using more efficient optical and electronic devices. Any osmotic gradients during the sample handling can be avoided by dialysis against or chromatography with aqueous solutions containing nonfluorescent and noninteracting additives of the same concentration as the indole derivatives. It is further hoped that in natural vesicle-like particles or cells the endogeneous tryptophan-containing (e.g., cytoplasmatic) proteins can play the same role as the so far artificially introduced tryptamine molecules.

So far, measurements above the phase transition temperature are still poor because of technical and experimental reasons. Evidently tryptamine seems to leak faster out of the intravesicular compartment at temperatures above T_c so that the response signal becomes rather small. In principle any extravesicular tryptamine molecules do not interfere with the discussed effects (the time response for these molecules is beyond the stopped-flow limits); however, the extravesicular tryptamine increases the fluorescence background and makes the detection of the signal response due to the intravesicularly remaining tryptamine molecules more difficult. Above T_c the time course due the permeation of D_2O becomes rather fast but still measurable by stopped-flow techniques especially for large vesicles.

In conclusion an easy method has been described to measure the permeation of water (D_2O or alternatively H_2O) across vesicular lipid bilayers and—possibly under favorable conditions—also across intact biological membranes. The method is based on a solvent-isotope effect of fluorescence quantum yields of indole chromophores. Various factors involved have been discussed. Preliminary experiments using phospholipid vesicles where tryptamine resides almost only within the intravesicular compartment show that the new methods gives reliable results. Experimental details together with further results will be reported later.

Acknowledgment. I thank Drs. E. Helmreich and K.-H. Korfsmeier for the use of the stopped-flow apparatus and the performance of the electron micrographs, respectively. Dr. F. W. Schneider's stimulating discussions and support are highly acknowledged.

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Cyanoketenes. Mechanism of *tert*-Butylcyanoketene Cycloaddition to Methyl- and Dimethylketene

Sir:

Ketene dimerizations are fraught with ambiguities regarding their operative mechanisms. In certain cases it appears that the mechanism is a concerted $[_\pi 2_s + {}_\pi 2_a]$ process. For example, dimethylketene dimerization shows a high negative entropy of activation and little solvent polarity dependence.[1] Also, from a concerted dimerization of unsymmetrical ketoketenes, the resulting cyclobutane-1,3-diones would be expected to show predominantly cis stereochemistry for the bulkier substituent, and such has been observed for the homodimerizations of benzylphenyl and benzylmethylketenes.[2] In other cases data appear more consistent with a nonconcerted, stepwise mechanism. For example, when methylchloro- and *tert*-butylchloroketene, generated in situ from the corresponding acid chlorides, cycloadd to methyl-*n*-propyl- and methylisopropylketene, equal amounts of isomeric *cis*- and *trans*-cyclobutane-1,3-diones result.[3] Another anomolous observation for a concerted mechanism is the formation of 2-oxetanone products which are often observed in many homodimerizations of aldoketenes.[4] Examples are the dimerizations of ketene itself,[5] methylketene,[6] butylketene,[7] and phenylketene.[8] Mixed dimerizations of ketoketones and aldoketenes also often yield 2-oxetanone products.[3] In addition, bis(trifluoromethyl)ketene cycloadds to dimethylketene to give a mixture of the corresponding cyclobutane-1,3-dione and 2-oxetanone.[9] Clearly, the above results suggest that both concerted and stepwise mechanisms are possible, but little unambiguous mechanistic data has appeared.

Our objective regarding the above general problem was to gain mechanistic information concerning the cycloaddition of an electron-deficient ketene to electron-rich aldo- and ketoketene analogues. Specifically, we report here a mechanistic study of the cycloaddition of *tert*-butylcyanoketene (**1**) to methyl-and dimethylketene which unambiguously establishes these cycloadditions to be nonconcerted dipolar processes. *The most unique observation of this study is that the zwitterionic intermediate proposed in a ketene to ketene cycloaddition has, for the first time, been independently generated, trapped, and shown to give the same products as observed in the cycloadditions themselves.* The genesis of this mechanistic probe stems from our earlier reports that zwitterionic intermediates are readily generated from the thermolysis of appropriately substituted cyclic vinyl azides,[10,11] and the results here further document this to be a most powerful tool for the study of cyanoketene cycloadditions.

Methylketene was generated and condensed at liquid nitrogen temperature.[12] It was then treated with a toluene solution of *tert*-butylcyanoketene[13] and the reaction solution allowed to warm to ambient temperature. After 30 min the solvent was removed in vacuo and the crude oil purified to give the 2-oxetanone (**2**, Scheme I) as a colorless oil in 49% purified

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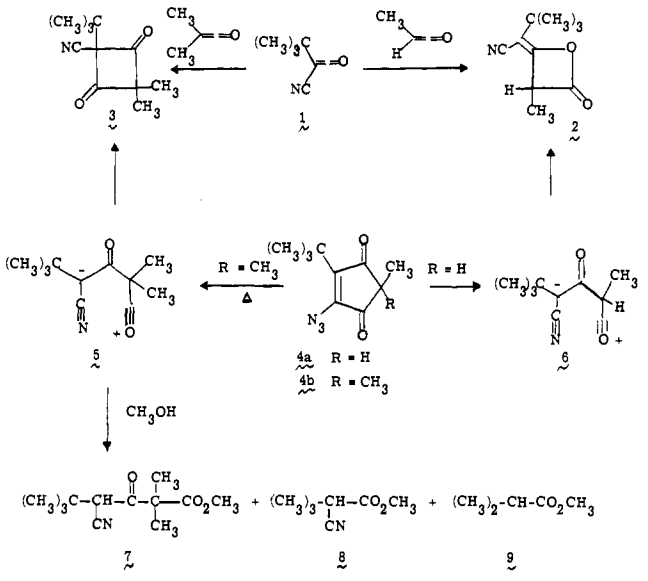
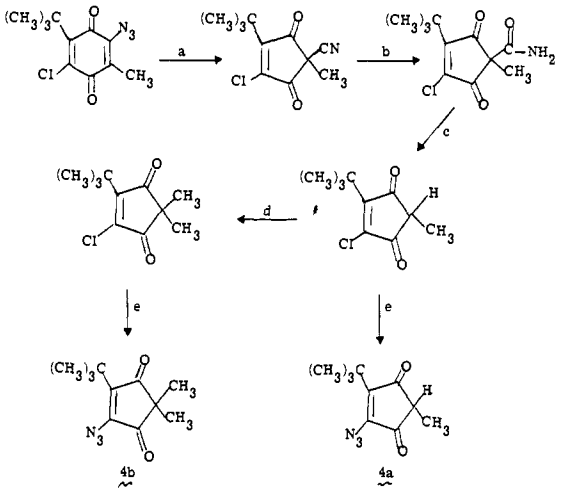
Scheme I



Scheme II



a) C_6H_6, Δ, 66%; b) H_2SO_4, 93%; c) 6N HCl/DME, Δ, 93%; d) KH/CH_3I, 88%; e) NaN_3/CH_3OH[18]

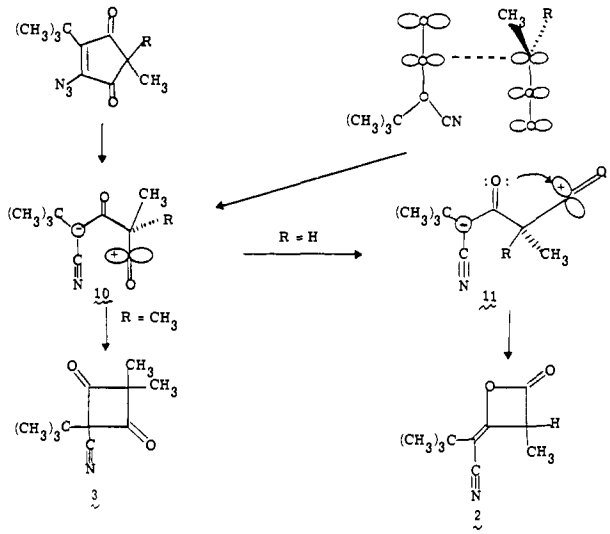
yield.[14] None of the cyclobutane-1,3-dione dimer was detected in the crude reaction product by ^1H NMR or IR analysis. In an analogous fashion, *tert*-butylcyanoketene and dimethylketene[15] cycloadd to give only the cyclobutane-1,3-dione dimer (**3**) in 37% purified yield.[16] Characteristic structural data for the dimers **2** and **3** are given below. **2:** IR (neat, cm^{-1}) 2215 (CN), 1912 (C=O), 1680 (C=C); ^1H NMR ($CDCl_3$, δ) 4.34 (1 H, q, J = 7 Hz), 1.56 (3 H, d, J = 7 Hz), 1.22 (9 H, s); ^{13}C NMR ($CDCl_3$, δ) 165.9, 159.8, 115.6, 99.2, 53.4, 34.0, 29.1, 10.7; mass spectrum 179 (M^+). **3:** IR (Nujol, cm^{-1}) 2212 (CN), 1763 (C=O); ^1H NMR ($CDCl_3$, δ) 1.55 (3 H, s), 1.27 (3 H, s), 1.19 (9 H, s); ^{13}C NMR ($CDCl_3$, δ) 199.9, 112.7, 77.4, 76.6, 38.2, 25.8, 22.3, 15.1; mass spectrum 193 (M^+). Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82. Found: C, 68.37, H, 7.76.

It was anticipated that, if the above cycloadditions proceed via the respective zwitterions, **5** and **6**, such intermediates could be independently generated upon thermolysis of the corresponding 4-azido-5-*tert*-butylcyclopentene-1,3-diones (**4a,b**).[10,11] Thus, these were synthesized as outlined in Scheme II and subjected to thermolysis in benzene at 55–65 °C. Remarkably, thermolysis of **4a** gave only the 2-oxetanone (**2**, 82% purified yield), and **4b** gave only the cyclobutane-1,3-dione (**3**, 90% purified yield). These results alone clearly do not establish a common intermediate to the ketene dimers, **2** and **3**, from both the azidocyclopentene-1,3-diones **4** and the ketene cycloadditions, since the conversions of **4a** to **2** and **4b** to **3** could conceivably arise by at least three possible pathways, i.e., (1) a concerted ring contraction; (2) fragmentation to *tert*-butylcyanoketene plus methyl- or dimethylketene followed by subsequent cycloadditions; (3) respective cleavage of **4a** and **4b** to the zwitterions **6** and **5** and their subsequent ring closure to products.

The first of the above possibilities, i.e., the concerted process, is untenable with the results. That is, even though one can envisage a concerted ring contraction of **4b** to **3**, which will ultimately be ruled out, such would not be possible for the conversion of **4a** to the oxetanone, **2**, since lactone bond formation would seemingly be impossible from a concerted process. Thus, assuming that **4a** and **4b** react by analogous pathways, a concerted ring contraction can be rejected. Further unambiguous evidence for a stepwise dipolar mechanism came from zwitterion trapping experiments. Specifically, thermolysis of **4b** in refluxing methanol gave methyl 2-cyano-3,3-dimethylbutanoate (**8**)[19] and methyl 2-methylpropanoate (**9**)[20] in roughly equal amounts and, significantly, the β-keto ester **7** (41%). In a control experiment the cyclobutane-1,3-dione (**3**) was also subjected to methanolysis under the same conditions as above, and the exclusive product was the β-keto ester **7**: colorless solid, mp 28–30 °C; IR (neat, cm^{-1}) 2225 (CN), 1751 and 1726 (C=O); NMR ($CDCl_3$, δ) 3.71 (3 H, s), 3.62 (1 H, s), 1.43 (3 H, s), 1.36 (3 H, s), 1.09 (9 H, s). Anal. Calcd. for $C_{12}H_{19}NO_3$: C, 63.98; H, 8.50. Found: C, 63.94; H, 8.61. However, the rate of methanolysis of **3** is appreciably slower than that observed for **4b**. For example, a 5-mL methanol solution containing 2.4 mmol of **4b** has completely reacted after 1.5 h at reflux, while an analogous solution of **3** has gone only to 38% completion during the same length of time. The salient point of these data is that the β-keto ester **7** is formed upon methanolysis of **4b**, and that this product is not arising exclusively from the methanolysis of cyclobutane-1,3-dione (**3**). Thus, some, if not all, of it must be coming from methanolysis of the zwitterion **5**. Therefore, a concerted mechanism for the conversion of **4b** to **3** lacks credence. Also, a pure ketene mechanism is unreasonable, since, if this were so, one would certainly expect the methanolysis of **4b** to give only the esters **8** and **9**. Yet the major product is in fact the β-keto ester **7**. That leaves as the most reasonable alternative, a mechanism in which the azidocyclopentene-1,3-dione (**4b**) cleaves to the zwitterion **5** and that this partitions between ring closure to **3** and equilibration with *tert*-butylcyanoketene and dimethylketene. When the decomposition of **4b** is accomplished in methanol, the zwitterion **5** is trapped to give **7** and the respective ketenes give **8** and **9**. Finally, since the cycloadditions of *tert*-butylcyanoketene with dimethyl- and methylketene give exactly the same products as the thermolysis of, respectively, **4b** and **4a**, both processes must involve common zwitterionic intermediates.

These data suggest still a further significant feature of the cycloaddition mechanism, mainly that the two ketenes undergo initial bond formation from a head-to-tail orientation to give the zwitterion represented by conformer **10** (Scheme III). Such an interpretation is possible, since **10** would be the expected conformer to arise directly when the zwitterion is independently generated from the cyclopentenedione precursors. Direct ring closure of **10** (R = CH_3) to **3** would involve the orthogonal enolate anion and acyl cation orbitals. In the less sterically hindered example **10** (R = H), rapid rotation to **11** is allowed and subsequent ring closure to the β-lactone **2** may be most facile since it could involve a carbonyl nonbonding e^- pair in an orbital which is now not orthogonal to the acyl cation orbitals.[21]

Scheme III



In conclusion, we wish to emphasize the significant points resulting from this study: (1) for the first time, the zwitterion resulting from the interaction of a ketene with a ketene has been independently generated and shown to give the same products as the cycloaddition itself; (2) the fact that zwitterions are formed in the thermolysis of **4** further establishes our earlier prediction and provides a most powerful predictive model for the thermal chemistry of appropriately substituted vinyl azides;[10,11] (3) these results suggest a potentially general mechanistic probe for the investigation of the cycloadditions of a variety of cyano compounds since suitably substituted cyclic vinyl azides can be viewed as precursors to possible cyano substituted zwitterionic intermediates in [2 + 2], [3 + 2], and [4 + 2] cycloadditions.

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(12) Methylketene was prepared as described by A. J. Jenkins, *J. Chem. Soc.*, 2563 (1952), with a modified apparatus.
(13) W. Weyler, Jr., W. G. Duncan, M. G. Liewen, and H. W. Moore, *Org. Synth.*, **55**, 32 (1976).
(14) A crude yield of >80% was observed by ^{1}H NMR analysis. Although ^{1}H NMR showed little impurity, an appreciable amount of polymeric material was left behind after vacuum distillation of the crude product.
(15) Dimethylketene was generated by the pyrolysis of commercially available tetramethylcyclobutane-1,3-dione at 580 °C (1 Torr).
(16) A crude yield of 83% was obtained which showed it to be >90% by ^{1}H NMR analysis. Again a large amount of polymer remained as a residue after vacuum distillation. When the reaction was followed by IR analysis, one observed the ketene absorption to decrease in intensity as the cyclobutanedione carbonyl absorption at 1763 increased. No higher carbonyl absorption was detected. Thus, it is unlikely that the cycloaddition initially gives a 2-oxetanone which rearranges to the cyclobutanedione, **3**, under the reaction conditions.
(17) The spectral and analytical properties of all these new compounds are in strict agreement with their molecular formulations.
(18) The corresponding azido compounds were not purified because of their inherent instability. However, no impurities could be detected by IR or ^{1}H NMR analysis.
(19) Prepared independently as described by W. Weyler, Jr., W. G. Duncan and H. W. Moore, *J. Am. Chem. Soc.*, **97**, 6187 (1975).
(20) Prepared independently from the commercially available isobutanoyl chloride and MeOH.
(21) The possibility of a common, zwitterionic intermediate for the formation of β-lactones and butanediones in ketene dimerizations has been previously noted by R. B. Woodward and G. Small, Jr., *J. Am. Chem. Soc.*, **72**, 1297 (1950), and R. Huisgen, R. Grashey, and J. Sauer in "The Chemistry of Alkenes", S. Patai, Ed., Wiley, Ltd., 1964, p 790.
(22) Taken in part from the Ph.D. Thesis of D. Scott Wilbur.

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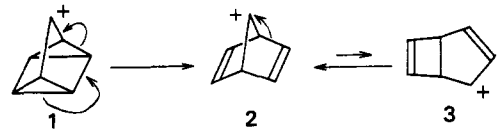
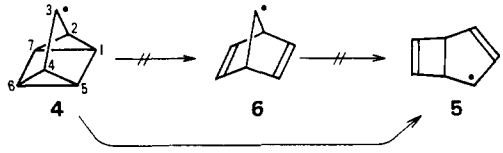
Fast Rearrangement of 3-Quadricyclyl Radical to Bicyclo[3.2.0]hepta-3,6-dien-2-yl Radical

Sir:

3-Quadricyclyl cation (**1**) rearranges to 7-norbornadienyl cation (**2**) which undergoes a partially degenerate rearrangement; the mechanism proposed for the latter is ring contraction of **2** to bicyclo[3.2.0]hepta-3,6-dien-2-yl cation (**3**) followed by ring expansion back to **2**.[1] In contrast to the cationic ana-



logues, we report here that 3-quadricyclyl radical (**4**) rearranges quite rapidly to bicyclo[3.2.0]hepta-3,6-dien-2-yl radical (**5**); 7-norbornadienyl radical (**6**) is not involved in this rearrangement.



The radical chain reduction[2] of 3-chloroquadricyclane (**7**) by a stannane affords an opportunity to examine rearrangement of **4**. When 0.20 mmol of **7**,[3] 0.11 mmol of tri-*n*-butylstannane, and 0.004 mmol of di-*tert*-butyl peroxide are reacted in 0.15 mL of *n*-hexane in a degassed sealed tube at 130 °C for 6 h, the stannane was consumed as shown by the absence of the absorption at 1810 cm^{-1} ($\nu_{Sn\text{-}H}$) in the IR spectrum of the reaction mixture. A GLC analysis of the reacted mixture showed that 0.10 mmol of **7** was consumed and bicyclo[3.2.0]hepta-2,6-diene (**8**)[4] was formed to the amount of 90 mol % of the consumed **7**. No other volatile product (neither quadricyclane nor norbornadiene) was present in >1 mol % of the consumed **7**. A control experiment without the stannane showed that ~80% of **7** persisted under the present reaction condition.[5] These results indicate that most of **4**, generated by homolytic chlorine atom abstraction from **7** by tri-*n*-butylstannyl radical, rearranges to **5** followed by hydrogen atom transfer from the stannane. To trap **4** before the rearrangement, **7** was dechlorinated in tri-*n*-butylstannane solvent in a reaction condition in which >80% of quadricyclane persists in the stannane solvent. When 0.16 mmol of **7** was heated in 0.15 mL (0.58 mmol) of the stannane in the presence of 2 mol % of azoisobutyronitrile at 80 °C for 3 h in a sealed degassed tube, 80% of **7** decayed and **8** was detected to the extent of 15

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