neat)[19]: −87 [$N(CH_3)_2$ and CH], −51 and −44 c.p.s. (CH_3 groups).

Quaternization and Hydrolysis of I.—A solution of 84 g. (0.5 mole) of 3-dimethylamino-2,2,4,4-tetramethylcyclobutanone and 93 g. (0.5 mole) of methyl tosylate was heated overnight on a steam bath. When a solution of 56 g. (1.0 mole) of potassium hydroxide in 200 ml. of water was added to the solid product at room temperature, the mixture became quite hot and trimethylamine evolved. The solution was heated on a steam bath for 6 hr., then cooled, and extracted with ether. The aqueous layer was acidified by the slow addition of concentrated hydrochloric acid. The organic layer which separated was taken up in ether, washed with water, and dried over anhydrous magnesium sulfate. Distillation through a 10-in. packed column gave 43.2 g. (71%) of 2,2,4-trimethyl-3-pentenoic acid (II), b.p. 86° (2 mm.), $n^{20}\mathrm{D}$ 1.4472.

Anal. Calcd. for $C_8H_{14}O_2$: C, 67.6; H, 9.9; neut. equiv., 142. Found: C, 67.6; H, 10.1; neut. equiv., 142. Infrared maxima (smear): 3.87, 3.9 (OH), 5.87 (COOH), 10.6 (OH deformation), 12.22 μ (C=CH). N.m.r. (neat): −490 (COOH), −208 (C=CH), −64 and −67 [$(CH_3)_2C{=}CH$], −52 c.p.s. [$C(CH_3)_2$]. With a warm sample and higher resolution, the peak at −208 c.p.s. was resolved into seven peaks and the doublet at −64 and −67 c.p.s. into two sets of doublets with the same coupling constant. This pattern, from spin–spin interaction of the methyl groups and the olefinic proton, is characteristic of the grouping $(CH_3)_2C{=}CH—$.

***trans*-3-Dimethylamino-2,2,4,4-tetramethylcyclobutanol** (IV).—A solution of 3.8 g. (0.1 mole) of sodium borohydride in 25 ml. of water was added slowly to a stirred solution of 50 g. (0.3 mole) of 3-dimethylamino-2,2,4,4-tetramethylcyclobutanone (I) in 75 ml. of ethyl alcohol. The temperature of the exothermic reaction was kept at 25–30° by a water bath. The mixture was stirred for 1 hr. after addition was complete, then heated in an evaporating dish on the steam bath until most of the ethyl alcohol was removed. The residue was extracted with 300 ml. of ether, and the ether layer was separated, washed with water, and dried over anhydrous magnesium sulfate. Evaporation of the ether yielded 46.8 g. (92%) of *trans*-3-dimethylamino-2,2,4,4-tetramethylcyclobutanol (IV), m.p. 69–72°. An analytical sample was prepared by dissolving some IV in warm hexane and chilling the solution in Dry Ice. Rapid filtration of the solid gave a sample, m.p. 70–72°.

Anal. Calcd. for $C_{10}H_{21}NO$: C, 70.2; H, 12.3; N, 8.2; neut. equiv., 171. Found: C, 70.3; H, 12.5; N, 8.1; neut. equiv., 171.8. Infrared maxima (KBr pellet): 3.12 (OH), 3.53, 3.59 μ [$N(CH_3)_2$]. N.m.r. spectrum (saturated chloroform solution): −155 (OH), −130 (O—CH), −84 [$N(CH_3)_2$], −63 (N—CH), —41 c.p.s. (CH_3 groups).

The *N*-phenylurethane was prepared from IV and phenyl isocyanate, with *N*,*N*,*N*′,*N*′-tetramethyl-1,3-butanediamine used as a catalyst. The derivative, recrystallized twice from hexane, melted at 134.5–135.5°.

Anal. Calcd. for $C_{17}H_{26}N_2O_2$: C, 70.4; H, 9.0; N, 9.7. Found: C, 70.4; H, 9.0; N, 9.7.

***cis*-3-Dimethylamino-2,2,4,4-tetramethylcyclobutanol** (IV).—A solution of 100 g. of 3-dimethylamino-2,2,4,4-tetramethylcyclobutanone in 500 ml. of isooctane was hydrogenated in a stainless steel rocking autoclave over 30 g. of 5% ruthenium on powdered carbon at 100° and 3000 p.s.i. for 4 hr. The catalyst was removed by filtration and washed with 300 ml. of methanol. Analysis of the combined filtrates by vapor phase chromatography showed no starting material was present. The filtrate was distilled through a 6-in. Vigreux column to a base temperature of 150°. The residue solidified on cooling and was recrystallized from hexane to give 32.0 g. of crude *cis*-IV, m.p. 124.5–128.5°. Another recrystallization from hexane raised the melting point to 129–130°.

Anal. Calcd. for $C_{10}H_{21}NO$: C, 70.2; H, 12.3; N, 8.2. Found: C, 70.4; H, 12.7; N, 8.1. Infrared maxima (KBr pellet): 3.15 (OH), 3.55 and 3.62 μ [$N(CH_3)_2$]. N.m.r. spectrum (20% solution in chloroform): −41 and −49 (CH_3), −78 (N—CH), −83 [$N(CH_3)_2$], −113 (OH), −134 c.p.s. (O—CH). The picrate, recrystallized from ethyl alcohol, melted at 238–239°.

Anal. Calcd. for $C_{16}H_{24}N_4O_3$: C, 48.0; H, 6.0; N, 14.0. Found: C, 48.0; H, 6.1; N, 13.6.

Evaporation of the filtrate yielded 53.7 g. of solid material consisting mostly of *trans*-IV.

5-Dimethylamino-2,2,4,4,6,6-hexamethyl-1,3-cyclohexanedione (III).—Over a period of 30 min., 210 g. (3.0 moles) of dimethylketene was added to a stirred solution of 297 g. (3.0 moles) of *N*,*N*-dimethylisobutenylamine in 700 ml. of acetonitrile. The temperature of the exothermic reaction was kept at 30–40° by an ice bath. Stirring was continued for several hours at room temperature, and the solvent then was evaporated on a steam bath. The residue (374.3 g.) was taken up in dilute hydrochloric acid and extracted with ether. The aqueous residue was made alkaline with sodium hydroxide, and the organic layer which separated was taken up in ether and dried over an-

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[14] E. Benzing, *Angew. Chem.*, **71**, 521 (1959).

[15] K. C. Brannock, A. Bell, R. D. Burpitt, and C. A. Kelly, *J. Org. Chem.*, **26**, 625 (1961).

[16] G. Opitz, H. Hellman, and H. W. Schubert, *Ann.*, **623**, 112 (1959).

[17] R. H. Hasek and E. U. Elam (to Eastman Kodak Co.), Canadian Patent 618,772 (1961).

[18] Infrared spectra were determined on a Baird AB2 instrument. Significant maxima are reported in microns (μ).

[19] N.m.r. spectra were obtained with a Varian V4300B spectrometer at 40 Mc. Unless otherwise noted, spectra are quoted in cycles per second (c.p.s.) relative to tetramethylsilane as an internal standard.

hydrous magnesium sulfate. Distillation through a 12-in. packed column gave 123 g. of 3-dimethylamino-2,2,4,4-tetramethylcyclobutanone (I) and 115.1 g. (32%) of 5-dimethylamino-2,2,4,4,6,6-hexamethyl-1,3-cyclohexanedione (III), b.p. 132–134° (4 mm.), n^{20}_{D} 1.4948.

Anal. Calcd. for $C_{14}H_{25}NO_2$ (III): mol. wt., 239. Found: mol. wt., (ebullioscopic in benzene), 244. Infrared maxima (smear): 3.61 $[N(CH_3)_2]$, 5.75 μ (C=O). N.m.r. spectrum (50% solution in benzene): −98 $[N(CH_3)_2]$, −94 (N—CH), −68 $[—COC(CH_3)_2CO—]$, −52 and −47 c.p.s. (CH_3 groups). With dilution of the sample, the peak at −68 c.p.s. separated into a doublet.

The black residue from the distillation was extracted with 200 ml. of hot acetone. Evaporation of the acetone left 27.5 g. of solid residue, which was recrystallized from ethyl alcohol and then from toluene to give 19.4 g., m.p. 168–169°. Elemental analysis and molecular weight determination indicated that this compound was an adduct of three molecules of dimethylketene and one molecule of *N*,*N*-dimethylisobutenylamine.

Anal. Calcd. for $C_{18}H_{31}NO_3$: C, 69.9; H, 10.1; N, 4.6; mol. wt., 309. Found: C, 70.1; H, 10.5; N, 4.6; mol. wt. (ebullioscopic in benzene), 318. Infrared maxima (mineral oil mull): 3.5, 3.6 $[N(CH_3)_2]$, 5.74 μ (C=O).

2,2,4,4,6,6-Hexamethyl-5-piperidino-1,3-cyclohexanedione.—Dimethylketene (280 g., 4.0 moles) was added to a stirred solution of 280 g. (2.0 moles) of *N*-isobutenylpiperidine in 500 ml. of dimethylformamide. The exothermic reaction was kept at 40–50° by an ice bath. The reaction mixture was stirred for 6 hr. and then distilled through a 10-in. packed column to give 104.3 g. (25%) of 2,2,4,4-tetramethyl-3-piperidinocyclobutanone and 180.4 g. (31%) of 2,2,4,4,6,6-hexamethyl-5-piperidino-1,3-cyclohexanedione, b.p. 134–136° (1.2 mm.), n^{20}_{D} 1.5090.

Anal. Calcd. for $C_{17}H_{29}NO_2$: mol. wt., 279. Found: mol. wt. (ebullioscopic in benzene), 280. Infrared maxima (smear): 3.55, 3.62 ($C_5H_{10}N$), 5.76 μ (C=O).

A solid product which precipitated in the still during the above distillation was removed by filtration and recrystallized from toluene to give 51.3 g. of a 3:1 adduct, m.p. 216.5–217.5°.

Anal. Calcd. for $C_{21}H_{35}NO_3$: C, 72.2; H, 10.0; mol. wt., 349. Found: C, 72.0; H, 10.2; mol. wt. (ebullioscopic in benzene), 345. Infrared maxima (mineral oil mull): 3.55 ($C_5H_{10}N$), 5.78 μ (C=O).

2,2,4,4,6,6-Hexamethyl-5-piperidino-1,3-cyclohexanediol.—A solution of 50 g. (0.185 mole) of 2,2,4,4,6,6-hexamethyl-5-piperidino-1,3-cyclohexanedione in 100 ml. of tetrahydrofuran was added slowly to a stirred solution of 11.4 g. (0.3 mole) of lithium aluminum hydride in 200 ml. of tetrahydrofuran at 10–20°. The solution was refluxed for 1 hr., cooled, and 12 ml. of water, 9 ml. of 20% sodium hydroxide solution, and 38 ml. of water were added successively. The mixture was filtered and the solid was washed with several portions of tetrahydrofuran. Evaporation of the filtrate left 49.4 g. (97%) of crude product, m.p. 208–211°. Recrystallization from toluene gave 36.3 g. (72%) of 2,2,4,4,6,6-hexamethyl-5-piperidino-1,3-cyclohexanediol, m.p. 212–213°.

Anal. Calcd. for $C_{17}H_{33}NO_2$: C, 72.1; H, 11.7; N, 5.0. Found: C, 71.9; H, 11.5; N, 4.9. Infrared maxima (mineral oil mull): 2.98 (OH), 3.65 μ $[N(CH_3)_2]$.

5-Dimethylamino-2,2,4,4,6,6-hexamethyl-1,3-cyclohexanediol.—By the same procedure, 5-dimethylamino-2,2,4,4,6,6-hexamethyl-1,3-cyclohexanedione (III) was reduced with lithium aluminum hydride to the corresponding glycol, m.p. 208–210°.

Anal. Calcd. for $C_{14}H_{29}NO_2$: C, 69.2; H, 11.9; N, 5.8. Found: C, 68.8; H, 12.0; N, 5.6. Infrared maxima (mineral oil mull): 3.01 (OH), 3.6 μ $[N(CH_3)_2]$.

2-Butyl-3-dimethylamino-2-ethyl-4,4-dimethylcyclobutanol.—A solution of 70 g. (0.31 mole) of 2-butyl-3-dimethylamino-2-ethyl-4,4-dimethylcyclobutanone in 100 ml. of ether was added slowly to a stirred suspension of 8.8 g. (0.23 mole) of lithium aluminum hydride in 200 ml. of ether. The temperature was maintained at 10–15° by an ice bath. After the addition was complete, the mixture was stirred for 1 hr. at room temperature. A small amount of ethyl acetate was added to destroy the excess lithium aluminum hydride, followed by slow addition of 9 ml. of water, 7 ml. of 20% sodium hydroxide solution, and 27 ml. of water. An ice bath was used for cooling during these additions. The white solid that formed was removed by filtration and washed with several portions of ether. The combined ether layers were dried over anhydrous magnesium sulfate and distilled through a 12-in. packed column to give 59 g. (84%) of 2-butyl-3-dimethylamino-2-ethyl-4,4-dimethylcyclobutanol, b.p. 99–102° (1.3 mm.), n^{20}_{D} 1.4804. Infrared maxima (smear): 3.12 (OH), 3.55, 3.61 μ $[N(CH_3)_2]$.

1-Dimethylamino-4-methyl-1-penten-3-one (VI).—Gaseous ketene was passed into a rapidly stirred solution of 316 g. (3.2 moles) of *N*,*N*-dimethylisobutenylamine in 300 ml. of ethyl ether to a weight increase of 147 g. (3.5 moles). The exothermic reaction was kept at 20–30° by intermittent use of an ice bath. The reaction solution was stirred at room temperature for an additional hour and distilled through a 12-in. packed column to give 409.6 g. (93%) of 1-dimethylamino-4-methyl-1-penten-3-one, b.p. 105–107° (2 mm.), n^{20}_{D} 1.5301.

Anal. Calcd. for $C_8H_{15}NO$: C, 68.0; H, 10.6; N, 9.9. Found: C, 68.0; H, 10.9; N, 9.7. Infrared maxima: 6.05, 6.25, 6.38 μ (N—C=C—C=O).

1-Dimethylamino-2,2-dimethylcyclobutanol.—Ketene was passed into a rapidly stirred solution of 99 g. (1 mole) of *N*,*N*-dimethylisobutenylamine in 400 ml. of ethyl ether at −15 to −20° to a weight increase of 42 g. (1 mole). The cold reaction mixture was stirred for 1 hr. and then was added slowly to a stirred suspension of 28.4 g. (0.75 mole) of lithium aluminum hydride in 500 ml. of ethyl ether at 15–25°. Stirring was continued for 2 hr. after the addition. Excess lithium aluminum hydride was destroyed by the addition of ethyl acetate, followed by successive additions of 28 ml. of water, 21 ml. of 20% sodium hydroxide solution, and 115 ml. of water. The white solid was removed by filtration and washed several times with ether. Distillation of the combined filtrates through an 8-in. Vigreux column gave 118.2 g. (83%) of 1-dimethylamino-2,2-dimethylcyclobutanol, b.p. 88–91° (7 mm.), which solidified on cooling. An analytical sample recrystallized from hexane melted at 58–60°. Infrared maxima: 3.0 (OH), 3.56 and 3.62 μ $[N(CH_3)_2]$.

1,1′-(1,4-Piperazinediyl)bis[4-methyl-1-penten-3-one].—A solution of 194 g. (1.0 mole) of 1,4-diisobutenylpiperazine in 400 ml. of ethyl ether was cooled in an ice bath and stirred rapidly as ketene was added to a weight increase of 84 g. (2.0 moles). A large amount of solid precipitated. The entire reaction mixture was evaporated on a steam bath to 256 g. of solid residue, which was recrystallized from aqueous ethyl alcohol to give 201.7 g. (73%) of 1,1′-(1,4-piperazinediyl)bis[4-methyl-1-penten-3-one], m.p. 253–254°.

2-Ethyl-4-methyl-1-piperidino-1-penten-3-one (XI).—Seventy grams (1.0 mole) of dimethylketene was added to a stirred solution of 139 g. (1.0 mole) of 1-(1-butenyl)piperidine in 400 ml. of ether under a nitrogen atmosphere over 15 min. The reaction mixture was stirred for 30 min. after the addition and then distilled through a 10-in. packed column to give 172 g. (82%) of 2-ethyl-4-methyl-1-piperidino-1-penten-3-one (XI), b.p. 119–121° (0.6 mm.), n^{20}_{D} 1.5424.

2-Ethyl-4,4-dimethyl-3-piperidinocyclobutanone (VII) **and 2-Ethyl-4,4-dimethyl-3-piperidinocyclobutanol.**—Thirty-five grams (0.5 mole) of dimethylketene was added to a stirred solution of 69.5 g. (0.5 mole) of 1-(1-butenyl)piperidine in 200 ml. of ether at −20° to 0°. An infrared spectrum, taken an hour after addition was complete, showed a strong absorption at 5.65 μ, indicative of the cycloadduct, 2-ethyl-4,4-dimethyl-3-piperidinocyclobutanone. The cold solution was added slowly to a stirred suspension of 14.2 g. (0.375 mole) of lithium aluminum hydride in 250 ml. of ether at 10–20°. After addition was complete, stirring was continued for 1 hr. at room temperature; 14 ml. of water was added carefully, with cooling, followed by 10 ml. of 20% sodium hydroxide solution and 50 ml. of water. The solid that formed was removed by filtration and washed with several portions of ether. The combined filtrates were distilled through a 10-in. packed column to give 71.2 g. (68%) of 2-ethyl-4,4-dimethyl-3-piperidinocyclobutanol, b.p. 87–89° (0.5 mm.), n^{20}_{D} 1.4870.

2-Ethyl-3-piperidinocyclobutanone (VIII) **and 2-Ethyl-3-piperidinocyclobutanol.**—Ketene was passed into a stirred solution of 69.5 g. (0.5 mole) of 1-(1-butenyl)piperidine in 200 ml. of ether at −20° to a weight increase of 25.5 g. (0.6 mole). The reaction solution was stirred at −20° for 1 hr. after the addition. An infrared spectrum of the solution showed an absorption at 5.65 μ, characteristic of a cyclobutanone (VIII). The cold solution was added slowly to a stirred suspension of 14.2 g. (0.375 mole) of lithium aluminum hydride in 250 ml. of ether at 15–25°. After addition was complete, stirring was continued for 1 hr. at room temperature, and 14 ml. of water was added carefully, with cooling, followed by 10 ml. of 20% sodium hydroxide solution and 49 ml. of water. The solid that formed was removed by filtration and washed with several portions of ether. The combined filtrates were distilled through a 10-in. packed column to give 65.1 g. (71%) of 2-ethyl-3-piperidinocyclobutanol, b.p. 98° (0.8 mm.), $n^{20}D$ 1.4930.

The rearrangement of VIII to a mixture of 2-ethyl-1-piperidino-1-buten-3-one and 1-piperidino-1-hexen-3-one was followed by infrared spectra. A small sample of the ether solution of VIII described previously was allowed to stand for a few days at room temperature. Periodic examination by infrared spectroscopy showed a gradual disappearance of the band at 5.65 μ and a corresponding appearance of bands at 6.05, 6.25, and 6.38 μ.

2-Ethyl-1-piperidino-1-buten-3-one (IX) and 1-Piperidino-1-hexen-3-one (X).—Ketene was added to a stirred solution of 139 g. (1 mole) of 1-(1-butenyl)piperidine in 400 ml. of benzene to a weight increase of 42 g. (1 mole). Frequent cooling was required to maintain the reaction temperature at 10 to 25°. The solution was stirred for 1 hr. after the addition, and then distilled through a 10-in. packed column to give 109.2 g. (60%) of a mixture of IX and X, b.p. 137° (0.3 mm.), $n^{22}D$ 1.5544.

Anal. Calcd. for $C_{11}H_{19}NO$: C, 72.9; H, 10.5; N, 7.8. Found: C, 72.7; H, 10.5; N, 7.7. N.m.r. spectrum (50% solution in CCl_4): IX, singlet at −301 (C=CH—N), broad peaks at −150 and −85 ($C_5H_{10}N$), −100 ($CH_3C=O$), −108 (CH_2), −60 c.p.s. (CH_3); X, doublets centered at −308 and −216 (CH=CH—N), broad peaks at −150 and −85 ($C_5H_{10}N$), −108 ($CH_2C=O$), −85 (CH_2), −60 c.p.s. (CH_3). Relative areas of peaks corresponding to C=CH—N protons indicated the ratio of IX to X was approximately 1:2.

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An Unusual Fragmentation–Rearrangement under Acyloin Reaction Conditions[1,2c]

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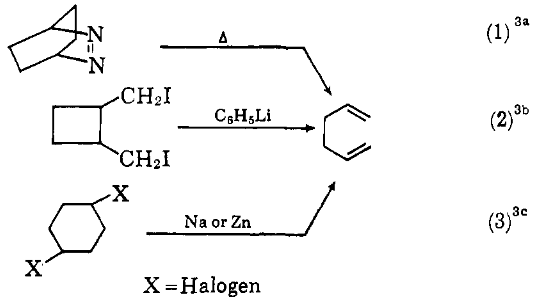
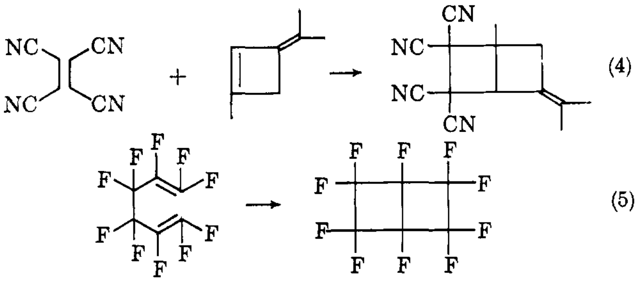
Attempted acyloin ring closure on *cis*-1,2-dicarbethoxycyclobutane leads, by an apparent fragmentation reaction, to 2-carbethoxycyclopentanone.

The bicyclo[2.2.0]hexane skeleton has eluded most attempts toward its synthesis.[3] The result of many previous investigations has been a fragmentation reaction[3c] as the following examples indicate.



Only unusual reagents or combinations of reagents, *e.g.*, tetracyanoethylene and 1-methyl-3-isopropylidenecyclobutene,[4] the isomerization of perfluoro-1,5-hexadiene,[5] or photochemical reactions[6] have been successful in producing the bicyclo[2.2.0]hexane system. In fact, the first example of "Dewar benzene," a bicyclo[2.2.0]hexadiene, has been produced by a photochemical reaction.[7]



Cope and Herrick,[8] in their synthesis of bicyclo[4.2.0]octane-7-ol-8-one from 1,2-dicarbethoxycyclohexane, demonstrated that the acyloin reaction can produce a four-membered ring. Because the generally accepted mechanism for the acyloin reaction involves the dimerization of intermediate radical ions[9] and because the fragmentation reactions known to us when this work was started involved purely ionic intermediates[3c,10] it was felt that bicyclo[2.2.0]hexane-2-ol-3-one might be prepared simply from 1,2-dicarbethoxycyclobutane following the example of Cope and Herrick.

When this reaction was conducted in liquid ammonia,[11] the major product (40%) was 2-carbethoxycyclopentanone, identical in all respects with an authen-

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[2] (a) To whom inquiries concerning this communication should be addressed; (b) Participant in the National Science Foundation supported Research Participation for College Teachers program in the Summer of 1962. (c) NOTE ADDED IN PROOF.—After this paper was accepted, we learned, by personal communication, that the observations reported here had been made independently (*and prior to our work*) by Dr. H. Ogura and Dr. J. Meinwald at Cornell University. Dr. P. G. Gassman at Ohio State University has also independently observed this rearrangement.

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[5] A. H. Fainberg and W. T. Miller, *ibid.*, **79**, 4170 (1957).

[6] (a) S. Cremer and R. Srinivasan, *Tetrahedron Letters*, No. **21**, 24 (1960); (b) W. G. Dauben and G. J. Fonken, *J. Am. Chem. Soc.*, **81**, 4060 (1959).

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[9] S. M. McElvain, "Organic Reactions," Coll. Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1948, p. 256.

[10] C. A. Grob, *Experentia*, **13/3**, 126 (1957).

[11] *Cf.*, J. C. Sheehan, R. A. Coderre, and P. A. Cruickshank, *J. Am. Chem. Soc.*, **75**, 6231 (1953).