Ketenes. XIV. Adducts of Dimethylketene with C=N Compounds[1]

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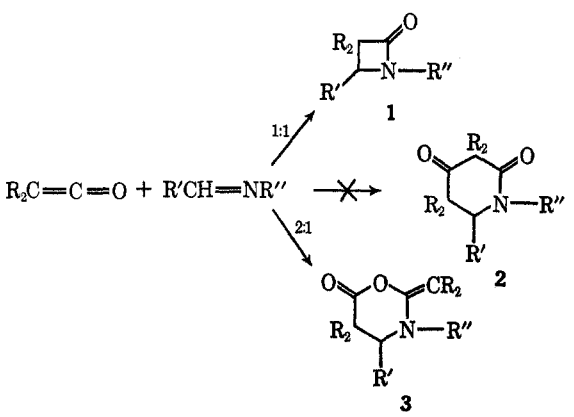
Received June 11, 1970

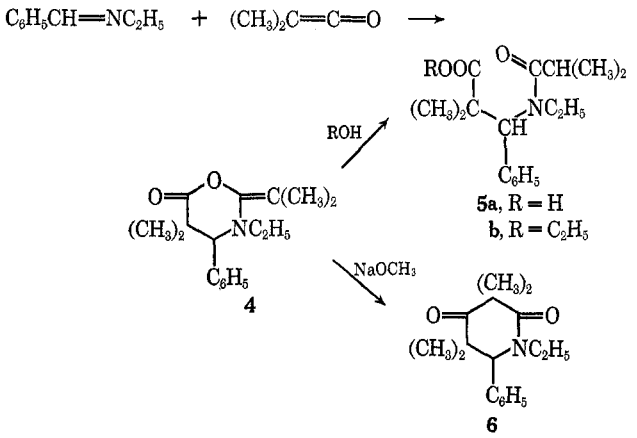
The structures of the 2:1 adducts of dimethylketene with azomethines and N heterocycles were incorrectly assigned in the early literature. These materials are oxazinone derivatives rather than piperidinediones. For some C=N compounds, bulky substituents on the nitrogen of the azomethine and use of solvents of low polarity favor β-lactam formation at the expense of oxazinone.

In his pioneering work on ketenes, Staudinger described in detail the preparation and properties of adducts of ketenes with various azomethine compounds and N heterocyles.[2-6] The 1:1 adducts were β-lactams **1**; the 2:1 adducts, the so-called "ketene bases," were formulated as piperidinediones **2**. Despite the suspiciously facile hydrolysis of these latter compounds and the puzzling appearance of hydrolytically stable isomers,[2] the piperidinedione structure went unchallenged for over 50 years.[7] Preliminary studies in these laboratories,[8] and simultaneous work by Taylor and coworkers,[9] showed that most "ketene bases" are, in fact, dihydrooxazinones **3**.

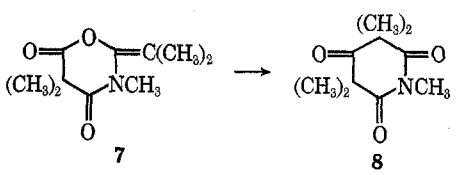


The present paper is a detailed account of the structural assignments of the adducts from C=N compounds and ketenes, reactions of these adducts, and variations of reactivity with structure of C=N compounds. Rigorous structural assignments were made for the dimethylketene adducts with *N*-benzylideneethylamine and quinoline. These C=N compounds represent widely different types and both adducts are well known in the literature.[2-6]

Dimethylketene and *N*-benzylideneethylamine reacted in benzene (and more rapidly in acetonitrile) to give 3-ethyldihydro-2-isopropylidene-5,5-dimethyl-4-phenyl-2*H*-1,3-oxazin-6(5*H*)-one (**4**) in high yield. This product was sensitive to moisture and hydrolyzed overnight in moist air to 3-(*N*-ethyl-2-methylpropionamido)-2,2-dimethyl-3-phenylpropionic acid (**5a**). Refluxing **4** in 10% aqueous sodium carbonate solution effected the same hydrolysis to **5a** (97% yield) in 30 min. When **4** was heated with a small amount of sodium methoxide in refluxing cyclohexane, a facile and virtually quantitative rearrangement to the piperidinedione **6** occurred. **6** was resistant to hydrolysis; it was recovered unchanged after prolonged refluxing in 10% sodium carbonate solution.[10]



The rearrangement of the oxazinone **4** to the piperidinedione **6** is equivalent to that of the derivative **7** from dimethylmalonyl chloride and *N*-methylisobutyramide to the piperidinetrione **8**.[11] The pair of isomers **4** and **6** provided models for characterization of other derivatives by infrared and nmr spectra.



Hydride reductions of the oxazinones produced derivatives of the piperidinediones, presumably by the base-catalyzed rearrangement cited above. Treatment of **4** with sodium borohydride in *tert*-butyl alcohol gave the hydroxypiperidone **9** as a mixture of isomers. Oxidation of **9** with dichromate in sulfuric acid produced the piperidinedione **6**. The action of lithium aluminum

(1) Paper XIII in this series: J. C. Martin, R. D. Burpitt, P. G. Gott, M. Harris, and R. H. Meen, *J. Org. Chem.*, **36**, 2205 (1971).

(2) H. Staudinger, H. W. Klever, and P. Kober, *Justus Liebigs Ann. Chem.*, **374**, 1 (1910).

(3) H. Staudinger and H. W. Klever, *Ber.*, **39**, 968 (1906).

(4) H. Staudinger, *ibid.*, **40**, 1145 (1907).

(5) H. Staudinger, *ibid.*, **39**, 3062 (1906).

(6) H. Staudinger and H. W. Klever, *ibid.*, **40**, 1149 (1907).

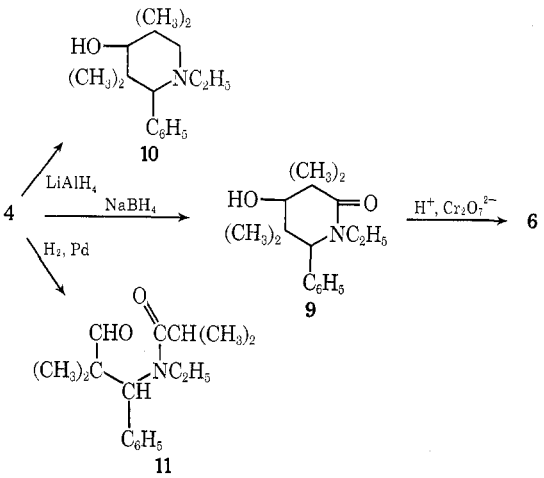
(7) S. A. Ballard, D. S. Melstrom, and C. W. Smith in "The Chemistry of Penicillin," H. T. Clarke, J. R. Johnson, and R. Robinson, Ed., Princeton University Press, Princeton, N. J., 1949, p 992.

(8) J. C. Martin, V. A. Hoyle, Jr., and K. C. Brannock, *Tetrahedron Lett.*, 3589 (1965).

(9) (a) R. N. Pratt, S. A. Proctor, and G. A. Taylor, *Chem. Commun.*, 574 (1965); (b) R. N. Pratt, G. A. Taylor, and S. A. Proctor, *J. Chem. Soc. C*, 1569 (1967).

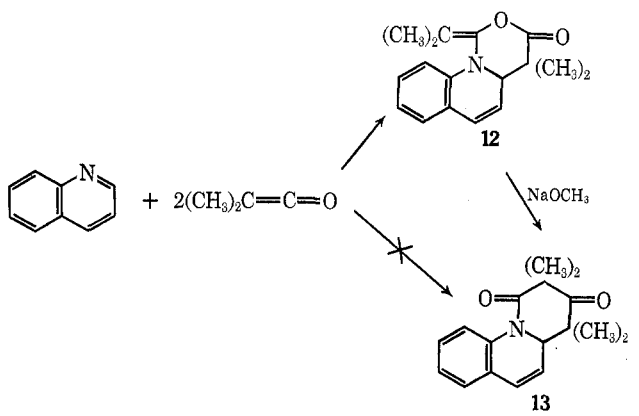
(10) In the reaction of *N*-benzylidenemethylamine with dimethylketene, Staudinger[2] found an isomeric 2:1 adduct, mp 115°, in a 3% yield. The piperidinedione made by isomerization of the initially formed dihydrooxazinone melts at 115°, and we conclude that Staudinger's small amount of isomeric material was actually the piperidinedione.

(11) J. C. Martin, K. C. Brannock, and R. H. Meen, *J. Org. Chem.*, **31**, 2966 (1966).

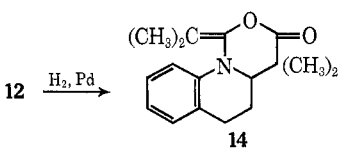


hydride on **4** gave the piperidinol **10**. A corresponding rearrangement occurred in the reduction of the 2:1 adduct of dimethylketene and *N*-*N*-dialkylisobutenylamines.[12] The catalytic hydrogenation of **4** over palladium did not effect saturation of the isopropylidene groups, but gave instead the unusual hydrogenolysis to the acyclic aldehyde **11**.

Dimethylketene and quinoline reacted rapidly in acetonitrile to afford the 2:1 adduct **12** in 92% yield. Rearrangement of this product, catalyzed by sodium methoxide, produced the piperidinedione **13** in 76%



yield. Structural assignments for these compounds were made by methods cited for the benzylideneethylamine derivatives. Catalytic hydrogenation of **12** over palladium did not affect the oxazinone structure but only saturated the endocyclic double bond to give the corresponding tetrahydroquinoline **14**.



With few exceptions, 1:1 cycloadditions of ketenes and azomethines have been limited to fully aromatic Schiff bases, *i.e.*, anils of aromatic aldehydes or ketones; studies of the reaction have been concerned with substituent effects. Huisgen, *et al.*,[13] described the reaction of diphenylketene and benzylidenemethylamine and reported that a change in the order of addition greatly changed the relative amounts of 1:1 and 2:1 adducts formed. In the addition of dimethylketene to a series of *N*-benzylidenealkylamines, we noted two significant factors which affected the mode of cycloaddition; β-lactam formation was favored, at the expense of 2:1 cycloaddition, by the presence of bulky *N*-alkyl groups and by the use of nonpolar solvents. The magnitudes of these effects are shown in Table I.

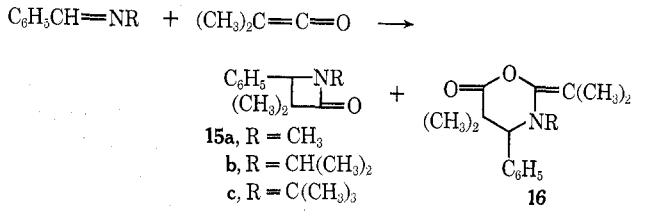
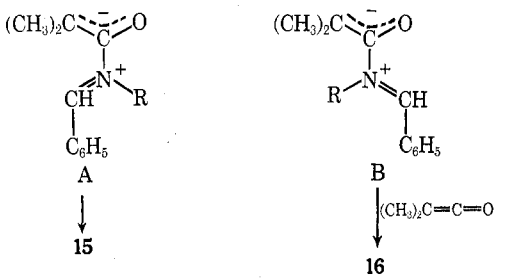


TABLE I

YIELDS OF PRODUCTS FROM $C_6H_5CH{=}NR$ AND DIMETHYLKETENE

	In hexane solvent		In acetonitrile solvent	
R	**15**, %	**16**, %	**15**, %	**16**, %
a, Methyl	40	60	0	100
b, Isopropyl	88	12	15	85
c, *tert*-Butyl	95	5	24	76

The effects observed here are compatible with a mechanism involving a dipolar intermediate, generated by combination of the electrophilic center of dimethylketene with the nitrogen atom to give the zwitterions A and B. In polar solvents the zwitterion is stabilized,



and another molecule of dimethylketene reacts with the dipolarophile B to afford the 2:1 adduct **16**. The presence of a bulky R group would sterically favor the less hindered rotamer A, which is the favored conformation for collapse to the β-lactam **15**. There is an alternative explanation that the reaction is proceeding by a combination of mechanisms, concerted and stepwise polar, and that the polar solvents favor the dipole mechanism at the expense of the concerted pathway.

Imines derived from aliphatic aldehydes also reacted with dimethylketene to give dihydrooxazinones. The general reaction was also extended to include butylethylketene. A list of dihydrooxazinones prepared is presented in Table II. In Table III, other piperidinediones prepared by rearrangement of dihydrooxazinones are listed.

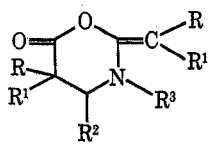
Several C=N heterocycles reacted with dimethylketene to give the dihydrooxazinones listed in Table IV. Benzoxazole and benzothiazole gave the oxazinone type of closure rather than the piperidinedione closure reported for these compounds with diphenylketene.[14] Benzoxazole gave a low yield in this reaction, but 2-

(12) J. C. Martin, P. G. Gott, and H. U. Hostettler, *J. Org. Chem.*, **32**, 1654 (1967).

(13) R. Huisgen, B. A. Davis, and M. Morikawa, *Angew. Chem.*, **80**, 802 (1968).

(14) R. D. Kimbrough, Jr., *J. Org. Chem.*, **29**, 1242 (1964).

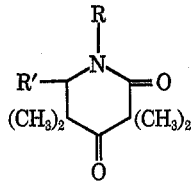
TABLE II
DIHYDROOXAZINONES FROM KETENES AND ACYCLIC C=N COMPOUNDS[a]



R	R¹	R²	R³	Yield, %	Mp or bp (mm), °C	Registry no.
CH_3	CH_3	C_6H_5	CH_3	80	126-129	29668-71-1
CH_3	CH_3	C_6H_5	$(CH_3)_3C$	35	100-103	29668-72-2
CH_3	CH_3	$(CH_3)_2CH$	C_3H_7	80	102 (1)	29668-73-3
CH_3	CH_3	C_2H_5	C_3H_7	59	82 (0.1)	29668-74-4
CH_3	CH_3	$(CH_3)_2CH$	C_2H_5	71	92-97 (0.5)	29668-75-5
CH_3	CH_3	$-(CH_2)_5-$[b]	C_3H_7	86	124-125 (0.1)	29668-76-6
CH_3	CH_3	H	$(CH_3)_3C$	75	96-97	29668-77-7
C_2H_5	C_4H_9	C_6H_5	CH_3	90	130-170 (0.1)	29668-78-8

[a] Satisfactory analytical values (±0.35% for C and H) were reported for all compounds in the table: Ed. [b] Spiro structure.

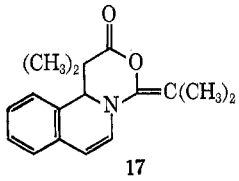
TABLE III
PIPERIDINEDIONES FROM DIHYDROOXAZINONES[a]



R	R′	Yield, %	Mp, °C	Formula	Registry no.
CH_3	C_6H_5	89	115	$C_{16}H_{21}NO_2$	29668-79-9
C_3H_7	$(CH_3)_2CH$	89	95-97	$C_{15}H_{27}NO_2$	29668-80-2

[a] Satisfactory analytical values (±0.35% for C and H) were reported for all compounds in the table: Ed.

methylbenzoxazole gave an exothermic reaction and a high yield of product. Isoquinoline and dimethylketene gave the oxazinone **17**.



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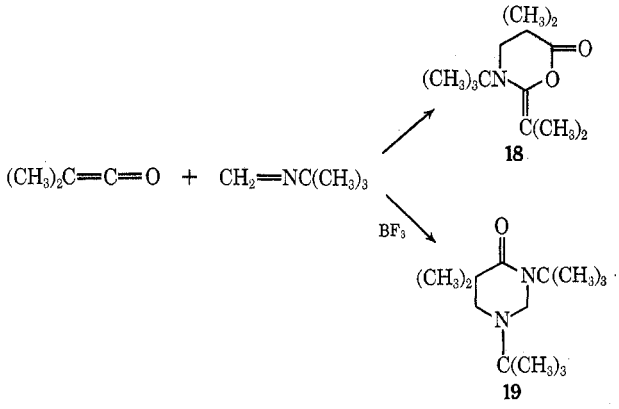
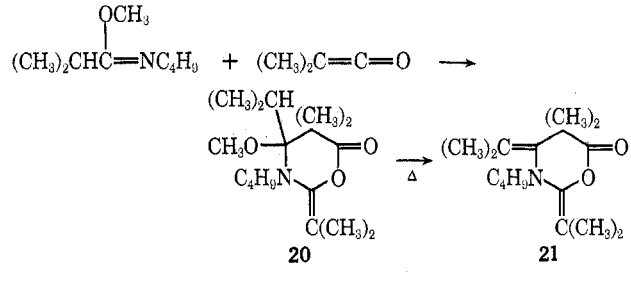
Yields and physical constants of β-lactams prepared in this study are given in Table V.

When *N*-methylene-*tert*-butylamine and dimethylketene reacted under the usual conditions and with no catalyst present, the oxazinone **18** was formed, but,



when a catalytic amount of boron trifluoride was present, the adduct **19** from 2 mol of azomethine and 1 mol of ketene was obtained. There is precedent for this in the work of Clemens and Emmons, who found that ketene and *N*-methylene-*tert*-butylamine gave a structure analogous to **19**.[15] However, the reaction of dimethylketene with benzylideneethylamine in the presence of boron trifluoride gave only the usual oxazinone adduct.

Holley and Holley[16] reported that an imino thioether and dimethylketene gave a β-lactam. We found that a compound of a similar type, an imino ether, gave a 2:1 adduct **20**, which lost methanol on distillation to give the oxazinone **21**.



The reaction of dimethylketene with C=N compounds seems to be general for a wide variety of C=N linkages. The products were shown to be dihydrooxazinones, not the piperidinediones previously reported.[2-6] Heterocyclic C=N compounds always gave 2:1 adducts of the dihydrooxazinone type, while azomethines afforded 2:1 and 1:1 adducts in varying ratios depending upon structure of the azomethine and polarity of the reaction solvent.

(15) D. H. Clemens and W. D. Emmons, *J. Org. Chem.*, **26**, 949 (1961).
(16) A. D. Holley and R. W. Holley, *J. Amer. Chem. Soc.*, **73**, 3172 (1951).

TABLE IV

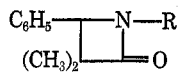
DIHYDROOXAZINONES FROM DIMETHYLKETENE AND HETEROCYCLIC C=N COMPOUNDS[a]

C=N compound	Yield, %	Mp, °C	Formula	Registry no.
6-Methoxyquinoline	72	85–86.5	$C_{18}H_{21}NO_3$	29668-81-3
Isoquinoline	60	107–110	$C_{17}H_{19}NO_2$	29784-72-3
Benzoxazole	25	103–104	$C_{15}H_{17}NO_3$	29668-82-4
Benzothiazole	90	83.5–85	$C_{15}H_{17}NO_2S$	29668-83-5
2-Methylbenzothiazole	93	100.5–101.5	$C_{16}H_{19}NO_2S$	29668-84-6

[a] Satisfactory analytical values (±0.35% for C and H) were reported for all compounds in the table: Ed.

TABLE V

β-LACTAMS FROM DIMETHYLKETENE AND C=N COMPOUNDS[a]



R	Yield, %	Mp or bp (mm), °C	Formula	Registry no.
CH_3	24	117–121 (4.6)	$C_{12}H_{15}NO$	29668-85-7
C_2H_5	88	101–103 (1)	$C_{13}H_{17}NO$	29668-86-8
$(CH_3)_3C$	81	85.5–87	$C_{15}H_{21}NO$	29668-87-9

[a] Satisfactory analytical values (±0.35% for C and H) were reported for all compounds in the table: Ed.

Experimental Section

3-Ethyldihydro-2-isopropylidene-5,5-dimethyl-4-phenyl-2*H*-1,3-oxazin-6(5*H*)-one (4).—Dimethylketene (21.0 g, 0.3 mol) was added to a solution of 20.0 g (0.15 mol) of benzylideneethylamine in 100 ml of acetonitrile at −20° over a period of 10 min. The characteristic yellow color of dimethylketene was discharged rapidly and the temperature rose to −10°. The mixture was allowed to warm to room temperature, and the acetonitrile was then removed *in vacuo*. The residual white solid was washed with several portions of pentane and dried in a vacuum desiccator to obtain 34.0 g (83%) of **4**: mp 101.5–104°; ir (CCl_4) 5.72 and 5.92 μ; nmr (CCl_4) δ 0.98 (t, 3), 1.04 (s, 3), 1.07 (s, 3), 1.78 (s, 3), 1.85 (s, 3), 2.80 (m, 2), 4.07 (s, 1), and 7.43 (s, 5).

Anal. Calcd for $C_{17}H_{23}NO_2$: C, 74.7; H, 8.5; N, 5.1. Found: C, 74.9; H, 8.2; N, 5.1.

1-Ethyl-3,3,5,5-tetramethyl-6-phenyl-2,4-piperidinedione (6).—A mixture of 50.0 g of **4**, 1.5 g of sodium methoxide, and 200 ml of cyclohexane was refluxed for 2 hr. The mixture was filtered to remove a small amount of solid and then washed with two 100-ml portions of water. The organic layer was concentrated and cooled. The white solid that precipitated was filtered and dried to give 46.0 g (92%) of **6**, mp 86–90°. A sample for analysis was recrystallized from an ethyl alcohol–water mixture: mp 89.5–91°; ir (cyclohexane) 5.87 and 6.10 μ; nmr (CCl_4) δ 0.83 (s, 3), 1.08 (t, 3), 1.43 (s, 6), 1.50 (s, 3), 2.78 (m, 1), 3.81 (m, 1, NCH_2), 4.25 (s, 1), and 7.14 (m, 5).

Anal. Calcd for $C_{17}H_{23}NO_2$: C, 74.7; H, 8.5; N, 5.1. Found: C, 74.7; H, 8.7; N, 5.1.

3-(*N*-Ethyl-2-methylpropionamido)-2,2-dimethyl-3-phenylpropionic Acid (5a).—A mixture of 7.0 g (0.025 mol) of **4**, 2.5 g of sodium carbonate, and 23 ml of water was refluxed for 3 hr. The resulting solution was acidified with dilute HCl, and the solid that formed was removed by filtration, washed with water, and dried to give 7.1 g (97%) of **5a**, mp 118–120°. A sample for analysis was recrystallized from aqueous methanol: mp 120–121° (lit.[7] 114–114.5°); ir (KBr) 5.82 and 6.22 μ; nmr (CCl_4) δ 0.50 (t, 3), 1.10 and 1.19 (two sets of doublets, 6), 1.31 (s, 3), 1.36 (s, 3), 2.82 (septet, 1), 3.45 (q, 2), 6.15 (s, 1), 7.50 (broad peak, 5), and 9.1 (s, 1).

Anal. Calcd for $C_{17}H_{25}NO_3$: C, 70.1; H, 8.6; N, 4.8. Found: C, 70.4; H, 8.5; N, 5.0.

Ethyl 3-(*N*-Ethyl-2-methylpropionamido)-2,2-dimethyl-3-phenylpropionate (5b).—The quantity of **4** that resulted from mixing 100 g (0.75 mol) of benzylideneethylamine and 135 g (1.5 mol) of dimethylketene in 200 ml of acetonitrile was treated with 259 ml of ethyl alcohol and stirred for 8 hr at room temperature. Distillation of this solution through a 6-in. packed column gave 221 g (93%) of **5b**, bp 128–130° (0.4 mm). This material solidified on standing. A sample for analysis was recrystallized from cyclohexane: mp 44–45°; ir (KBr) 5.84 and 6.12 μ; nmr (CCl_4) δ 0.51 (t, 3), 1.16 (t, 3), 1.08 (s, 3), 1.20 (s, 3), 1.40 (s, 3), 2.86 (septet, 1), 3.45 (q, 2), 4.15 (q, 2), 6.30 (s, 1), and 7.25–7.75 (m, 5).

Anal. Calcd for $C_{19}H_{29}NO_3$: C, 71.4; H, 9.2; N, 4.4. Found: C, 71.7; H, 9.5; N, 4.3.

1-Ethyl-4-hydroxy-3,3,5,5-tetramethyl-6-phenyl-2-piperidinone (9).—A solution of 50.0 g (0.18 mol) of **4** in 150 ml of *tert*-butyl alcohol was heated to 40°, and 3.7 g of sodium borohydride was then added. The temperature was kept at 65° for 20 hr, and then 15 ml of acetic acid was added. The mixture was added to 500 ml of water and 30 ml of 10% HCl. The alcohol was removed on a steam bath, and the remaining organic layer was extracted with ether. Evaporation of the ether layer gave 42 g of syrup. Washing with ether and water gave 11 g (22%) of **9**, mp 188–189°, as a mixture of isomers: ir (KBr) 2.93, 6.22, and 9.40 μ.

Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.1; H, 9.1; N, 5.1. Found: C, 74.4; H, 8.8; N, 5.0.

1-Ethyl-3,3,5,5-tetramethyl-2-phenyl-4-piperidinol (10).—**4** (25 g) was added slowly to a slurry of 6 g of lithium aluminum hydride in 300 ml of ether. The mixture was refluxed for 2 hr after the addition. Ethyl acetate (25 ml) was added to destroy the excess hydride, followed by 6 ml of water, 4.5 ml of 20% sodium hydroxide solution, and 21 ml of water. The mixture was filtered to remove the solid, and the filtrate was then distilled to give 17.5 g (73%) of **10**, bp 115° (0.5 mm), which partly solidified on standing.

Anal. Calcd for $C_{17}H_{27}NO$: C, 78.1; H, 10.4; N, 5.4. Found: C, 78.3; H, 10.5; N, 5.7.

***N*-Ethyl-*N*-(2-formyl-2-methyl-1-phenylpropyl)-2-methylpropionamide (11).**—A solution of 27.0 g (0.1 mol) of **4** in 200 ml of ethyl acetate was hydrogenated in a magnetically stirred pressure bottle over 2 g of 5% palladium on powdered carbon at 25° (40 psi). A reaction time of 9 hr was required for the absorption of 0.1 mol of hydrogen. The catalyst was removed by filtration, and the solvent was then removed *in vacuo* to give 27.0 g (99%) of practically pure **11**, which, after two washings with pentane, melted at 84–85°: ir (KBr) 5.86 and 6.09 μ; nmr (CCl_4) δ 0.82 (t, 3), 1.05 (s, 6), 1.15 (d, 6), 2.75 (septet, 1), 3.35 (q, 2), 4.92 (s, 1), 6.41 (m, 5), and 9.68 (s, 1, CHO).

Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.2; H, 9.1; N, 5.1. Found: C, 73.7; H, 9.2; N, 4.8.

4,4a-Dihydro-1-isopropylidene-4,4-dimethyl-1*H*-1,3-oxazino-[3,4-*a*]quinolin-3-one (12).—Dimethylketene (28.9 g, 0.4 mol) was added to a stirred solution of 26.0 g (0.2 mol) of quinoline in 100 ml of acetonitrile at −35°. The reaction was rapid and exothermic, and the temperature rose to 10°. The mixture was stirred for 2 hr at room temperature and then distilled through a 6-in. Vigreux column to give 50.0 g (92%) of **12**, bp 143–147° (0.1–0.2 mm). This material solidified on standing. A sample for analysis was recrystallized from an ethyl alcohol–water mixture: mp 82–83.5° (lit.[2] mp 81–82°); ir (CCl_4) 5.75 and 5.92 μ; nmr (CCl_4) δ 1.18 (s, 6), 1.49 (s, 3), 1.83 (s, 3), 4.27 (d, 1), 5.55 (pair of doublets, 1), and 6.30 to 7.10 (m, 5).

Anal. Calcd for $C_{17}H_{19}NO_2$: C, 75.8; H, 7.1; N, 5.2. Found: C, 75.9; H, 7.2; N, 4.9.

4,4a-Dihydro-2,2,4,4-tetramethyl-1*H*-benzo[*c*]quinolizine-1,3-(2*H*)-dione (13).—A solution of 5.0 g of **12** and 0.1 g of sodium methoxide in 50 ml of cyclohexane was heated at 65° for 2 hr. The infrared spectrum of the solution indicated that the starting material was gone and a new compound had been formed. The solution was concentrated *in vacuo*, and the solid that precipitated was removed by filtration and dried to give 3.8 g (76%) of **13**, mp 84–86°. A sample for analysis was recrystallized from methanol: mp 87–88°; ir (cyclohexane) 5.92 and 6.00 μ; nmr (CH_2Cl_2) δ 1.13 (s, 3), 1.28 (s, 3), 1.32 (s, 3), 1.38 (s, 3), 4.38 (t, 1, J = 2.4 Hz, 4a proton), 5.82 (pair of doublets, 1, J = 9.8 and 2.4 Hz, 5 proton), 6.55 (pair of doublets, 1, J = 9.8 and 2.4 Hz, 6 proton), 7.07 (m, 1), and 7.73 (m, 3).

4,4a,5,6-Tetrahydro-1-isopropylidene-4,4-dimethyl-1*H*-1,3-oxazino[3,4-*a*]quinolin-3-one (14).—A solution of 10 g (0.037 mol) of **12** in 75 ml of cyclohexane was hydrogenated over 2 g of 75% palladium on carbon at 25° (40 psi) in a magnetically stirred pressure bottle until 0.037 mol of hydrogen had been absorbed. The reaction mixture was filtered to remove the catalyst and the filtrate concentrated *in vacuo*. The residual oil crystallized and was recrystallized from hexane to give 7.5 g (74%) of **14**, mp 97–98°. A sample for analysis was recrystallized from methanol: mp 97–98°; ir (CCl_4) 5.70 and 5.91 μ; nmr (CCl_4) δ 1.21 (s, 3), 1.30 (s, 3), 1.40 (s, 3), 1.83 (s, 3), 2.02 (m, 2, methylene group at 5 position), 2.75 (m, 2, methylene group at 6 position), 3.40 (m, 1, 4a proton), 6.80 (m, 4).

Anal. Calcd for $C_{17}H_{21}NO_2$: C, 75.3; H, 7.8; N, 5.2. Found: C, 75.6; H, 7.7; N, 5.4.

Data for Table I.—Dimethylketene (0.1 mol) was added rapidly to 0.1 mol of an *N*-benzylidenealkylamine in 100 ml of either hexane or acetonitrile, and the reaction mixture was kept at 68–70° for 18 hr. The mixture was assayed by glpc (5% silicone fluid FS-1265 QF-1 on Chromosorb P). The only products formed were **15** and **16**, and the values reported in the table are percentages of the total area of **15** and **16**.

1-Isopropyl-3,3-dimethyl-4-phenyl-2-azetidinone (15b).—Dimethylketene (41.3 g, 0.59 mol) was added rapidly to a refluxing solution of 73.6 g (0.5 mol) of *N*-benzylideneisopropylamine in 500 ml of refluxing hexane. Refluxing was continued for 6 hr. Examination of the reaction solution by glpc (5% silicone fluid FS-1265 QF-1 on Chromosorb P) showed 88% **15b** and 12% **16b**. Distillation through a 6-in. packed column gave 89.0 g (82%) of **15b**: bp 114° (2 mm); ir (KBr) 5.70 μ; nmr (CCl_4) δ 0.70 (s, 3), 1.09 and 1.31 (pair of doublets, 6, isopropyl methyls), 1.29 (s, 3), 3.57 (septet, 1), 4.29 (s, 1), and 7.22 (s, 5).

Anal. Calcd for $C_{14}H_{19}NO$: C, 77.4; H, 8.8; N, 6.4. Found: C, 77.4; H, 9.1; N, 6.2.

3-Isopropyl-2-isopropylidene-5,5-dimethyl-4-phenyl-2*H*-1,3-oxazin-6(5*H*)-one (16b).—Dimethylketene (30.8 g, 0.44 mol) was added to a stirred solution of 29.4 g (0.2 mol) of *N*-benzylideneisopropylamine in 100 ml of acetonitrile. The reaction was quite exothermic, and the temperature was kept at 30–60° by a water bath. The yellow color of the dimethylketene was discharged in about 10 min. Examination of the reaction solution by glpc (5% silicone fluid FS-1265 QF-1 on Chromosorb P) showed 15% **15b** and 85% **16b**. The solid that precipitated on cooling was removed by filtration and dried to give 43 g (76%) of **16b**, mp 108–110°. Recrystallization from hexane gave 38.0 g: mp 111–113°; ir (CCl_4) 5.72 and 5.91 μ; nmr (CCl_4) δ 0.87, 1.11 (pair of doublets, 6, isopropyl methyls), 0.99 (s, 3), 1.17 (s, 3), 1.78 (s, 3), 1.92 (s, 3), 3.25 (septet, 1), 4.00 (s, 1), and 7.42 (m, 5).

Anal. Calcd for $C_{18}H_{25}NO_2$: C, 75.2; H, 8.8; N, 4.9. Found: C, 74.9; H, 8.8; N, 4.8.

4,4a-Dihydro-1-isopropylidene-4,4,4a-trimethyl-1*H*,3*H*-[1,3]oxazino[4,3-*b*]benzoxazol-3-one.—Dimethylketene (16.1 g, 0.23 mol) was added to a stirred solution of 13.3 g (0.1 mol) of 2-methylbenzoxazole in 75 ml of acetonitrile. The solution was stirred for 15 hr at room temperature, and the solvent was then removed *in vacuo*. The white, crystalline residue weighed 27.3 g, and, after recrystallization from hexane, gave 19.5 (72%) of 4,4a-dihydro-1-isopropylidene-4,4,4a-trimethyl-1*H*,3*H*-[1,3]-oxazino[4,3-*b*]benzoxazol-3-one: mp 103–104°; ir (KBr) 5.65 and 5.85 μ; nmr ($CDCl_3$) δ 1.37 (s, 3), 1.42 (s, 3), 1.50 (s, 3), 1.75 (s, 3), 1.92 (s, 3), and 6.75 (m, 4).

Anal. Calcd for $C_{16}H_{19}NO_3$: C, 70.3; H, 7.0; N, 5.1. Found: C, 70.3; H, 6.9; N, 4.8.

1,3-Di-*tert*-butyltetrahydro-5,5-dimethyl-4(1*H*)-pyrimidinone (19).—Dimethylketene (9.1 g, 0.13 mol) was added rapidly to a stirred solution of 23 g (0.27 mol) of *N*-methylene-*tert*-butylamine and 1 ml of boron trifluoride etherate in 100 ml of ethyl acetate. An exothermic reaction took place, and some cooling was necessary to keep the temperature under 35°. The solvent was removed *in vacuo* to give 27 g of residue that slowly crystallized. Glpc indicated that this residue contained 63% **19**. This quantity represented a yield of 56%. Distillation through a 4-in. packed column gave 10.3 g (32%) of **19**, bp 96–100° (1.2 mm), that was pure by glpc. A sample recrystallized from hexane melted at 60–61°: ir (KBr) 6.13 μ; nmr ($CHCl_3$) δ 1.01 (s, 6), 1.10 (s, 9), 1.37 (s, 9), 2.38 (s, 2), and 3.96 (s, 2, $-NCH_2N-$).

Anal. Calcd for $C_{14}H_{28}N_2O$: C, 70.0; H, 11.7; N, 11.7. Found: C, 70.2; H, 11.8; N, 11.8.

3-Butyl-4-isopropyl-2-isopropylidene-4-methoxy-5,5-dimethyl-2*H*-1,3-oxazin-6(5*H*)-one (20) and 3-Butyl-2,4-bis(isopropylidene)-5,5-dimethyl-2*H*-1,3-oxazin-6(5*H*)-one (21).—Dimethylketene (12.5 g, 0.18 mol) was added rapidly to a stirred solution of 14 g (0.089 mol) of *N*-(1-methoxy-2-methylpropylidene)butylamine in 75 ml of acetonitrile. The reaction solution was stirred for 15 hr at room temperature. The solvent was then removed *in vacuo* to give 24.5 g of crude **20** as an oily residue: ir (neat) 5.70, 5.91, and 9.28 μ; nmr (CCl_4) δ 0.90 (m, 3), 1.02, 1.15 (pair of doublets, 6, isopropyl methyls), 1.27 (s, 6), 1.35 (m, 4), 1.65 (s, 3), 1.69 (s, 3), 2.22 (septet, 1), 3.00 (m, 2), and 3.05 (s, 3). Distillation of crude **20** through a 3-in. Vigreux column gave methanol as a forecut and 15.1 g (57%) of **21**: bp 110–121° (0.15–0.25 mm); ir (neat) 5.65 and 5.82 μ; nmr (CCl_4) δ 0.90 (t, 3), 1.28 (m, 4), 1.49 (s, 6), 1.67 (s, 3), 1.73 (s, 3), 1.79 (s, 3), 1.84 (s, 3), and 2.68 (m, 2).

Anal. Calcd for $C_{16}H_{27}NO_2$: C, 72.5; H, 10.2; N, 5.3. Found: C, 72.2; H, 10.1; N, 5.2.

Registry No.—**4**, 6082-57-1; **5a**, 6082-60-6; **5b**, 6082-59-3; **6**, 6982-58-2; **9**, 6082-61-7; **10**, 6082-62-8; **11**, 29683-09-8; **12**, 4612-76-4; **13**, 6082-64-0; **14**, 4612-77-5; **15b**, 29683-13-4; **16b**, 29683-14-5; **19**, 29683-15-6; **20**, 29784-71-2; **21**, 29668-70-0; dimethylketene, 598-26-5; 4,4a-dihydro-1-isopropylidene-4,4,4a-trimethyl-1*H*,3*H*-]1,3]oxazino-4,3-*b*]benzoxazol-3-one, 29668-88-0.