THE DIELS-ALDER REACTIVITY OF SOME NEW SULFUR (SELENIUM) SUBSTITUTED HALOBUTADIENES

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Summary.   3-PhS(e)-(1),2-(di)halobutadienes undergo BF_3 catalysed cycloadditions with methyl vinyl ketone at 25°C, to give good yields of adducts in which the regiochemistry of addition is mainly controlled by the sulfur (selenium) atom.

In the preceding paper[1] we described the synthesis of ten new asymmetrically substituted butadienes. In this paper we wish to report that the chalcogen containing dienes (1a-d) and 2(a-d) are all reactive in Diels-Alder cycloadditions, and that, despite the instability of several of the dienes, moderate to excellent yields of cycloadducts can be obtained using Lewis acid catalysis. Aromatization of the adducts allowed for an unambiguous assignment of the regiochemical preferences of the dienes in the cycloadditions; in the cases of dienes (2a-d) this provides proof of their actual structures.

The reactions of all ten dienes with methyl vinyl ketone (MVK) were investigated. MVK is a moderately reactive dienophile which shows relatively low regioselectivity in similar cyclo-additions.[2] Early results with the sulfur containing dienes (1a) and (1b) demonstrated that these dienes were insufficiently stable to withstand thermal cycloadditions, and therefore BF_3 catalysed room temperature conditions were subsequently employed.

Thiodienes (1a and b) were very difficult to isolate, polymerizing rapidly when neat. However, when concentrated hexane extracts of (1a) or (1b) were added to a large excess of MVK under N_2, containing BHT stabilizer, followed by small quantities (10-20 μl) of BF_3·etherate, cycloadducts could be obtained in multigram quantities with yields [based on the diene precursor (8)] of 45-68% from diene (1a) and 20-33% from diene (1b). Selenodienes (1c and d) could be isolated briefly, and exposure of these crude dienes to the above reaction conditions led to good yields of the corresponding cycloadducts (see Table 1).

3a-d; R=CH_3
6; R = H, X = Br, Ar = PhS

5a-d; R = CH_3
7; R = H, Ar = PhS
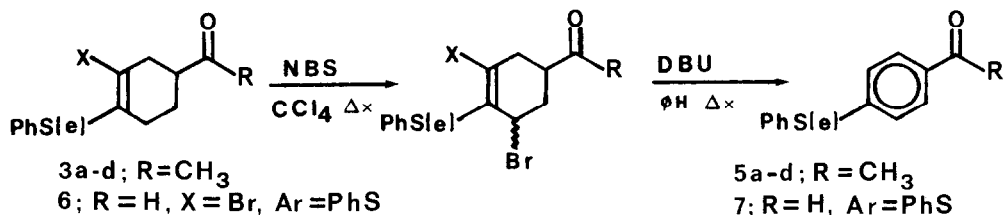
Scheme 1.

All four of the cycloadditions described above led to mixtures of regioisomers (3) and (4) with ratios (Table 1) varying from 2:1 for (3b):(4b) to 5:1 for (3a):(4a). To determine the structures of the major regioisomers, the mixtures were allylically brominated with N-bromo-
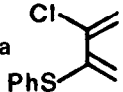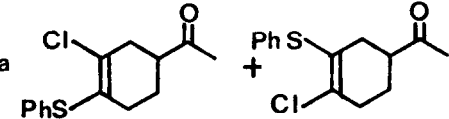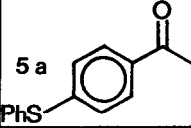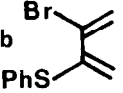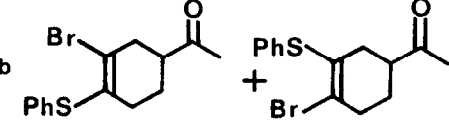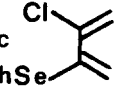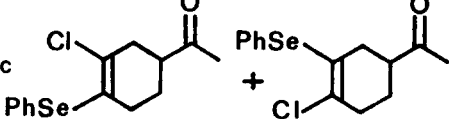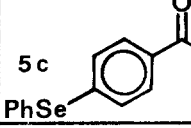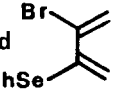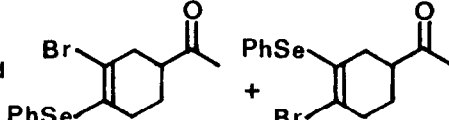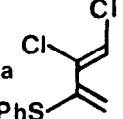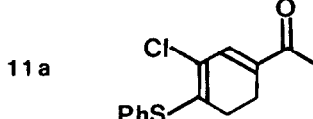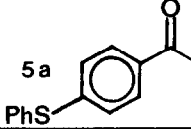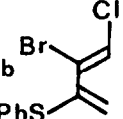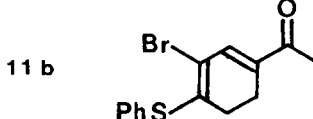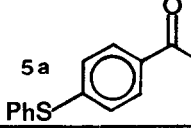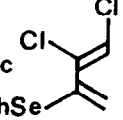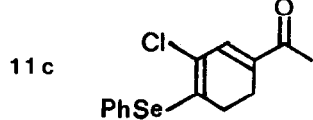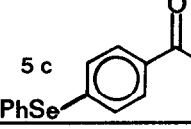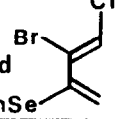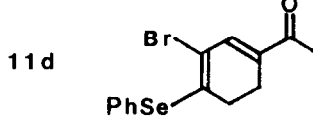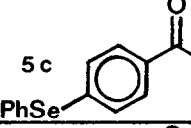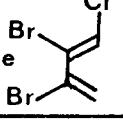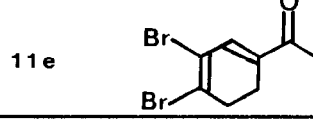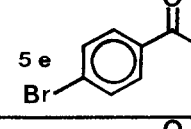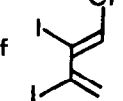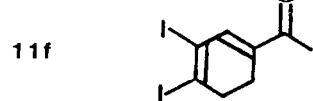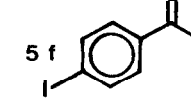
DIENE	(major;3) ADDUCT (minor;4)	Ratio	Yield %a	AROMATIC	Yield %
1a (Cl, PhS)	a (Cl/PhS acetyl adducts)	5:1	68[b]	5a (PhS-phenyl acetyl)	68
1b (Br, PhS)	b (Br/PhS acetyl adducts)	2:1	33[b]	—	—
1c (Cl, PhSe)	c (Cl/PhSe acetyl adducts)	4:1	76	5c (PhSe-phenyl acetyl)	53
1d (Br, PhSe)	d (Br/PhSe acetyl adducts)	≥4:1	51	—	—
2a (Cl, Cl, PhS)	11a (Cl/PhS acetyl)	—	57	5a (PhS-phenyl acetyl)	100
2b (Br, Cl, PhS)	11b (Br/PhS acetyl)	—	56	5a (PhS-phenyl acetyl)	100
2c (Cl, Cl, PhSe)	11c (Cl/PhSe acetyl)	—	86	5c (PhSe-phenyl acetyl)	40
2d (Br, Cl, PhSe)	11d (Br/PhSe acetyl)	—	62	5c (PhSe-phenyl acetyl)	28
2e (Br, Cl, Br)	11e (Br/Br acetyl)	—	75	5e (Br-phenyl acetyl)	88
2f (I, Cl, I)	11f (I/I acetyl)	—	12	5f (I-phenyl acetyl)	95

TABLE 1. Diels-Alder Adducts and their Aromatization Products.

a) All yields of purified isolated compounds on a 5-20 mmol scale. b) Yield based on diene precursors (8a) and (8b).

succinimide, and then aromatized, by a double dehydrohalogenation with 1,8-diazobicyclo[5.4.0]-undec-7-ene (DBU), as shown in Scheme 1. The chloroadducts (3a) and (3c), gave > 50% yields of aromatized products, which the nmr spectra showed to be predominately the para-substituted acetophenones (5a)[3] and (5c),[4a] but neither bromoadduct (3b) nor (3d) aromatized satisfactorily. However acrolein, with BF_3 catalyst, reacted with bromodiene (1b) to give a single adduct (6) in 28% yield which on aromatization as shown in Scheme 1 gave paraphenylthiobenzaldehyde (7)[5] in 58% yield, indicating that the bromo and chlorodienes express similar regiochemistry. Thus it appears that chalcogen dominates halogen regiochemistry, just as it dominates oxygen in some similar systems.[2,6] Not surprisingly, the smallest selectivity is seem competing the second row chalcogen, sulfur, against the third row halogen, bromine.
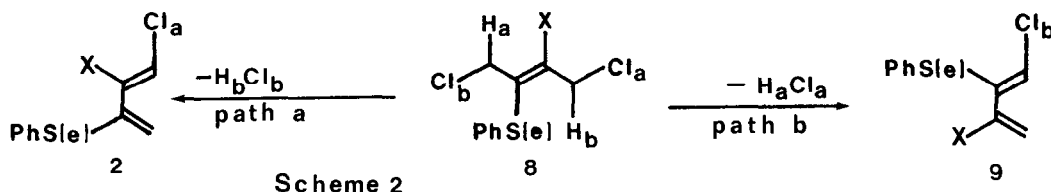
Scheme 2

With the trisubstituted dienes (2a-d) there are two regiochemical considerations. The dienes are produced by 1,4-elimination of HCl from the precursors (8a-d), and the two possible pathways, (a and b) are shown in Scheme 2, with pathway b leading to an alternative structure (9) for the dienes. This duality, combined with the regiochemical possibilities of the cyclo-addition, means that aromatization alone cannot determine the structure of the cycloadduct. Fortunately extra regiochemical information was available, since dienes (2a-d) all underwent ready BF_3-catalyzed cycloadditions with MVK, to form single adducts, in 57-86% yields, which were not the expected simple adducts (10a-d) but the dienones (11a-d). Their structures, except for the regiochemistry of X and Y, were established by the proton nmr spectra which showed only five ring protons for each adduct including always an allylically broadened, one proton singlet at 6.7-6.9δ, and by ir which showed several intense bands in the 1650-1685 cm^{-1} region. Additionally, dienone 11a analysed correctly[4b] and dienone (11b) spontaneously aroma-tized on standing to form the para substituted acetophenone (5a), as did all four dienones (11a-d) on treatment with DBU.
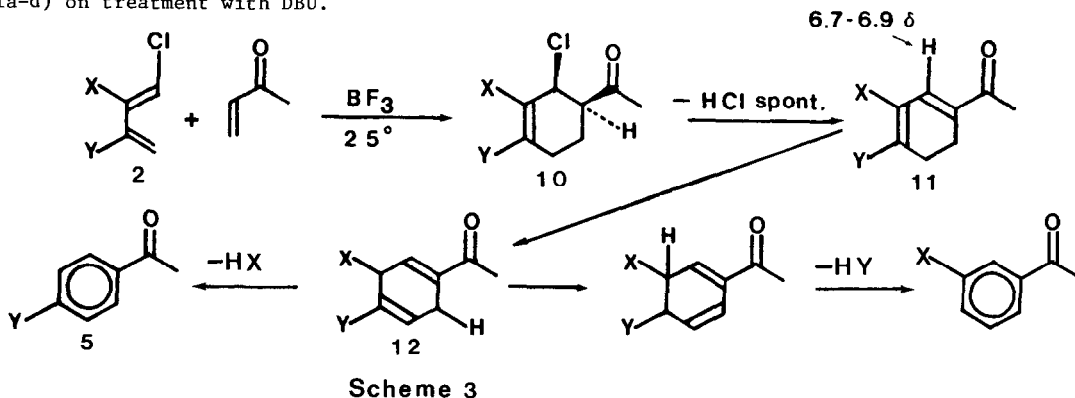
Scheme 3

With this additional information all the desired regiochemical data can be extracted (Scheme 3). The only reasonable structure to undergo a spontaneous dehydrohalogenation under cycloaddition conditions is the β-chloroketone (10). This requires an orientation of cyclo-addition as shown, with the 1-chloro substituent of the diene, and the acetyl substituent of the dienophile "ortho". It follows that the second dehydrohalogenation can only give para-substituted aromatics when X is halogen and Y arylchalcogen in Scheme 3. This establishes structures (11) and (10), and requires the diene structures to be (2a-d). The Z-stereochemistry is indicated by the high cycloaddition reactivity of the dienes.[7]

The trihalodienes (2e) and (2f) proved to be much less reactive in cycloadditions than the other dienes, giving no product under catalysed conditions. However their intrinsically greater stability allowed them to be used in thermal cycloadditions, and in refluxing MVK, in the presence of excess Na$_2$CO$_3$, both dienes underwent slow reaction to give adducts (8e) and (8f). The low yield of (8f) is presumably largely a reflection of low reactivity as large quantities of unreacted (2f) were routinely recovered from these reactions. Both adducts aromatized readily on treatment with DBU to give the para haloacetophenones (4e) and (4f). The loss of the "meta" halogen is to be expected since the first intermediate of Scheme 3 that can aromatize (12) should lead to para products via a facile 1,4-elimination.

A typical procedure is as follows: E,2-Phenylthio-1,3,4-trichlorobut-2-ene (2.62 g, 10 mmol) was added to a mixture of aluminum amalgam [from Al foil (0.52 g, 20 mmol) and Hg(OAc)$_2$ (1.0 g, 3 mmol)] and NH$_4$Cl (3.2 g, 60 mmol) in stirred methanol (50 ml) under N$_2$ at 25°C. After 15 minutes when the foil had dissolved, the reaction mixture was poured onto water (25 ml) and extracted with hexane (3 x 20 ml). The hexane extracts were washed with water (25 ml), saturated brine (25 ml) and dried (MgSO$_4$). The solvent was concentrated under reduced pressure to give a yellow oil (1.8 g) which was immediately added to freshly distilled MVK (10 ml, 120 mmol) containg BHT (50 mg) under N$_2$ at 25°C. BF$_3$·Etherate (20 μl) was added and the solution was stirred for 72 h at 25°C. The volatiles were removed under reduced pressure. The residue was dissolved in ethyl acetate/hexane (1:9) and vacuum filtered through t.l.c. grade silica gel. The filtrate was concentrated under reduced pressure and subjected to mplc on silica gel (97 x 2.5 cm) eluting with ethyl acetate/hexane (1:9) to give adducts (3a)[4c] and (4a) (1.82 g, 68%) in a 5:1 ratio as a yellow oil (δCH$_3$ 1.95; ν CO 1720 cm^{-1}).

References

1. A.J. Bridges and J.W. Fischer, preceding paper.
2. B.M. Trost, W.C. Vladuchick and A.J. Bridges, J. Amer. Chem. Soc., 102, 3554 (1980).
3. E. Fournier, L. Patit, J. Pishon-Gouet and M. Dursin, Bull. Soc. Chim. France, 1754 (1966).
4. a) Calc. for C$_{14}$H$_{12}$OSe C; 61.00, H; 4.39. Found C; 61.17, H; 4.33. b) Calc. for C$_{14}$H$_{13}$ClOS C; 63.50, H; 4.96. Found C; 63.60, H, 4.97. c) Analysed as 2,4-DNPH derivative Calc. for C$_{20}$H$_{19}$ClN$_4$O$_4$S C; 53.74, H; 4.29, N; 12.54. Found C; 53.50, H; 4.51, N; 13.17.
5. The MeLi adduct of (6) was shown to be identical to the NaBH$_4$ reduction product of (5a).
6. T. Cohen, R.J. Ruffner, D.W. Shull, W.D. Daniewski, R.M. Ottenbrite and P.V. Alston J. Org. Chem., 43, 4052 (1978).
7. J.C. Sauer, Angew. Chem. Int. Edn. Eng., 6, 16 (1967).