Ketenes. II. Cycloaddition of Dialkyl Ketenes to Vinyl Ethers[1]

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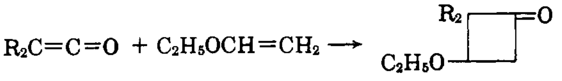
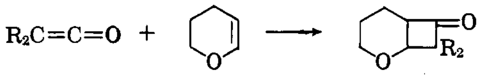
Dimethylketene adds readily to a variety of vinyl ethers to form 3-alkoxy-2,2-dimethylcyclobutanones. Higher dialkyl ketenes, which dimerize much more slowly than dimethylketene, can be forced into cycloaddition to the less reactive allyl ethers and vinyl esters.

The cycloaddition of diphenylketene[3] and dimethylketene[4] to vinyl ethers was first noted by Staudinger in 1920. A few years ago, Hurd and Kimbrough reexamined the cycloadduct of diphenylketene and ethyl vinyl ether, and corrected Staudinger's original structural assignment by demonstrating that the product was 3-ethoxy-2,2-diphenylcyclobutanone (Ia).[5] They also prepared and characterized the corresponding cycloadducts, IIa and IIb, of ketene and diphenylketene with dihydropyran. Here it was apparent that ketene added to the olefinic bond much less readily than diphenylketene, and in this respect the behavior of the two ketenes followed the relative reactivities in cycloadditions to cyclopentadiene.[3,6-8] On the other hand, Kimbrough found that diphenylketene failed to yield cycloadducts with higher alkyl vinyl ethers,[9] which is rather surprising in view of its well-known ease of addition to a variety of other (and presumably less nucleophilic) olefinic compounds.



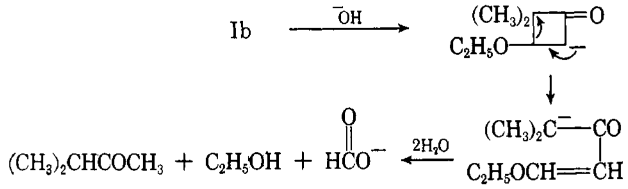
Ia, R = C_6H_5
b, R = CH_3



IIa, R = H
b, R = C_6H_5
c, R = CH_3

Dimethylketene is rated as less active than diphenylketene in cycloaddition reactions.[10] For example, dimethylketene does not react with styrene,[4] while diphenylketene forms an adduct.[3,6a] The reaction of dimethylketene with ethyl vinyl ether at −20° required three or four days and was accompanied by some dimerization of the ketene. Neither the yield nor the structure of the product was determined.[4]

In the light of these observations, the ready addition of dialkyl ketenes to a variety of vinyl ethers was somewhat unexpected. The cycloadduct of dimethylketene and ethyl vinyl ether was obtained in 80% yield by adding the ketene to the ether at room temperature. Formulation of the product as 3-ethoxy-2,2-dimethylcyclobutanone (Ib) was compatible with infrared and n.m.r. spectra and with the alkaline degradation to 3-methyl-2-butanone. The mechanism of this degradation probably involves an opening of the ring, followed by a saponification and cleavage similar to that of hydroxymethylene ketone derivatives.[11]



Vinyl ethers with larger alkyl groups, which failed to yield adducts with diphenylketene,[9] reacted readily with dimethylketene to form alkoxy cyclobutanones in good yields. Inert substituents, such as chloro and phenoxy, on the alkyl group had no adverse effect on the reaction. In a vinyl ether containing an amino group, a vigorous acylation of the amine function occurred; the derivative then underwent normal cycloaddition with more dimethylketene. An attempt to use a vinyl ether containing a tertiary amino group gave only a polymer of dimethylketene, in keeping with the well-known catalytic action of trialkyl amines on dimethylketene.[12]

Ethyl propenyl ether formed an adduct with dimethylketene in good yield, but ethyl isobutenyl ether failed to react. The latter addition presumably failed because steric effects override the nucleophilic reactivity of the vinyl ether; the more nucleophilic enamines of analogous structure (isobutenyl amines) react readily with ketenes.[1] It is noteworthy that the vinyl ethers, unlike enamines, did not form 1:2 and 1:3 adducts with dimethylketene; furthermore, the cycloaddition product of ethyl propenyl ether and dimethylketene consisted of two isomers in amounts corresponding to the ratio of *cis–trans* isomers in the starting propenyl ether. These results, indicating a 1:1 stereospecific addition, are too fragmentary to afford any significant conclusions, but they suggest that the cycloaddition of ketenes to vinyl ethers is a

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[2] To whom inquiries should be sent.

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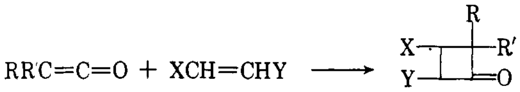
TABLE I

CYCLOADDUCTS OF DIALKYL KETENES



R	R'	X	Y	Method[a]	Yield, %	B.p. °C.	B.p. mm.	$n^{20}D$	% C Calcd.	% C Found	% H Calcd.	% H Found
CH_3	CH_3	OC_2H_5	H	A	80	82–83	38	1.4270	67.6	67.8	9.9	10.0
CH_3	CH_3	OC_2H_5	CH_3	A	64	90–92	34		69.2	68.8	10.3	10.3
CH_3	CH_3	OC_4H_9	H	A	65	72–78	6.5	1.4323	70.6	70.0	10.6	10.6
CH_3	CH_3	$OCH_2CH(CH_3)_2$	H	A	54	70	6.9	1.4287	70.6	70.7	10.6	10.9
CH_3	CH_3	$OCH(C_2H_5)(C_4H_9)$	H	A	56	85	0.7	1.4419	74.3	74.2	11.5	11.6
CH_3	CH_3	OCH_2CH_2Cl	H	A	70	91.5–93.5	4.9	1.4578	54.7	54.6	7.5	7.5[b]
CH_3	CH_3	$OCH_2CH_2OC_6H_5$	H	A	67	118–119	0.5	1.5104	71.8	71.7	7.7	7.8
CH_3	CH_3	$OCH_2CH_2NHCOCH(CH_3)_2$	H	A	80	62–67	0.003–0.007	1.4666	63.5	63.9	9.3	9.3[c]
CH_3	CH_3	$OC_6H_4OCH_3$ (*p*)	H	A	46	134–138	3.5	1.5290	76.4	76.7	7.9	7.8
CH_3	CH_3	$SCH_2CH_2OCOCH_3$	H	A	41	119–124	1.5		55.6	55.5	7.4	7.4[d]
CH_3	CH_3	$-OCH_2CH_2CH_2-$		A	80	89–90	11	1.4632	70.1	70.4	9.2	9.1
CH_3	CH_3	$-OCH(OC_2H_5)CH_2CH_2-$		A	85	116[e]	3		66.6	66.5	9.2	9.2
CH_3	CH_3	OC_2H_5	OC_2H_5	A	20	90–92.5	9.7	1.4355	64.5	63.9	9.7	9.7
C_2H_5	*n*-C_4H_9	OC_2H_5	H	B	81	80	1.6	1.4443	72.8	72.8	11.1	11.3
C_2H_5	*n*-C_4H_9	$OCOCH_3$	H	C	30	97	0.5	1.4554	67.9	67.8	9.5	9.4
C_2H_5	*n*-C_4H_9	$CH_2OC_2H_5$	H	C	31	76	0.4	1.4497	73.5	73.0	11.4	11.4
C_2H_5	*n*-C_4H_9	$CH_2OC_6H_5$	H	C	15	133–134	0.4		78.4	78.3	9.3	9.4
C_2H_5	*i*-C_4H_9	$OCOCH_3$	H	C	31	64	0.6	1.4550	67.9	67.7	9.5	9.4
C_2H_5	*i*-C_4H_9	$-CH_2OCH_2-$		C	30	*f*			73.4	73.8	10.3	10.2
C_6H_5	C_6H_5	$OCOCH_3$	H	A	72	114–115.5[g]			77.1	77.1	5.7	5.8
C_6H_5	C_6H_5	$SCH_2CH_2OCOCH_3$	H	A	87	90–91[h]			70.6	70.7	5.9	6.0

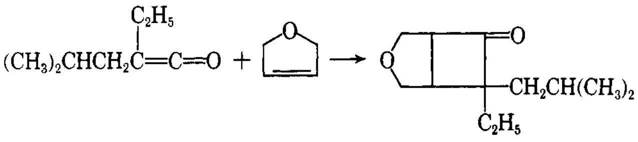
[a] A, reaction in inert solvent at room temp.; B, reactants heated at 100° (no solvent); C, reactants heated at 180° (autoclave). [b] % Cl: calcd., 19.6; found, 19.5. [c] % N: calcd., 6.2; found, 6.1. [d] % S: calcd., 14.8; found, 15.3. [e] Product solidified, m.p. 55° (from ethyl alcohol). [f] Purified by gas–liquid chromatography (see Experimental). [g] Melting point (from benzene–hexane). [h] Melting point (from ethyl alcohol).

more concerted process than the addition to enamines.[13]

Steric effects were also noted in the cycloaddition of dimethylketene to cyclic structures. Dihydropyran was very reactive and gave the bicyclic adduct IIc in excellent yield, but butyl 1-cyclohexen-1-yl ether failed to react.

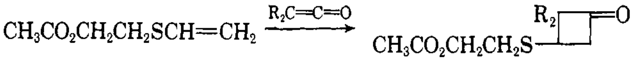
Although polarity is an important factor in the reactivity of nucleophilic olefins with ketenes, the symmetrical vinyl ether, 1,2-diethoxyethylene, added to dimethylketene to give 3,4-diethoxy-2,2-dimethylcyclobutanone in 20% yield. A measure of the electron-donating effect of the alkoxy group was shown by the cycloaddition of *p*-methoxystyrene to dimethylketene; styrene itself does not react.

The nucleophilic character of the olefinic linkage is sharply reduced in allyl ethers, and the rapid dimerization of dimethylketene nullified efforts to obtain cycloadducts with such compounds. Higher dialkyl ketenes, due to their much lower rates of dimerization,[16] could be forced into cycloadditions with allyl ethers at elevated temperatures. Butylethylketene, heated with allyl ethyl ether at 180° for 8 hr. gave the adduct in 24% yield. Under similar conditions, ethylisobutylketene and 2,5-dihydrofuran afforded the bicyclic adduct III in 32% yield.



III

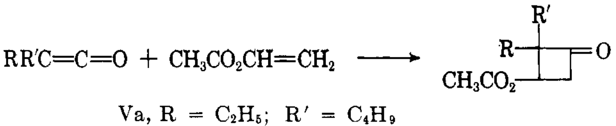
Vinyl thioethers also added to disubstituted ketenes; 2-(vinylthio)ethyl acetate gave adducts IVa and IVb with dimethylketene and diphenylketene in 41 and 87% yields, respectively.



IVa, R = CH_3

b, R = C_6H_5

Vinyl acetate exhibited a relatively low reactivity, comparable to that of allyl ethers, in its cycloaddition to ketenes. Butylethylketene and ethylisobutylketene, heated with vinyl acetate at 180°, gave the acetoxycyclobutanones Va and Vb in 30% yields. Diphenylketene and vinyl acetate combined very slowly at room temperature to give the cycloadduct Vc in 72% yield.



Va, R = C_2H_5; R' = C_4H_9

b, R = C_2H_5; R' = $CH_2CH(CH_3)_2$

c, R = R' = C_6H_5

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(13) It is tempting to suggest a correlation with the question of one- and two-step Diels–Alder mechanisms[14]; however, 1,2-cycloadditions of strongly nucleophilic and electrophilic partners, while they may involve a similar mechanistic question, exhibit fundamental differences from Diels–Alder reactions (*e.g.*, pronounced solvent effects).[15]

(14) For a review, see J. A. Berson and A. Remanick, *J. Am. Chem. Soc.*, **83**, 4947 (1961); C. Walling and H. J. Schugar, *ibid.*, **85**, 607 (1963).

(15) C. A. Stewart, Jr., *ibid.*, **84**, 119 (1962).

(16) The rates of dimerization of dialkyl ketenes fall off rapidly with increase in size and branching of alkyl groups. At room temperature, approximate rate constants ($k \times 10^6$) are dimethyl-, 70; ethylmethyl-, 10; diethyl-, 0.2[17]; butylethyl-, 0.04; and ethylisobutyl-, 0.006.[18]

(17) H. Staudinger, H. Schneider, P. Schotz, and P. M. Strong, *Helv. Chim. Acta*, **6**, 219 (1923).

(18) Unpublished estimates from the authors' laboratory.

Table I is a summary of the data obtained from all the cycloadducts prepared from ketenes and unsaturated ethers during the course of this work.

Experimental

Dialkyl ketenes were prepared by pyrolysis of the corresponding anhydrides.[19] Diphenylketene was prepared by dehydrohalogenation of diphenylacetyl chloride. 1,2-Diethoxyethylene was prepared by the method of McElvain and Stammer[20]; benzyl vinyl ether, by vinylation of benzyl alcohol with acetylene at 150° using potassium hydroxide as a catalyst; allyl vinyl ether, by an exchange reaction between allyl alcohol and butyl vinyl ether[21]; and 2-(vinylthio)ethyl acetate, by acetylation of the alcohol obtained from Rohm and Haas Company. Allyl ethyl ether was obtained from Distillation Products Industries, 2,5-dihydrofuran from General Aniline and Film Corporation, *p*-methoxystyrene from Monomer–Polymer Laboratories, and the remainder of the unsaturated ethers from Union Carbide Chemicals Division of Union Carbide Corporation.

3-Ethoxy-2,2-dimethylcyclobutanone (Ib).—To 960 g. (13.3 moles) of ethyl vinyl ether, stirred at room temperature under a nitrogen atmosphere, 600 g. (8.6 moles) of dimethylketene was added over a period of 4 hr. The mixture was stirred at room temperature for several hours. Distillation through a 12-in. Vigreux column gave 315 g. (4.4 moles) of unchanged ethyl vinyl ether and 975 g. (80%) of 3-ethoxy-2,2-dimethylcyclobutanone, b.p. 82–83° (38 mm.).

The n.m.r. spectrum of Ib[22] contained a single peak at 1.12 (CH$_3$), a triplet at 1.2 and a quartet at 3.47 (OCH$_2$CH$_3$), a pair of doublets at 2.98 and 3.08 (CH$_2$), and a triplet at 3.82 p.p.m. (CH).

Hydrolysis of 3-Ethoxy-2,2-dimethylcyclobutanone (Ib).—A mixture of 96 g. (0.675 mole) of Ib and 150 ml. of 20% sodium hydroxide solution was refluxed with stirring for 10 hr. The organic layer was extracted with two 400-ml. portions of ether; the extracts were washed with water, dried over anhydrous magnesium sulfate, and distilled through a 10-in. packed column to give 43 g. (74%) of 3-methyl-2-butanone, b.p. 90–91°. The 2,4-dinitrophenylhydrazone of this material melted at 123–124°, lit.[23] m.p. 124.7.

3-(2-Ethylhexyloxy)-2,2-dimethylcyclobutanone.—Under a nitrogen atmosphere, 140 g. (2 moles) of dimethylketene was added to a stirred solution of 312 g. (2 moles) of 2-ethylhexyl vinyl ether in 1000 ml. of ether. The solution was stirred at room temperature for 6 hr. and then distilled through a 12-in. packed column to give 103 g. of recovered vinyl 2-ethylhexyl ether and 253 g. (57%) of 3-(2-ethylhexyloxy)-2,2-dimethylcyclobutanone, b.p. 85° (0.1 mm.).

8,8-Dimethyl-2-oxabicyclo[4.2.0]octan-7-one (IIc).—Approximately 2 moles of dimethylketene was passed into a solution of 252 g. (3 moles) of freshly distilled dihydropyran in 1000 ml. of ether over a period of 1 hr. The solution was stirred for several hours at room temperature and distilled through an 18-in. packed column to give 99.8 g. (1.18 moles) of recovered dihydropyran and 224.3 g. (73%) of 8,8-dimethyl-2-oxabicyclo[4.2.0]octan-7-one, b.p. 89–90° (11 mm.).

2-Butyl-3-(ethoxymethyl)-2-ethylcyclobutanone.—A mixture of 63 g. (0.5 mole) of butylethylketene and 65 g. (0.75 mole) of allyl ethyl ether was heated in an autoclave at 180° for 8 hr. The solution was distilled through a 12-in. packed column to give 43 g. of recovered allyl ethyl ether and 33 g. (31%) of 2-butyl-3-(ethoxymethyl)-2-ethylcyclobutanone, b.p. 76° (0.4 mm.).

3-(2-Acetoxyethylthio)-2,2-diphenylcyclobutanone (IVb).—Admixture of 24 g. (0.12 mole) of diphenylketene and 18 g. (0.12 mole) of 2-(vinylthio)ethyl acetate produced an exothermic reaction which appeared complete in a few hours. The viscous solution slowly crystallized over a period of several days. The yield of crude solid, m.p. 86–89°, was nearly quantitative. An analytical sample, prepared by recrystallization from ethyl alcohol, melted at 90–91°.

N-[2-(2,2-Dimethyl-3-oxocyclobutyloxy)ethyl]-2-methylpropionamide.—Under a nitrogen atmosphere, 136 g. (1.94 moles) of dimethylketene was added to a stirred solution of 84 g. (0.97 mole) of 2-(vinyloxy)ethylamine in 300 ml. of benzene. The reaction of the first mole of dimethylketene was very exothermic and extensive cooling was required. After the addition was complete, the reaction solution was stirred at room temperature for 5 hr., then distilled at 3 mm. to a base temperature of 150°. The residue was distilled in a molecular still to give 175 g. (80%) of N-[2-(2,2-dimethyl-3-oxocyclobutyloxy)ethyl]-2-methylpropionamide, b.p. 62–67° (3–7μ).

7-Ethyl-7-isobutyl-3-oxabicyclo[3.2.0]heptan-6-one (III).—A mixture of 63 g. (0.5 mole) of ethylisobutylketene and 70 g. (1.0 mole) of 2,5-dihydrofuran was heated in an autoclave at 180° for 8 hr. The resulting solution was separated into two fractions by distillation through a 12-in. packed column under reduced pressure. By gas–liquid chromatography (20% Carbowax 20M on Chromosorb P), the first fraction, 35 g., b.p. 69.5–71.5° (0.3 mm.), contained about 70% of III and 30% of 2,4-diethyl-2,4-diisobutyl-1,3-cyclobutanedione (the dimer of ethylisobutylketene); the second fraction, 17 g., b.p. 71.5–77.0° (0.3 mm.), contained 25% of III and 75% of dimer. A pure sample of III was isolated by a preparative-scale chromatography unit (same packing).

3-Oxo-2,2-diphenylcyclobutyl Acetate (Vc).—A mixture of 9.7 g. (0.05 mole) of diphenylketene and 4.3 g. (0.05 mole) of vinyl acetate was sealed in a flask under a nitrogen atmosphere. After several days, the mixture crystallized. The solid was rinsed with cold hexane to give 11.4 g. of crude 3-oxo-2,2-diphenylcyclobutyl acetate. An analytical sample, recrystallized from a mixture of benzene and hexane, melted at 114–115.5°.

Acknowledgment.—The authors thank V. Wilson Goodlett for interpretation of n.m.r. spectra and E. U. Elam and Mary B. Miller for preparation of some compounds.

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

[20] S. M. McElvain and C. H. Stammer, *J. Am. Chem. Soc.*, **73**, 915 (1951).

[21] G. A. Weeks and W. J. Grant (to British Oxygen Co., Ltd.), British Patent 709,106 (1954).

[22] N.m.r. spectra were recorded on a Varian A-60 instrument at 60 Mc. Values reported are parts per million (p.p.m.) referred to tetramethylsilane as an internal standard.

[23] E. M. McMahon, J. N. Roper, Jr., W. P. Utermohlen, Jr., R. H. Hasek, R. C. Harris, and J. H. Brant, *J. Am. Chem. Soc.*, **70**, 2976 (1948).