222 (13), 204 (12), 186 (100), 128 (29), 126 (28), 110 (100), 95 (92), 94 (90), 78 (80).

Anal. Calcd for $C_{12}H_{14}O_2S$: C, 64.86; H, 6.31. Found: C, 64.62; H, 6.29. The ^{13}C nmr spectrum of this material, however, suggested the presence of a major and minor isomer; ^{13}C nmr (acetone) in parts per million upfield from ^{13}C = 0 of solvent (major isomer) δ 78.4 (4 C, olefinic), 81.3 (2 C, olefinic), 82.5 (2 C, olefinic), 137.1 (2 C, C–O), and 160.5 ppm (2 C, C–S); (minor isomer) δ 78.8 (2 C, olefinic), 79.1 (2 C, olefinic), 81.5 (2 C, olefinic), 82.2 (2 C, olefinic), 137.3 (2 C, C–O), and 160.7 ppm (2 C, C–S).

The major product could be converted to a pure, crystalline diacetate in 67% yield from reaction of the mixture with acetic anhydride in pyridine: mp 115.5–116.5°; ir ($CHCl_3$) 3045, 3000, 2940, 1730, 1375, 1225, 1020, 995, and 915 cm^{-1}; λ max (95% C_2H_5OH) 258 nm (ϵ 6760), 283 nm (ϵ 3570 sh); pmr ($CDCl_3$) ($CH_{3'8}$) 2.08, ($H_{1'8}$) 5.60, ($H_{8'8}$) 3.85, ($H_{2-5'8}$) 5.7–6.5 with J_{1-2}, $J_{1-6} < 1$, and $J_{5-6} = 4.5$;[54] ^{13}C nmr ($CHCl_3$) relative to $^{13}CHCl_3$ δ 92.9 (2 C, C=O), −50.1 (2 C, olefinic), −48.3 (2 C, olefinic), −46.7 (2 C, olefinic), −43.5 (2 C, olefinic), 7.7 (2 C, *C*–OAc), 35.5 (2 C, C–S), and 56.1 ppm (2 C, CH_3–); mass spectrum 188 (4), 187 (12), 186 (72), 185 (37), 184 (15), 171 (6), 152 (6), 109 (7), 78 (16), 77 (17), 69 (10), 65 (12), 60 (37), 52 (8), 51 (37), 50 (15), 45 (89), 43 (100), 42 (17), and 39 (17).

Anal. Calcd for $C_{16}H_{18}O_4S$: C, 62.80; H, 5.88. Found: C, 62.68; H, 5.69.

The above reaction was repeated on 100 mg of **1** but without the pentane wash to provide a 72% yield of crude products. The ^{13}C nmr spectrum of this sample showed the above two isomers to be present in approximately equal amounts. In addition, about one-third of the sample had dehydrated to **15**, which was identified from its tlc properties and pmr spectrum. Neither ^{13}C nmr nor pmr gave any indication that this sample of **15** was a mixture of stereoisomers. An approximately 1:1 mixture of the bis sulfides above was stored in chloroform at room temperature until more than 50% decomposition had occurred (R_f 0.35 for bis sulfides, 0.60 for **15**, and 0.90 for diphenyl sulfide; chloroform–ethyl acetate, 1:2). The pmr (100 MHz) spectra of the starting bis sulfide mixture and the recovered bis sulfide mixture were identical but could not be assigned since two superimposed spectra were clearly present. Irradiation of the vinyl protons or substitution by deuterium (see below) enables this to be seen more clearly. At 4° the two isomers are separable by tlc (solvent above), provided small amounts of material are applied to the plates. The compound at high R_f (0.38) was crystalline; pmr spectrum, (H_1) 4.32, (H_{2-5}) 5.8–6.2, (H_6) 3.62 with J_{1-2} = 4.5, J_{1-6} = 4.5, J_{5-6} = 4.6. The lower R_f (0.32) isomer remained an oil; pmr spectrum (H_1) 4.27, (H_{2-5}) 5.7–6.2, (H_6) 3.59 with J_{1-2} = 4.8, J_{1-6} = 2.9, J_{5-6} = 5.2. These spectra were measured at 220 MHz after exchange with D_2O. The crystalline and oily isomers show identical mass spectra at 20 eV.

In summary, the ^{13}C nmr spectrum of the crystalline isomer requires that the same stereochemistry be present in both rings. Similarly, the pmr spectra of the separated isomers indicate the same stereochemistry is present in both rings of each molecule. In addition, both isomers dehydrate at about the same rate and give only **15**, which eliminates the possibility that either is cis,cis. The only remaining possibility is that the two isomers are the meso and racemic trans,trans structures **18a** and **18b**, bis(6-*trans*-1-hydroxycyclohexadien-2,4-yl) sulfide.

Through the use of **1**-*3,6-d*$_2$ and **1**-*1,2,3,4,5-d*$_5$, it was established that the additions for both rings in both isomers occurs exclusively by 1,2 opening; *cf.* reactions of azide and thiophenoxide with deuterated **1** for method of analysis.

Acknowledgment. The authors express their gratitude to Dr. D. D. Traficante of M.I.T. and Mr. E. A. Sokoloski of NIH for determining several of the nmr spectra reported here. In addition, we are grateful to Dr. H. Fales and Dr. P. Roller of NIH for obtaining the accurate mass measurements reported.

(54) The previous assignment of J_{1-6} = 4.5 Hz is incorrect.[28] Note also the change in numbering system used here.

Stereochemical Aspects of the Reaction of 2-Phenyl-Substituted Alkenylidenecyclopropanes with Chlorosulfonyl Isocyanate[1]

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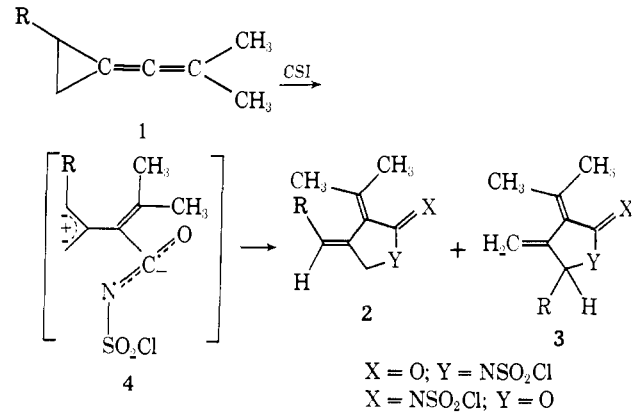
Contribution from the Department of Chemistry, University of Notre Dame, Notre Dame, Indiana 46556. *Received March 12, 1974*

Abstract: The stereochemical aspects of the reactions of alkenylidenecyclopropanes with CSI to produce bisalkylidenecyclopentane derivatives have been studied using (−)-(*R*)-2-phenylisobutenylidenecyclopropane ((−)-(*R*)-**5**) and a mixture of (*E*)- and (*Z*)-2-phenyl-1-(2,4-dimethyl-1-pentenylidene)cyclopropane (**13**). At 0° and below (−)-(*R*)-**5** reacts to form **6** in a highly stereoselective manner with inversion of configuration. The diene **7** is also formed optically active, the right-handed helicity of the diene being assigned on the basis of stereochemical interrelations and mechanistic arguments. At +30° the reaction proceeds with partial loss of optical activity, while at 61.2° complete loss of optical activity is observed. The observations are discussed in terms of the relative rates of bond rotation (leading to loss of optical activity) *vs.* collapse of the dipolar intermediate formed in the reaction. The results derived with **13** show that the facial selectivity of attack by CSI on the alkenylidenecyclopropane is sensitive to the steric features of groups attached to the terminal allene carbon and on the three-membered ring indicating that the CSI must attack the perpendicular (to the ring) p orbital on C_4 of the C_1–C_4 double bond.

Alkenylidenecyclopropanes (**1**) react with chlorosulfonyl isocyanate (CSI) to produce, in part depending on the nature of the functions attached to the three-membered ring, cycloaddition adducts of structure **2** and **3**.[2] The mechanism for the formation of **2** and **3** was visualized as proceeding *via* electrophilic attack on the perpendicular (with respect to the plane of the three-membered ring) p orbital on C_4 resulting in the formation of a cyclopropyl cation which underwent disrotatory ring opening to produce a dipolar intermediate (**4**). Collapse of **4** by nucleophilic attack by nitrogen or oxygen on either end of the allyl cation portion of **4**

(1) Part VII of a series Cycloaddition Reactions of Cyclopropane-Containing Compounds. For part VI see D. J. Pasto and J. K. Borchardt, *J. Amer. Chem. Soc.*, **96**, 6220 (1974).

(2) D. J. Pasto, A. F.-T. Chen, G. Ciurdaru, and L. A. Paquette, *J. Org. Chem.*, **38**, 1015 (1973).

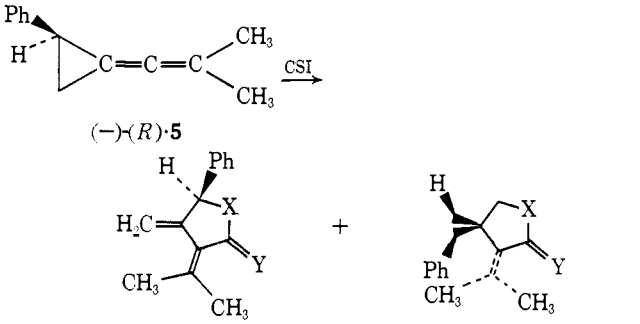


forms either **2** or **3**.[3] The possible concerted cycloaddition of CSI with an alkenylidenecyclopropane to give directly **2** and **3** was ruled out by the fact that cis 2,3-disubstituted alkenylidenecyclopropanes produce only *Z* products (about the 4-alkylidene group), whereas trans isomers produce mixtures of *E* and *Z* products.[2] In contrast, a concerted cycloaddition pathway with the cis and trans isomers would produce only enantiomerically related products (at C_5) as evidenced by the reactions of cis and trans disubstituted alkenylidenecyclopropanes with 4-phenyl-1,2,4-triazoline-3,5-dione.[4]

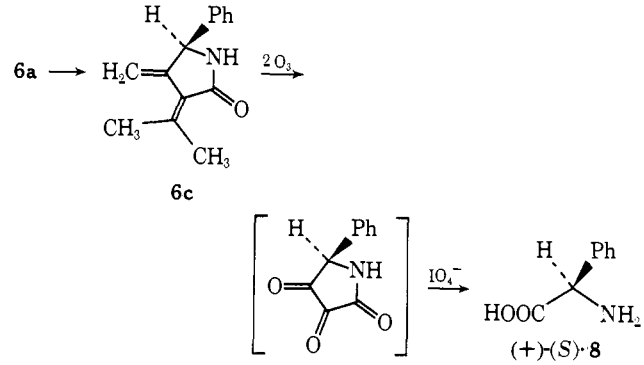
In order to gain further stereochemical evidence concerning the mode of electrophilic attack and the relative rates of bond rotation in **4** (leading to racemization) *vs.* collapse of the dipolar intermediate, we have investigated the stereochemical aspects of the reactions of (−)-(*R*)-2-phenylisobutenylidenecyclopropane[5] and (*E*)-2-phenyl-1-(2,4-dimethyl-1-pentenylidene)cyclopropane with CSI.

Results

Reaction of (−)-(*R*)-2-Phenylisobutenylidenecyclopropane (5) with CSI. The reaction of (−)-(*R*)-**5**[5] (64.2 ± 1.0% enantiomeric purity)[6] with CSI at 0° in methylene chloride solution produced a mixture of adducts, **6a**, **6b**, **7a**, and **7b**, *all of which were optically active*. The absolute configurations of the adducts were assigned as outlined in the following paragraphs.

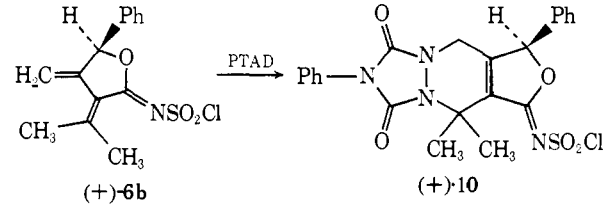


Reaction of adduct **6c**, derived from **6a** by hydrolysis,[2]



with slightly greater than 2 molar equiv of ozone in methylene chloride–pyridine solution at −70° followed by warming to room temperature and direct treatment with an aqueous solution of sodium metaperiodate produced (+)-(*S*)-phenylglycine (**8**) ([α]^{25}D (4 *N* HCl) +41.9°, 62.6 ± 1.5% enantiomeric purity). The enantiomeric purity of **6c** was determined by nmr techniques by complexation with the chiral shift reagent tris(trifluoroacetylcamphorato)europium(III) [Eu(tfac)$_3$] (**6a** shows no tendency to complex with Eu(tfac)$_3$) which transforms the enantiomeric hydrogens at C_5 in (*R*)- and (*S*)-**6c** into diastereomeric hydrogens of different chemical shifts. Direct integration gives an enantiomeric purity for **6c** of 63.9 ± 1.0%. Thus, the reaction of (−)-(*R*)-**5** with CSI has occurred with inversion and complete stereospecificity within experimental error.

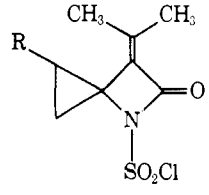
The enantiomeric purity of **6b** could not be directly determined by nmr techniques, **6b** showing no tendency to complex with Eu(tfac)$_3$. Attempted hydrolysis of **6b** to the corresponding lactone was not particularly effective owing to the hydrolytic instability of the lactone. Treatment of **6b** with PTAD, however, produced adduct **10** whose enantiomeric composition



could be determined by nmr techniques giving a value of 64.2 ± 1.2%. Attempts to determine the absolute configuration of **6b** were unsuccessful, the assigned configuration being based by mechanistic analogy with the formation of **6a** (*vide infra*).

The assignment of the chirality of the skewed diene chromophores[7] is based on three lines of evidence. The diene chromophores **7a** and **7b** are illustrated as

(3) No evidence could be obtained for the possible intermediacy of a [2 + 2] cycloadduct of structure i by nmr techniques at low temperatures.[2]



i

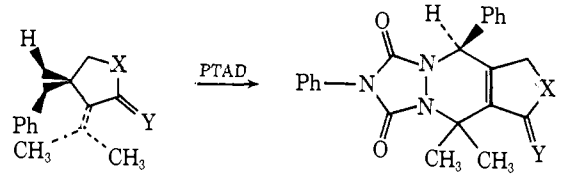
(4) (a) D. J. Pasto and A. Chen, *J. Amer. Chem. Soc.*, **93**, 2562 (1971); (b) D. J. Pasto, A. F.-T. Chen, and G. Binsch, *ibid.*, **95**, 1553 (1973).

(5) D. J. Pasto and J. K. Borchardt, *Tetrahedron Lett.*, 2517 (1973).

(6) All percentages are in terms of enantiomeric purities as determined directly by nmr techniques using chiral shift reagents (*vide infra*).

(7) For a brief discussion of the steric factors causing distortion of the planarity of the diene chromophore see reference in footnote 1. The details of an X-ray structural analysis of a similar skewed diene adduct will be reported and discussed in the near future.

right-handed helical dienes and, thus, are expected to possess positive rotations.[8] This assignment is tenuous, however, owing to the presence of a number of substituents on the diene chromophore which could possibly affect the sign of rotation. The second stereochemical correlation involves the conversion of **7a** and **7b** into **11a** and **11b**, respectively, with 4-phenyl-1,2,4-



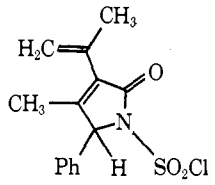
(+)-**7a**, X = NSO_2Cl; Y = O (−)-**11a**, X = NSO_2Cl; Y = O
(+)-**7b**, X = O; Y = NSO_2Cl (−)-**11b**, X = O; Y = NSO_2Cl

triazoline-3,5-dione (PTAD), and correlation of the sign of rotation of **11a** and **11b** with the signs of rotation and configurations of the 1:1 and 2:1 adducts of (−)-(*R*)-**5** with PTAD,[9] all containing the same attachment atoms at the chiral atom. Previous studies in our laboratories have shown that the cycloaddition of 1,2-bisalkylidenecyclopentanes such as **7a** and **7b** occurs by attack of the dienophile (PTAD) on the least hindered face of the diene chromophore, in these cases at the face opposite the phenyl group.[4b] In these cycloaddition reactions a substrate possessing a chiral plane is converted into a product containing a chiral center of *opposite* absolute configuration (and opposite sign rotation) compared to **6a** and the 1:1 cycloaddition product of (−)-(*R*)-**5** with PTAD.[9]

The enantiomeric purity of **11a** and **11b** was established by nmr analysis in the presence of $Eu(tfac)_3$ indicating enantiomeric purities of 58.9 ± 1.0 and 58.6 ± 1.0%, respectively. These enantiomeric purities do not correspond with those of **6a** and **6b** indicating that (1) either **7a** and **7b** were not formed in the same degree of stereoselectivity as were **6a** and **6b**, or (2) the reactions of **7a** and **7b** with the very reactive PTAD were not facial specific, or (3) partial racemization of **7a** and **7b** occurred during isolation and separation. We prefer the second explanation in that conversion of the 1:1 chiral diene adduct of (−)-(*R*)-**5** with PTAD into the similar 2:1 adduct occurs to produce a 2:1 adduct of the same enantiomeric purity (58.7 ± 1.0%),[9] and that **7a** and **7b** are stereochemically stable for periods of time considerably longer than those required for the separation and reaction procedures.[9] We believe that **7a** and **7b** are also formed in highly stereoselective reactions (*vide infra*) and that the reported optical rotations correspond to enantiomeric purities of 64.2 ± 1.0%. The final line of evidence in support of the proposed chiralities of **7a** and **7b** derive from mechanistic relationships in the formation of adducts **6a** and **7a** and **7b** (*vide infra*).

Effect of Reaction Temperature on the Enantiomeric Purities of 6 and 7. The reaction of (−)-(*R*)-**5** with CSI was carried out at −30, 0, +30, and +61.2°, and the enantiomeric purities of the adducts were determined as described in the foregoing section. The data are given in Table I. At −30 and 0° the reactions are stereospecific; however, at +30° the retention of optical activity is less than 50%, and at 61.2° *all products are racemic.*

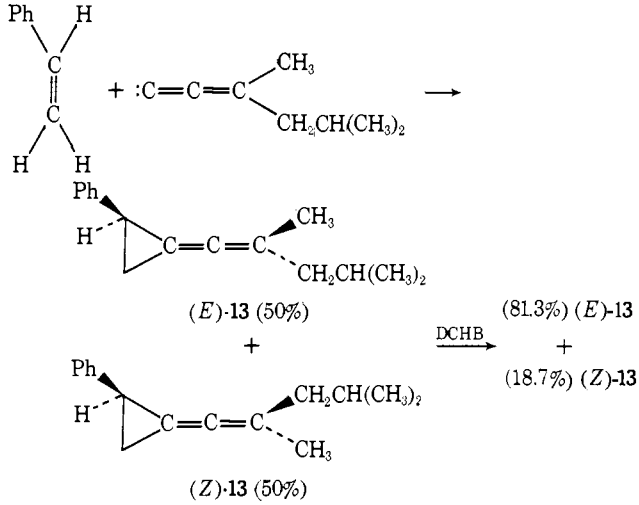
In addition to formation of the four adducts previously characterized (*i.e.*, **6** and **7**),[2] adduct **12** is formed in 2.8 and 8.5% at +30 and +61.2° and is optically inactive. Adduct **12** is a primary reaction



12

product and is not formed by thermal rearrangement of any of the adducts **6** or **7**.[10] At 61.2° two other as yet unidentified adducts are formed in <1% yield.

Reaction of 2-Phenyl-1-(2,4-dimethylpentenylidene)-cyclopropane (13). The reactions of unsymmetrically substituted allenecarbenes with alkenes produce 50:50 mixtures of *E* and *Z* isomers of the alkenylidenecyclopropane.[11] All attempts to separate the *E,Z* mixtures failed. Enrichment of one isomer, however, could be accomplished by chemical means. 2-Phenylisobutenylidenecyclopropane has been shown to react almost exclusively at the face of the C_1–C_4 double bond opposite the phenyl group with diimide and diisopinocampheylborane.[5] Making use of these observations, the 50:50 mixture of (*E*)- and (*Z*)-**13** was treated twice



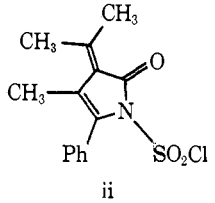
(*E*)-**13** (50%) (81.3%) (*E*)-**13**
+ DCHB + +
(*Z*)-**13** (50%) (18.7%) (*Z*)-**13**

with a deficient amount of dicyclohexylborane (DCHB) and the unreacted **13** was isolated. Nmr analysis indicated that an 81.3:18.7 mixture of the two isomers remained. The major isomer is assigned the *E* stereo-

(8) A. W. Burgstahler, H. Ziffer, and U. Weiss, *J. Amer. Chem. Soc.*, **83**, 4660 (1961); A. Moscowitz, E. Charney, U. Weiss, and H. Ziffer, *ibid.*, **83**, 4661 (1961).

(9) D. J. Pasto and J. K. Borchardt, *J. Amer. Chem. Soc.*, **96**, 6944 (1974).

(10) Adducts **6a**, **6b**, **7a**, and **7b** are both chemically and stereochemically stable at temperatures up to 100° for short periods of time. Prolonged heating of **6a** at 100° leads to double bond migration to produce ii, isolated previously from the treatment of **6a** with iodine in chloro-



ii

form at 70° for 3 hr.[2]

(11) D. J. Pasto and J. K. Borchardt, unpublished observations.

Scheme I

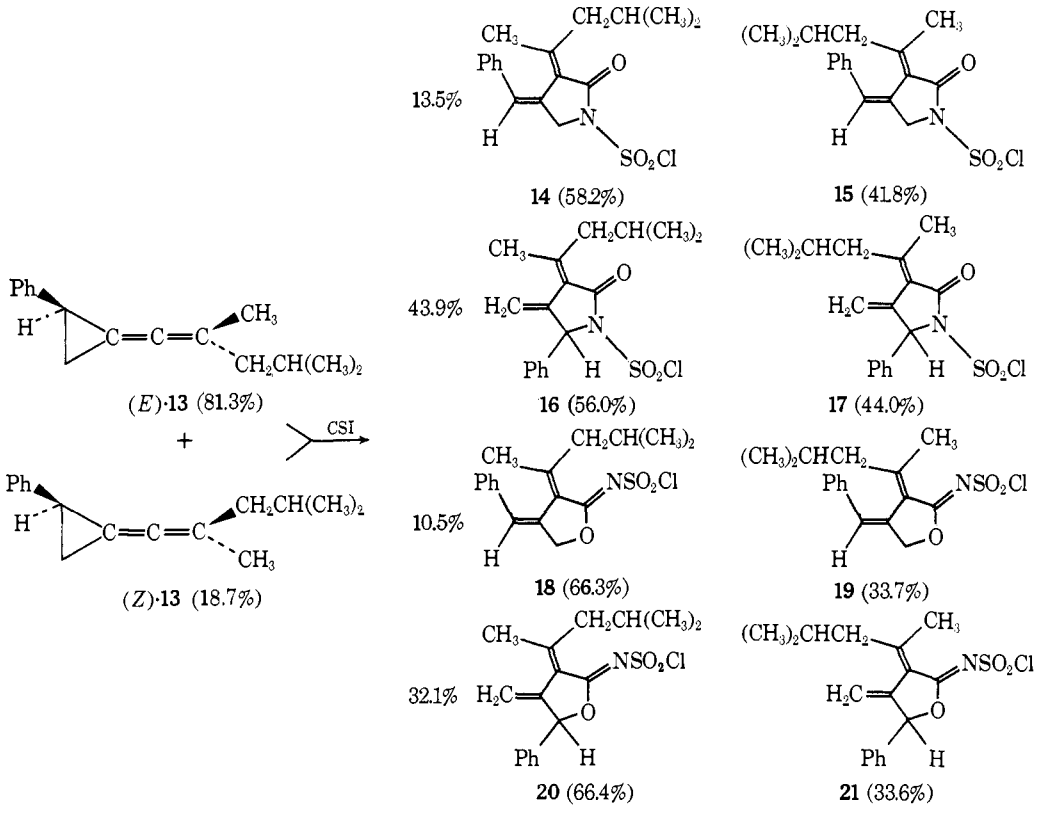


Table I. Enantiomeric Purities of Adducts **6a**, **6b**, **7a**, and **7b** as a Function of Reaction Temperature[a]

	Enantiomeric purity, %			
	Reaction temp			
Adduct	−30°	0°	+30°	+61°
6a	62.4 ± 0.5	63.9 ± 1.0	55.8 ± 1.2	50.0 ± 1.0
6b[b]	63.4 ± 0.5	64.2 ± 1.2	56.5 ± 1.2	50.0 ± 1.0
7a[c]	59.9 ± 0.7	58.9 ± 0.9	52.9 ± 1.0	50.0 ± 1.0
7b[c]	58.6 ± 0.6	58.6 ± 0.9	53.2 ± 1.0	50.0 ± 1.0

[a] Average of three nmr determinations with the associated average deviations. [b] Enantiomeric purity of **10** formed by reaction with PTAD. [c] Enantiomeric purity of **11a** and **11b** formed by reaction with PTAD.

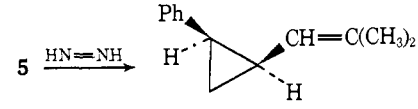
chemistry on the basis of steric considerations and nmr evidence. Attack by DCHB on the face of the C_1–C_4 double bond opposite the phenyl should occur more rapidly with (*Z*)-**13** thus leaving a mixture rich in (*E*)-**13**. The nmr spectrum of the 81:19 mixture contains two methyl singlets, the higher field singlet being more intense. Long-range shielding by the phenyl group is expected to cause the methyl of the *E* isomer to be more shielded relative to the methyl of the *Z* isomer. Similar shifts in the resonances of the isobutyl group are noted; however, they are in a direction opposite that observed for the methyl groups.

The reaction of the enriched *E*,*Z* mixture of **13** with CSI produced a mixture of adducts which could be separated into mixtures of two adducts isomeric about the C_6 4-methyl-2-pentylidene group. Although further separation of the mixtures was not possible, the stereochemical composition of each fraction could be determined by analysis of the nmr spectra. Assignment of the stereochemistry of the adducts is based on the long-range shielding effects of the phenyl and/or adjacent C=O or C=N functions on the methyl and isobutyl resonances.[2] The percentages indicated to the left of each pair of compounds (Scheme I) represents the yield of that pair of adducts, while the percentages given below the structures indicate the composition of that fraction.

Discussion

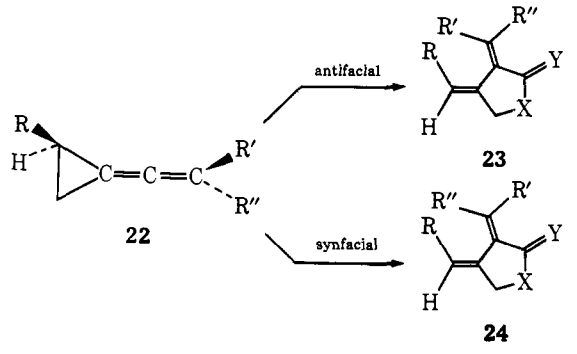
The mechanism initially proposed to account for the formation of products **2** and **3** implies electrophilic attack by CSI on the p orbital of C_4 of the C_1–C_4 double bond resulting in cyclopropyl cation formation and disrotatory opening to dipolar intermediate **4** and collapse to **2** and **3**. Stereochemical evidence pertaining to the orbital and facial selectivity of attack by the electrophile and stereoselectivity in the collapse of the dipolar intermediate was not available owing to the lack of appropriate asymmetry in the alkenylidenecyclopropanes. The results derived with **13** clarify the orbital and facial selectivity aspects of the reaction, while those derived with (−)-(*R*)-**5** provide interesting information concerning the structure and properties of the dipolar intermediate.

Reactions at the C_1–C_4 double bond of **5** show a high degree of facial selectivity arising from steric effects of the phenyl group. For example, reduction of **5** with diimide occurs only by attack at the face opposite the phenyl group.[5] Diisopinocampheylborane similarly reacts with **5**.[6] In the unsymmetrically C_5-substituted **13** the differing steric effects of the isobutyl and methyl



groups play an additional role in determining the facial selectivity of attack on the C_1–C_4 double bond.[12]

The facial selectivity of the attack on the C_1–C_4 double bond is readily inferred from the stereochemistry at C_3 of the adducts. Antifacial attack on an unsymmetrically substituted alkenylidenecyclopropane (**22**)



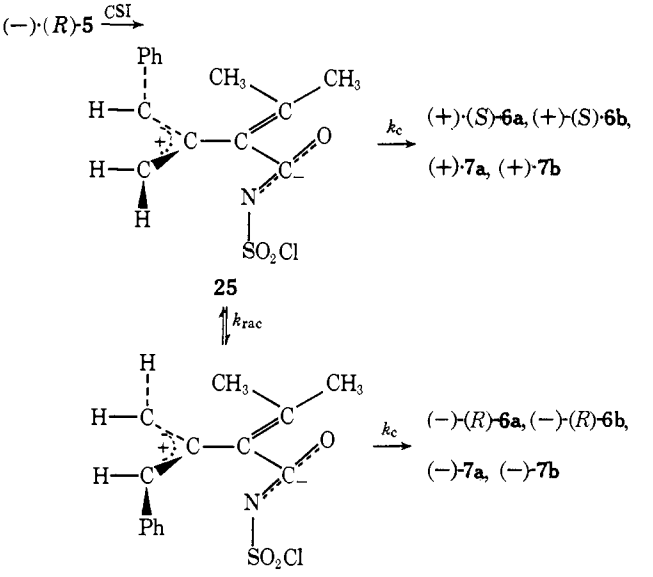
results in the exclusive formation of adduct **23**, while synfacial attack leads to formation of **24**. In the case of the reaction of the enriched mixture of (*E*)- and (*Z*)-**13** an antifacial specific attack (relative to the phenyl group) would produce a mixture of the stereoisomeric adducts (**14**, **16**, **18**, and **20** and **15**, **17**, **19**, and **21**) in an 81.3:18.7 ratio. Such is not the case. Assuming that (*Z*)-**13** reacts in an antifacial specific manner, owing to the combined steric effects of the larger phenyl and isobutyl groups on the same face of the C_1–C_4 double bond, (*E*)-**13** must undergo both anti- and synfacial attack by CSI in a ratio of 3.2:1.0. The observed facial selectivity in the reaction of CSI with **13** is consistent only with attack by the electrophile on the perpendicular p orbital on C_4 of the C_1–C_4 double bond.

The stereochemical results derived from the reaction of (−)-(*R*)-**5** with CSI provide considerable information concerning the stereochemistry of attack on **5** and the structural features of the dipolar intermediate. Antifacial attack by CSI on (−)-(*R*)-**5** results in the formation of the dipolar intermediate **25** in which the phenyl-substituted allyl cation resides in a plane orthogonal to the plane of the remainder of the intermediate. Immediate collapse of **25** by nucleophilic attack by nitrogen or oxygen from the "underside" of the allyl cation portion of **25** produces **6a** and **6b** with inversion of configuration at C_2 of **5**, and **7a** and **7b** of the indicated chirality. (Synfacial attack by CSI on (−)-(*R*)-**5** would result in formation of **6a** and **6b** with *retention* of configuration.) At temperatures below 0° **25** rapidly collapses to form **6a**, **6b**, **7a**, and **7b** in a highly stereoselective manner (Scheme II).

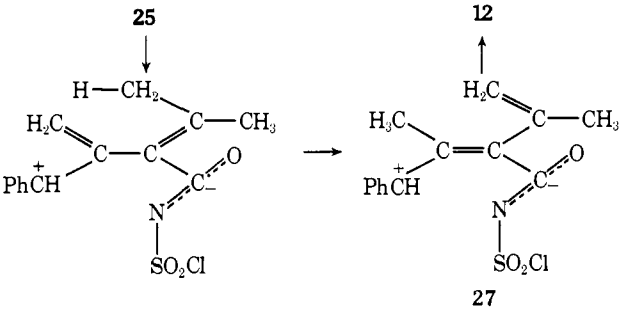
The formation of racemic product involves rotation about the C_1–C_4 bond in **25** to produce the enantiomeric dipolar intermediate **26** which then collapses to the enantiomeric adducts. At 0° the rate of collapse (k_c) is much greater than the rate of C_1–C_4 bond rotation (k_{rac}), at 30° the rates are competitive, whereas at 61.2° k_{rac} is much greater than k_c.

(12) The latter stereochemical feature does not affect the facial selectivity of attack on the C_4–C_5 double bond owing to the plane of symmetry in the nodal plane of the C_4–C_5 double bond. In contrast to the facial selectivity noted in the reaction of **13** with CSI (*vide infra*), the reaction of **13** with PTAD, which involves attack on the in-plane p orbital on C_4, occurs with complete lack of stereoselectivity.[9]

Scheme II



The formation of **12** can be viewed as arising by a [1.5]sigmatropic rearrangement in the planar conformation of the dipolar intermediate giving the new dipolar intermediate **27** which can collapse only to **12**. Adduct



12 is formed only when racemization occurs, the yield increasing with increasing loss of optical activity in the products.

Experimental Section

Melting points were determined using a Mel-Temp melting point apparatus and are uncorrected. Optical rotations were determined in chloroform solution at 25° using an O. C. Rudolph and Sons polarimeter. Proton magnetic resonance spectra were obtained with a Varian XL-100 spectrometer. The reported coupling constants are derived by first-order analyses of the nmr spectra. Enantiomeric and isomeric purities were determined by expansion of the appropriate nmr absorption peaks to a 25-Hz sweep and integration using a planimeter. High-resolution mass measurements and mass spectra were recorded on a Picker-Nuclear MS-902 spectrometer.

Reaction of (−)-(*R*)-5 with CSI. To a stirred 0.1 *M* solution of 1.70 g (10 mmol) of (−)-(*R*)-**5**[5] in dichloromethane maintained at 0° was slowly added a 0.1 *M* solution of 1.42 g (10 mmol) of CSI in dichloromethane. After 30 min the reaction was allowed to warm to room temperature and was stirred for an additional 30 min. The solvent and any unreacted CSI were removed under vacuum. Separation of the CSI adducts was accomplished by column chromatography on silica gel as previously described.[2] After recrystallization from ether, the isolated adducts **6a** ($[\alpha]^{25}D$ +20.5°), **6b** ($[\alpha]^{25}D$ +15.2°), **7a** ($[\alpha]^{25}D$ +9.3°), and **7b** ($[\alpha]^{25}D$ +24.7°) exhibited ir and nmr spectral properties identical with those previously reported for the racemic compounds.[2] (Rotations of the fractions derived directly from the chromatographic column were, within

Table II. Optical Rotations and Enantiomeric Purities of 6 and 7 at Various Temperatures

Adduct	Temperature −30° [α]²⁵D	−30° EA, %	+30° [α]²⁵D	+30° EA, %	+61.2° [α]²⁵D	+61.2° EA, %
6a	+20.6	62.4 ± 0.5	+10.1	55.8 ± 1.2	0.0	0.0
6b	+18.7	63.4 ± 0.5	+9.1	56.5 ± 1.2	0.0	0.0
7a[a]	+9.5	59.9 ± 0.7	+4.2	52.9 ± 1.0	0.0	0.0
7b[b]	+24.5	58.6 ± 0.6	+12.2	53.2 ± 1.0	0.0	0.0

[a] Enantiomeric purity of the PTAD adduct **11a**. [b] Enantiomeric purity of the PTAD adduct **11b**.

experimental error, the same as those of the once-recrystallized adducts.)

Determination of the Enantiomeric Purity of 6a. Adduct **6a** did not complex with the chiral shift reagent Eu(tfac)$_3$ and thus direct determination of the enantiomeric purity of **6a** could not be accomplished by nmr techniques. Adduct **6a** was hydrolyzed to the lactam **6c** in 20% aqueous dioxane by titration with aqueous potassium hydroxide as described previously[2] ([α]²⁵D +13.9°). Integration of the resonances of the hydrogen attached to the chiral carbon atom obtained in the presence of 0.50 molar equiv of Eu(tfac)$_3$ ($\Delta\delta$ = 0.14 ppm) indicated an enantiomeric purity of 63.9 ± 1.0%.

Determination of the Absolute Configuration of Lactam 6c. A solution of 0.11 g (0.53 mmol) of **6c** in 10 ml of 2% pyridine–methylene chloride was cooled to −78° (Dry Ice–acetone bath) and an excess of ozone was bubbled through the solution.[13] The reaction mixture was allowed to warm to room temperature and the solvent was removed on a rotary evaporator. The nmr spectrum of the residue indicated the loss of the methyl and methylene absorptions of the starting material: nmr ($CDCl_3$) δ 5.10 (br s, 1 H), 7.35 (m, 6 H).

The ozonolysis product was dissolved in 50 ml of acetone and was added dropwise with stirring to 50 ml of 0.03 *M* aqueous sodium metaperiodate cooled in an ice bath. After 6 hr the reaction mixture was allowed to warm to room temperature and was stirred for an additional 66 hr. The solvent was removed under vacuum and the white solid residue was extracted with 500 ml of dichloromethane. The solvent was removed under vacuum and the residue was recrystallized from acetone (23% overall): mp 301–302° dec; ir and nmr spectra identical with those of authentic *dl*-α-phenylglycine with mp 300–302° dec (Aldrich Chemical Co.); [α]²⁵D (1.5 *M* is 4 *N* HCl) +41.9° corresponding to an enantiomeric purity of 62.6 ± 1.5%.[14]

Determination of the Enantiomeric Purity of Adduct 6b. As adduct **6b** does not complex with Eu(tfac)$_3$ and the basic hydrolysis to the lactone proceeds in very poor yield, adduct **6b** was converted to **10**. To a stirred solution of 0.060 g (0.19 mmol) of **6b** in 10 ml of dichloromethane cooled to 0° in an ice bath was added 1.0 molar equiv of PTAD (0.033 g) dissolved in 10 ml of dichloromethane. After 20 min the solvent was removed under vacuum and the residue was recrystallized twice from ether (27.6%): mp 156–157° dec; nmr ($CDCl_3$) δ 1.70 and 1.90 (s, 3 H each), 4.13 and 4.25 (AB doublets, J = 15.0 Hz, 1 H each), 5.56 (br s, 1 H), 7.30 (m, 10 H).

Upon the addition of 0.4 molar equiv of Eu(tfac)$_3$ to the nmr tube of adduct **10**, the resonance at δ 5.56 due to the hydrogen atom attached to the chiral center separated into two peaks ($\Delta\delta$ = 0.03 ppm). Integration of the two peaks indicated an enantiomeric purity of 64.2 ± 1.0%.

Conversion of 7a to 11a and Determination of the Enantiomeric Purity. To a stirred 0.1 *M* solution of 0.074 g (0.22 mmol) of **7a** in dichloromethane at room temperature was added 1.0 molar equiv (0.041 g) of PTAD dissolved in 2 ml of dichloromethane. After 2 hr the solvent was removed under vacuum and the product was recrystallized twice from ether (30.4%): mp 144–146° dec; nmr ($CDCl_3$) δ 1.72 and 2.18 (s, 3 H each), 4.21 and 4.53 (AB doublets, J = 18.0 Hz, 1 H each), 5.77 (s, 1 H), 7.36 (m, 10 H); mass spectrum *m/e* 486.074 (calcd for $C_{22}H_{19}ClN_4O_5S$, 486.076); [α]²⁵D −27.2°. Upon addition of 0.4 molar equiv of Eu(tfac)$_3$ to the nmr sample, the resonance of the proton at the newly formed chiral center (δ 5.77) separated into two peaks ($\Delta\delta$ = 0.06 ppm). Integration of the two peaks indicates an enantiomeric purity of 58.9 ± 0.9%.

Conversion of 7b to 11b and Determination of the Enantiomeric Purity of 11b. PTAD (0.0323 g, 0.18 mmol) was treated with 0.0573 g (0.18 mmol) of **7b** as described above. After recrystallization twice from ether, 0.0309 g (34.6%) of adduct **11b** was isolated: mp 176–177° dec; nmr ($CDCl_3$) δ 1.70 and 2.16 (s, 3 H each), 4.90 and 5.29 (AB doublets, J = 18.5 Hz, 1 H each), 5.86 (s, 1 H), 7.30 (m, 10 H); [α]²⁵D −44.0°. Upon the addition of 0.4 molar equiv of Eu(tfac)$_3$ to the nmr sample, the resonance at δ 5.86 due to the hydrogen atom at the newly formed chiral center split into two peaks ($\Delta\delta$ = 0.06 ppm). Expansion and integration of the peaks indicated an enantiomeric purity of 58.6 ± 0.9%.

Determination of Enantiomeric Purities as a Function of Reaction Temperature. The reaction of (−)-(*R*)-**5** with CSI was carried out at −30 ± 1° (25% ethanol, 25% glycerine, 50% ice temperature bath,[15] 30 ± 1° (water bath), and 61.2° (refluxing chloroform), and the adducts were isolated and their enantiomeric purities were determined as described above. The results are summarized in Table II.

In addition to adducts **6** and **7**, adduct **12** was formed in 2.8 and 8.5% at +30 and +61.2°, respectively: ir (CCl_4) 1760 (C=O), 1640 (C=C), 1415 and 1190 cm^{-1} (−SO_2−); nmr ($CDCl_3$) δ 1.82 (d, J = 0.7 Hz, 3 H), 2.09 (dd, J = 0.4 and 1.5 Hz, 3 H), 5.18 (q, J = 0.4 Hz, 1 H), 5.33 (m, 1 H). 5.38 (m, 1 H), and 7.34 (br s, 5 H); [α]²⁵D 0.0°. Ozonolysis of **12** in 2% pyridine–methylene chloride followed by glpc analysis on a 6 ft Carbowax 20M on Chromosorb W column indicated the absence of acetone and benzaldehyde.

Preparation of a 1:1 Mixture of (*E*)- and (*Z*)-13. Using the method of Hennion and Nelson,[16] 63 g (0.5 mol) of 3-methyl-1-pentyn-3-ol (Eastman Organic Chemicals) in 200 ml of ether was added to a stirred mixture of 167 ml of 12 *M* HCl, 37 g of calcium chloride, and 0.1 g of copper–bronze powder cooled to 0° in an ice bath. After 1 hr a dark oil had formed on top of the solution. This layer was decanted and washed twice with 25-ml portions of cold water and then with 25 ml of 5% sodium bicarbonate. The organic layer was dried (K_2CO_3) and distilled from potassium carbonate giving 3-chloro-3,5-dimethyl-1-hexyne: bp 55–56° (25 mm); ir (CCl_4) 2120 cm^{-1}; nmr ($CDCl_3$) δ 1.04 (d, J = 5.8 Hz, 6 H), 1.82 (s, 3 H), 1.86 (d, J = 5.0 Hz, 2 H), 2.00 (m, 1 H), 2.61 (s, 1 H). Reaction of 3-chloro-3,5-dimethyl-1-hexyne with styrene in the presence of potassium *tert*-butoxide using the method of Hartzler[17] gave a 31% yield of a 1:1 mixture of (*E*)- and (*Z*)-**13**. The excess styrene and 2-methyl-2-propanol were removed under vacuum. Attempts to distill the product at 0.05 mm resulted in extensive decomposition and polymerization. The product was purified by chromatography on a 1 × 12 in. column of silica gel using hexane as an eluent: ir (CCl_4) 2010 cm^{-1}; nmr ($CDCl_3$) (*E*)-**13** δ 0.89 (d, J = 5.5 Hz, 6 H), 1.49 (dd, J = 8.6, 5.2 Hz, 1 H), 1.68 (m, 1 H), 1.736 (s, 3 H), 1.86 (m, 3 H), 2.78 (dd, J = 8.2, 5.3 Hz, 1 H), 7.11 (s, 5 H); (*Z*)-**13** δ 0.85 (d, J = 5.5 Hz, 6 H), 1.52 (dd, J = 8.6, 5.2 Hz, 1 H), 1.62 (m, 1 H), 1.741 (s, 3 H), 1.80 (m, 3 H), 2.78 (dd, J = 8.2, 5.3 Hz, 1 H), 7.11 (s, 5 H).

Partial Hydroboration of the 1:1 Mixture of (*E*)- and (*Z*)-13 with Dicyclohexylborane. To 43 ml of 0.7 *M* borane (0.030 mol) in tetrahydrofuran at 0° was added 5.4 g (0.066 mol) of cyclohexene. The reaction mixture was stirred at 0° for 30 min and 10.5 g (0.050 mol) of the 1:1 mixture of (*E*)- and (*Z*)-**13** in 20 ml of tetrahydrofuran was rapidly added. The reaction mixture was stirred for 15 min and 50 ml of 10% sodium hydroxide and 14 ml of 30% hydrogen peroxide was added. The mixture was stirred for 30 min, poured into 200 ml of water, and was extracted twice with 100-ml portions of ether. The extract was dried ($MgSO_4$), the solvent was removed

(13) D. J. Pasto and C. J. Johnson, "Organic Structure Determination," Prentice-Hall, Englewood Cliffs, N. J., 1969, p 333.

(14) The highest rotation reported for α-phenylglycine is 166.9° (1.5 *M* in 16% HCl): P. A. Levene and R. E. Steiger, *J. Biol. Chem.*, **86**, 703, 709 (1930). The rotation is not a function of the acid concentration.

(15) "International Critical Tables," Vol. I, Maple Press, York, Pa., 1926, p 62.

(16) G. F. Hennion and K. W. Nelson, *J. Amer. Chem. Soc.*, **79**, 2142 (1957).

(17) H. D. Hartzler, *J. Amer. Chem. Soc.*, **83**, 4990 (1961).

Table III. Chemical Shifts of Protons (δ) in Compounds **14–21**

Compd	H^1	H^2	H^3	H^4	H^5	H^6	H^7	Aromatic H
14	1.30	0.79 (d, J = 6.5 Hz)	2.82 (m)	2.54 (d, J = 6.5 Hz)		6.54	4.37 (d, J = 2.0 Hz)	7.17
15	2.14	0.47 (d, J = 6.5 Hz)	1.70 (m)	1.42 (d, J = 6.5 Hz)		6.44	4.32 (d, J = 2.5 Hz)	7.23
16	1.94	0.72 (d, J = 6.5 Hz)	2.80 (m)	2.74 (d, J = 7.0 Hz)	5.28	5.02	5.43 (t, J = 1.2 Hz)	7.20
17	2.33	0.62 (d, J = 6.5 Hz)	2.50 (m)	2.21 (d, J = 7.5 Hz)	5.23	5.02	5.41 (t, J = 1.2 Hz)	7.20
18	1.49	0.97 (d, J = 6.6 Hz)	*a*	2.90 (d, J = 6.2 Hz)		5.10 (d, J = 2.1 Hz)	6.64 (t, J = 2.1 Hz)	7.22
19	2.24	0.90 (d, J = 6.6 Hz)	*a*	2.67 (d, J = 6.6 Hz)		5.43 (d, J = 2.1 Hz)	6.10 (t, J = 2.1 Hz)	7.32
20	2.24	1.04 (d, J = 6.2 Hz)	*a*	2.92 (d, J = 6.6 Hz)	5.45	5.10 (d, J = 2.1 Hz)	6.09 (t, J = 2.1 Hz)	7.32
21	2.49	0.96 (d, J = 6.2 Hz)	*a*	2.44 (d, J = 6.5 Hz)	5.44	5.04 (d, J = 2.1 Hz)	6.10 (t, J = 2.1 Hz)	7.29

[a] Could not be unambiguously assigned.

under reduced pressure, and the residue was chromatographed on Florisil. Elution with Skelly Solve B gave 4.7 g of **10** enriched in the *E* isomer. The above procedure was repeated using 16 ml of 0.7 *M* borane, 2.42 g of cyclohexene, and the 4.7 g of **13** enriched in the *E* isomer. Final chromatography on Florisil gave 1.85 g of 81.3 ± 1.5% (*E*)-**13** and 18.7 ± 1.5% (*Z*)-**13** as determined by integration of the nmr spectrum.

Reaction of a Mixture of 81.3% (*E*)- and (*Z*)-13 with CSI. The reaction of CSI with an 81.3% (*E*)- and 18.7% (*Z*)-**13** mixture in methylene chloride at 0° was carried out as described above. Chromatographic separation on a 0.75 × 20 in. column of silica gel with elution with 5% ether–hexane gave fractions containing a mixture of **14** (58.2%) and **15** (41.8%) (ir (CCl_4) 1753 (C=O), 1600 (C=C), 1415 and 1185 cm^{-1} ($-SO_2-$); nmr, see Table III) followed by fractions containing a mixture of **16** (56.0%) and **17** (44.0%) (ir (CCl_4) 1752 (C=O), 1630 (C=C), 1411 and 1186 cm^{-1} ($-SO_2-$); nmr, see Table III). Elution with 10% ether–hexane produced fractions containing a mixture of **18** (66.3%) and **19** (33.7%) (ir (CCl_4) 1610 (C=C), 1579 (C=N), 1380 and 1176 cm^{-1} ($-SO_2-$); nmr, see Table III) followed by fractions containing **20** (66.4%) and **21** (33.6%) (ir (CCl_4) 1620 (C=C), 1575 (C=N), 1380 and 1175 cm^{-1} ($-SO_2-$); nmr, see Table III). Integration of the nmr spectrum of the initial reaction mixture containing **14–21** indicated the presence of 13.5% **14** and **15**, 43.9% **16** and **17**, 10.5% **18** and **19**, and 32.1% **20** and **21**.

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