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Highly Heteroatom-dependent π-Facial Stereoselectivity in the Diels-Alder Reaction of 1,3-Cyclopentadienes Having a Heteroatom Substituent at 5-Position1)

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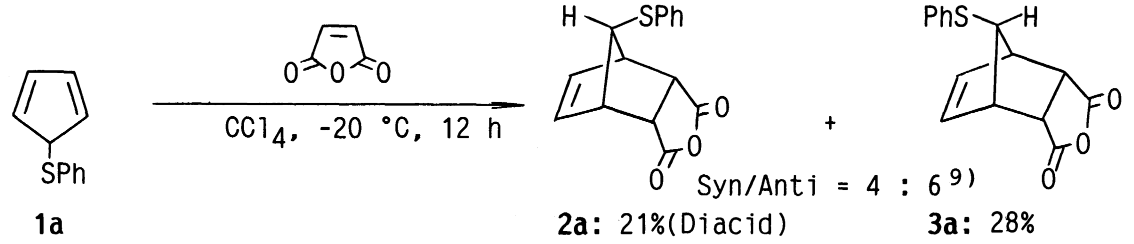
5-Phenylthio-1,3-cyclopentadiene reacted with maleic anhydride to give a 4 : 6 mixture of *syn-* and *anti*-attack adducts. In contrast, the selenium isologue, 5-phenylseleno-1,3-cyclopentadiene reacted with dienophiles with remarkable *anti*-π-facial selectivity to give the corresponding *anti*-attack adducts, exclusively.

The origin of π-facial stereoselectivity in Diels-Alder reactions of 5-substituted cyclopentadienes, the simplest dienes with unsymmetric π-plane, has been one of the subjects of intensive studies2-6) and the following π-facial stereoselectivities were reported: 1) 5-Acetoxy- and 5-hydroxy-1,3-cyclopentadienes react with dienophiles with remarkable *syn*-π-facial selectivity and 1,2,3,4,5-pentachlorocyclopentadiene4,6) reacts with *syn*-π-facial preference; 2) The dienes having 5-alkyl or 5-trimethylsilyl group give opposite results.3a,c,5) The *anti*-selectivity can be simply explained by steric approach control, but the *syn*-selectivity is still not fully understood.

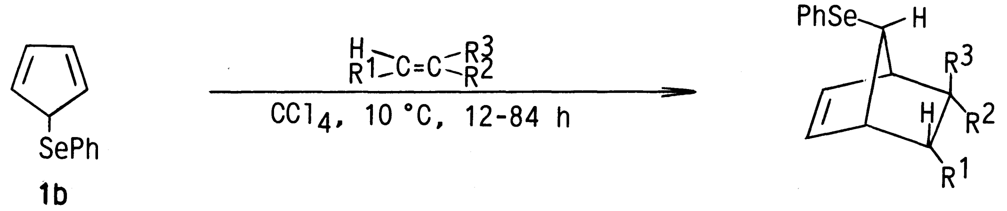
In this paper, we wish to report the first synthesis of 5-phenylseleno-1,3-cyclopentadiene (**1b**) and show a high dependence of π-facial stereoselectivity upon heteroatom substituents in Diels-Alder reactions of 5-phenylthio-1,3-cyclopentadiene (**1a**) and the diene **1b**.

5-Phenylthio-1,3-cyclopentadiene (**1a**) was prepared from the reaction of thallium cyclopentadienide and phenylsulfenyl chloride in carbon tetrachloride.7) The diene **1a** was very easily isomerized due to [1,5] proton transfer.3a,7,8) Thus, after removal of precipitated thallium chloride, an equimolar amount of maleic anhydride was immediately added. The reaction mixture was allowed to stand at -20 °C for 12 h to give a 4 : 6 mixture of *syn-* and *anti*-attack products, 8-*endo*- and 8-*exo*-phenylthio-3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1,3-dione, (**2a**) and (**3a**) [isolated yields: **2a**(as diacid); 21%, **3a**; 28%](Scheme 1).9-11) The structures of **2a** and **3a** were determined on the basis of their ^{1}H-NMR solvent shifts and chemical correlations.6a,14) Low π-facial selectivity in Diels-Alder reaction of **1a** was contrasting to the remarkable *syn*-π-facial selectivities observed in the oxygen examples.4)



Scheme 1.

In contrast, 5-phenylseleno-1,3-cyclopentadiene (**1b**) reacted with dienophiles with remarkable *anti*-π-facial stereoselectivity. The diene **1b** was similarly prepared from phenylselenenyl bromide and thallium cyclopentadienide in carbon tetrachloride at 10 °C under nitrogen atmosphere.[3a,7] Although, the diene **1b** was rather stable than **1a**, isolation of **1b** failed.[12] After removal of thallium bromide, an equimolar amount of maleic anhydride was added. After standing at 10 °C for 84 h, *anti*-attack product, 8-*exo*-phenylseleno-3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1,3-dione (**3b**) was exclusively obtained in 69% yield (mp 121-124 °C).[13] The reactions of the diene **1b** with N-phenylmaleimide and dimethyl fumarate also exclusively gave the corresponding *anti*-attack products **4b** and **5b** in 32 and 34% yields, respectively (Scheme 2).[14] ^{1}H-NMR monitoring of the reaction mixture showed no formation of any other stereoisomers.

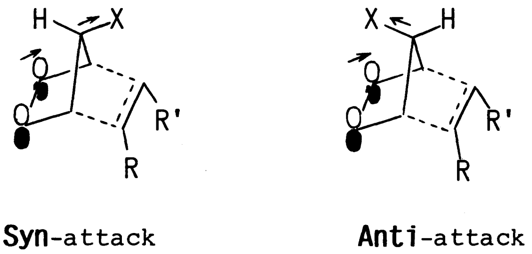


Scheme 2.

3b: R^1,R^2= (CO)OCO, R^3= H, 69%, mp 121-124 °C
4b: R^1,R^2= (CO)N(Ph)CO, R^3= H, 32%, mp 211-212 °C
5b: $R^1=R^3$= CO_2CH_3, R^2= H, 34%*, mp 79-80 °C
*in the presence of $AlCl_3 \cdot Et_2O$

No existing theories can generally account for the fact: 5-hydroxy- and 5-acetoxydienes react with remarkable *syn*-π-facial selectivity,[4] 5-phenylthiodiene **1a** without π-facial selectivity and 5-phenylseleno diene **1b** with remarkable *anti*-π-facial selectivity. At present time, we wish to tentatively explain the selectivity of the oxygenated dienes based on the hypothesis founded on the relative stabilities of the *syn*- and *anti*-attack transition states (Fig. 1).

The *syn*-attack transition state may be more stable due to the favorable



Transition states
Fig. 1.

interaction of π-electrons with the polarized C(7)-X bond from the back side. Since the electronegativities of heteroatoms decrease in the order of oxygen > sulfur > selenium, the *syn*-π-facial selectivity will be decreased in that order.[16,17] In the reaction of the diene **1b**, *anti*-π-facial selectivity can be simply accounted for in terms of steric approach control.

Further investigations on the selectivity and synthetic application of the dienes **1a** and **1b** are now in progress.

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9) The ratio was determined on ^{1}H-NMR. **2a** was isolated as diacid form, since fractional recrystallization of the mixture gave **2a** in low yields.

10) **2a**: mp 91-93 °C; IR (KBr) 1860, 1780cm^{-1}; ^{1}H-NMR (CDCl$_3$) δ 3.40 (m, 2H, CH), 3.58 (t, J= 1.4 Hz, 1H, CH-SPh), 3.94 (dd, J= 2.8, 1.6 Hz, 2H, CH), 6.40 (m, 2H, CH=CH), 7.3-7.4 (m, 5H, Ph); ^{1}H-NMR(C$_6$D$_6$) δ 2.73 (m, 2H, CH), 2.90 (t, J= 1.4 Hz, 1H, PhS-CH), 3.07 (m, 2H, CH), 5.67 (m, 2H, CH=CH), 6.9-7.1 (m, 5H, Ph); ^{13}C-NMR (Acetone-d$_6$) δ 46.7, 50.1, 69.1, 128.4, 130.2, 132.2, 134.5, 137.3, 172.5 (*C=O); EIMS(20 eV), m/z (rel intensity) 272 (M$^+$, 27), 244

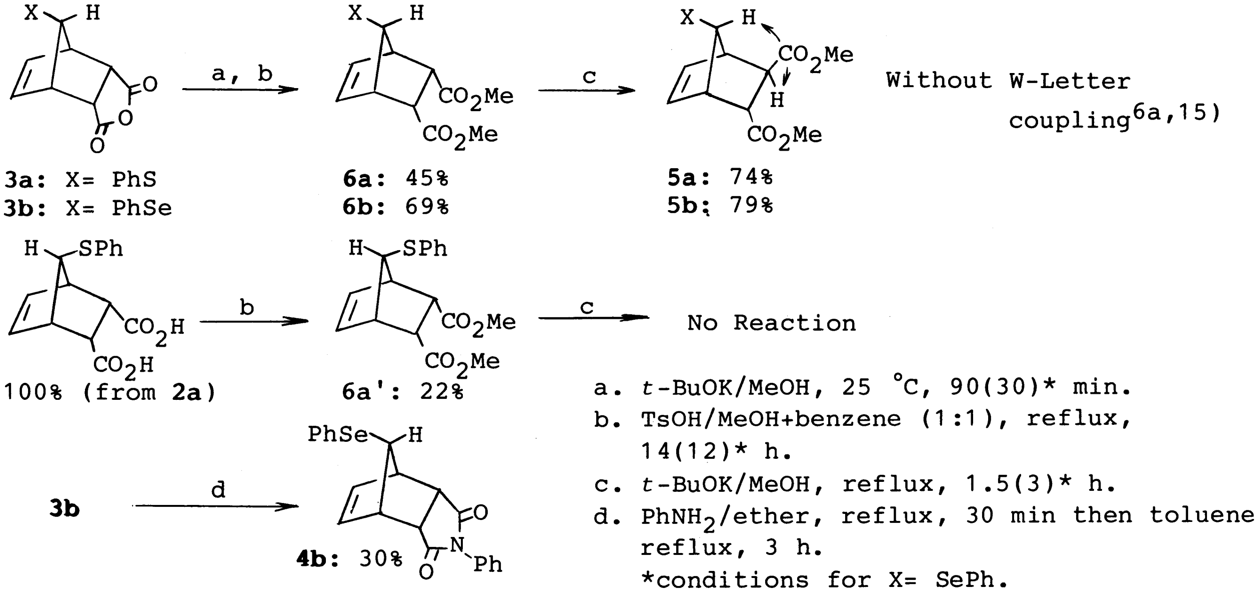
(18), 199 (100), 174 (45), 135 (11), 110 (13), 91 (49), 85 (61).
Anal. Found:C, 65.92; H, 4.55%. Calcd for $C_{15}H_{12}O_3S$: C, 66.16; H, 4.44%.

11) **3a**: mp 165-168 °C; IR(KBr) 1860, 1785 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 3.40 (s, 1H, CH-SPh), 3.65 (br s, 4H, CH), 6.37 (br s, 2H, CH=CH), 7.2-7.4 (m, 5H, Ph); ^{1}H-NMR (C_6D_6) δ 2.37 (dd, J= 1.6, 2.9 Hz, 2H, CH), 2.57 (m, 1H, CH-Ph), 2.95 (m, 2H, CH), 5.74 (m, 2H, CH=CH), 6.9-7.2 (m, 5H, Ph); ^{13}C-NMR (Acetone-d_6) δ 46.9, 51.5, 70.3, 127.3, 129.9, 130.7, 134.8, 136.7, 171.8 (*C=O); EIMS (20 eV), m/z (rel intensity) 272 (M$^+$, 33), 244 (10), 199 (100), 174 (12), 135 (19), 110 (12), 91 (51).
Anal. Found: C, 66.23; H, 4.53%. Calcd for $C_{15}H_{12}O_3S$: C, 66.16; H, 4.44%.

12) The ^{1}H-NMR ($CDCl_3$) of **1b** showed a singlet peak at δ= 4.68 and AA'BB' multiplet peak at δ= 6.42 due to olefinic protons.

13) **3b**: mp 121-124 °C; IR (KBr) 1860, 1790 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 3.30 (t, J= 1.65 Hz, 1H, CH-SePh), 3.62 (dd, J=2.93, 1.65 Hz, 2H, CH), 3.70 (m, 2H, CH), 6.37 (m, 2H, CH=CH), 7.1-7.5 (m, 5H, Ph); ^{1}H-NMR (C_6D_6) δ 2.35 (brs, 2H, CH), 2.53 (s, 1H, CH-SePh), 3.03 (s, 2H, CH), 5.74 (s, 2H, CH=CH), 7.0-7.3 (m, 5H, Ph); ^{13}C-NMR (Acetone-d_6) δ 47.1, 52.4, 66.0, 127.9, 129.9, 130.7, 133.7, 135.8, 171.5 (*C=O); EIMS(20 eV), m/z (rel intensity), 320 (M$^+$, 43), 222 (27), 142 (28), 141 (100), 135 (28), 91 (41).
Anal. Found: C, 56.16; H, 3.83%. Calcd for $C_{15}H_{12}O_3Se$: C, 56.44; H, 3.79%.

14) Structural confirmation of the products **2a**, **3a**, **3b**, **4b**, and **5b**.



Without W-Letter coupling[6a,15]

3a: X= PhS
3b: X= PhSe

6a: 45%
6b: 69%

5a: 74%
5b: 79%

100% (from **2a**)

6a': 22%

No Reaction

3b

4b: 30%

a. *t*-BuOK/MeOH, 25 °C, 90(30)* min.
b. TsOH/MeOH+benzene (1:1), reflux, 14(12)* h.
c. *t*-BuOK/MeOH, reflux, 1.5(3)* h.
d. $PhNH_2$/ether, reflux, 30 min then toluene reflux, 3 h.
*conditions for X= SePh.

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