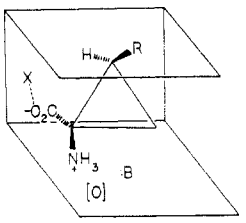

Figure 3. Active-site cartoon of the ethylene-forming enzyme.

neweaver–Burk analysis in Figure 2, which yields identical values of K_I and K_m, 0.5 mM, provides necessary but not sufficient proof that this is the case.

Discussion

This study establishes MeACC as a substrate and inhibitor of the ethylene-forming enzyme. The characteristics of its processing by the EFE are surprising. A priori, its 20% slower turnover might have been attributed to steric interactions which cause looser binding. No change in K_m and a smaller K_{cat} suggests that steric factors, while unimportant in binding, do become important in the transition state.

MeACC is the strongest competitive inhibitor of the EFE yet described. Its preparation from optically pure precursors of unambiguous absolute configuration provides a useful route to this chiral analogue as well as firmly establishing the chirality required of analogues by the active center for ethylene production. The synthetic methodology used provides a general route to alkylated ACC derivatives in just two steps from 1,2-dibromides.

The fact that MeACC is a better substrate than the corresponding ethyl compound, along with our other previous results,[17] allows us to further refine the active-site picture of the EFE as shown in Figure 3. These additions include a "roof" which interacts with alkyl groups at the 2-position; a binding group X which interacts with the carboxyl group, since neither alkyl groups[10-12] or hydroxymethyl (Pirrung, M. C., unpublished) can substitute at this position; bases in position to remove protons from nitrogen as the oxidation proceeds; and an oxidant positioned adjacent to nitrogen. The nature of this oxidant is currently unknown. Our previous model work has shown that one-electron oxidation can lead to ethylene production[17] but also indicates that a hydrogen atom-abstracting oxidant could accomplish the desired goal.[28] Baldwin has shown that high-valent metal oxo derivatives may also be competent.[29] What this picture does not adequately explain is how this reputedly "tight" active site allows α-aminoisobutyric acid to enter,[30] or how free-radical traps like propyl gallate intercept the intermediates in ethylene formation.

MeACC may have another use in ethylene biosynthesis studies. It has recently been established[31,32] that cyanide is produced from C1–N1 of ACC during ethylene biosynthesis. It has been suggested[32] that of the physiological changes associated with ethylene biosynthesis, the shift to a cyanide-insensitive electron transport system may be connected with cyanide production. Since MeACC is converted to propene, which has ca. 60 times less physiological activity than ethylene,[8] yet will also produce cyanide, a comparison of the physiological responses to ACC and MeACC will allow the effects of each substance to be sorted out. Such studies are currently underway.

Acknowledgment. Advice from Professor Mosher concerning the determination of optical purity is appreciated. Financial support from FMC Corp. and the U. S.–Israel Binational Agricultural Research and Development Fund, Grant No. I-643-83, is gratefully acknowledged. NMR spectra were obtained on a Nicolet NMC-300 spectrometer purchased with funds provided by the National Science Foundation (CHE-8109064).

Note Added in Proof: Baldwin has recently reported the results of processing of the alkyl deuterated ACC's: Baldwin, J. E.; Adlington, R. M.; Lajoie, G. A.; Rawlings, B. J. *J. Chem. Soc., Chem. Commun.* **1985**, 1496–1498.

(28) Pirrung, M. C. *Biochemistry* **1986**, *25*, 114–119.
(29) Baldwin, J. E.; Jackson, D. E.; Adlington, R. M.; Rawlings, B. J. *J. Chem. Soc., Chem. Commun.* **1985**, 206–207.
(30) Yang, S. F.; Liu, Y.; Su, L. *Planta* **1984**, *161*, 439–443.
(31) Peiser, G. D.; Wang, T.-T.; Hoffman, N. E.; Yang, S. F.; Liu, H.-W.; Walsh, C. T. *Proc. Natl. Acad. Sci. U.S.A.* **1984**, *81*, 3059–3063.
(32) Pirrung, M. C. *Bioorg.* Chem. **1985**, *13*, 219–226.

Analysis of the Factors Contributing to the Large Changes in the Product Distributions Observed in Radical-Chain Addition and Cycloaddition Reactions of Ethylallene and Ethylallene-*3,3*-d_2

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The radical-chain addition of benzenethiol to ethylallene (ETA) and to a 1:1 mixture of ETA and 3,3-dideuterioethylallene (ETA-d_2) produces substantially different product distributions (Scheme I). Much larger differences in product (and d_2) distributions are observed in the cycloaddition reactions with 1,1-dichloro-2,2-dichloroethene (1122) and *N*-phenylmaleimide (NPMI) (Schemes II and III). These changes in product distributions are attributed to four cooperative effects: a difference in the regioselectivity for reaction between the (*E*)- and (*Z*)-ethyl-substituted allyl radicals which is steric in nature favoring reaction at the ethyl-substituted end of the allyl radical in the (*Z*)-isomer and three isotope effects. Deuterium substitution is shown to favor formation of the (*Z*)-alkyl-substituted allyl radical (a steric isotope effect) and also to favor atom transfer and ring closure at the ethyl-substituted end of the allyl radical in the intermediates. The ring-closure reaction is dominated by a rotational isotope effect.

During the past decade efforts in the author's laboratories have been directed toward gaining a thorough understanding of the mechanistic details of addition and cycloaddition reactions of substituted allenes. The results

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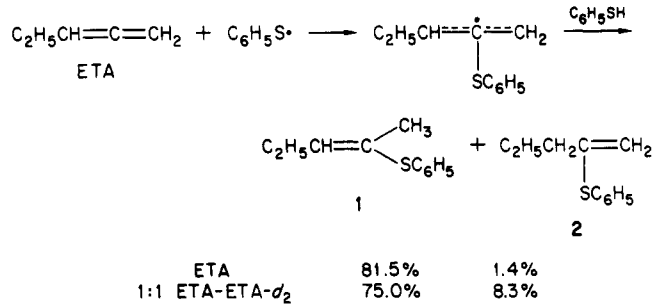
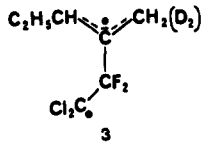
Scheme I



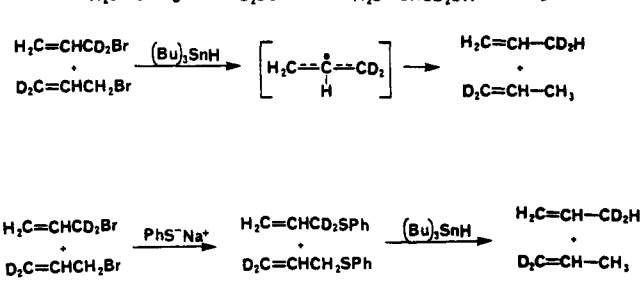
of these studies have indicated that the (2 + 2) cycloaddition reactions of substituted allenes with common dienophiles occur via two-step, diradical-intermediate (TSDI) pathways,[1] and considerable information on the structures of the diradical intermediates and on the relative rates of formation, cleavage, internal rotation, and ring closure of the intermediates has been accumulated.[1] In our early studies kinetic isotope effect (KIE) measurements were carried out on radical-chain[2] and the cycloaddition reactions[1a,b] in order to gain information concerning which π-system was undergoing attack and the extent of rotation and bending of the orthogonal allene systems in the transition states for intermediate radical and diradical formation. These KIE studies also gave information on the product and H–D distributions in the products. Large changes in product distributions were noted in the radical-chain and cycloaddition reactions of ethylallene (ETA) and 3,3-dideuterioethylallene (ETA-d_2), for which at that time no reasonable explanations were available. Only one example was reported, that being for the radical-chain addition of benzenethiol to ETA, the results of which are shown in Scheme I. In the radical-chain addition to ETA hydrogen atom transfer to the ethyl-substituted end of the intermediate allyl radical occurs to produce **2** in 1.4% yield.[3] The addition of benzenethiol to a 1:1 mixture of ETA and ETA-d_2 resulted in an increase in the yield of **2** to 8.3%! From the measured H_2:D_2 ratios and the product distributions an IE of 2.7 ± 0.8 was calculated for the preference for hydrogen atom abstraction at the ethyl-substituted end of the allyl radical intermediate in the D_2 system compared to the H_2 system. This IE was calculated on the basis of the assumption that substitution of H by D would have no affect on the ratio of (*E*)- and (*Z*)-ethyl-2-(phenylthio)allyl radicals formed in the reaction and that the regioselectivity of the *E* and *Z* radicals toward hydrogen atom abstraction were the same. This IE was reported, noting that its magnitude is unrealistically large and that its source was not understood.[2b] Subsequently we observed even larger changes in product distributions in the cycloaddition reactions of mixtures of ETA and ETA-d_2 with 1,1-dichloro-2,2-difluoroethene (1122) and *N*-phenylmaleimide (NPMI).

The product distributions and D_2 percentages observed in the reaction of 1122 with a mixture of ETA and ETA-d_2 (51.09% ETA-d_2) are shown in Scheme II. The numbers under the column heading H_2 are the yields of the three cycloadducts derived from ETA.[2a,3,4] The entries under the column heading H_2:D_2 are the yields of the adducts derived from the mixture of ETA and ETA-d_2 (left) and the percent d_2 cycloadduct (right). The entries under the column heading D_2 are the calculated yields from ETA-d_2 based on the product distribution observed from ETA and the percent ETA-d_2 in the H_2–D_2 mixture. Three dramatic differences are immediately obvious: (1) The yields of **3** and **4** increase markedly with ETA-d_2; (2) the relative yield of **4** increases significantly relative to that of **3**; (3) the d_2 content of **3** and **4** increase, while that of **5** decreases.[5]



The product distributions derived in the reactions with NPMI are shown in Scheme III. Similar changes in product distributions are observed; i.e., the yields of **8** and **9** increase at the expense of **6** and **7**.[6] The changes in product and d_2 distributions shown in Schemes II and III will be specifically accounted for by the results reported in this article.

We have recently directed efforts to determine the sources(s) of these product distribution IE's (PDIE's). The results of these studies now allow for a reasonable explanation of the PDIE's. A review of the literature revealed that several secondary IE studies had been carried out on the formation of radicals by the addition of a radical to a substituted alkene;[7] however, we are not able to find any report on the measurement of the secondary IE's in atom transfer or ring closure of radical and diradical systems. Accordingly it was felt that even though such an effect would be far too small to explain our PDIE's it was necessary to measure the IE for atom transfer to an allyl radical. Recent results obtained in the author's laboratories have shown that the PDIE's for atom transfer from tributyltin hydride to the 1,1-dideuterioallyl radical generated from 1,1- and 3,3-dideuterioallyl bromide and phenyl sulfide are 1.056 (at 50 °C) and 1.080 (at 80 °C),[8] respectively. As expected these values are far too small to account for the large observed PDIE's described above.



Our efforts were then focused on testing the validity of the assumption that D substitution for H would not affect

(1) (a) Pasto, D. J.; Warren, S. E. *J. Am. Chem. Soc.* **1982**, *104*, 3670. (b) Pasto, D. J.; Heid, P. F.; Warren, S. E. *Ibid.* **1982**, *104*, 3676. (c) Pasto, D. J.; Yang, S. H. *Ibid.* **1984**, *106*, 152. (d) Pasto, D. J.; Yang, S. H. *J. Org. Chem.*, in press.

(2) (a) Pasto, D. J.; Warren, S. E.; Morrison, M. A. *J. Org. Chem.* **1981**, *46*, 2837. (b) Pasto, D. J.; Warren, S. E. *Ibid.* **1981**, *46*, 2842.

(3) The remaining product is formed by the initial addition of the benzenethiyl radical to C_3 of ETA (ref 2).

(4) The reaction of 1122 with ETA is very clean, producing only the three cycloadducts shown in Scheme II. The Yields are determined by direct NMR analysis of the reaction mixture.

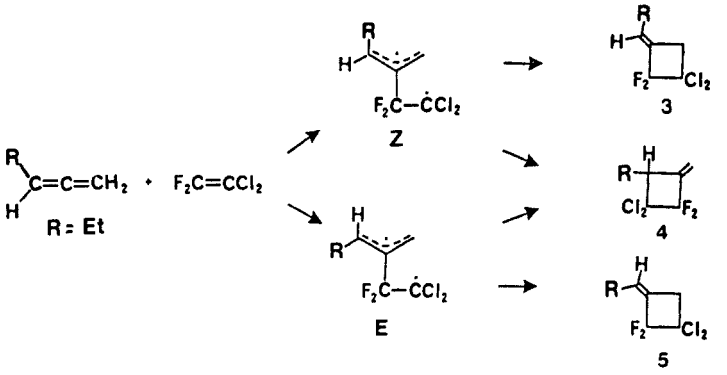
(5) The overall H_2 (ETA) and D_2 (ETA-d_2) balances based on starting and recovered ethylallene and the isotopic content of the cycloadducts is <0.7% based on ETA and <0.4% based on ETA-d_2.

(6) In competition with the formation of **6**–**9** via the stereoisomeric diradical intermediates, two ene-type products are also formed (ref 1b). This, along with the fact that **6** and **8** were isolated as an inseparable mixture by HPLC, does not allow for a comparison in differences in d_2 compositions of **6**–**9**.

(7) Feld, M.; Stefani, A. P.; Szwarc, M. *J. Am. Chem. Soc.* **1962**, *84*, 4451. Stefani, A. P.; Chuang, L.-Y.Y.; Todd, H. E. *Ibid.* **1978**, *92*, 4168. Pryor, W. A.; Henderson, R. W.; Ratsiga, R. A.; Carroll, N. *Ibid.* **1966**, *88*, 1199.

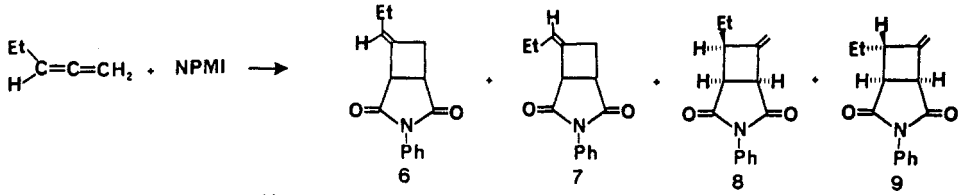
(8) Pasto, D. J.; Huang, N.-Z. *J. Org. Chem.* **1986**, *51*, 412.

Scheme II



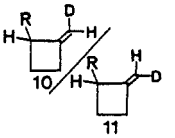
	H_2	$H_2:D_2$		D_2
	49.4	41.9	53.77	34.6
	21.8	34.5	52.53	46.6
	28.8	23.7	46.49	18.8

Scheme III



		6	7	8	9
	H_2	48.1	35.1	5.4	11.4
1:1	$H_2:D_2$	36.6	20.9	17.0	25.5
	D_2	25.1	6.8	28.6	39.5

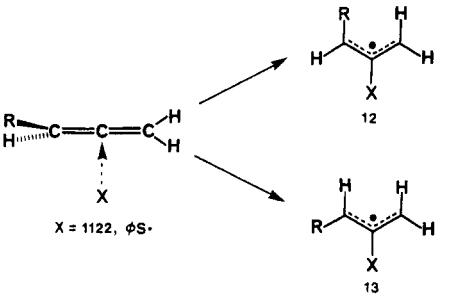
Scheme IV



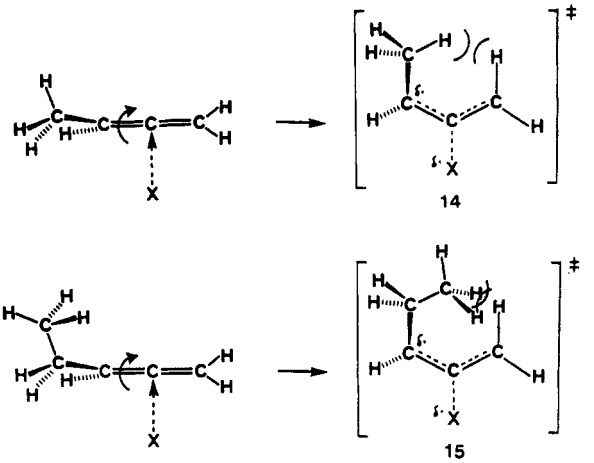
DMA	1.00
Et–	1.06
t-Bu–	1.22

the ratio of the (*E*)- and (*Z*)-allyl radical intermediates derived from ETA or any other substituted allene. In order to test the validity of this assumption we have prepared 3-deuterio-1,1-dimethylallene (DMA-d_1), -1-ethylallene (ETA-d_1), and -1-*tert*-butylallene (TBA-d_1) and have measured the ratios of the (*E*)- and (*Z*)-deuteriomethylene cycloadducts **10** and **11** derived from the cycloadditions reactions with 1122. The results are shown in Scheme IV. There is no discrimination apparent in the formation of **10** vs. **11** from DMA-d_1 (R = H = CH_3). In the reactions with ETA-d_1 and TBA-d_1 significant preferences are indicated for the formation of the (*Z*,*Z*)-1-alkyl-3-deuterioallyl radicals which undergo ring closure to form **10**. (It must be noted that the reaction of ETA with 1122 produces both (*E*)- and (*Z*)-1-ethylallyl radical intermediates, whereas the reaction with TBA produces *only* the (*Z*-*tert*-butylallyl radical intermediate.[1a] Therefore, the **10**:**11** ratio observed with ETA-d_1 is "diluted" by the formation of the (*E*)-ethyl-substituted allyl radical.)

These IE's can reasonably be explained on the basis of steric effects generated in the transition states for the formation of the diradical intermediates. KIE and steric effect data[1a,b,2] indicate that the transition states occur late along the reaction coordinate; extensive rotation and bending of the originally linear, orthogonal allene system having occurred in the transition states. As the size of the alkyl group increases, the steric interactions between the alkyl group and the approaching reagent increase in the transition state for formation of **13**, thereby favoring the formation of **12**, even though **12** is less thermodynamically favored. Because of this steric effect any group larger than

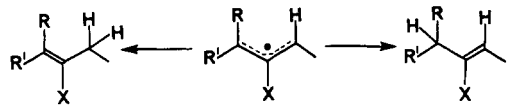


hydrogen that is attached to the carbon atom attached to the allene chromophore will be oriented away from the direction of the approaching reagent. This conformation will be retained in going to the transition state for the formation of **12**. When the alkyl group is methyl there appears to be little or no adverse steric interaction between the hydrogen of the methyl group and the hydrogen in the *Z* orientation at C_3 of the allyl fragment in the transition state **14**. However, when the alkyl group is an ethyl group,



or particularly the *tert*-butyl group, severe steric interactions must develop in the transition state between a methyl group and the C_3 hydrogen as shown in **15**. We believe that the IE's shown in Scheme IV are steric in nature, the C–D bond being slightly shorter than the C–H bond,[9] and thus D acts as if it is smaller than H. Thus, our assumption that the substitution of H by D would not effect the ratio of the (*E*)- and (*Z*)-allyl radical intermediates formed in these reactions is shown not to be valid. The IE's given in Scheme IV, however, are not of sufficient magnitude to account for the much larger changes observed in the product distributions, even recognizing that the IE exerted by ETA-d_2 should be the square of the value shown in Scheme IV for the reaction of ETA-d_1.

The only factors remaining for consideration are possible differences in regioselectivities for hydrogen atom abstraction or ring closure in the (*E*)- and (*Z*)-alkyl-substituted radicals and the effect of rotational IE's in the ring closure reaction. Little is known concerning possible differences in the regioselectivities of stereoisomeric allyl radicals toward hydrogen atom transfer or ring closure. Atom transfer or ring closure at C_3 in **16** results in a shortening of the C_1–C_2 bond length and maintains rigidity about the forming C_1–C_2 π bond, thus increasing the steric interaction between R and H. Reaction at C_1, however,



16

results in the lengthening of the C_1–C_2 bond as well as allowing for rotation of the R group out of the plane of the forming C_2–C_3 π bond, thus reducing the steric interactions between R and H. The inspection of models suggest that the changes in R–H interactions should be greater than the changes in the R′–X interactions. Therefore differences in regioselectivities are to be expected and should be dependent on the size of the R and R′ groups. There is some experimental evidence in support of this proposal. In the radical-chain addition of benzenethiol to alkylallenes hydrogen atom transfer to C_1 in the ethyl- and isopropyl-substituted allyl radical intermediates occurs to the extent of only ~3%, whereas in the *tert*-butyl-substituted systems 50% of the product is derived from transfer to C_1.[2a] In the ring closure of the alkyl-substituted diradical intermediates formed in the cycloaddition reactions of alkylallenes with 1122 the percents of ring closure at the alkyl-substituted end of the allyl radical (C_1) in the ethyl-, isopropyl-, and *tert*-butyl-substituted intermediates are observed to be 15.4%, 25.0%, and 39.1%, respectively.[1a,10]

The final factor contributing to the large changes in the product distributions in the cycloaddition reactions to ETA and ETA-d_2 must be the effects of D vs. H in the ring-closure steps. There are two components to the IE that will be operative in this step: a small, less-than-unity secondary IE arising from the change in hybridization at carbon during bond formation and an IE arising from the rotation of the terminal CD_2 in order to facilitate the bond-forming process. The theoretical maximum for this rotational IE is 2.00, and the magnitude of its contribution should be significantly greater than that of the hybridization IE. Rather significant IE's for preferential ring closure at CH_2 relative to CD_2 in ring-closure reactions have been reported earlier. The IE's for ring closure in the diradical intermediates formed in the cycloaddition reactions of 1,1-dideuterioallene with acrylonitrile and 1122 are >1.21 and >1.17.[11] The ring closure of *gem*-dideuteriotrimethylenemethane exhibits an IE of 1.37.[12] These IE's are a product of the secondary hydridization and rotational IE's. An essentially pure rotational IE of 1.15 (75% of the theoretical maximum) has been observed in the formation of the diradical intermediate in the reaction of 1,1-bis(trideuteriomethyl)allene with 1122.[1a] These rotational IE's favor the formation of **4** and **8** and **9** in Schemes II and III.

The combination of the IE's also nicely explains the observed d_2 contents of the cycloadducts **3** and **5**, the d_2 content of **3** being higher and reflecting the increased d_2 content in the Z intermediate at the expense of the E intermediate.

With an understanding of the regioselectivities and IE's operative in the formation and ring-closure reactions of the diradical intermediates E and Z in Scheme II, the d_2 contents of the cycloadducts can now be interpreted in terms of the competition between the two modes of ring closure for the two diradical intermediates. The cycloadduct **3** derived from Z is expected to have a higher d_2 content when formed from the 1:1 mixture of ETA and ETA-d_2 than that of **5** derived from E. Adduct **4**, which can be derived from both E and Z diradicals, should have a d_2 content intermediate between those of **3** and **5**. The d_2 content of **4** is intermediate in value;[13] however, it is much closer in value to that of **3** than to that of **5**. This suggests that **4** is formed mostly from Z. As the d_2 contents of **3** and **5** represent the d_2 contents in the E and Z intermediates, respectively, one can calculate that only 17% of the total of **4** is formed from E and 83% from Z. (This is quite reasonable considering the steric interactions generated between R and the CCl_2 radical center on ring closure to form **4**). This now allows one to calculate the ratio of Z and E intermediates formed in the reaction as being 68:32, a ratio slightly higher than that suggested earlier based solely on the **3**:**5** ratio of 63:37.

Summary

The significant differences in the product distributions between the cycloaddition reactions of ETA and ETA-d_2 thus arise from a combination of steric effects on the regioselectivity of reactions of substituted allyl radicals and three IE's which affect the ratio of the (*E*)- and (*Z*)-alkyl-substituted radicals formed and the regioselectivities of their ring-closure reactions. In the radical-chain addition reactions of substituted allenes only the rotational IE is not operative. The smaller change in the product distributions observed in the radical-chain addition of benzenethiol to ETA and ETA-d_2 suggests that the rotational IE is the dominant factor controlling the product distributions.

Experimental Section

Cycloaddition of ETA–ETA-d_2 Mixture with 1122. A mixture of ETA and ETA-d_2[2b] (150 μL, 51.09% ETA-d_2) was placed in a heavy-walled Pyrex tube. The tube was cooled in dry ice, and ~600 μL of 1122 was condensed in the tube. The contents of the tube were triply freeze-degassed, and the tube was sealed

(9) Steric isotope effects have been proposed previously, the largest to the author's knowledge 1.20 ± 0.04 (Sherrod, S. A.; da Costa, R. L.; Barnes, R. A.; Boekelheide, V. *J. Am. Chem. Soc.* **1974**, *96*, 1565).

(10) The study of the regioselectivities of stereoisomerically related allyl radicals is under further study in the authors laboratories.

(11) Dai, S.-H.; Dolbier, W. R., Jr. *J. Am. Chem. Soc.* **1968**, *90*, 5028; **1972**, *94*, 3946.

(12) Crawford, R. J.; Cameron, D. M. *J. Am. Chem. Soc.* **1966**, *88*, 2589.

(13) The ± values for the d_2 content analyses of **3**, **4**, and **5** are ±0.34%, ±0.62%, and ±0.35% based on 40–50 mass spectral scans per run for two individual analyses with a 2σ rejection level.

under reduced pressure. The tube was heated in a sand bath at 160 °C for 2 days. The tube was removed from the sand bath, chilled in dry ice, and cracked open. A portion of the contents was removed and the 300-MHz NMR spectrum was recorded showing the complete disappearance of the ETA and the presence of peaks representing only **3–5**. The relative yields of **3–5** were determined by integration of the NMR spectrum.

The unreacted 1122 was allowed to evaporate and the reaction mixture was separated by preparative GLC on a 12 ft × $^1/_4$ in. Carbowax 20 M on Chromasorb P column. The individual samples were analyzed for d_2 content by mass spectrometry, by measuring the relative peak heights (flat-topped) of the M and M + 2 (product-d_2) peaks. Between 40 and 50 repetitive scans were made and the relative intensities were averaged. The relative yields of **3–5** and their percent d_2 content are given in Scheme II.

Cycloaddition of ETA and ETA-d_2 Mixture with NPMI. In a thick-walled Pyrex tube were placed 100 μL of a mixture of ETA and ETA-d_2 (51.09% ETA-d_2), 2 mol equiv of NPMI, and 1.0 mL of benzene. The contents of the tube were triply freeze-degassed, and the tube was sealed under vacuum. The tube was heated in a sand bath at 160 °C for 5 days. The tube was removed from the bath, cooled, and opened. NMR analysis of the contents of the tube showed the complete disappearance of ETA and the formation of only **6–9**. The benzene was removed from the reaction mixture, and the residue was separated by preparative HPLC on a 5-μm silica gel column using hexane–methylene chloride gradient elution. The d_2 contents of the fractions were determined by mass spectral techniques as described above. The relative yields (integration of the NMR spectrum of the crude reaction mixture) and d_2 compositions are given in Scheme III.

Preparation of 3-Deuterio-1,1-dimethylallene. 3-Deuterio-1,1-dimethylallene was prepared by the reduction of 3-chloro-3-methyl-1-butyne with lithium aluminum deuteride using the previously published procedure for the reduction of propargyl chlorides with lithium aluminum hydride.[2a] The product was isolated by preparative GLC using a 15-ft Carbowax 20 M column at 80 °C. Mass spectral analysis indicated the presence of >99.5% DMA-d_1.

Preparation of 3-Deuterio-1-ethylallene. 3-Deuterio-1-ethylallene was prepared by the reduction of 3-chloro-1-pentyne with lithium aluminum deuteride employing the previously described procedure for the reduction of propargyl chlorides with lithium aluminum hydride.[2a] The product was isolated by preparative GLC. Mass spectral analysis indicated the presence of >99.5% ETA-d_1.

Preparation of *tert*-Butyl-3-deuterioallene. A solution of 0.53 g (5.3 mmol) of *tert*-butylallene in 10 mL of ether and 10 mL of tetrahydrofuran contained in a 50-mL round-bottom flask equipped with a side-arm equilibrating addition funnel was cooled to −80 °C (dry ice–2-propanol bath). The reaction mixture was maintained under a nitrogen atmosphere. *tert*-Butyllithium (10% mol excess) was added dropwise and the reaction mixture was allowed to warm to −60 °C. After the mixture was stirred for 2 h at −60 °C, 2 mL of deuterium oxide was added, and the reaction mixture was allowed to warm to 25 °C. The organic layer was washed with 15 mL of ice–water and was dried ($MgSO_4$). The organic solvents were removed by fractional distillation, and the product was purified by preparative GLC using a 12 ft × $^1/_4$ in. SE-30 column at 80 °C. Mass spectral analysis indicated the presence of 92.7% d_1 and 7.3% d_0 *tert*-butylallene.

Cycloaddition of the Monodeuterioalkylallenes with 1122. The cycloaddition reactions of the monodeuterioalkylallenes were carried out at 160 °C as described previously.[1a] The ratios of **10** and **11** were determined directly on the reaction mixtures by integration of the vinyl hydrogen region of the NMR spectra.

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Registry No. **1122**, 79-35-6; ETA, 591-95-7; NPMI, 941-69-5; DMA-*d*, 101933-73-7; ETA-*d*, 101933-74-8; TBA-*d*, 101933-75-9; PhSH, 108-98-5; D_2, 7782-39-0.

Oxymetalation. 20.[1] Conversion of Cyclopropanes into 1,2-Dioxolanes via *tert*-Butyl Peroxymercuriation, Bromodemercuriation, and Silver Salt Induced Cyclization

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The *tert*-butyl peroxymercuriations of cyclopropane and ethyl-, phenyl-, 1,1-dimethyl-, 1-methyl-1-phenyl-, and 1,1-diphenylcyclopropane (**1a–f**) have been carried out by using mercury(II) acetate, a onefold excess of *tert*-butyl hydroperoxide, and 20 mol % of perchloric acid. After anion exchange with aqueous potassium bromide, the derived γ-(bromomercurio)alkyl *tert*-butyl peroxides (**2a–f**) have been isolated (33–51%; 10% for **2a**) by silica chromatography. These have been converted into the corresponding γ-bromoalkyl *tert*-butyl peroxides (**3a–f**) (84–100%) by reaction with bromine and sodium bromide in methanol. The bromides (**3a–e**) have, in turn, been converted into the corresponding 1,2-dioxolanes (**4a–e**) (>80%) by treatment with silver trifluoroacetate. However, the reaction of **3f** with silver trifluoroacetate afforded a phenoxyacetal derived from β-*tert*-butoxyethyl phenyl ketone, which was identified by conversion into phenol plus the corresponding (2,4-dinitrophenyl)hydrazone upon treatment with acidic (2,4-dinitrophenyl)hydrazine. The exceptional behavior of **3f** supports the suggestion that the final step in this three-stage synthesis of 1,2-dioxolanes proceeds via trialkylperoxonium intermediates.

In a far-reaching discovery, Kopecky et al.[2] found that certain alkenes may be converted into 1,2-dioxetanes via hydroperoxybromination and silver salt induced cyclization (e.g., eq 1). The analogous conversion of cyclopropanes into 1,2-dioxolanes (eq 2) has been investigated by Adam et al.[3] and found to be problematical. Thus, the ring-opening step only proceeded at an acceptable rate when the cyclopropane possessed at least one aryl substituent, and even then reaction times of 20–150 h were required. Furthermore, the hydroperoxybromination was subject to unpredictable amounts of competing aromatic bromina-

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