Preparation and Diels-Alder Reactivity of Several New Chalcogen-Halogen Substituted Butadienes[1]

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Addition of halogens and pseudohalogens across one π-bond of 1,4-dichlorobut-2-yne, followed by a 1,4-elimination, is an efficient synthesis of several new polysubstituted butadienes. If the product dienes have a sulfur or selenium substitutent they are quite reactive, undergoing cycloaddition with the moderately reactive dienophile methyl vinyl ketone at 20 °C in the presence of boron trifluoride etherate. The regiochemistry of the cycloadditions was elucidated, and the limitations of the methodology are discussed.

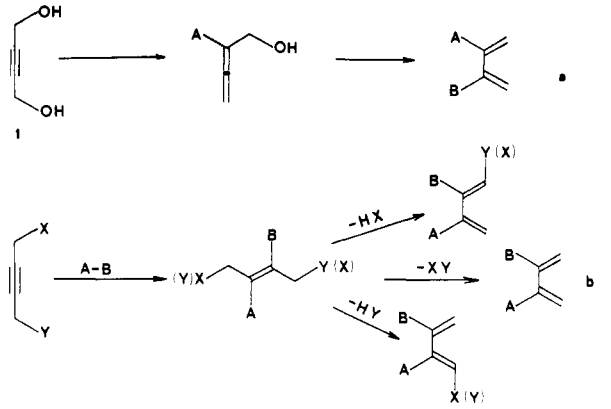
Introduction

In recent years the synthesis of heteroatom-substituted butadienes has been intensely studied,[2] mainly because the dienes have proven to be very useful in Diels-Alder reactions. Although many new butadienes have been prepared, there are still a rather limited number known with multiple heteroatom substituents. Our primary targets were dienes containing a sulfur or selenium atom and at least one other substituent. Several ((1- and ((2-alkylaryl)thio)butadienes are known to undergo Diels-Alder reactions,[3,4] but they are not reactive enough to be very useful.[5] Dienes with both sulfur and an oxygen substituent are much more reactive, and the 1,2-,[6,7] 1.4-,[8] and 2,3-disubstitution[9] patterns have been investigated.

For our starting material we chose butyne-1,4-diol (1). Since diol 1 has a linear four-carbon skeleton, two π bonds, and two substituents it can be thought of as a scrambled butadiene. Migration of both double bonds, with direct or allylic displacement of substituents, could lead to a wide variety of 1,2-, 2,3-, and 1,4-disubstituted butadienes.

Initially we examined two different strategies for the conversion of diol 1 into asymmetrically di- and trisubstituted dienes. One strategy, (Scheme Ia) has been reported on elsewhere.[10] The second strategy, consists of an electrophilic addition across the central triple bond followed by a 1,4-elimination. This process has been used in a preparation of 2-(triethylsilyl)butadiene.[11] In principle it could lead to a very wide variety of substituted butadienes as illustrated in Scheme Ib. However, the method has several obvious limitations. Monofunctionalized butynediol derivatives are made in low yields,[12] and the desired regiochemistry, in both the addition and elimination steps, may not be obtained. Also the triple bond may be too unreactive to add the electrophile, especially if the substituents are electron withdrawing.

Scheme I[a]



[a] If A = B, or A ≠ B, or A = H there are 12 possible 1,4-elimination products.

Results and Discusion

Diene Preparation. We decided to use 1,4-dichlorobut-2-yne (2) as our starting material since electrophilic additions should give no regiochemical problems, and 1,4-eliminations can be carried out, either by a reductive dehalogenation[13] or by base induced dehydrochlorination.

Alkyne (2) reacted with a series of pseudohalogens and halogens to form adducts **3a-f** as shown in Table I. The reactions with PhSeCl or PhSCl[14] were carried out in

(1) Preliminary communication: Bridges, A. J.; Fischer, J. W. *Tetrahedron Lett.* **1982**, *24*, 445, 447.

(2) Some recent examples. (a) Oxygen-substituted dienes: Danishefsky, S.; Kitahara, T.; Yan, C. F.; Morris, J. *J. Am. Chem. Soc.* **1979**, *101*, 6996. Danishefsky, S.; Yan, C. F.; Singh, R. K.; Gammill, R. B.; McCurry, M.; Fritsch, N.; Clardy, J. *Ibid.* **1979**, *101*, 7001. Dowd, P.; Weber, W. *J. Org. Chem.* **1982**, *47*, 4774. Hiranuma, H.; Miller, S. I. *Ibid.* **1982**, *47*, 5083. Gupta, R. C.; Harland, P. A.; Stoodley, R. J. *J. Chem. Soc., Chem. Commun.* **1983**, 754. (b) Nitrogen-substituted dienes: Overman, L. E.; Clizbe, L. A.; Freerks, R. L.; Marlowe, C. K. *J. Am. Chem. Soc.* **1981**, *103*, 2807. Overman, L. E.; Freerks, R. L.; Petty, C. B.; Clizbe L. A.; Ono, R. K.; Taylor, G. F.; Jessup, P. J. *Ibid.* **1981**, *103*, 2816. Gillard, M.; T'Kint, C.; Sonveaux, E.; Ghosez, L. *Ibid.* **1979**, *101*, 5837. Oppolzer, W.; Bieber, L.; Francotte, E. *Tetrahedron Lett.* **1979**, 4537. (c) Silicon-substituted dienes: Fleming, I.; Percival, A. *J. Chem. Soc., Chem. Commun.* **1978**, 178. Koreeda, M.; Ciufolini, M. A. *J. Am. Chem. Soc.* **1982**, *104*, 2308. Negishi, E.; Luo, F. T. *J. Org. Chem.* **1983**, *48*, 1560. (d) Selenium-substituted dienes: Toshimitsu, A.; Vemura, S.; Okano, M. *J. Chem. Soc., Chem. Commun.* **1982**, 965. Reich, H. J.; Rusek, J. J.; Olson, E. *J. Am. Chem. Soc.* **1979**, *101*, 2225.

(3) Wijers, H. E.; Brandsma, L.; Arens, J. F. *Recl. Trav. Chim. Pays-Bas* **1966**, *85*, 601. Jacobs, T. L.; Michaelovski, A. *Tetrahedron Lett.* **1967**, 2607.

(4) Cohen, T.; Mura, A. J.; Shull, D. W.; Fogel, E. R.; Ruffner, R. J.; Falck, J. R. *J. Org. Chem.* **1976**, *41*, 3218.

(5) Gouesnard, J. P.; Martin, G. J.; Blain, M. *Tetrahedron* **1974**, *30*, 151.

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(8) Trost, B. M.; Godleski, S. A.; Ippen, J. *J. Org. Chem.* **1978**, *43*, 4559.

(9) Trost, B. M.; Vladuchick, W. C.; Bridges, A. J. *J. Am. Chem. Soc.* **1980**, *102*, 3548, 3554.

(10) Bridges, A. J.; Fischer, J. W. *J. Chem. Soc., Chem. Commun.* **1982**, 665.

(11) Balt, D. C.; Ganem, B. *Tetrahedron Lett.* **1978**, 3323.

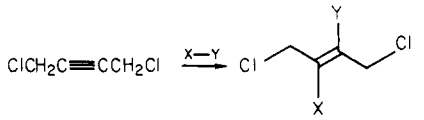
(12) Bailey, W. J.; Pfeiffer, C. R. *J. Org. Chem.* **1955**, *20*, 1337. Dupont, G.; Dulou, R.; Lefevbre, G. *Bull. Soc. Chim. Fr.* **1954**, 816. Frazer, M. M.; Raphael, R. L. *J. Chem. Soc.* **1955**, 4280.

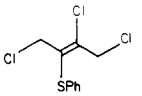
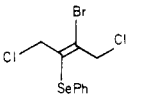
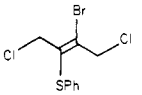
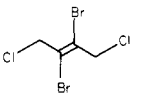
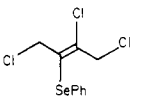
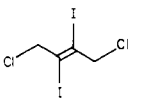
(13) Criegee, R.; Horauf, W.; Schellenberg, W. D. *Chem. Ber.* **1953**, *86*, 126.

(14) Hopkins, P. B.; Fuchs, P. L. *J. Org. Chem.* **1978**, *43*, 1208.

0022-3263/84/1949-2954$01.50/0

Table I. Additions to 1,4-Dichlorobut-2-yne (2)



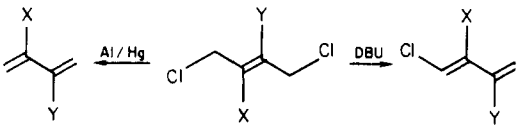
electrophile	adduct 3		yield, %	electrophile	adduct 3		yield, %
PhSCl	a		98	PhSeBr	d		93
PhSBr	b		80	Br_2	e		97
PhSeCl	c		100	I_2	f		86

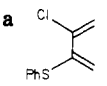
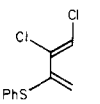
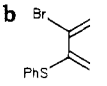
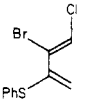
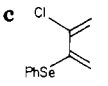
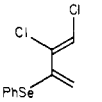
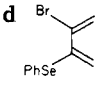
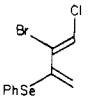
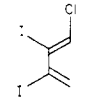
CH_3CN and were rapid, whereas PhSBr[15] and PhSeBr[16] (produced in situ in $CHCl_3$ and CH_2Cl_2, respectively) added slowly to **2** (5 days). (In a related reaction, addition of CH_3CN as a cosolvent was shown to accelerate PhSBr addition markedly.) Bromine also added immediately to **2**, but iodine did not react at all with **2** until the reaction was carried out in refluxing dichloroethane. The addition was reversible and the adduct **3f** had to be stored at −20 °C to prevent decomposition. This result contrasts sharply with the reported easy addition of iodine to diol **1**[17] and probably reflects the electron deficient nature of alkyne **2**.

In order to look at a wider range of diene precursors several other addition reactions of **2** were examined. **2** did not react with either acetyl hypobromite[18] or acetyl hypoiodite under a wide range of conditions. Several attempts were made to trap the intermediate cyclic onium ions with external nucleophiles [PhSeCl/CH_3CN,[19] PhSeCl/NaOAc,[20] and PhSCl/NaOAc] but all were unsuccessful, as was an attempted intramolecular trapping involving the addition of PhSCl to 1,4-diacetoxybut-2-yne, which gave only the simple 2,3-adduct.

With the precursors in hand some 1,4-dehalogenations were examined. Active zinc[21] in refluxing ethyl acetate dehalogenated both trihalides (**3a** and **3b**), but was not satisfactory as extensive polymerization occurred both during the reaction, probably because the dienes produced have very limited thermal stability, and after workup, probably because residual $ZnCl_2$ could not be completely removed from the product, even by chromatography. Both of these problems could be overcome by the use of a more powerful reducing system, aluminum amalgam in buffered methanol.[22] At 20 °C all the Al dissolved exothermically

Table II. 1,4-Eliminations



3	diene 4	yield, %	diene 5	yield, %
a, X = Cl; Y = SPh	a 	⩾68	a 	85
b, X = Br; Y = SPh	b 	⩾40	b 	63
c, X = Cl; Y = SePh	c 	75	c 	46
d, X = Br; Y = SePh	d 	76	d 	68
e, X = Br; Y = Br			e 	85
f, X = I; Y = I			f 	81

in 1–2 h reducing the trihalobutenes (**3a–d**) completely with the results shown in Table IIa. 3-Chloro-2-(phenylthio)butadiene (**4a**) could be obtained consistently in ~80% crude yields, but it still polymerized readily when neat, making accurate yields and full characterization difficult. In practice it was best not to isolate diene **4a** pure, but to strip most of the solvent, and to use the concentrated (~50%) hexane solution immediately. The diene was characterized by its proton NMR spectrum and subsequent Diels–Alder reactions. The NMR spectrum consists of a broad singlet at 7.22–7.47 δ (5 H, aromatic) and four somewhat broadened one-proton singlets at 6.36,

(15) To generate PhSBr we initially followed the preparation of tritylsulfenyl bromide from the corresponding sulfenyl chloride and NaBr in acetone. (Ciuffarin, E.; Guaraldi, G. *J. Org. Chem.* **1970**, *35*, 2006.) However addition of PhSCl to a stirred suspension of NaBr in acetone led to immediate loss of the orange-red sulfenyl halide color, and the only products isolated were (phenylthio)propanone and diphenyl disulfide. Attempts to generate PhSBr and PhSI in situ using either the halide exchange in DMF containing alkyne **2**, or diphenyl disulfide/bromine in in CH_2Cl_2 (Trost, B. M.; Ziman, S. D. *J. Org. Chem.* **1973**, *38*, 933) were also totally unsuccessful. However, modification of Fuchs[14] PhSCl preparation using NBS instead of NCS proved to be very satisfactory for in situ PhSBr additions.

(16) Reich, H. J. *J. Org. Chem.* **1974**, *39*, 428.

(17) Hollins, R. A.; Campos, M. P. A. *J. Org. Chem.* **1979**, *44* 3931.

(18) Levine, S. G.; Wall, M. E. *J. Am. Chem. Soc.* **1959**, *81*, 2826.

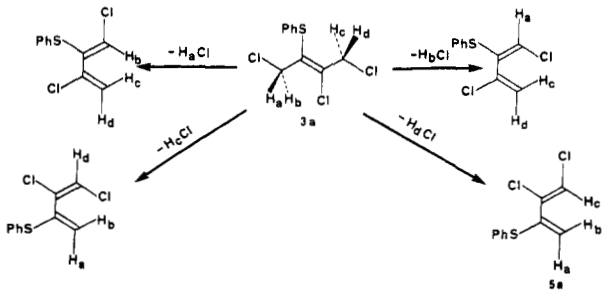
(19) Toshimitsu, A.; Aoai, T. *J. Org. Chem.* **1981**, *46*, 4727.

(20) Sharpless, K. B.; Lauer, R. F. *J. Org. Chem.* **1974**, *39*, 429.

(21) Smith, C. W.; Norton, D. G. "Organic Syntheses"; Wiley: New York, 1963; Collect. Vol. 4, p 348.

(22) Roedig, A.; Detzer, N.; Bonse, G. *Liebigs Ann. Chem.* **1971**, *752*, 60.

Scheme II

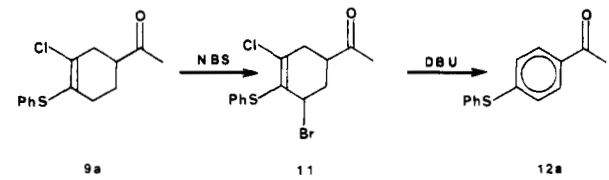


5.95, 5.68, and 5.50 δ. Several similar 1,1,[23] 1,2-,[24] and 1,3-S,Cl-substituted[25] butadienes have been reported, but only in one case was a cycloadduct, a [2 + 2] product with tetracyanoethylene, reported.[26] The yield quoted for diene **4a** in Table II is based upon the overall isolated yields of a Diels-Alder adduct from trihalide **3a**, so must represent a minimum true yield. The same is true of 3-bromo-2-(phenylthio)butadiene (**4b**), which was so unstable, that only once was a good quality NMR spectrum obtained on it. In contrast both selenodienes (**4c** and **4d**) were stable enough to isolate and characterize spectroscopically, so the yields quoted are of isolated dienes. A ^{13}C NMR spectrum of 3-chloro-2-(phenylseleno)butadiene (**4c**) showed four vinyl peaks at 118.4, 126.2, 135.3, and 138.0 δ, of which the former two were triplets and the latter two singlets, in an off resonance decoupled spectrum, unequivocally demonstrating the 2,3-disubstitution pattern.

The dehydrohalogenation of adducts **3a–f** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) was examined. Reaction of trihalide **3a** with 1 equiv of DBU in benzene at 25 °C was rapid, giving good yields of a crude diene, which showed four singlets in a 5:1:1:1 ratio, at 7.22, 7.10, 6.12, and 5.65 δ in the proton NMR, and eight signals, all between 121.9 and 136.9 δ, in the ^{13}C NMR spectrum. This showed that only a single diene had been produced by the dehalogenation, but did not distinguish between the four possibilities shown in Scheme II. The other trihalides **3b–d** also dehydrohalogenated cleanly under the same conditions to give single products. The bromine adduct **3e** reacted under the same conditions, but iodine adduct **3f** reacted much more slowly and required 2 equiv of DBU to drive the reaction to completion. All of these dienes were at least stable enough to survive PLC purification, but only the dibromodiene **5e** and diiododiene **5f** appeared to be stable for extended periods of time.

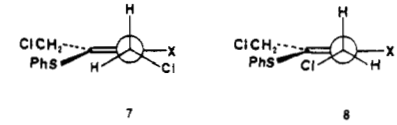
The assignment of structures to dienes **5a–f** was made principally by their subsequent Diels–Alder chemistry, which clearly indicated that, where there were two possible regiochemistries, i.e., dienes **5a–d**, only the 1,2-dihalo dienes were obtained. Stereochemistry was assigned in the same way. The *Z* isomers would be expected to be considerably more reactive in Diels–Alder reactions than the *E* isomers,[27] so dienes **5a–f** were assigned the *Z* stereochemistry. All five of these dienes had similar NMR spectra with H1 appearing at 7.15–7.29 δ and H4 appearing at 6.12–6.42 and 5.65–5.80 δ. The iododiene **5f** showed a different pattern with H1 at 7.15 δ and the H4 protons at 6.75 and 6.18 δ. Coupled with its slow formation, and the fact that it was by far the least reactive of the dienes in Diels–Alder reactions, this information suggested that this

Scheme III



diene may be the *E* isomer **6**.

The regiospecificity seen in these eliminations is not easy to explain, but the stereospecificity may be explained by looking at conformations **7** and **8**. Unless the group X is



very large (iodine perhaps?) conformation **7** leading to the *Z* diene should have less steric hindrance than conformation **8** leading to the *E* diene.

Diels–Alder Reactions. The first Diels–Alder reaction to be examined was that between 3-chloro-2-(phenylthio)butadiene (**3a**) and methyl vinyl ketone (MVK). The reaction mixture polymerized when a thermal Diels–Alder reaction in refluxing MVK was attempted. However when the diene was added as a ~50% solution in hexane, to a large excess of freshly distilled MVK containing BHT stabilizer and a trace of $BF_3{\cdot}Et_2O$ catalyst, a Diels–Alder reaction occurred. Working up the reaction, after 3 days at 25 °C, gave, after MPLC purification, a Diels–Alder adduct in 45–68% yield based upon starting trihalide **3a**. (See Table III.

NMR and HPLC analysis of the crude reaction mixture, and the purified product showed that it contained a 5.5:1 mixture of two very similar compounds, presumably the regioisomeric adducts **9a** and **10a**. In order to identify the major regioisomer unequivocally, it was decided to aromatize the product mixture, since the meta- and para-substituted acetophenones produced would be easy to identify. The adduct mixture brominated readily with N-bromosuccinimide (NBS) in CCl_4 at reflux to give a mixture of allylically brominated adducts, e.g., **11**, which were reacted with 2 equiv of DBU in refluxing benzene for 3 h. After chromatographic purification *p*-(phenylthio)-acetophenone (**12a**),[28] readily identified by ^1H and ^{13}C NMR spectra, was obtained in 68% yield, with no trace of the meta isomer. Since the overall yield was high enough to preclude confusion of products from the two isomers, structure **9a**, the product of sulfur regiocontrol, can be assigned to the major isomer, as illustrated in Scheme III.

On BF_3-catalyzed reaction with acrolein, diene **4a** gave a single adduct **13a** in 40% yield, which gave *p*-(phenylthio)benzaldehyde (**14**)[29] on NBS/DBU aromatization, showing augmented sulfur regiocontrol of the reaction. Bromodiene (**4b**) reacted with both MVK and acrolein under catalytic conditions to give much lower yields of products, probably due to the greater instability of the diene. The MVK adduct was a 2:1 mixture of isomers **9b** and **10b**, whilst the acrolein adduct **13b** was a 10:1 isomer mixture. The MVK products (**9b, 10b**) did not react with NBS so the regiochemistry could not be determined, but the acrolein adduct mixture was readily aromatized to **14** in 58% overall yield, confirming that the major isomer is

(23) Radchenko, S. I.; Petrov, A. A. *Zh. Org. Khim.* **1965**, *1*, 987.
(24) Butler, P. E.; Mueller, W. H. *Tetrahedron Lett.* **1966**, 2179. Parham, W. E.; Kajigaeshi, S.; Groen, S. H. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 509.
(25) Pariza, R. J.; Fuchs, P. L. *J. Org. Chem.* **1983**, *48*, 2304.
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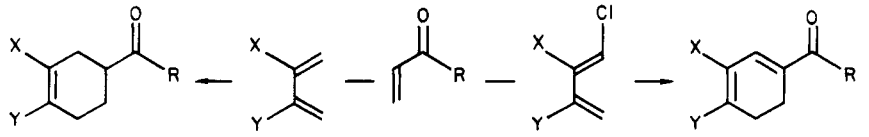
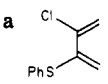
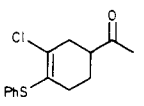
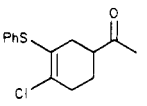
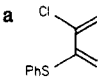
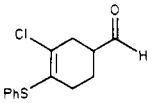
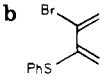
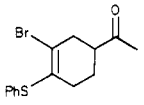
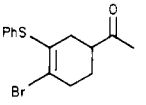
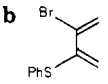
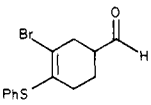
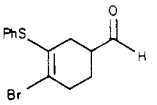
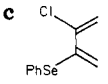
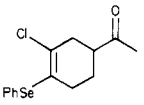
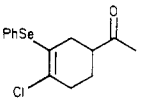
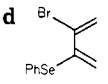
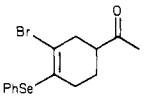
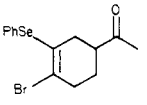
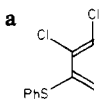
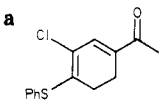
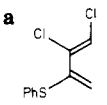
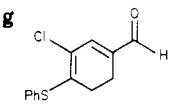
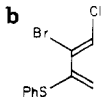
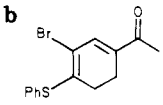
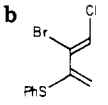
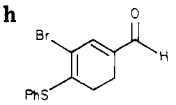
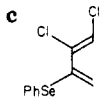
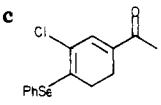
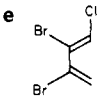
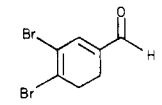
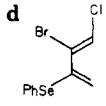
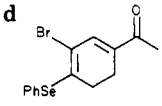
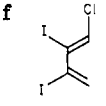
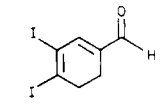
Table III. Diels-Alder Reactions of Dienes



diene 4	Diels-Alder adduct major 9	Diels-Alder adduct minor 10	ratio	yield, %
Disubstituted Dienes				
a 	 **a**		5.5:1	68
a 	**13a** 			40
b 	 **b**		2:1	40
b 	**13b** 		10:1	27
c 	 **c**		100:1	72
d 	 **d**		50:1	70

diene 5	product 15	yield, %	diene 5	product 15	yield, %
Trisubstituted Dienes					
a 	**a** 	57	**a** 	**g** 	21
b 	**b** 	56	**b** 	**h** 	14
c 	**c** 	47	**e** 	**e** 	51
d 	**d** 	62	**f** 	**f** 	12

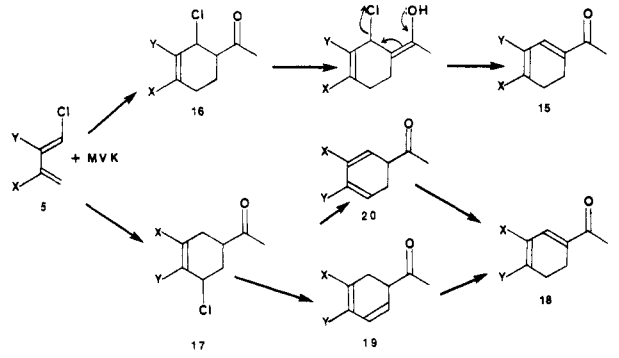
13b with sulfur controlling the regiochemistry. By analogy the major isomer of the MVK reaction was assigned structure **9b**. Reactions of chlorodiene **4a** with acrylonitrile, methyl acrylate, crotonaldehyde, and benzoquinone, or between bromodiene **4b** and methyl propynoate or propynoic acid were all unsuccessful.

The proton NMR spectra of the reaction mixtures of the seleno dienes **4c** and **4d** with MVK were initially interpreted as indicating 4:1 regioisomer ratios,[1] but later ^{13}C NMR and HPLC analysis showed the true isomer ratios to be 100:1 and 50:1, respectively. Aromatization of adduct **9c** gave *p*-(phenylseleno)acetophenone (**12c**), but the bromo adduct **9d**, just like its thio analogue **9b**, failed to react with NBS, so the structure was again assigned by analogy.

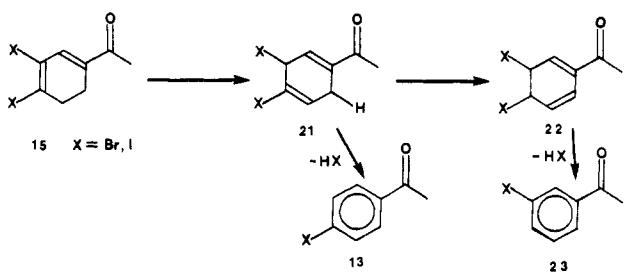
Some Diels–Alder reactions of the trisubstituted dienes **5a–f** were also examined with the results shown in Table III. The dihalothio/dihaloselenodienes **5a–d** gave good yields of single products with MVK under the usual catalytic conditions. After 3 days dibromo diene **5e** was only 25% consumed, and diiodo diene **5f** did not react at all. Repeating these last reactions without catalyst, in refluxing MVK for 2 days, led to products in 51% and 13% yields, respectively. Both reactions required solid Na_2CO_3 to mop up HCl produced and were difficult to purify due to the presence of MVK dimer,[30] and large quantities of diene **5f** were recovered unchanged. Thio dienes **5a** and **5b** also

(30) Tamura, F.; Yulakaka, S.; Murata, N. *Kogyo Kagaku Zasshi* **1963**, *66*, 1344.

Scheme IV



Scheme V



gave low yields of single adducts with acrolein under the usual catalytic conditions.

Spectroscopic analysis of all of these products revealed that they were 1,3,4-trisubstituted cyclohexa-1,3-dienes of general formula **15** rather than the Diels–Alder adducts **16** or **17**. In each case the proton NMR spectrum showed only four saturated ring protons in the 2–3 δ range, some appearing as obvious AA'BB' systems. Each compound also showed a narrow multiplet ($J < 2$ Hz) at 6.7–6.9 δ for the only other ring proton. The ^{13}C spectrum of **15e** showed four vinyl signals between 110.4 and 143.7 δ, and a rather shielded carbonyl signal at 196.6 δ. **15c** has λ_{max} at 361 nm (ϵ 1.28 × 10^4), and IR spectra of all the products showed a stronger band at 1660 cm^{-1} than at 1710 cm^{-1}.

Products such as **15** could arise in two different ways as shown in Scheme IV. The more direct route (a) goes through adduct **16**, which can undergo HCl elimination to give **15**. The alternative pathway (b) involves the other cycloaddition to give adduct **17**. Dehydrohalogenation, followed by two double bond migrations, or a 1,4-elimination and single migration would lead to adduct **18**, isomeric to **15** but not easily distinguishable from it. It is very important to decide between these possibilities, not just to prove the regiochemistry of the cycloaddition, but also to prove the regiochemistry of the trisubstituted dienes **5a–d**. Spontaneous elimination is not intrinsic to all acyldihalocyclohexenes, as was demonstrated by the failure of allyl bromide **11** to eliminate spontaneously even at 80 °C. This argues strongly against path b, where the elimination from **17** to give **19** or **20** is entirely unactivated. By contrast the conversion of **16** to **15** is simply a dehydrohalogenation of a β-chloro ketone, producing a highly conjugated system directly, which should be a very easy process. Therefore, it was concluded that the Diels–Alder reactions always produced the 1,2-adducts **16** initially.

With this problem solved an aromatization would reveal the regiochemistry of the original dienes. In fact some adducts aromatized spontaneously on standing for a few days, and they were all aromatized on treatment with 1 equiv of DBU in refluxing benzene, and in every case the products were para-substituted acylbenzenes **13** or **14**. This means that the cyclohexadienone adducts must have the structures **15a–j** and dienes **5a–d** must be 1,2-dihalo-3-chalcogenobutadienes.

There was still one question to be answered. The dihalocyclohexadienes **15e** and **15f** have two halogen atoms, but only one, the 3-substituent is eliminated. Since both halogen atoms are initially vinylic, the first step must be a double bond migration. The C5 protons are acidified, so the initial migration will move a double bond to that position to give the cyclohexa-1,4-diene **21** as shown in Scheme IV. This allyl halide would be expected to undergo 1,4-elimination, to give *p*-acetophenone (**13e,f**) much more readily that it would rearrange a second time to give **22**, the precursor to the meta product **23**, as shown in Scheme V.

Conclusions

This paper describes very straightforward preparations of ten asymmetrically substituted butadienes, most in excellent overall yields, so that all can be easily obtained on a multigram scale. The technique is limited by the availability of the precursors, and the tendency of the dienes to polymerize.

Several points came out of the examination of the Diels–Alder reactions. Sulfur and selenium significantly increase the reactivity of the dienes. They also dominate the regiochemistry when present. This is not surprising since Trost[8,9] and Cohen[6] have shown that sulfur is a more powerful regiocontrolling element than oxygen. That sulfur is more powerful than chlorine is suggested by the results of the thermal cycloadditions of 2-chloro- and 2-(phenylthio)butadiene with methyl acrylate. With 2-(phenylthio)butadiene the 1,4-disubstituted product is the only isolated product,[4] whereas with chloroprene the 1,4- and 1,3-stereoisomers are obtained in a 6:1 ratio.[31] These results are also in accord with the predictions of simple FMO theory.[32] The orbital coefficients published for 2-chlorobutadiene show a difference of 0.149 (0.546–0.397, by CNDO/2)[33] whereas those published for 2-(phenylthio)butadiene show a much larger difference of 0.335 (0.532–0.197, by MINDO/3).[9] Sulfur is a much more polarizing substituent for the diene than chlorine, so when the two are in direct competition sulfur should dominate the regiochemistry. The 2:1 regioisomer ratio with bromothiodiene **4b** and MVK suggests that descending a period increases the regiochemical directing influence. This trend can be seen even more dramatically in the regiochemistry of the selenodienes **4c** and **4d** where selenium dominates halogen much more strongly (~50–100:1) than sulfur does. With the trisubstituted dienes **5a–d** the 1-substituent should augment the directing influence of the 3-substituent.[32] In the trihalodienes **5e,f** the 2- and 3-substituents effectively cancel one another out, so the 1-substituent should control regiochemistry. This was exactly what was observed with minor isomers (if any) being present in quantities, too small to detect. It should be borne in mind that almost all of these regioisomer ratios were obtained under conditions of BF_3 catalysis,[9,34] and that thermal ratios would be considerably lower (if obtainable).

Experimental Section

General Procedures. All solvents were redistilled prior to use, and if drying was required, they were stirred over powdered CaH_2 prior to decanting or distillation. MVK and acrolein were

(31) Mukai, T.; Kojima, T. *J. Org. Chem.* **1971**, *36*, 924.
(32) Fleming, I. "Frontier Orbitals and Organic Chemical Reactions"; Wiley: New York, 1976.
(33) Alston, P. V.; Ottenbrite, R. M.; Shillady, D. D. *J. Org. Chem.* **1973**, *38*, 4075.
(34) Yates, P.; Eaton, P. *J. Am. Chem. Soc.* **1960**, *82*, 4436.

distilled from molecular sieves onto a little BHT stabilizer under N_2 immediately before use. Proton NMR spectra were obtained as 10–25% solutions in $CDCl_3$ on a Varian A60A spectrometer or IBM NR80 spectrometer and ^{13}C spectra at 20 MHz on the IBM NR80 spectrometer. IR spectra were obtained on a Pye-Unicam 3-200 spectrometer as thin films, unless otherwise stated, and UV spectra on a Varian 2340 UV spectrometer in ethanol. Melting points were obtained on a Fisher-Johns melting point apparatus and are uncorrected. Microanalyses were carried out within the department on a Perkin-Elmer 240 elemental analyzer. HPLC was carried out on a Waters Associates 6000 A system with Perkin Elmer LC 75 detector with a Bondapak C18 reverse-phase column, eluting with acetonitrile. 1,4-Dichlorobut-2-yne,[35] 4-(phenylthio)acetophenone (**12a**),[28] and benzenesulfenyl chloride[14] were prepared according to literature procedures.

(*E*)-2-(Phenylthio)-1,3,4-trichlorobut-2-ene (3a). Benzenesulfenyl chloride (7.2 g, 50 mmol) was added dropwise to a stirring solution of 1,4-dichloro-2-butyne (6.1 g, 50 mmol) in acetonitrile (100 mL) at 25 °C under nitrogen. After 3 h, the solvent was removed under reduced pressure to give **3a** (13.1 g, 100%) as a light yellow oil, which could be Kugelrohr distilled at 80 °C (0.005 mmHg). Calculated for $C_{10}H_9Cl_3S$: C, 44.88; H, 3.40. Found: C, 44.85; H, 3.53. ^1H NMR δ 7.4 (5 H, br s, aromatics), 4.70 (2 H, s, allylic CH_2), 4.2 (2 H, s, allylic CH_2); IR 3060, 1580, 1480, 1440, 1425, 1275, 1085, 950, 740, 710, 685 cm^{-1}.

(*E*)-2-(Phenylthio)-3-bromo-1,4-dichlorobut-2-ene (3b). Thiophenol (2.0 mL, 20 mmol) was added dropwise to a stirring suspension of NBS (3.60 g, 20 mmol) in chloroform (50 mL) at 25 °C under nitrogen. The reaction was exothermic and became dark orange. After 0.5 h, 1,4-dichloro-2-butyne (2.44 g, 20 mmol) was added dropwise and the mixture was stirred an additional 16 h at 25 °C. The reaction mixture was poured onto water (100 mL) and the layers were separated. The aqueous layer was extracted with chloroform (2 × 25 mL) and the combined organic layers were washed with water (100 mL) and saturated brine (100 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure, and residual volatiles by pumping under vacuum for 16 h to yield **3b** (4.91 g, 80%) as a viscous orange oil. An analytical sample was prepared by PLC on silica gel eluting with 10% $CHCl_3$ in hexane. Calculated for $C_{10}H_9BrCl_2S$: C, 38.49; H, 2.91. Found: C, 38.34; H, 3.20. ^1H NMR δ 7.35 (5 H, br s, aromatic), 4.79 (2 H, s, allylic CH_2), 4.20, (2 H, s, allylic CH_2); IR 3060, 1585, 1475, 1440, 1425, 1265, 1075, 945, 745, 720, 690 cm^{-1}.

(*E*)-2-(Phenylseleno)-1,3,4-trichlorobut-2-ene (3c). Benzeneselenyl chloride (3.84 g, 20 mmol) and 1,4-dichloro-2-butyne (2.44 g, 20 mmol) were stirred together in acetonitrile (25 mL) at 25 °C for 20 h under nitrogen. The color changed from deep red to yellow. The solvent was removed under reduced pressure to yield (3c) (6.28 g, 100%) as an orange oil. ^1H NMR δ 7.3–7.6 (5 H, m, aromatics), 4.66 (2 H, s, allylic CH_2), 4.25 (2 H, s, allylic CH_2); IR 3060, 1600, 1575, 1475, 1440, 1425, 1270, 1090, 945, 740, 720, 690 cm^{-1}.

(*E*)-2-(Phenylseleno)-3-bromo-1,4-dichlorobut-2-ene (3d). Bromine (1.6 g, 10 mmol) was added dropwise to a stirring solution of diphenyl diselenide (3.12 g, 10 mmol) in dichloromethane (40 mL)[17] at 25 °C under nitrogen. After 1.5 h, 1,4-dichloro-2-butyne (2.44, 20 mmol) was added and the reaction mixture was refluxed for 5 days. The brown-black solution was cooled and poured onto water (50 mL) and the layers were separated. The aqueous layer was extracted with chloroform (2 × 15 mL) and the combined organic layers were washed with water (25 mL) and saturated brine (25 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure, and residual volatiles by pumping under vacuum (0.1 mm) for 1 h to give **3d** (6.67 g, 93%) as a brown oil: ^1H NMR δ 7.1–7.6 (5 H, m, aromatics), 4.73 (2 H, s, allylic CH_2), 4.23 (2 H, s, allylic CH_2); IR 3060, 1575, 1475, 1435, 1265, 1075, 940, 740, 720, 690 cm^{-1}.

(*E*)-2,3-Dibromo-1,4-dichlorobut-2-ene (3e). Bromine (0.52 mL, 10 mmol) was added dropwise to 1,4-dichloro-2-butyne (1.22 g, 10 mmol) stirring in CCl_4 (20 mL) under nitrogen at 20 °C. After 4 h, the reaction mixture was poured onto dilute aqueous $Na_2S_2O_3$ solution (1 M, 25 mL) and the layers were separated. The aqueous layer was extracted with chloroform (2 × 20 mL) and the combined organic layers were washed with water (50 mL) and saturated brine (50 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure to yield **3e** (2.73 g, 97%), mp 41–43 °C (lit.[36] mp 58 °C) as a white solid: ^1H NMR δ 4.51 (s); IR (KBr pellet) 1425, 1405, 1265, 1080, 940, 725 cm^{-1}.

(*E*)-2,3-Diodo-1,4-dichloro-2-butene (3f). 1,4-Dichloro-2-butyne (1.22 g, 10 mmol) and iodine (2.54 g, 10 mmol) were refluxed together for 5 days in dichloroethane (25 mL) under nitrogen. The reaction mixture was then poured onto aqueous $Na_2S_2O_3$ solution (1 M, 25 mL) and extracted with ether (3 × 20 mL). The ether layers were combined and washed with water (25 mL) and saturated brine (25 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure to yield **3f** (3.22 g, 86%) as a rod-like white crystals, mp 122–123.5 °C (lit.[37] 121–123 °C), 59%, which decomposed gradually on standing at 25 °C: ^1H NMR δ 4.55 (s); IR (KBr pellet) 1420, 1260, 1180, 1070, 935, 715 cm^{-1}.

General Procedure for 2,3-Disubstituted Diene Preparation by Aluminum Amalgam Reductive Eliminations. Freshly made aluminum amalgam (2 molar equiv) [made by stirring Al foil with mercuric acetate (0.3 equiv) in methanol until all the acetate had dissolved and gas evolution was observed; the methanol was decanted and the foil was washed with methanol and ether and stored under ether until used] was added to a solution (~0.2 M) of the appropriate trihalide **3** in methanol containing solid NH_4Cl (6 equiv) stirred under N_2 at 25 °C. A mildly exothermic reaction occurred and the Al foil all dissolved within 1–2 h. At this point the mixture was poured onto water (~2 × volume of MeOH) and extracted with small portions of hexane (3 × 10–25 mL). The combined hexane layers were washed with water and saturated brine and dried ($MgSO_4$). The solvent was removed under reduced pressure. In some cases, a small portion of solvent was left to prevent polymerization. The experimentals give product, (crude) yield, starting material, scale, comments, and spectroscopic data.

3-Chloro-2-(phenylthio)butadiene (4a): ~80%, from (*E*)-2-(phenylthio)-1,3,4-trichlorobut-2-ene (**3a**), 20 mmol. Solvent was normally not completely removed due to polymerization. ^1H NMR δ 7.47–7.22 (5 H, m, aromatics), 6.36, 5.95, 5.68, 5.5. (all 1 H, s, vinyl H).

3-Bromo-2-(phenylthio)butadiene (4b): ~40%, from (*E*)-3-bromo-1,4-dichloro-2-(phenylthio)but-2-ene (**3b**), 20 mmol. Solvent was not normally completely removed due to polymerization. ^1H NMR δ 7.1–7.5 (5 H, m, aromatic), 6.4 (1 H, d, J = 2 Hz, vinyl), 6.15 (1 H, s, vinyl), 5.7 (2 H, narrow m, vinyl).

3-Chloro-2-(phenylseleno)butadiene (4c): 0.91 g, 75%, from (*E*)-2-(phenylseleno)-1,3,4-trichlorobut-2-ene (**3c**), 5 mmol. Polymerizes within 48 h. ^1H NMR δ 7.2–7.6 (5 H, m, aromatics), 6.48, 6.06, 5.80, 5.63 (all 1 H, all br s, vinyls); ^{13}C NMR δ (ORD multiplicity) 138.0 (s), 135.3 (s), 132.9 (d), 130.0 (s), 129.5 (d), 127.8 (d), 126.2 (t), 118.4 (t); IR 1575, 1475, 1440, 1360, 1070, 1020, 930, 895, 740, 690, 670 cm^{-1}.

3-Bromo-2-(phenylseleno)butadiene (4d): 1.10 g, 76%, from (*E*)-3-bromo-1,4-dichloro-3-(phenylseleno)but-2-ene (**3c**), 5 mmol. Polymerizes within 48 h. ^1H NMR δ 7.2–7.65 (5 H, m, aromatics), 6.35 (2 H, s, vinyl), 5.7–5.8 (2 H, br s, vinyls); ^{13}C NMR δ 136.2, 132.9, 130.0, 129.5, 128.4, 128.1, 127.8, 123.1; IR 1570, 1475, 1440, 1060, 1020, 895, 740, 690 cm^{-1}.

General Procedure for 1,2,3-Trisubstituted Diene Preparation by DBU Elimination. DBU (1 equiv) was added dropwise to the appropriate tri- or tetrahalide **3** in dilute benzene solution (0.25 M) stirring at 25 °C under nitrogen. There was an exothermic reaction, a thick preicpitate appeared within 5 minutes, and the reaction mixture became dark brown. After 1 h, the mixture was poured onto excess aqueous 1 M HCl and the layers were separated. The aqueous layer was extracted with ether. The combined organic layers were washed with water and saturated brine and dried ($MgSO_4$). The solvent was removed under reduced pressure to give a brown mobile oil. Purification was completed by prep TLC eluting with 10% $CHCl_3$ in hexane, unless otherwise stated.

(*Z*)-1,2-Dichloro-3-(phenylthio)butadiene (5a): 1.96 g, 85%, from (*E*)-2-(phenylthio)-1,3,4-trichlorobut-2-ene (**3a**), 10 mmol.

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Polymerized within 48 h. ^{1}H NMR δ 7.2 (5 H, br s, aromatic), 7.10 (1 H, s, C 1), 6.12 (1 H, s, C4), 5.65 (1 H, s, C 4); ^{13}C NMR δ 136.9, 133.8, 133.0, 130.1, 129.5, 127.5, 125.0, 121.9.

(*Z*)-2-Bromo-1-chloro-3-(phenylthio)butadiene (5b): 1.75 g, 63%, from (*E*)-3-bromo-1,4-dichloro-3-(phenylthio)but-2-ene (3b), 10 mmol. Polymerized within 48 h. ^{1}H NMR δ 7.2–7.7 (6 H, aromatics and Cl), 6.12 (1 H, d, J = 0.5 Hz, C4), 5.69 (1 H, d, J = 0.5 Hz, C4); ^{13}C NMR δ (ORD mutliplicity) 138.2 (s), 133.7 (s), 130.3 (d), 129.5 (d), 129.2 (s), 127.5 (d), 126.3 (t), 124.9 (d).

(*Z*)-1,2-Dichloro-3-(phenylseleno)butadiene (5c): 1.20 g, 86%, from (*E*)-2-(phenylseleno)-1,2,4-trichlorobut-2-ene (3c), 5 mmol. ^{1}H NMR δ 7.2–7.6 (5 H, m, aromatic), 7.15 (1 H, s, Cl), 6.42 (1 H, s, C4), 5.80 (1 H, s, C4).

(*Z*)-2-Bromo-1-chloro-3-(phenylseleno)butadiene (5d): 0.78 g, 68%, from (*E*)-3-bromo-1,4-dichloro-2-(phenylseleno)but-2-ene (3d), 5 mmol. ^{1}H NMR δ 7.15–7.6 (6 H, m, aromatic and Cl), 6.31 (1 H, s, C4), 5.73 (1 H, s, C4).

(*Z*)-1-Chloro-2,3-dibromobutadiene (5e): 0.89 g, 85%, from (*E*)-2,3-dibromo-1,4-dichlorobut-2-ene (3e) 4.2 mmol. Not purified at all. ^{1}H NMR δ 7.29 (1 H, s, Cl)m 6.40 (1 H, d, J = 2.5 Hz, C4), 5.85 (1 H, d, J = 2.5 Hz, C4); IR 3085, 1600, 1395, 1170, 980, 900, 875, 800 cm^{-1}.

(*Z*)-1-Chloro-2,3-diiodobutadiene (5f): 2.37 g, 81%, from (*E*)-2,3-diiodo-1,4-dichlorobut-2-ene (3f), 8.6 mmol. Required 2 equiv of DBU to effect complete elimination. Not purified further. ^{1}H NMR δ 7.15 (1 H, s, Cl), 6.75 (1 H, d, J = 2 Hz, C4), 6.18 (1 H, d, J = 2 Hz, C4).

Diels–Alder Reactions. General Procedure. The diene (crude) was made into a 1–2 molar solution in the dienophile (freshly distilled from 4A molecular sieves) containing BHT stabilizer and stirred under N_2 at 25 °C. BF_3 etherate (10–50 μL) was then added and the resulting mixture was stirred at 25 °C for 2–3 days. The color always darkened at least a little. The excess dienophile was then removed under reduced pressure leaving a thick viscous oil which was dissolved in 10% ethyl acetate/hexane and vacuum filtered through TLC grade silica gel on a sintered glass funnel to remove polymeric residue. The resulting bright yellow oils were purified by either gravity, or MPLC, silica gel columns (95 × 2.5 cm) eluting with 10–30% ethyl acetate/hexane. The experimentals quote major product, yield, isomer ratios where appropriate, starting diene and dienophile, purification, and analytical data. Except where stated only the major isomer NMR spectrum is quoted. In no case were regioisomers separated during chromatographic purification.

1-(3-Chloro-4-(phenylthio)cyclohex-3-enyl)ethanone (9a): 1.82 g, 68% from trichloride **3a**, 5.5:1 ratio, 3-chloro-2-(phenylthio)butadiene (**4a**) and MVK, 10 mmol. 10% EtOAc/hexane. ^{1}H NMR δ 7.3–7.6 (5 H, m, aromatic), 2.5–3.2 (4 H, m, allylic CH_2), 1.95–2.3 (6 H, m, other ring H, methyl ketone, 1.95, s); IR 2970, 1720, 1590, 1485, 1175, 815, 750 cm^{-1}. Analyzed as 2,4-dinitrophenylhydrazone, mp 148–149 °C. Anal. Calcd for $C_{20}H_{19}ClN_4O_4S$: C, 53.75; H, 4.29; N, 12.54. Found: C, 53.50; H, 4.51; N, 13.17. ^{1}H NMR δ 8.2 (1 H, s, C3 aromatic), 7.95 (1 H, s, C5 aromatic), 7.8 (1 H, s, C6 aromatic), 7.35 (5 H, br s, phenylthio), 2.5–3.3 (7 H, m, ring protons), 2.1 (3 H, s, methyl); IR (KBr pellet) 3300, 1620, 1590, 1405, 1340, 740 cm^{-1}.

3-Chloro-4-(phenylthio)cyclohex-3-enecarbaldehyde (13a): 2.0 g, 40% from trichloride **3a**, 3-chloro-2-(phenylthio)butadiene (**4a**) and acrolein, 20 mmol. MPLC 10% EtOAc/hexane followed by PLC 30% EtOAc/hexane. Anal. Calcd. for $C_{13}H_{13}ClOS$: C, 61.77; H, 5.18. Found: C, 61.79; H, 5.51. ^{1}H NMR δ 9.67 (1 H, s, CHO), 7.2–7.8 (5 H, m, aromatics), 1.5–3.0 (7 H, m, ring protons); IR 2900, 2700, 1715, 1615, 1580, 1470, 1330, 800, 690 cm^{-1}.

1-(3-Bromo-4-(phenylthio)cyclohex-3-enyl)ethanone (9b): 2.0 g, 40% from trihalide **3b**, 2:1 ratio, from 3-bromo-2-(phenylthio)butadiene (**4b**) and MVK, 16 mmol. MPLC 10% EtOAc/hexane. ^{1}H NMR δ 7.2–7.5 (5 H, m, aromatic), 2.2–3.2 (5 H, m, allylic CH_2 and ring Cl), 2.10 (3 H, s, methyl ketone) 1.9–2.05 (2 H, m, ring CH_2); IR 2930, 1700, 1580, 1470, 1430, 1350, 1170, 740, 690 cm^{-1}.

3-Bromo-4-(phenylthio)cyclohex-3-enecarbaldehyde (13b): 1.60 g, 27% from trihalide **3b**, 10:1 ratio, from 3-bromo-2-(phenylthio)butadiene (**4b**) and acrolein, 20 mmol, MPLC 10% EtOAc/hexane. ^{1}H NMR δ 9.65 (1 H, s, CHO), 7.0–7.9 (5 H, m, aromatic), 1.6–3.4 (7 H, m, ring protons); IR 3040, 2700, 1720, 1470, 1125, 780 cm^{-1}.

1-(3-Chloro-4-(phenylseleno)cyclohex-3-enyl)ethanone (9c): 0.61 g, 72%, from 3-chloro-2-(phenylseleno)butadiene (**4c**) and MVK, 2.7 mmol. MPLC 10% EtOAc/hexane. ^{1}H NMR δ 7.2–7.7 (5 H, m, aromatics), 1.0–3.0 (10 H, m, ring protons and 2.13, s, methyl); ^{13}C NMR δ 208.7, 136.1, 129.3, 128.9, 127.4, 127.3, 126.5, 47.9, 35.7, 31.5, 27.9, 25.5; IR 1710, 1440, 1370, 1355, 1170, 740, 690 cm^{-1}.

1-(3-Bromo-4-(phenylseleno)cyclohex-3-enyl)ethanone (9d): 0.64 g, 70%, from 3-bromo-2-(phenylseleno)butadiene (**4d**) and MVK, 2.5 mmol. MPLC 10% EtOAc/hexane. ^{1}H NMR δ 7.2–7.7 (5 H, m, aromatics), 2.5–2.95 (4 H, m, allylic CH_2), 1.2–2.3 (6 H, m, ring protons plus 2.13, s, methyl); ^{13}C NMR δ 208.6, 136.3, 130.2, 129.3, 128.7, 127.8, 118.5, 48.5, 38.4, 32.3, 27.9., 25.5; IR 2930, 1705, 1475, 1435, 1370, 1355, 1330, 1170, 765, 745, 695 cm^{-1}.

1-(3-Chloro-4-(phenylthio)cyclohexa-1,3-dienyl)ethanone (15a): 0.53 g, 57%, from (*Z*)-1-2-dichloro-3-(phenylthio)butadiene (**5a**) and MVK, 3.5 mmol. MPLC 10% EtOAc/hexane. Anal. Calcd for $C_{14}H_{13}ClOS$: C, 63.50; H, 4.96. Found: C, 63.88; H, 5.02. ^{1}H NMR δ 7.3–7.7 (5 H, m, aromatics), 6.85 (1 H, br s, C2), 2.1–2.7 (7 H, m, ring protons), 2.25 (s, methyl ketone); IR 3030, 1725, 1660, 1540, 1390, 1270, 820, 765 cm^{-1}.

3-Chloro-4-(phenylthio)cyclohexa-1,3-dienecarbaldehyde (15g): 1.07 g, 21%, from (*Z*)-1,2-dichloro-3-(phenylthio)butadiene (**5a**) and acrolein, 20 mmol. MPLC 10% EtOAc/hexane. Anal. Calcd for $C_{13}H_{11}ClOS$: C, 62.27; H, 4.42. Found: C, 62.61; H, 4.55. ^{1}H NMR δ 9.50 (1 H, s, CHO), 7.2–7.7 (5 H, m, aromatics), 6.79 (1 H, br s, C2), 2.0–2.4 (4 H, m, allylic CH_2); IR 3060, 2920, 1720, 1680, 1580, 1440, 1190, 910, 750 cm^{-1}.

1-(3-Bromo-4-(phenylthio)cyclohexa-1,3-dienyl)ethanone (15b): 0.50 g, 57%, from (*Z*)-2-bromo-1-chloro-3-(phenylthio)-butadiene (**15b**) and MVK, 3 mmol. MPLC 10% EtOAc/hexane. Compound aromatized slowly on standing. ^{1}H NMR δ 7.3–7.5 (5 H, m, aromatics), 6.93 (1 H, br s, C2), 1.95–2.5 (7 H, m, allylic CH_2 plus s, 2.29, methyl ketone); ^{13}C NMR δ 196.6, 143.7, 137.9, 135.4, 134.8, 130.5, 130.2, 129.5, 110.4, 29.5, 25.0, 20.6; IR 1710, 1655, 1525, 1265, 1220, 1160, 750, 705, 690 cm^{-1}; UV (EtOH) λ_{max} 361 nm (ε 1.28 × 10^4).

3-Bromo-4-(phenylthio)cyclohexa-1,3-dienecarbaldehyde (15h): 0.70 g, 17%, from (*Z*)-2-bromo-1-chloro-3-(phenylthio)-butadiene (**5b**) and acrolein, 14 mmol. MPLC 10% EtOAc/hexane then PLC 10% EtOAc/hexane. Compound rapidly aromatized spontaneously. ^{1}H NMR δ 9.65 (1 H, s, CHO), 7.0–7.9 (5 H, m, aromatic), 6.76 (1 H, br, s, C2 vinylic), 2.2–2.5 (4 H, approx AB, q, J_{AB} = 7 Hz, allylic CH_2); IR 3050, 2820, 2720, 1660, 1580, 1510, 1185, 1155, 750, 690 cm^{-1}.

1-(3-Chloro-4-(phenylseleno)cyclohexa-1,3-dienyl)-ethanone (15c): 0.63 g, 47%, from (*Z*)-1,2-dichloro-3-(phenylseleno)butadiene (**5c**) and MVK, 4.3 mmol. MPLC 10% EtOAc/hexane. ^{1}H NMR 7.2–7.8 (5 H, m, aromatics), 6.71 (1 H, br s, C2), 2.0–3.0 (7 H, m, allylic methylenes plus 2.27, s, methyl ketone); IR 3060, 1710, 1660, 1540, 1440, 1385, 1265, 1220, 1160, 1070, 970, 810, 745, 695 cm^{-1}.

1-(3-Bromo-4-(phenylseleno)cyclohexa-1,3-dienyl)-ethanone (15d): 0.75 g, 62%, from (*Z*)-2-bromo-1-chloro-3-(phenylseleno)butadiene (**5d**) and MVK, 3.4 mmol. MPLC 10% EtOAc/hexane. ^{1}H NMR 7.1–7.7 (5 H, m, aromatics), 6.81 (1 H, br s, C2 vinylic), 2.2–3.2 (7 H, m, allylic CH_2 plus 2.26, s, methyl ketone); IR 3050, 1705, 1655, 1525, 1380, 1260, 745, 690 cm^{-1}.

1-(3,4-Dibromocyclohexa-1,3-dienyl)ethanone (15e): 0.63 g, 51%, from (*Z*)-1-chloro-2,3-dibromobutadiene (**5e**) and MVK, refluxed in the presence of 3 molar equiv of Na_2CO_3 for 2 days, 4.4 mmol. ^{1}H NMR 6.90 (1 H, br s, C2), 2.55–2.9 (4 H, broadened AB quartet J ~ 6 Hz, allylic CH_2), 2.35 (3 H, s, methyl ketone); IR 1670, 1565, 1390, 1260, 1220 cm^{-1}.

1-(3,4-Diiodocyclohexa-1,3-dienyl)ethanone (15f): yield estimated by NMR at 13%, as it could not be separated from MVK dimer. From (*Z*)-1-chloro-2,3-diiodobutadiene (**5f**) and MVK, refluxed in the presence of 3 molar equiv of Na_2CO_3 for 2 days. ^{1}H NMR peaks at δ 7.00 (t, J = 1 Hz), 2.35–2.9 (m), and 2.28 (s) attributed to **15f**. All other peaks belonged to 6-acetyl-2-methyl-$\Delta^{2,3}$-tetrahydropyran.

General Procedure for Aromatization of Disubstituted Diene Diels–Alder Adducts. The Diels–Alder adduct (**9** or **13**) (1 equiv) and NBS (1 equiv) were refluxed in CCl_4 under nitrogen for 2 h. The reaction mixture was cooled and poured onto water and the layers were separated. The aqueous layer was extracted

with chloroform and the combined organic layers were washed with water, saturated brine, and dried ($MgSO_4$). The solvent was removed under reduced pressure. The residue and DBU (2 equiv) were refluxed together in benzene under nitrogen for 3 h. The mixture became black and formed a thick precipitate. The reaction mixture was cooled to 20 °C and poured onto excess dilute HCl and the layers separated. The aqueous layer was extracted with ether and the combined organic layers were washed with water and saturated brine and dried ($MgSO_4$). Solvent was removed under reduced pressure, and the residual oils were purified by preparative TLC to give, as the major or only product, the para-substituted product, as shown by NMR comparison with known compounds. Compound **9a** gave **12a** in 68% yield. Compounds **13a** and **13b** both gave **14a** in 58% yield. Compound **9c** gave **12c** in 53% yield.

General Procedure for Aromatization of Trisubstituted Diene Diels–Alder Adducts. The dienone **15** (1 equiv) and DBU (1 equiv) were refluxed together in benzene under nitrogen for 3 h. The reaction became black and formed a thick precipitate. The mixture was cooled to 20 °C and poured onto excess dilute HCl. The layers were separated and the aqueous layer was extracted with ether. The combined organic layers were washed with water and saturated brine and dried ($MgSO_4$). The solvent was removed under reduced pressure, and the residual oil was purified by preparative TLC to give as the major, or only aromatic product, the para-substituted aromatic as shown by NMR comparison with known compounds. Compounds **15a** and **15b** both gave **12a** in 100% yields. Compounds **15 g** and **15 h** gave **14** in 70% and 100% yields, respectively. Compounds **15c** and **15d** gave **12c** in 40% and 100% yields, respectively. Compound **15e** gave **12e** in 88% yield. Compound **15f** gave **12f** in undetermined yield (due to the presence of MVK dimer).

***p*-(Phenylseleno)acetophenone (12c).** Acetyl chloride (0.13 mL, 1.8 mmol) was added dropwise to a stirring solution of diphenyl selenide (0.41 g, 1.8 mmol) and anhydrous aluminum chloride (0.29 g, 2.2 mmol) in carbon disulfide (5 mL) at 20 °C under nitrogen. There was a violent exothermic reaction, and the mixture was stirred for 1.5 h after the addition was completed. The reaction was quenched by pouring onto water (10 mL) and the layers were separated. The aqueous layer was extracted with ether (2 × 10 mL). The combined organic layers were washed with water (10 mL) and saturated brine (10 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure to yield a yellow oil which was purified by preparative TLC eluting with 10% ethyl acetate/hexane to give **13c** (0.14 g, 28%). Recrystallization from 95% EtOH gave yellow crystals: mp 47.5–49 °C. Anal. Calcd for $C_{14}H_{12}OSe$: C, 61.10; H, 4.29. Found: C, 61.17; H, 4.33. ^1H NMR δ 7.76 (2 H, half of AB quartet, J = 9 Hz, C2 aromatics), 7.4–7.7 (5 H, m, PhSe), 7.20 (2 H, half of AB quartet, J = 9 Hz, aromatics), 2.52 (3 H, s, methyl ketone); IR (KBr pellet) 1680, 1585, 1395, 1270, 955, 825, 750, 695 cm^{-1}.

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Registry No. **3a**, 85972-06-1; **3b**, 85972-07-2; **3c**, 85972-08-3; **3d**, 85972-09-4; **3e**, 85415-22-1; **3f**, 85972-10-7; **4a**, 85972-11-8; **4b**, 85972-12-9; **4c**, 85972-13-0; **4d**, 85972-14-1; **5a**, 85972-15-2; **5b**, 85972-16-3; **5c**, 85972-17-4; **5d**, 85972-18-5; **5e**, 85972-19-6; **5f**, 85972-20-9; **9a**, 85972-21-0; **9b**, 85895-55-2; **9c**, 85972-22-1; **9d**, 85972-32-3; **10a**, 85972-29-8; **10b**, 85972-30-1; **10c**, 85972-31-2; **10d**, 85972-33-4; **12c**, 85972-34-5; **13a**, 90606-71-6; **13b**, 90606-72-7; **15a**, 85972-23-2; **15b**, 85972-24-3; **15c**, 85972-25-4; **15d**, 85972-26-5; **15e**, 85972-27-6; **15f**, 85972-28-7; **15g**, 90606-73-8; **15h**, 90606-74-9; MVK, 78-94-4; $ClCH_2C{\equiv}CCH_2Cl$, 821-10-3; PhSCl, 931-59-9; PhSBr, 28074-23-9; PhSeCl, 5707-04-0; PhSeBr, 34837-55-3; Br_2, 7726-95-6; I_2, 7553-56-2; acrolein, 107-02-8.

Syntheses, Conformational Studies, and Reactions of Heteromacrocycles. Bis(2-pyridyl) Ketone Derivatives[1]

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A new series of spiromacrocycles were prepared by nucleophilic displacement of bromide from bis(6′-bromo-2′-pyridyl)-1,3-dioxolane; nucleophiles employed included the dianions of $HO(CH_2CH_2O)_nH$, n = 1–6, $HS(CH_2CH_2S)_nH$, n = 1,2, and $(HSCH_2CH_2)_2O$. Single-crystal X-ray diffraction studies on the 1:1 diethylene and 1:1 tetraethylene glycol ketal coronands showed them to have conformations dominated by the requirements of the pyridyl ketal unit (pyridine N anti to ketal O) and an inherent imidate moiety (N–C–O–C torsion angle near 0°). Besides the 1:1 coronands, isolated from most of the reactions, the higher oligomers and acyclic products were also obtained and characterized. ^1H NMR and elemental analytical data indicate that several of these macrocycles sequester $CHCl_3$. All of the 1:1 ketal crown ethers, and several of the 2:2 macrocycles, were hydrolyzed to the corresponding ketonic macrocycles. X-ray diffraction analysis indicated that the hexaethylene glycol ketonic coronand formed a neutral component complex with a water molecule, whereas the smaller tetraethylene glycol coronand did not. Reduction of the ketonic coronands with $NaBH_4$ produced the corresponding carbinol macrocycles, all of which were oils that were slowly transformed back to the corresponding ketone via air oxidation.

Introduction

Modified crown ether macrocycles containing a 2,6-pyridinediyl or 2,2′-bipyridine-6,6′-diyl subunit exhibit a penchant for the formation of neutral component complexes.[2] X-ray diffraction experiments confirm that **20e** and **1** bind a water molecule in the polyethylene portion of their structures,[2-4] whereas no evidence for this sort of neutral host–guest interaction is displayed by either **20c**

(1) (a) Part 98 in the Chemistry of Heterocyclic Compounds Series. (b) Taken from the PhD dissertation of HCRT, LSU, 1983.

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