Registry No. **1a**, 89909-33-1; **1b**, 89909-34-2; **1c**, 16801-14-2; **2a**, 81316-37-2; **2b**, 57699-36-2; **2c**, 57699-30-6; **3a**, 81316-44-1; **3b**, 81316-43-0; **5**, 89909-36-4; CuCN, 544-92-3; O_2, 7782-44-7; *p*-$MeOC_6H_4C(CH_3)(OH)CN$, 69813-75-8; MeOH, 67-56-1; *p*-$MeOC_6H_4\dot{C}CN$, 89909-35-3; DCN, 3029-30-9; TMB, 366-29-0; TEA, 121-44-8; TME, 563-79-1; $DCN^{-}\cdot$, 68331-38-4; $TMB^{+}\cdot$, 21296-82-2; DMHD, 764-13-6; 1,2,4-trimethoxybenzene, 135-77-3; 1,4-dibromonaphthalene, 83-53-4.

Stereoselective Addition Reactions of Allylic Sulfides to Acetylenic Esters: *E/Z* Stereochemical Variations by Lewis Acid

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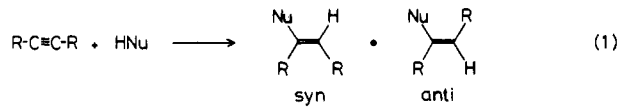
The Lewis acid catalyzed addition reactions of allylic sulfides to methyl propiolate (MP) and dimethyl acetylenedicarboxylate (DMAD) have been investigated. The stereochemical outcome is considerably influenced by the Lewis acid. While the $AlCl_3$-catalyzed reactions of MP afforded *E* adducts **2** as the major products, the use of $ZnCl_2$ resulted in the inversion of stereoselectivity to give *Z* adducts **3** mainly. The reactions of DMAD showed the similar change in the stereoselectivity, though these reactions had a higher trend of *E* selectivity. The stereochemical assignments of these adducts were made on the basis of the spectroscopic data as well as the chemical transformations. The reasonable reaction mechanism and the remarkable stereochemical effects of a Lewis acid are discussed in detail.

The stereochemistry of nucleophilic additions to acetylenic compounds is an object of current attention.[1] The theoretical studies by Houk et al.[2] and Dykstra et al.[3] have predicted on the basis of ab initio calculations that nucleophilic additions to unactivated acetylenes proceed via a single transition state to give anti products, and this is observed experimentally.[4] In contrast, nucleophilic additions to activated acetylenes are known to give variable stereochemical results, i.e., syn and anti adducts (eq 1),



(1)

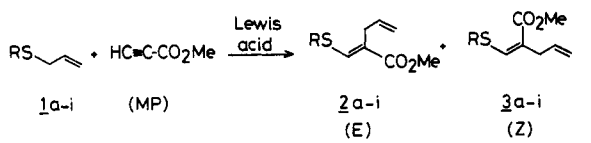
depending on the substituents, nucleophiles, and reaction media.[1,4-8] These are also compatible with the recent ab initio calculations by Caramella and Houk,[9] which indicate that the vinyl anions formed by nucleophilic addition to acetylenes are bent but the barrier to inversion is considerably lowered by electron-withdrawing substituents. On the other hand, less attention has been paid to the stereochemical effect of the Lewis acids, whereas the Lewis acids have been often employed to activate the acetylenic esters in their addition reactions.[10,11]

Table I. Lewis Acid Catalyzed Addition Reaction of Allylic Sulfides 1 with Methyl Propiolate (MP)[a]

entry	allylic sulfide 1, R =	Lewis acid	% yield[b] 2 + 3	*E:Z* ratio[c] (2:3)
1	**1a**, C_6H_5	$AlCl_3$	71	72:28
2		$FeCl_3$	45	80:20
3		$TiCl_4$	69	80:20
4		$EtAlCl_2$	51	67:33
5		$BF_3{\cdot}Et_2O$	77	65:35
6		$SnCl_4$	20[d]	50:50
7		$ZnCl_2$	92	3:97
8	**1b**, cyclohexyl	$AlCl_3$	80	90:10
9		$ZnCl_2$	94	29:71
10	**1c**, $CH_2CH{=}CH_2$	$AlCl_3$	73	78:22
11		$ZnCl_2$	95	10:90
12	**1d**, $CH_2CO_2CH_3$	$AlCl_3$	71	77:23
13		$ZnCl_2$	80	>98Z
14	**1e**, *n*-C_5H_{11}	$AlCl_3$	77	80:20
15	**1f**, CH_2Ph	$AlCl_3$	73	86:14
16	**1g**, CH_2CH_2OH	$AlCl_3$	complex mixture	
17	**1h**, CH_2CH_2OAc	$AlCl_3$	41	71:29
18	**1i**, $CH_2CH_2CH_2Br$	$AlCl_3$	83	79:21

[a] All reactions were carried out at 25 °C in methylene chloride by using 1.0 equiv of allylic sulfide 1, 1.2 equiv of methyl propiolate, and 1.1 equiv of the Lewis acid. Reactions using $ZnCl_2$ were carried out without the solvent. [b] Isolated yields. [c] The olefin ratio was determined by a combination of GLC and ^1H NMR analyses. [d] The deallylation products (**7**) were also isolated in 23% yield.

We previously reported a novel $AlCl_3$-catalyzed reaction of methyl propiolate and allylic sulfides to produce the 1:1 adducts with syn (i.e., *E*) stereoselectivity (see eq 2).[12] It



(2)

1a-i (MP) 2a-i (E) 3a-i (Z)

(1) Houk, K. N.; Strozier, R. W.; Rozeboom, M. D.; Nagase, S. *J. Am. Chem. Soc.* **1982**, *104*, 323 and references cited therein.
(2) Strozier, R. W.; Caramella, P.; Houk, K. N. *J. Am. Chem. Soc.* **1979**, *101*, 1340.
(3) Dykstra, C. E.; Arduengo, J. E.; Fukunaga, T. *J. Am. Chem. Soc.* **1978**, *100*, 6007.
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(9) Caramella, P.; Houk, K. N. *Tetrahedron Lett.* **1981**, *22*, 819.
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(11) Medici, A.; Fogagnolo, M.; Pedrini, P.; Dondoni, A. *J. Org. Chem.* **1982**, *47*, 3844.

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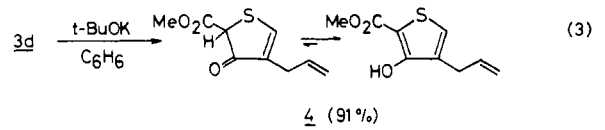
is now found that the use of different Lewis acids as the catalyst in this reaction causes a dramatic change in the stereoselectivity. In this paper we describe the full details of this work including the reasonable mechanism, and the unique stereochemical effects of Lewis acids are discussed on the basis of the acid strength.

Results and Discussion

Reactions with Methyl Propiolate (MP). While only a sluggish reaction took place between methyl propiolate (MP) and allyl phenyl sulfide (**1a**) at the elevated temperature (200 °C, neat; <4%), producing a large amount of polymeric substances, the use of $AlCl_3$ as a catalyst remarkably accelerated the reaction and led to the smooth formation of the 1:1 adducts even under the mild conditions. Thus, treatment of **1a** with MP in benzene at room temperature in the presence of $AlCl_3$ gave a mixture of (*E*)- and (*Z*)-methyl 2-allyl-3-(phenylthio)acrylates **2a** and **3a** in 3:1 ratio (eq 2; Table I, entry 1). The optimal yield of the reaction was obtained by using a slight excess of $AlCl_3$, while the olefin ratio was not affected by the amount of the Lewis acid used. Table I reveals that the reaction proceeds equally well with $AlCl_3$ for the substrates bearing various functional groups with *E* stereoselectivity. The reaction of alcohol **1g** led to a complex mixture (entry 16), but its acetate **1h** gave the corresponding adducts in moderate yield (entry 17).

The reaction was also catalyzed by the other commonly used Lewis acids, but the stereochemical outcome was subject to considerable influences by changing the Lewis acid catalyst (Table I, entries 1–7). It is most interesting to note that the *E* stereoselectivity obtained with a strong Lewis acid such as $AlCl_3$ diminishes with decrease of the acidity of Lewis acids,[13,14] and finally a complete inversion of stereoselectivity is observed with $ZnCl_2$, a weak Lewis acid. Notably the $ZnCl_2$-catalyzed reactions of **1a** (entry 7) and **1d** (entry 13) proceeded almost stereospecifically to give the anti (i.e., *Z*) adducts.

The structural assignments of these products were made on the basis of elemental analyses and mass, IR, and ^1H NMR spectra, which are summarized in Table III, (supplementary material). The olefin ratio was determined by GLC and ^1H NMR spectroscopy with the aid of the characteristic chemical shift of the β-vinyl proton of trisubstituted olefins. The *E* isomers **2**[15] were characterized by the downfield absorption (δ 7.3–7.8) compared to that of *Z* isomers **3** (δ 6.5–6.9).[16] The stereochemical assignment was further confirmed by the chemical conversions (vide infra). For example, treatment of **3d** with *t*-BuOK in benzene afforded a high yield of the Dieckmann condensation product **4** (eq 3), while its *E* isomer **2d** was recovered unchanged from the same treatment.



(3)

4 (91%)

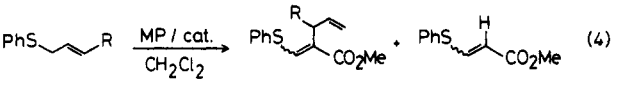
(12) Hayakawa, K.; Kamikawaji, Y.; Kanematsu, K. *Tetrahedron Lett.* **1982**, *23*, 2171.
(13) House, H. O. "Modern Synthetic Reactions"; W. A. Benjamin: Los Angeles, CA, 1972.
(14) Susz, B. P. *Bull. Soc. Chim. Fr.* **1965**, *2671*.
(15) The pure (*E*)-**2a** was obtained as follows; hydrolysis (KOH/aqueous CH_3OH) of a mixture of **2a** and **3a** (80:20) and the recrystallization from *n*-hexane gave the pure *E* acid (mp 74–74.5 °C), th esterification (diazomethane/Et_2O) of which afforded **2a** in the pure form.
(16) Isobe, K.; Fuse, M.; Kosugi, H.; Hagiwara, H.; Uda, H. *Chem. Lett.* **1979**, *785*.

Table II. $AlCl_3$- and $ZnCl_2$-Catalyzed Addition Reaction of Allylic Sulfides 1 with Dimethyl Acetylenedicarboxylate (DMAD)[a]

entry	allylic sulfide 1, R =	Lewis acid	% yield[b] 13	% yield[b] 14	E:Z ratio (13:14)
1	**1a**, C_6H_5	$AlCl_3$	39	11	78:22
2		$ZnCl_2$	20	30	40:60
3	**1b**, cyclohexyl	$AlCl_3$	80	8	91:9
4		$ZnCl_2$	63	35	64:36
5	**1c**, $CH_2CH{=}CH_2$	$AlCl_3$	61	6	91:9
6		$ZnCl_2$	31	63	33:67
7	**1d**, $CH_2CO_2CH_3$	$AlCl_3$	69	9	88:12
8		$ZnCl_2$	22	34	39:61
9	**1e**, *n*-C_5H_{11}	$AlCl_3$	71	7	91:9

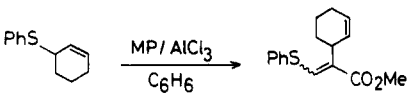
[a] The reactions of allylic sulfide 1 (1 equiv) and DMAD (1 equiv) were carried out at 25 °C in benzene when $AlCl_3$ (1.3 equiv) was used or in methylene chloride when $ZnCl_2$ (1 equiv) was used. [b] The stereoisomers of products were separated chromatographically in all cases, and the yields given here are the isolated yields.

The reaction described above, however, has some limitations in scope. Introduction of substituents onto the allylic moiety of **1** like **5** and **8** substantially suppressed the formation of the adducts (**6** and **9**, respectively), and instead a considerable amount of deallylation product **7** was formed (eq 4 and 5), though the product ratio varied



(4)

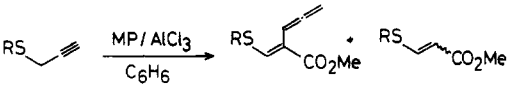
5	cat.	6 (E/Z)	7 (E/Z)
a, R = Me	$AlCl_3$	15% (54:46)	51% (50:50)
	$BF_3{\cdot}Et_2O$	32% (33:67)	35% (40:60)
	$ZnCl_2$	33% (5:95)	32% (8:92)
b, R = Ph	$AlCl_3$	none	72% (60:40)



(5)

8 9 (7%) 7 (67%)

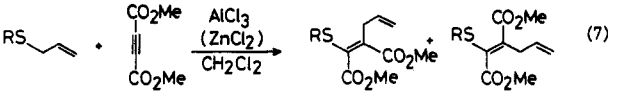
with the Lewis acids used. The weaker Lewis acid gave a greater amount of addition products. The propargyl sulfides **10** and MP underwent the similar reaction in the presence of $AlCl_3$ to give the allenic products **11** again together with the corresponding dealkylation products **12** (eq 6).



(6)

10		11	12 (=7)
a	R = Ph	a (25%)	a (25%)
b	R = cyclohexyl	b (38%)	b (19%)

Reactions with Dimethyl Acetylenedicarboxylate (DMAD). Dimethyl acetylenedicarboxylate (DMAD) was also found to react smoothly with various allylic sulfides **1a–e** in the presence of the Lewis acid catalyst (eq 7). The

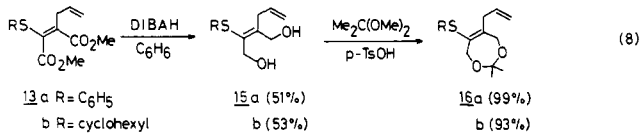


(7)

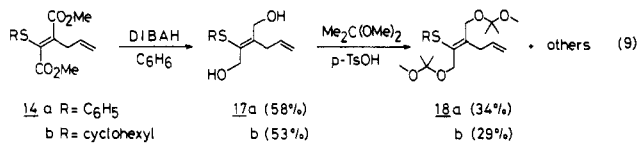
1a-e (DMAD) 13a-e (E) 14a-e (Z)

results are summarized in Table II, in which $AlCl_3$ and $ZnCl_2$ are used as the representative Lewis acid. As in the case of MP, the inversion of stereoselectivity was observed between $AlCl_3$- and $ZnCl_2$-catalyzed reactions, although the reactions of DMAD generally showed a higher trend of *E* selectivity compared to those of MP.

In these cases, each isomer of products could be easily isolated by column chromatography. In the ^1H NMR spectra (Table III, supplementary material) the chemical shift of the diallylic protons is diagnostically different between products **13** and **14**. That signal (d, 2 H) of *Z* isomers **14** appeared at the higher field (δ 3.05–3.14) compared to that of *E* isomers **13** (δ 3.25–3.36), presumably due to the shielding effect of the cis carbomethoxy group. However, the spectral differences between these two isomers were relatively small and less informative for the stereochemical assignments. Therefore, the stereochemistry of the tetrasubstituted double bonds of DMAD adducts was confirmatively determined by the following chemical transformations (eq 8 and 9). Although the



13 a R = C_6H_5 15 a (51%) 16 a (99%)
b R = cyclohexyl b (53%) b (93%)

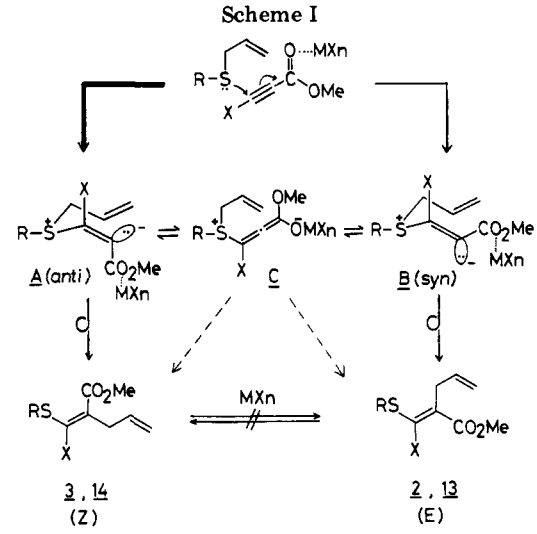


14 a R = C_6H_5 17a (58%) 18a (34%)
b R = cyclohexyl b (53%) b (29%)

$LiAlH_4$ reduction led to a complex mixture of several minor products, the reduction of both isomers **13a,b** and **14a,b** with DIBAH (4 equiv) in benzene afforded the corresponding diols **15a,b** and **17a,b**, respectively. While the treatment of **15a,b** with excess of 2,2-dimethoxypropane in the presence of *p*-TsOH gave almost quantitatively the cyclic ketals **16a,b** (eq 8), the same treatment of **17a,b** gave the acyclic diketals **18a,b** along with a mixture of monoketals (eq 9). These results clearly indicated the *E* configuration of **13** and the *Z* configuration of **14**.

Reaction Mechanism. It is most noteworthy that the *E*/*Z* ratio of products in the above reactions changes remarkably, depending on the Lewis acid employed. It was confirmed that no *E*/*Z* stereoequilibration of each product occurred under the reaction conditions. For example, treatment of **2a**(*E*) with 1 equiv of $ZnCl_2$ (CH_2Cl_2, 1 week), and **3a** (>95% *Z*) with 1 equiv of $AlCl_3$ (benzene, 2 days) caused no isomerizations and resulted in the recovery of unchanged **2a** and **3a**, respectively. Therefore, the above results can be most reasonably explained by a stepwise mechanism as shown in Scheme I. As for acetylenes,[1] nucleophilic addition of allylic sulfides **1** to the acetylenic esters (MP and DMAD) activated by Lewis acid would first give kinetically preferred anti zwitterion (A), which, however, would equilibrate with the more stable zwitterion B presumably via the linear zwitterion C[9] when the barrier to inversion is sufficiently lowered, although a direct formation of B is not completely precluded. The zwitterionic intermediates A and B thus formed undergo the formal ionic [3.3]-sigmatropic rearrangements to give (**3** and **14**) and *E* products (**2** and **13**), respectively. Considering the geometrical difficulty of the conversion of A to *Z* products, the rearrangement most probably proceeds via a tight ion pair. This is also suggested by the fact that introduction of a cation-stabilizing substituent on the allylic sulfides **5** and **8** increases the formation of deallylation products

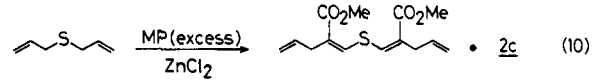
Scheme I



7 at the cost of the [3.3]-sigmatropic rearrangement.

The remarkable stereochemical effects of Lewis acid observed in the above reactions, therefore, should be attributed to its influences on the equilibration of the zwitterionic intermediates. In the reaction using a weak Lewis acid such as $ZnCl_2$, the initially formed anti zwitterion A undergoes the rearrangement to *Z* products faster than the inversion to B since the barrier seems to be still high.[18] However, when the acetylenic esters are activated by complexation with more active Lewis acid, this barrier to inversion would be more effectively lowered[9] so that the equilibration of these zwitterions ultimately leads to the formation of greater amount of *E* products. In accord with this, the reaction of **1a** and MP at the lower temperature (−53 °C) gave the more *Z* product compared to that at room temperature (see Table I); ex., with $TiCl_4$ (68%, **2a/3a** (*E*/*Z*) = 57:43) and with $SnCl_4$ (32%, **2a/3a** = 15:85). The above results are in good accordance with Houk's theoretical predictions.[1] The higher trend of *E* selectivity in the reactions with DMAD can be attributed to the further stabilization of syn zwitterion B due to the cyclic chelate formation by coordination of both ester groups to the Lewis acid.

The reaction of diallyl sulfide **1c** and MP provided an interesting result supporting the above rationalization. While the treatment of **1c** with excess of MP (2–3 equiv) in the presence of $AlCl_3$ afforded only a *E*/*Z* mixture of the 1:1 adducts (**2c/3c** = 78:22) as shown in Table I (entry 10), the same reaction using $ZnCl_2$ as the catalyst gave the 1:2 *Z*,*Z* adduct **19** (70%) along with the 1:1 *E* adduct (**2c**) (8%) (eq 10). This indicates that $AlCl_3$ complexes strongly



1c 19 (70 %) (8 %)

with the initially formed 1:1 adducts to deactivate the second allylic sulfide moiety for the next reaction.[17] It is also interesting to note that only the 1:1 *Z* adduct **3c** seems to react with the second mole of MP in the presence of

(17) It is reported that $AlCl_3$ complexes preferentially with vinylic esters rather than acetylenic esters: Snider, B. B.; Rodini, D. J.; Conn, R. S. E.; Sealfon, S. *J. Am. Chem. Soc.* **1979**, *101*, 5283.

(18) A referee suggests another possibility that a preference for the formation of the *Z* isomers with the use of soft Lewis acid like $ZnCl_2$ could be associated with an interaction of this Lewis acid with the soft sulfur of the sulfide as well as the ester carbonyl oxygen causing a cyclic interaction.

$ZnCl_2$. This was confirmed by the reaction using 1:1 adducts (**2c** and **3c**). Treatment of a mixture of **2c** and **3c** (78:22) obtained by the $AlCl_3$-catalyzed reaction with excess of MP in the presence of $ZnCl_2$ afforded **19** (18%) and recovered pure **2c** (70%).

In conclusion, we have demonstrated that the allylic sulfides and acetylenic estes (MP and DMAD) can smoothly undergo the novel addition reactions involving the allylic rearrangement in the presence of the Lewis acid. The stereoselectivity of these reactions is strongly influenced by the Lewis acid and can be controlled by choosing an appropriate Lewis acid catalyst. The synthetic utility of these unique reactions is currently under investigation.

Experimental Section

The melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectra were determined on a JASCO IR A-1 infrared spectrophotometer and reported in reciprocal centrimeters. ^1H nuclear magnetic resonance (^1H NMR) spectra were taken in deuteriochloroform on a JEOL PS-100 (100 MHz) spectrometer. Chemical shifts are reported in δ units (parts per million downfield from tetramethylsilane). Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Couplng constants are reported in herts. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were obtained on a JEOL FX-100 spectrometer. Chemical shifts are reported in δ units. Mass spectra (MS) were determined on a JEOL D-300 spectrometer equipped with a JMA 3100/3500 at an ionization voltage of 70 eV. Data are reported as m/e (relative intensity) values.

General Procedure for Lewis Acid Catalyzed Reactions. With $AlCl_3$. A mixture of methyl propiolat (MP) (202 mg, 2.6 mmol) or dimethyl acetylenedicarboxylate (DMAD) (284 mg, 2.0 mmol) and $AlCl_3$ (347 mg, 2.6 mmol) in dry benzene or methylene chloride (2 mL) was stirred at room temperature for 20 min, and then an appropriate allylic sulfide (2.0 mmol) was added dropwise under ice-cooling. The resulting solution was stirred at room temperature until the allylic sulfide was completely consumed (ca. 2 h). The reaction mixture was quenched with ice–water and extracted with ether. The combined organic phases were dried over Na_2SO_4, evaporated in vacuo, and chromatographed on a silica gel column by using *n*-hexane–ethyl acetate as eluent to give the products as an oil. The reactions with other Lewis acids were performed in the same way. The results are summarized in Tables I and II.

Compound 2a: IR (neat) 1710, 1225 cm^{-1}; ^1H NMR δ 3.17 (dm, J = 6.0 Hz, 2 H), 3.71 (s, 3 H), 4.95–5.25 (m, 2 H), 5.60–6.05 (m, 1 H), 7.72 (s, 1 H), 7.20–7.50 (m, 5 H); MS, m/e (relative intensity) 234 (M^+, 100), 125 (58). Anal. Calcd for $C_{13}H_{14}O_2S$: C, 66.64; H, 6.02. Found C, 66.66; H, 6.00.

Compound 3a: IR (neat) 1710, 1225 cm^{-1}; ^1H NMR δ 3.06 (dm, J = 6.0 Hz, 2 H), 3.88 (s, 3 H), 4.95–5.25 (m, 2 H), 5.60–6.05 (m, 1 H), 6.98 (s, 1 H), 7.20–7.50 (m, 5 H).

The spectroscopic data of other products are given in Table III (supplementary material section).

With $ZnCl_2$. To a stirred mixture of an allylic sulfide (2.0 mmol) and $ZnCl_2$ (275 mg, 2.0 mmol) was added dropwise MP (202 mg, 2.4 mmol) or DMAD (284 mg, 2.0 mmol). The resulting mixture was stirred at room temperature until the allylic sulfide was completely consumed. After water was added, the reaction mixture was extracted with ether, evaporated, and chromatographed to give the products. When the reaction was carried out in methylene chloride, a much longer reaction time was needed to complete the reaction. The results are summarized in Tables I and II.

2-Carbomethoxy-3-hydroxy-4-allylthiophene (4). A mixture of **3d** (100 mg, 0.43 mmol) and potassium *tert*-butoxide (150 mg, 1.3 mmol) in dry benzene (3 mL) was stirred at room temperature for 20 h. The reaction mixture was diluted with aqueous 10% HCl and extracted with ether. The combined organic phases were dried over Na_2SO_4, evaporated under the reduced pressure, and chromatographed on silica gel with *n*-hexane–ethyl acetate (7:1) as an eluent to give **4** (78 mg, 91%) as a colorless oil: IR (neat) 3300, 1665 cm^{-1}; ^1H NMR δ 3.29 (br d, J = 6.0 Hz, 2 H), 3.90 (s, 3 H), 4.90–5.33 (m, 2 H), 5.63–6.43 (m, 1 H), 7.07 (s, 1 H), 9.33 (s, 1 H, D_2O exchangeable).

(*E*)-2-(Phenylthio)-3-allyl-2-butene-1,4-diol (15a). General Procedure for DIBAH Reduction. To a solution of **13a** (300 mg, 1.03 mmol) in dry benzene (5 mL) was added a hexane solution of diisobutylaluminium hydride (2.3 mmol) at room temperature. The resulting solution was stirred under Ar for 20 h and then quenched with aqueous 10% HCl solution. The organic phase was extracted with ether, dried over Na_2SO_4, and concentrated in vacuo. The residual oil was chromatographed on silica gel with *n*-hexane–ethyl acetate (2:1) to give **15a** (90 mg, 51%) as a colorless oil: IR (neat) 3330, 1000 cm^{-1}; ^1H NMR δ 2.77 (br s, 2 H, D_2O exchangeable), 3.35 (dm, J = 6.0 Hz, 2 H), 4.25 (s, 2 H), 4.30 (s, 2 H), 4.87–5.35 (m, 2 H), 5.48–6.13 (m, 1 H), 7.10–7.50 (m, 5 H).

(*E*)-2-(Cyclohexylthio)-3-allyl-2-butene-1,4-diol (15b). The similar reduction of **13b** (244 mg, 0.82 mmol) gave **15b** (106 mg, 53%) as a colorless oil: IR (heat) 3350, 1000 cm^{-1}; ^1H NMR δ 1.05–2.30 (m, 10 H), 2.76 (br s, 2 H, D_2O exchangeable), 2.80–3.13 (m, 1 H), 3.29 (dm, J = 6.0 Hz, 2 H), 4.19 (s, 2 H), 4.32 (s, 2 H), 4.80–5.30 (m, 2 H), 5.45–6.20 (m, 1 H).

(*Z*)-2-(Phenylthio)-3-allyl-2-butene-1,4-diol (17a). The similar reduction of **14a** (300 mg, 1.03 mmol) gave **17a** (102 mg, 58%) as a colorless oil: IR (neat) 3330, 1000 cm^{-1}; ^1H NMR δ 1.92 (br s, 2 H, D_2O exchangeable), 3.22 (dm, J = 6.0 Hz, 2 H), 4.18 (s, 2 H), 4.47 (s, 2 H), 4.87–5.35 (m, 2 H), 5.55–6.28 (m, 1 H), 7.10–7.40 (m, 5 H).

(*Z*)-2-(Cyclohexylthio)-3-allyl-2-butene-1,4-diol (17b). The similar reduction of **14b** (200 mg, 0.67 mmol) gave **17b** (87 mg, 54%) as a colorless oil: IR (neat) 3350, 1005 cm^{-1}; ^1H NMR δ 1.05–2.03 (m, 10 H), 2.28 (br s, 2 H, D_2O exchangeable), 2.70–3.13 (m, 1 H), 3.06 (dm, J = 6.0 Hz, 2 H), 4.21 (s, 2 H), 4.40 (s, 2 H), 4.82–5.28 (m, 2 H), 5.47–6.20 (m, 1 H).

2,2-Dimethyl-5-(phenylthio)-6-allyl-4,7-dihydro-1,3-dioxepin (16a). A mixture of **15a** (125 mg, 0.53 mmol) and *p*-toluenesulfonic acid monohydrate (5 mg) in 4 mL of 2,2-dimethoxypropane was stirred at 0 °C for 1 h, and then aqueous K_2CO_3 solution (10 mL) was added. The organic phase was extracted with ether, dried over Na_2SO_4, evaporated in vacuo, and chromatographed on a short silica gel column with *n*-hexane–ethyl acetate (2:1) to give **16a** (144 mg, 99%) as a colorless oil: IR (neat) 1235, 1095 cm^{-1}; ^1H NMR δ 1.41 (s, 6 H), 3.08 (dm, J = 6.0 Hz, 2 H), 4.27 (s, 2 H), 4.30 (s, 2 H), 4.81–5.29 (m, 2 H), 5.40–6.05 (m, 1 H), 7.10–7.40 (m, 5 H); MS, m/e (relative intensity) 276 (M^+, 100), 190 (14), 149 (17), 123 (17), 110 (63), 109 (37).

2,2-Dimethyl-5-(cyclohexylthio)-6-allyl-4,7-dihydro-1,3-dioxepin (16b). The same treatment of **15b** (155 mg, 0.64 mmol) as above gave **16b** (168 mg, 93%) as a colorless oil: IR (neat) 1235, 1090 cm^{-1}; ^1H NMR δ 1.37 (s, 6 H), 1.05–2.20 (m, 10 H), 2.66–2.92 (m, 1 H), 3.12 (dm, J = 6.0 Hz, 2 H), 4.25 (s, 2 H), 4.31 (s, 2 H), 4.76–5.25 (m, 2 H), 5.37–6.03 (m, 1 H).

(*Z*)-7-Allyl-3,3,10,10-tetramethyl-6-(phenylthio)-2,4,9,11-tetraoxa-6-dodecene (18a). The similar treatment of **17a** (240 mg, 1.02 mmol) gave **18a** (131 mg, 34%) as the least polar product and unreacted **17a** (48 mg, 20%). **18a**, colorless oil: IR (neat) 1225, 1035 cm^{-1}; ^1H NMR δ 1.25 (s, 6 H), 1.35 (s, 6 H), 3.10 (s, 3 H), 3.18 (s, 3 H), 3.21 (dm, J = 6.0 Hz, 2 H), 4.03 (s, 2 H), 4.30 (s, 2 H), 4.85–5.30 (m, 2 H), 5.48–6.13 (m, 1 H), 7.10–7.40 (m, 5 H).

(*Z*)-7-Allyl-3,3,10,10-tetramethyl-6-(cyclohexylthio)-2,4,9,11-tetraoxa-6-dodecene (18b). The similar treatment of **17b** (175 mg, 0.72 mmol) gave **18b** (81 mg, 29%) as the least polar product: IR (neat) 1230, 1035 cm^{-1}; ^1H NMR δ 1.29 (s, 6 H), 1.35 (s, 6 H), 1.10–2.23 (m, 10 H), 2.67–2.95 (m, 1 H), 3.17 (s, 3 H), 3.24 (s, 3 H), 3.26 (dm, J = 6.0 Hz, 2 H), 3.99 (s, 2 H), 4.17 (s, 2 H), 4.83–5.26 (m, 2 H), 5.36–6.02 (m, 1 H).

Dimethyl (2*Z*,2′*Z*)-2,2′-Diallyl-3,3′-thiodiacrylate (19). A mixture of diallyl sulfide (**1c**) (190 μL, 1.47 mmol), methyl propiolate (232 μL, 3.74 mmol), and $ZnCl_2$ (220 mg, 1.47 mmol) was stirred at room temperature for 20 h, and then aqueous 10% HCl (10 mL) was added. The organic phase was extracted with ether, dried over Na_2SO_4, and concentrated in vacuo. The residue was chromatographed on silica gel with *n*-hexane–ethyl acetate (7:1) to give in the order of elution **2c** (24 mg, 8%) and **19** (290 mg, 70%) as colorless needles, mp 68–69 °C (*n*-hexane–ether): IR (Nujol) 1700, 1240 cm^{-1}; ^1H NMR δ 3.10 (dm, J = 6.0 Hz, 4 H),

3.82 (s, 6 H), 4.80–5.35 (m, 4 H), 5.50–6.27 (m, 2 H), 6.85 (s, 2 H); MS, m/e 282 (M^+). Anal. Calcd for $C_{14}H_{18}O_4S$: C, 59.55; H, 6.43. Found: C, 59.55; H, 6.37.

Registry No. **1a**, 5296-64-0; **1b**, 53439-63-7; **1c**, 592-88-1; **1d**, 72867-23-3; **1e**, 3393-13-3; **1f**, 6937-97-9; **1g**, 58965-04-1; **1h**, 82937-11-9; **1i**, 64871-50-7; **2a**, 82937-12-0; **2b**, 82937-15-3; **2c**, 82937-17-5; **2d**, 82937-21-1; **2e**, 82937-14-2; **2f**, 82937-19-7; **2h**, 82937-10-8; **2i**, 82937-24-4; **3a**, 82937-13-1; **3b**, 82937-16-4; **3c**, 82937-18-6; **3d**, 82937-22-2; **3e**, 83037-51-8; **3f**, 82937-20-0; **3h**, 82937-23-3; **3i**, 82937-25-5; **4**, 89889-98-5; **13a**, 89889-88-3; **13b**, 89889-90-7; **13c**, 89889-92-9; **13d**, 89889-94-1; **13e**, 89889-96-3; **14a**, 89889-89-4; **14b**, 89889-91-8; **14c**, 89889-93-0; **14d**, 89889-95-2; **14e**, 89889-97-4; **15a**, 89889-99-6; **15b**, 89890-00-6; **16a**, 89890-03-9; **16b**, 89890-04-0; **17a**, 89890-01-7; **17b**, 89890-02-8; **18a**, 89890-05-1; **18b**, 89890-06-2; **19**, 89890-07-3; MP, 922-67-8; DMAD, 762-42-5; $AlCl_3$, 7446-70-0; $FeCl_3$, 7705-08-0; $TiCl_4$, 7550-45-0; $EtAlCl_2$, 563-43-9; $BF_3{\cdot}Et_2O$, 109-63-7; $SnCl_4$, 7646-78-8; $ZnCl_2$, 7646-85-7; 2,2-dimethoxypropane, 77-76-9.

Supplementary Material Available: The spectroscopic data of compounds **2a–i**, **3a–i**, **6(E)**, **6(Z)**, **11a,b** **13a–e**, and **14a–e** (Table III) (4 pages). Ordering information is given on any current masthead page.

Field and Resonance Substituent Constants for Aromatic Derivatives: Limitations of Swain's Revised *F* and *R* Constants for Predicting Aromatic Substituent Effects

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Two key limitations of Swain's revised F and R constants are pointed out. First, they provide an incomplete separation of field and resonance effects. Second, the range of precise applicability of R is restricted to systems following σ or σ^+ while it fails badly for systems following σ^-. The first limitation is attributed to inappropriate criteria used to separate field and resonance effects while the second is more fundamental. It reflects the fact that no single resonance scale can predict the whole range of aromatic reactivity due to very significant variations in substituent resonance effects with electron demand. It is concluded that the F,R model should be abandoned in favor of lines of research involving approaches intermediate in complexity between those of Swain and of Taft.

Introduction

Fifteen years ago, Swain and Lupton introduced two parameters, F and R, which were claimed to respectively represent substituent field and resonance effects.[2] They also claimed that only one resonance parameter was necessary for each substituent to predict substituent effects for a wide variety of properties and reactions according to eq 1, where P_x is the value of a particular property for a

$$P_x = fF + rR + h \quad (1)$$

series of substituents X, f and r are transmission coefficients which only depend upon the reaction or property and conditions while h is the intercept for the correlation equation.[2] This approach contrasted with the earlier approach of Taft[3] who denoted the field and resonance components as σ_I and σ_R but presented detailed evidence that different resonance parameters (σ_R^+, σ_R(BA), σ_R^0 or σ_R^-) were necessary, depending upon the electron demand of the particular system or reaction.[4,5] Taft's was eq 2,

$$P_x = P_0 = \rho_I\sigma_I + \rho_R\sigma_R \quad (2)$$

where P_0 is the value of the property for the parent molecule (X = H), σ_R is one of the four resonance scales listed above and ρ_I and ρ_R correspond to f and r in 1.

Swain's approach is clearly the simpler of the two since it involves only two fixed scales. Probably for that reason, F and R constants have been quite extensively used, particularly in correlations of spectroscopic and biological data.[6] However, both the derivation and the utility of this approach have been seriously criticized by other leading physical organic chemists in articles, reviews, and books.[7] Nevertheless, Swain has recently reported revised values of F and R based upon a larger data set and more sophisticated statistical analysis, but still using the same basic, previously criticized, assumptions.[8] Although Swain presents what appears to be impressive statistical data to support his claim that he has developed a universal resonance scale,[8] close inspection reveals that certain of his conclusions result from the use of incomplete data sets and are unjustified. Consequently, we felt that it was important to point out the problems with the F,R approach so that organic chemists who make occasional use of dual (field and resonance) substituent constants would be aware of the serious limitations of this attractively simple model.

Discussion

(i) The Choice of R = 0 for $N(CH_3)_3^+$ as a Criterion for Separating *F* and *R* and Defining the Resonance Scale. The original R scale was determined by using the assumption that R = 0 for $N(CH_3)_3^{+2}$. It was quickly pointed out by several others that this assumption was probably incorrect and that R was consequently not a pure resonance scale.[7a,7b,9] However, the same

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