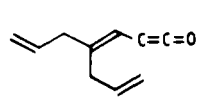
of two terminal double bonds because of the greater likelihood that one of them will be properly oriented for the cycloaddition.



1c

5

Increasing the chain length by one carbon practically suppresses the cycloaddition (entries e and f). This is not too surprising since, according to FMO theory,[4] the initial interaction between the olefin and the ketene should lead to bonding between C_1 and C_8 and, thus, to an eight-membered transition state. However, no bicyclic adduct (i.e., structure of type **5**) resulting from a C_1–C_7 interaction was observed.

Keteniminium salts are more electrophilic than ketenes and they do not dimerize.[5a] The requisite alkenylketeniminum salts **6** were generated in situ by slow addition of a 0.1 M solution of an unsaturated amide **4** and collidine (1.1 equiv) into a refluxing 0.1 M solution of freshly prepared triflic anhydride in 1,2-dichloroethane. The mixture was refluxed over a period of 20–40 h. The resulting cyclobutaniminium salt was directly hydrolyzed (H_2O–CCl_4, Δ) to the corresponding cyclobutanone **3** (Scheme II). As shown in table I (entries a and g–n) good yields of cycloadducts were obtained for a variety of chain lengths including those leading to cyclobutanones fused to a medium ring. The products **3g**, **3i** and **3k** resulting from α-substituted amides are interesting inasmuch as they are not available by the intermolecular [2 + 2] cycloadditions of keteniminium salts to olefins.

The reactions gave the cis-fused adducts except in the case of **4l**, which only produced the trans isomer **3l** probably as a result of an epimerization of the cis adduct under the reaction conditions.

The formation of the tricyclic ketone **3m** illustrates the generality of the method and indicates that it could become useful for the construction of spiranic skeletons. It also indicates that the regiochemistry of the cycloaddition is essentially governed by the electronic properties of the double bond: the less substituted terminal carbon atom becomes bonded to the electrophilic C_1 atom, a process that gives a tertiary carbenium intermediate[11] but also an eight-membered ring.

A limitation of the method is shown by the formation of **3n** from amide **4n**. This result indicates that, when the terminal olefinic carbon atom is more highly substituted, the cycloaddition does not occur but the olefin will be acylated by the keteniminum salt.

The present results clearly show the power of intramolecular cycloadditions of ketenes and keteniminium salts as a synthetic tool. The ketene reaction appears somewhat more limited by a competitive oligomerization of the ketene. Activation of the ketene by heteroatoms will probably provide a convenient solution to that problem.[8] The keteniminium route is more general and offers a potential for enantioselective intramolecular [2 + 2] cycloadditions.[12] We are pursuing our studies along these lines.

Acknowledgment. We are grateful to the Fonds National de la Recherche Scientifique (fellowship to I.M.) and the S.P.P.S. (Grant 79-84/13) for generous support in this work.

Registry No. **2a**, 21430-12-6; **2b**, 39764-81-3; **2c**, 95018-90-9; **2d**, 95018-91-0; **2e**, 95018-92-1; **3a**, 13756-54-2; **3b**, 5212-68-0; **3c**, 95019-02-6; **3d**, 95019-03-7; **3e**, 39778-69-3; **3g**, 57706-99-7; **3g** (semicarbazole), 20609-42-1; **3h**, 27655-70-5; **3i**, 95019-04-8; **3i** (semicarbazole), 95019-08-2; **3j**, 29783-22-0; **3j** (semicarbazole), 95019-09-3; **3k**, 95019-05-9; **3k** (semicarbazole), 95019-10-6; **3l**, 95019-06-0; **3l** (semicarbazole), 95019-11-7; **3m**, 95019-07-1; **3m** (semicarbazole), 95019-12-8; **3n**, 1502-22-3; **4a**, 95018-93-2; **4g**, 95018-94-3; **4h**, 95018-95-4; **4i**, 95018-96-5; **4j**, 95018-97-6; **4k**, 95018-98-7; **4l**, 95018-99-8; **4m**, 95019-00-4; **4n**, 95019-01-5.

Supplementary Material Available: Spectroscopic data and elemental analyses of **2a–d,f**, **3a–d,g–n**, and **4a,g–n** (4 pages). Ordering information is given on any current masthead page.

(11) Saimoto, H.; Houge, C.; Hesbain-Frisque, A. M.; Mockel, A.; Ghosez, L. *Tetrahedron Lett.* **1983**, 2251.

(12) Houge, C.; Frisque-Hesbain, A. M.; Mockel, A.; Ghosez, L. *J. Am. Chem. Soc.* **1982**, *104* 2920.

Intramolecular [2 + 2] Cycloadditions of Ketenes

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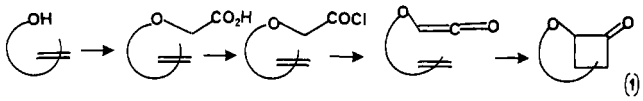
Received August 6, 1984

The stereospecific [2 + 2] cycloaddition of ketenes to alkenes has become a valuable method for the synthesis of cyclobutanones and compounds that can be derived from them.[2] It is one of the few general methods for carbofunctionalization of alkenes. Although isolated examples of intramolecular [2 + 2] cycloadditions of ketenes to alkenes are known,[3] the reaction has not been developed into a general synthetic method. The intramolecular reaction promises to extend the scope of the cycloaddition to less reactive alkenes and ketenes and to provide an efficient route to complex polycyclic compounds. The intramolecular nature of the reaction will lead to a high degree of stereo- and regioselectivity. We describe here our initial results which illustrate the validity of this approach. A complementary study by Ghosez, Greuter, and co-workers is described in an accompanying paper.[4]

Our initial exploratory work involved alkoxyketenes. This choice was based on the observation that ethoxyketene, generated from ethoxyacetyl chloride and NEt_3, adds to alkenes in 30–50% yield to give 2-ethoxycyclobutanones.[5] While these yields appear to be acceptable, they are achieved by using the alkene as the solvent. The related intramolecular reactions should proceed in better yield and provide synthetically useful products.

Reaction of an unsaturated alcohol with sodium hydride and bromoacetic acid in THF at reflux gave a 70–90% yield of the corresponding (alkenyloxy)acetic acid.[6] The acid was converted to the acid chloride by treatment with oxalyl chloride in benzene. The acid chloride (0.03 M) and NEt_3 were heated at reflux in benzene (2–4 h) under nitrogen to generate the ketene which reacted to give the cyclobutanone in 16–72% yield based on carboxylic acid (see eq 1). The results are shown in Table I.



(1)

Remarkably, the results indicate that the electronic effects of substituents on the double bond, rather than the connectivity pattern, control the regiochemistry of the cycloaddition.[2] Alkenes in which the internal carbon is more highly substituted react to give bicyclo[3.2.0]heptanes or bicyclo[4.2.0]octanes (entries 1–8). Alkenes in which the terminal carbon is more highly substituted react to give bicyclo[3.1.1]heptanes or bicyclo[4.1.1]octanes (entries 11 and 12). The formation of bridged ring compounds has not previously been observed in intramolecular cycloadditions of ketenes.

Alkenes with the substitution pattern of entries 1–5 are highly reactive since leading bond formation between the carbonyl carbon

(1) Fellow of the Alfred P. Sloand Foundation 1979–1983; Dreyfus-Teacher Scholar 1982–1987.

(2) (a) Brady, W. T. *Tetrahedron* **1981**, *37*, 2949. (b) Ghosez, L. "Stereoselective Synthesis of Natural Products"; Bartmann, W., Winterfeldt, E., Eds.; Excerpta Medica: Amsterdam–Oxford, 1979; pp 93–105. (c) Ghosez, L.; O'Donnell, M. J. "Pericyclic Reactions"; Marchand, A. P., Lehr, R. E., Eds.; Academic Press: New York, 1977; Vol. II, pp 79–140.

(3) (a) Baldwin, S. W.; Page, E. H., Jr. *J. Chem. Soc., Chem. Commun.* **1972**, 1337. (b) Bisceglia, R. H.; Cheer, C. J. *Ibid.* **1973**, 165. (c) Wolff, S.; Agosta, W. C. *Ibid* **1973**, 771. (d) Smit, A.; Kok, J. G. J.; Geluk, H. W. *Ibid.* **1975**, 513. (e) Becker, D.; Birnbaum, D. *J. Org. Chem.* **1980**, *45*, 570. (f) Moon, S.; Kolesar, T. F. *Ibid.* **1974**, *39*, 995. (g) Beereboom, J. J. *Ibid.* **1965**, *30*, 4230. (h) Sauers, R. R.; Kelly, K. W. *Ibid.* **1970**, *35*, 3286. (i) Yates, P.; Fallis, A. G. *Tetrahedron Lett.* **1968**, 2493.

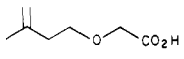
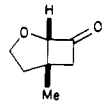
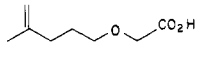
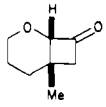
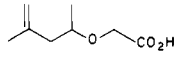
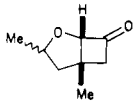
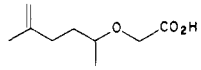
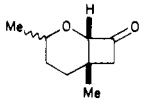
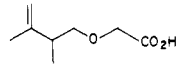
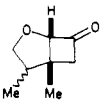
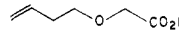
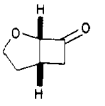
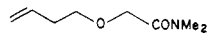
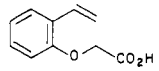
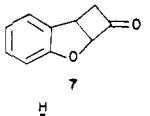
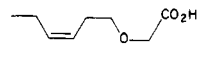
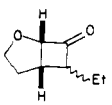
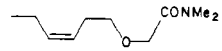
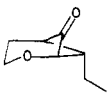
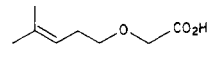
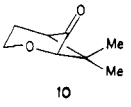
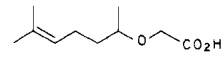
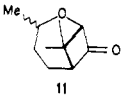
(4) Marko, I.; Ronsmans, B.; Hesbain-Frisque, A.-M.; Dumas, S.; Ghosez, L.; Ernst, B.; Greuter, H. *J. Am. Chem. Soc.*, preceding paper in this issue.

(5) DoMinh, T.; Strausz, O. P. *J. Am. Chem. Soc.* **1970**, *92*, 1766.

(6) Nakai, T.; Mikami, K.; Taya, S.; Kimura, Y.; Mimura, T. *Tetrahedron Lett.* **1981**, *22*, 69.

0002-7863/85/1507-2194$01.50/0

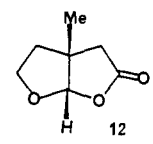
Table I. Intramolecular [2 + 2] Cycloaddition Reactions of Ketenes and Keteniminium Salts Derived from Alkoxyacetic Acids

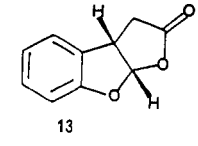
entry	alkoxyacetic acid	cyclobutanone	yield
1		 1	72%
2		 2	62%
3		 3	66% (α-CH_3) 7% (β-CH_3)
4		 4	58% (3:2)
5		 5	63% (4:3)
6		 6	16%
7			79%
8		 7	70%
9		 8	0%
10		 9	40% (**8**, β-CH_3) 7% (**8**, α-CH_3) 14% (**9**)
11		 10	52%
12		 11	13% (β-CH_3) 17% (α-CH_3)

of the ketene and the alkene occurs at a sterically unhindered unsubstituted carbon and any positive charge in the transition state is at a tertiary carbon. The styrene shown in entry 8 is also very reactive since any positive charge in the transition state is at a benzylic carbon. The monosubstituted alkene shown in entry 6 gives a low yield of adduct since any positive charge must be at a secondary carbon. 1,2-disubstituted alkenes, in which steric effects hinder addition, give no cycloadduct (entry 9). Entry 3 indicates the potential for high stereoselectivity, although entries 4 and 5 indicate that it is by no means assured.

The cycloaddition of keteniminium salts, developed by Ghosez and co-workers,[7] provides a solution in some cases where intramolecular [2 + 2] cycloadditions of ketenes fail (entries 6 and 9). Treatment of an unsaturated alcohol with sodium hydride and bromo-*N*,*N*-dimethylacetamide in THF gave a 70–82% yield of the (alkenyloxy)-*N*,*N*-dimethylacetamide. Treatment of the amide with 1 equiv of triflic anhydride and 1 equiv of collidine in an inert solvent gave the ketenimium salt which added to the double bond to give, after hydrolysis, the cyclobutanone. Using this procedure a monosubstituted alkene gives a 79% yield of adduct **6** (entry 7). The cycloaddition to a cis-1,2-disubstituted alkene gives a mixture of regioisomers **8** and **9** since the double bond is symmetrically substituted (entry 10). The *trans*-(3-hexenyloxy)keteniminium salt reacts to give only the Friedel–Crafts adduct tetrahydro-4-propylidene-3-pyranone in 65% yield. This alternative reaction is likely to occur whenever an allylic hydrogen can be transferred to the nitrogen.[7a]

These cycloadducts are useful synthetic intermediates. Baey-

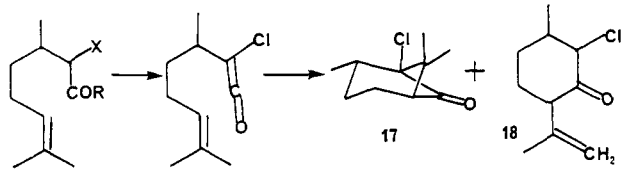

12


13

(7) (a) Ghosez, L.; Marchand-Brynaert, J. "Iminium Salts in Organic Chemistry Part 1;" Böhme, J.; Viehe, H. G., Eds.; Wiley: New York, 1976; pp 421–532. (b) Falmagne, J.-B.; Escudero, J.; Taleb-Sahraoui, S.; Ghosez, L. *Angew. Chim., Int. Ed. Engl.* **1981**, *20*, 879.

er–Villiger oxidation of **1** and **7** proceeds in 90% yield to give **12** and **13**, respectively. This approach is therefore useful for the synthesis of the furofuran moiety of aflatoxins and neoclerodane insect antifeedants.

The preparation of **10** (entry 11) suggests that intramolecular ketene cycloadditions can provide a simple route to the pinane skeleton. Unfortunately, treatment of acyl chloride **14** with NEt_3 in benzene at reflux gave no cyclobutanone. Since (chloroalkyl)ketenes are known to give higher yields of cyclobutanones from alkenes than simple alkylketenes, we prepared the corresponding chloro acid **15** in 81% yield by treatment of the dianion of the acid with carbon tetrachloride.[8] Conversion of **15** to the acid chloride **16** with oxalyl chloride, followed by treatment with NEt_3 in benzene at reflux, gave a 55% yield of the desired bridged cyclobutanone **17** (from **15**) and an 18% yield of the Friedel–Crafts adduct **18**. As expected,[7a] the keteniminium salt reacts to give



14, X = H, R = Cl
15, X = Cl, R = OH
16, X = Cl, R = Cl

only the Friedel–Crafts adduct isopulegone in low yield.

These results clearly indicate the power of intramolecular [2 + 2] cycloadditions of ketenes to alkenes to generate complex polycyclic systems efficiently. This reaction provides a remarkably simple route to the pinane skeleton. We are continuing our exploration of the scope of the intramolecular cycloaddition which should find widespread use in organic synthesis.

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Registry No. 1, 95123-29-8; **2**, 95123-30-1; **2** (semicarbazone), 95123-31-2; **3** (isomer 1), 95123-32-3; **3** (isomer 2), 95191-00-7; **4** (isomer 1), 95123-33-4; **4** (isomer 2), 95191-01-8; **4** (semicarbazone), 95123-34-5; **5** (isomer 1), 95123-35-6; **5** (isomer 2), 95191-02-9; **6**, 95123-36-7; **6** (semicarbazone), 18749-72-9; **7**, 95123-37-8; **8** (isomer 1), 95123-38-9; **8** (isomer 2), 95191-03-0; **9**, 95123-39-0; **10**, 95123-40-3; **11** (isomer 1), 95123-41-4; **11** (isomer 2), 95191-04-1; **12**, 95123-42-5; **13**, 95123-43-6; **14**, 36392-06-0; **16**, 95123-44-7; **17**, 95123-45-8; **18**, 95123-46-9; $CH_3C(=CH_2)(CH_2)_2OH$, 763-32-6; $CH_3(=CH_2)(CH_2)_3OH$, 22508-64-1; $CH_3C(=CH_2)CH_2CH(CH_3)OH$, 2004-67-3; $CH_3C(=CH_2)(CH_2)_2CH(CH_3)OH$, 50551-88-7; $CH_3C(=CH_2)CH(CH_3)CH_2OH$, 1708-93-6; $CH_2=CH(CH_2)_2OH$, 627-27-0; (*Z*)-$CH_3CH_2CH=CH(CH_2)_2OH$, 928-96-1; $(CH_3)_2C=CH(CH_2)_2OH$, 763-89-3; $(CH_3)_2C=CH(CH_2)_2CH(CH_3)OH$, 1569-60-4; $CH_3C(=CH_2)(CH_2)_2OCH_2CO_2H$, 95123-48-1; $CH_3C(=CH_2)(CH_2)_3OCH_2CO_2H$, 95123-49-2; $CH_3C(=CH_2)CH_2CH(CH_3)OCH_2CO_2H$, 95123-50-5; $CH_3C(=CH_2)(CH_2)_2CH(CH_3)OCH_2CO_2H$, 95123-51-6; $CH_3C(=CH_2)CH(CH_3)CH_2OCH_2CO_2H$, 95123-52-7; $CH_2=CH(CH_2)_2OCH_2CO_2H$, 95123-53-8; $CH_2=CH(CH_2)_2OCH_2CONMe_2$, 95123-54-9; *o*-$CH_2=CHC_6H_4OCH_2CO_2H$, 95123-55-0; (*Z*)-$CH_3CH_2CH=CH(CH_2)_2OCH_2CO_2H$, 95273-92-0; (*Z*)-$CH_3CH_2CH=CH(CH_2)_2OCH_2CONMe_2$, 95123-56-1; $(CH_3)_2C=CH(CH_2)_2OCH_2CO_2H$, 95123-57-2; $(CH_3)_2C=CH(CH_2)_2CH(CH_3)OCH_2CO_2H$, 95123-58-3; $(CH_3)_2C=CH(CH_2)_2CH(CH_3)CHCO_2^{-2}$, 95123-59-4; tetrahydro-4-propylidine-3-pyranone, 95123-60-7; 2-vinylphenol, 695-84-1; bromoacetic acid, 79-08-3; *N*,*N*-dimethyl-2-bromoacetamide, 39221-60-8.

Supplementary Material Available: ^1H and ^{13}C NMR and IR for **1–11** and **17** (3 pages). Ordering information is given on any current masthead page.

(8) This efficient approach to α-chloro acids will be described separately.

Novel Palladium-Catalyzed Reactions of Propargyl Carbonates with Carbonucleophiles under Neutral Conditions

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The palladium-catalyzed reactions of various allylic compounds with carbonucleophiles are well-established and useful synthetic methods.[1] We have shown that the allylation of carbonucleophiles can be carried out under neutral conditions by using allylic carbonates.[2-4] In contrast to the extensive studies on the palladium-catalyzed reactions of allylic compounds, very few studies have been carried out on the palladium-catalyzed reactions of propargyl compounds. The conversion of propargyl acetates or halides to 1,2-dienes by the reaction with hard carbonucleophiles such as alkyl magnesium or zinc compounds in the presence of palladium catalysts has been reported.[5] We wish to report here a new palladium-catalyzed reaction of propargyl carbonates with soft carbonucleophiles to give 2,3-disubstituted propenes **2** under neutral conditions as shown below.

$$\underset{\mathbf{1}}{HC{\equiv}CCH_2OCO_2Me} + 2NuH \xrightarrow{\text{Pd cat.}} \underset{\mathbf{2}}{CH_2{=}C(Nu)CH_2Nu} + CO_2 + MeOH$$

Reaction of methyl propargyl carbonate (**1**) with 2 equiv of methyl 2-methyl-3-oxopentanoate in boiling THF for 2 h in the presence of $Pd_2(dba)_3CHCl_3$ and 1,2-bis(diphenylphosphino)-ethane (dppe) (Pd/dppe = $^1/_2$, 5 mol %) gave the adduct **3**[6] in 69% yield. Reaction of dimethyl malonate with **1** in boiling THF for 2 h afforded a 1:1 mixture of the adducts **4** and **5** in 49% yield. In boiling dioxane for 9 h, the exo olefin of **4** isomerized almost completely to the stable conjugated olefin to give **5**[6] in 69% yield (Scheme I).

β-Keto esters and β-diketones bearing two active hydrogens react with propargyl carbonates in a 1:1 ratio. In other words, both C- and O-alkylations take place with these compounds to give 4-methylene-4,5-dihydrofurans and 4-methylfurans (Table I). Reaction of **1** with methyl acetoacetate in THF at room temperature for 2 h in the presence of Pd/dppe catalyst (5 mol %) gave 3-(methoxycarbonyl)-2-methyl-4-methylene-4,5-dihydrofuran (**6a**)[8] in 88% yield after chromatographic purification on alumina.[9] This smooth cyclization proceeded under completely neutral conditions. On the other hand, the addition of a base was

(1) For reviews, see: (a) Tsuji, J. "Organic Synthesis with Palladium Compounds"; Springer Verlag: Berlin, 1980. (b) Tsuji, J. *Pure Appl. Chem.* **1982**, *54*, 197–206. (c) Trost, B. M. *Tetrahedron* **1977**, *33*, 2615–2649. (d) Trost, B. M. *Acc. Chem. Res.* **1980**, *13*, 385–393.

(2) Tsuji, J.; Shimizu, I.; Minami, I.; Ohashi, Y. *Tetrahedron Lett.* **1982**, *23*, 4809–4812.

(3) Palladium-catalyzed neutral allylation using diene monoxides, see: (a) Tsuji, J.; Kataoka, H.; Kobayashi, Y. *Tetrahedron Lett.* **1986**, 2675–2578. (b) Trost, B. M.; Molander, G. A. *J. Am. Chem. Soc.* **1981**, *103*, 5969–5972. (c) Takahashi, T.; Kataoka, H.; Tsuji, J. *J. Am. Chem. Soc.* **1983**, *105*, 147–149.

(4) Palladium-catalyzed neutral allylation by desilylation–allylation, see: (a) Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1979**, *101*, 6432–6433; **1980**, *102*, 6359–6361; **1981**, *103*, 5972–5974; **1983**, *105*, 2326–2335. (b) Trost, B. M.; Self, C. R. *J. Am. Chem. Soc.* **1983**, *105*, 5942–5944.

(5) (a) Jeffery-Juong, T.; Linstrumelle, G. *Tetrahedron Lett.* **1980**, *21*, 5019–5020. (b) Ruitenberg, K.; Kleijn, H.; Elsevier, C. J.; Meijer, J.; Vermeer, P. *Tetrahedron Lett.* **1981**, *22*, 1451–1452. (c) Elsevier, C. J.; Stehouwer, P. M.; Westmijze, H.; Vermeer, P. *J. Org. Chem.* **1983**, *48*, 1103–1105.

(6) Satisfactory spectral data were obtained for these materials and satisfactory elemental analyses were obtained as well.

(7) Batty, J. W.; Howes, P. D.; Stirling, C. J. M. *J. Chem. Soc., Perkin Trans. 1* **1973**, 65–68.

0002-7863/85/1507-2196$01.50/0