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The Cheletropic Addition of Dichlorocarbene to 2-Phenylsulfonyl-2-azabicyclo[3.2.1]octa-3,6-diene and Its 8-Substituted Derivatives

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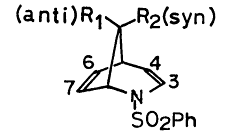
Synopsis. It was found that dichlorocarbene undergoes *exo* addition preferentially on the C_3–C_4 double bond of 2-phenylsulfonyl-2-azabicyclo[3.2.1]octa-3,6-diene and *endo* addition on that of 2-phenylsulfonyl-syn-8-benzoyloxy-2-azabicyclo[3.2.1]octa-3,6-diene.

Recently we have discovered that the 1,3-dipolar cycloadditions of phenylglyoxylonitrile oxide to 2-phenylsulfonyl-2-azabicyclo[3.2.1]octa-3,6-diene (**1**) and 2-phenylsulfonyl-syn-8-benzoyloxy-2-azabicyclo[3.2.1]-octa-3,6-diene (**3**) take place selectively with an *exo* attack on the C_6–C_7 double bond.[1] In order to explore further the reactivity of the C_3–C_4 and C_6–C_7 double bonds, particularly in their *exo* and *endo* sides, the addition of dichlorocarbene was investigated with azabicyclic dienes, **1**—**3**. Herein, we wish to report our findings on these reactions.



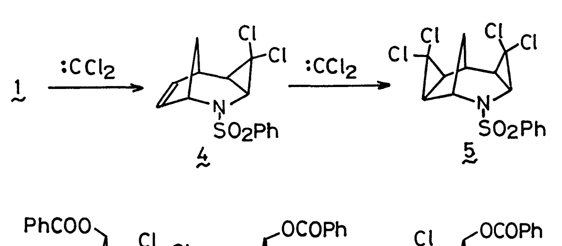
1: $R_1=R_2=H$
2: $R_1=PhCOO, R_2=H$
3: $R_1=H, R_2=PhCOO$

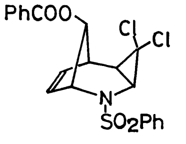
The reaction of diene **1** with dichlorocarbene, generated by the usual phase-transfer method,[2] afforded the 1:1 *exo* adduct (**4**) in a high yield after 30 min, as Table 1 shows. In a prolonged reaction, the 1:2 adduct (**5**) was produced by the subsequent addition of dichlorocarbene to adduct **4**. The reaction with diene **2**, in which the *exo* side of the C_6–C_7 double bond was blocked by the benzoyloxyl group, resulted in the formation of only the 1:1 *exo* adduct (**6**), even after 72 h, and the 1:2 adduct (**6′**) was not obtained at all. This indicates that the *endo* side of the C_6–C_7 double bond is much less reactive. On the other hand, when the *exo* side of the C_3–C_4 double bond was blocked by the benzoyloxyl group, the addition of dichlorocarbene was diverted to the *endo* side to afford the 1:1 *endo* adduct (**7**), together with the 1:2 adduct (**8**), as Table 1 shows.

Table 1. The yields of the products in the addition of dichlorocarbene to dienes 1—3

Dienes	Time/h	Adduct(yield/%)[a]
1	0.5	**4** (84), **5** (5)
1	3	**4** (65), **5** (23)
1	72	**4** (33), **5** (45)
2	3	**6** (91)
2	72	**6** (85)
3	3	**7** (77), **8** (20)
3	72	**7** (47), **8** (30)

a) Based on the dienes.





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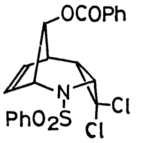

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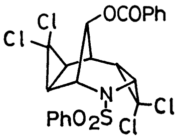

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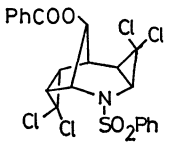

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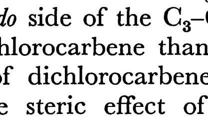
Next, the reactions of dienes **1**—**3** with dichlorocarbene were compared with those with phenylglyoxylonitrile oxide as a 1,3-dipole. The 1,3-dipolar addition to **2** in tetrahydrofuran at 0 °C afforded two *exo* adducts, **9** and **10**, in 47 and 22% yields respectively after 3 h. This phenomenon of the *exo* prevalence, which is observed even in the existence of the benzoyloxyl group in the C_6–C_7 side of **2**, agreed with the results in the cases of **1** and **3** reported previously.[1] As has been described above, we have found that dichlorocarbene exhibits an *exo* or *endo* attack preferentially on the C_3–C_4 double bond of dienes **1**—**3**, while phenylglyoxylonitrile oxide exhibits an *exo* attack on their C_6–C_7 double bonds, and that the *endo* side of the C_3–C_4 double bond is less reactive to dichlorocarbene than its *exo* side. Thus, the addition of dichlorocarbene to dienes **1**—**3** is governed by the steric effect of hydrogen or the substituent at the 8-position.



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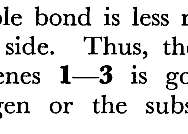

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Experimental

The melting points are uncorrected. The ^1H NMR spectra were taken at room temperature with a Hitachi R-24A spectrometer, using tetramethylsilane as the internal standard. The IR spectra were taken with a Hitachi 216 grating infrared spectrometer.

Materials. Dienes **1**—**3** were prepared from norbornadiene and 7-benzoyloxynorbornadiene according to the published procedures.[3] **2**: mp 121.5—122 °C; IR (KBr) 1715 cm^{-1} (CO), 1345, 1180 cm^{-1} (SO_2); ^{1}H NMR ($CDCl_3$) δ 2.76 (m, 1H, 5-H), 4.82 (brs, 2H, 1-H and 8-H), 5.15 (m, 2H, 4-H and 7-H), 6.09 (dd, 1H, $J_{6,7}$=5.3 Hz, $J_{5,6}$=2.3 Hz, 6-H), 6.28 (d, 1H, $J_{3,4}$=9.0 Hz, 3-H), 6.88—8.02 (m, 10H, aromatic). Found: C, 65.67; H, 4.63; N, 4.08%. Calcd for $2_{20}H_{17}NO_4S$: C, 65.40; H, 4.63; N, 3.81%. **3**: mp 114.5—115 °C; IR (KBr) 1710 cm^{-1} (CO), 1340, 1165 cm^{-1} (SO_2); ^{1}H NMR ($CDCl_3$) δ 2.75 (m, 1H, 5-H), 4.71 (m, 1H, 1-H), 5.07 (m, 2H, 4-H and 8-H), 5.39 (dd, 1H, $J_{6,7}$=6.0 Hz, $J_{1,7}$=3.0 Hz, 7-H), 6.09 (dd, 1H, $J_{6,7}$=6.0 Hz, $J_{5,6}$=3.3 Hz, 6-H), 6.57 (d, 1H, $J_{3,4}$=8.0 Hz, 3-H), 6.92—8.00 (m, 10H, aromatic). Found: C, 65.41; H, 4.64; N, 4.11%. Calcd for $C_{20}H_{17}NO_4S$: C, 65.40; H, 4.63; N, 3.81%.

*General Procedure for the Addition of Dichlorocarbene to Dienes **1**—**3**.* A 50% aqueous sodium hydroxide solution (6.5 g) was stirred, drop by drop, into a solution of dienes (2.72 mmol) in chloroform (10 g) with benzyltriethylammonium chloride (50 mg) for 30 min at room temperature. After a definite period of stirring, the reaction mixture was diluted with water and extracted with chloroform. After the removal of the chloroform *in vacuo*, the residue was chromatographed on a silica-gel column, using benzene, hexane, or ethyl acetate as the eluant.

*Reaction with **1**.* Two adducts, **4** and **5**, were obtained. **4**: mp 132.5—134 °C; IR (KBr) 1335 and 1168 cm^{-1} (SO_2); ^{1}H NMR (C_6D_6) δ 1.10 (m, 1H, 9-H_{anti}), 1.48 (dd, 1H, $J_{3,5}$=10.0 Hz, $J_{5,6}$=3.0 Hz, 5-H), 2.3 (d, 1H, $J_{9s,9a}$=11.3 Hz, 9-H_{syn}), 2.32 (m, 1H, 6-H), 3.2 (d, 1H, $J_{3,5}$=10.0 Hz, 3-H), 4.48 (m, 1H, 1-H), 5.40 (dd, 1H, $J_{7,8}$=5.7 Hz, $J_{1,8}$=2. 7Hz, 8-H), 5.64 (dd, 1H, $J_{7,8}$=5.7 Hz, $J_{7,9}$=2.3 Hz, 7-H), 6.75—8.00 (m, 5H, aromatic). Found: C, 51.07; H, 3.96; N, 4.55%. Calcd for $C_{14}H_{13}NO_2SCl_2$: C, 50.92; H, 3.97; N, 4.24%. **5**: mp 165—166.5 °C; IR (KBr) 1360 and 1172 cm^{-1} (SO_2); ^{1}H NMR (C_6D_6) δ 1.24 (d, 1H, $J_{3,5}$=10.7 Hz, 5-H), 1.32 (d, 1H, $J_{7,9}$=7.3 Hz, 7-H), 1.69 (d, 1H, $J_{7,9}$=7.3 Hz, 9-H), 1.80 (m, 2H, 10-CH_2), 2.17 (m, 1H, 6-H), 3.13 (d, 1H, $J_{3,5}$=10.7 Hz, 3-H), 4.38 (m, 1H, 1-H), 6.67—8.10 (m, 5H, aromatic). Found: C, 43.41; H, 2.91; N, 3.36%. Calcd for $C_{15}H_{13}NO_2SCl_4$: C, 43.61; H, 3.17; N, 3.39%.

*Reaction with **2**.* The adduct **6** was obtained: mp 136—137 °C; IR (KBr) 1720 cm^{-1} (CO), 1355, 1170 cm^{-1} (SO_2); ^{1}H NMR ($CDCl_3$) δ 2.22 (dd, 1H, $J_{3,5}$=10.0 Hz, $J_{5,6}$=3.0 Hz, 5-H), 3.27 (d, 1H, $J_{3,5}$=10.0 Hz, 3-H), 3.30 (m, 1H, 6-H), 4.91 (m, 1H, 1-H), 5.80 (m, 2H, 8-H and 9-H), 6.35 (dd, 1H, $J_{7,8}$=5.3 Hz, $J_{6,7}$=2.3 Hz, 7-H), 7.09—8.20 (m, 10H, aromatic). Found: C, 56.17; H, 3.66; N, 3.10%. Calcd for $C_{21}H_{17}NO_4SCl_2$: C, 56.01; H, 3.78; N, 3.11%. The small values of the coupling constants between H-5 and H-6 for **4** and **6** and between H-1 (H-6) and H-9 (H-7) for **5** indicated the *exo* configurations of **4**, **5**, and **6**.

*Reaction with **3**.* The adducts **7** and **8** were obtained. **7**: mp 130—130.5 °C; IR (KBr) 1720 cm^{-1} (CO), 1355, 1170 cm^{-1} (SO_2); ^{1}H NMR ($CDCl_3$) δ 1.93 (dd, 1H, $J_{5,6}$=8.0 Hz, $J_{3,5}$=10.7 Hz, 5-H), 3.66 (d, 1H, $J_{3,5}$=10.7 Hz, 3-H), 3.48 (m, 1H, 6-H), 4.49 (m, 1H, 1-H), 5.11 (t, 1H, $J_{1,8}$=$J_{7,8}$=4.7 Hz, 8-H), 6.00 (m, 2H, 7-H and 9-H), 6.94—8.00 (m, 10H, aromatic). Found: C, 56.13; H, 3.65; N, 3.11%. Calcd for $C_{21}H_{17}NO_4SCl_2$: C, 56.01; H, 3.78; N, 3.11%. **8**: mp 185—186 °C; IR (KBr) 1720 cm^{-1} (CO), 1360, 1170 cm^{-1} (SO_2); ^{1}H NMR [(2:1)C_6D_6–$CDCl_3$] δ 1.67 (dd, 1H, $J_{3,5}$=10.7 Hz, $J_{5,6}$=9.3 Hz, 5-H), 2.21 (d, 1H, $J_{7,9}$=8.0 Hz, 7-H), 2.41 (d, 1H, $J_{7,9}$=8.0 Hz, 9-H), 2.91 (dd, 1H, $J_{6,10}$=4.7 Hz, $J_{5,6}$=9.3 Hz, 6-H), 3.14 (d, 1H, $J_{3,5}$=10.0 Hz, 3-H), 4.36 (d, 1H, $J_{1,10}$=4.7 Hz, 1-H), 5.67 (t, 1H, $J_{1,10}$=$J_{6,10}$=4.7 Hz, 10-H), 6.74—7.90 (m, 10H, aromatic). Found: C, 49.55; H, 3.09; N, 2.65%. Calcd for $C_{22}H_{17}NO_4SCl_4$: C, 49.55; H, 3.19; N, 2.63%. The large values of the coupling constants between H-5 and H-6 for **7** and **8** indicated the *endo* configurations of **7** and **8**.

*Reaction of **2** with Phenylglyoxylonitrile Oxide.* A solution of a mixture of **2** (1.63 mmol) and α-chloro-α-(hydroxyimino)acetophenone (1.63 mmol) was cooled in an ice bath. Into the cooled solution, a solution of triethylamine (2.12 mmol) in tetrahydrofuran (20 cm^3) was then added and stirred. After 2 h, a precipitate was removed by filtration, and the filtrate was evaporated to dryness under reduced pressure. The residue was chromatographed on a silica-gel column, using (40:1) benzene–ethyl acetate as the eluant, to give two adducts, **9** (0.39 g, 47%) and **10** (0.19 g, 22%), puls a 23% recovery of **2**. **9**: mp 164—165 °C; IR (KBr) 1730 cm^{-1} (CO), 1355, 1170 cm^{-1} (SO_2); ^{1}H NMR ($CDCl_3$) δ 3.04 (d, 1H, $J_{1,10}$=7.3, 1-H), 3.96 (d, 1H, $J_{2,6}$=9.3 Hz, 6-H), 5.07 (m, 4H, 2-H, 7-H, 10-H, and 11-H), 6.51 (d, 1H, $J_{9,10}$=7.7 Hz, 9-H), 6.88—8.17 (m, 15H, aromatic). Found: C, 65.14; H, 4.22; N, 5.25%. Calcd for $C_{28}H_{22}N_2O_6S$: C, 65.37; H, 4.28; N, 5.44%. **10**: mp 147—148 °C; IR (KBr) 1725 cm^{-1} (CO), 1360, 1175 cm^{-1} (SO_2); ^{1}H NMR ($CDCl_3$) δ 3.18 (d, 1H, $J_{7,8}$=7.7 Hz, 7-H), 4.38 (d, 1H, $J_{2,6}$=9.3 Hz, 6-H), 4.86 (m, 2H, 1-H and 11-H), 5.10 (d, 1H, $J_{2,6}$=9.3 Hz, 2-H), 5.29 (dd, 1H, $J_{7,8}$=7.7 Hz, $J_{8,9}$=8.0 Hz, 8-H), 6.41 (d, 1H, $J_{8,9}$=8.0 Hz, 9-H), 6.98—8.11 (m, 15H, aromatic). Found: C, 65.18; H, 4.12; N, 5.27%. Calcd for $C_{28}H_{22}N_2O_6S$: C, 65.37; H, 4.28; N, 5.44%. The large difference in the chemical shifts between 2-H and 6-H indicated the orientation of adduct **9**.[4]

References

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