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SYNTHESIS AND CYCLOADDITION REACTION OF 2,3-DIMETHYLENE-7-ISOPROPYLIDENEBENZONORBORENE

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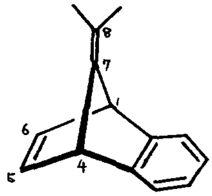
Summary: Synthesis of 2,3-dimethylene-7-isopropylidenebenzonorbornene (2) and its cycloaddition reactions with dichloroketene and dienophiles are described.

Recently, interesting stereoselectivities in cycloaddition reactions of molecules containing proximal π-bonds have been reported, and the factors controlling them have been extensively explored.[1] We have already reported that 7-isopropylidenebenzonorbornadiene 1 shows remarkable site-, stereo-, and regioselectivities in the cycloaddition reactions.[2] In this connection, the title compound 2, which has a cis diene moiety in place of the endocyclic double bond of 1, is of considerable theoretical and synthetic interest. We wish to report in this letter the synthesis and cycloaddition reactions of 2.



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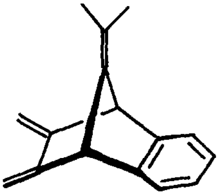

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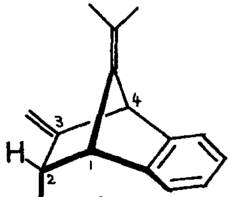

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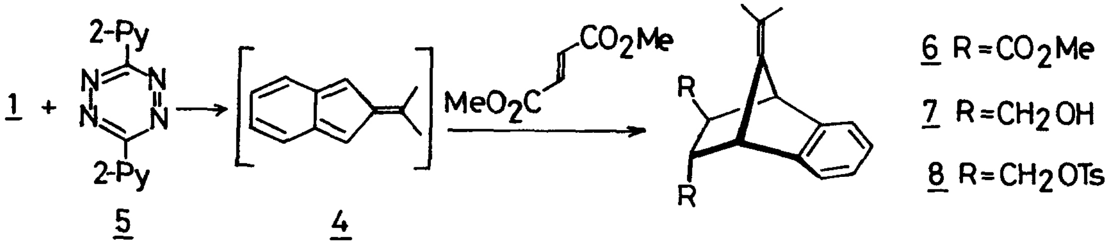
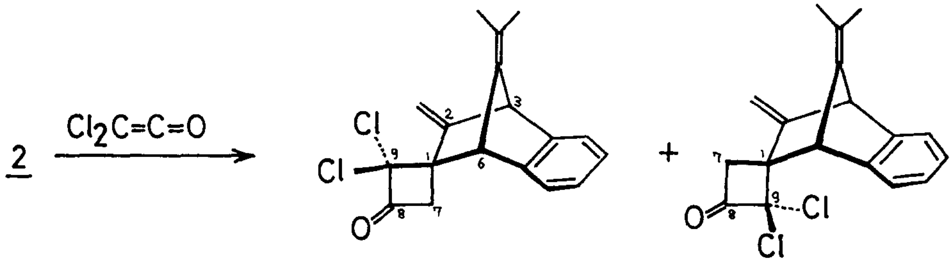
Compound 2 was prepared in a 48% overall yield from 1 via isobenzofulvene intermadiate (4). When 1 was allowed to react with 3,6-di(2'-pyridyl)-s-tetrazine 5 at ambient temperature in the presence of dimethyl fumarate, the diester 6 was obtained in 90% yield. The similar reactions



have been reported by Warrener[3] and Tanida.[4] Reduction ($LiAlH_4$/THF) of 6 furnished the diol 7 (95%), which was converted into the ditosylate 8[5] (70%). Treatment of 8 with t-BuOK/DMSO[6] gave the desired compound 2[7] in 80% yield. Careful catalytic hydrogenation of 2 over 5% Pd/C in ethyl acetate afforded dihydro compound 3[7] (55%), while 2 was inert toward the diimide reduction.

The unique electronic property of 2 was spectroscopically revealed.[7] The large split in the ^{13}C NMR chemical shifts of olefinic carbons indicated the polarization of all exocyclic double bonds and the intense UV absorption at 322 nm suggested the effective through-space conjugation of these unsaturated bonds. Reaction of 2 with dichloroketene[8] at room temperature gave two 1:1 adducts, 9 and 10, in 43% and 14% yields, respectively. Although the ^1H NMR spectra of both adducts[9] clearly indicated that dichloroketene addition took place at the less substituted exocyclic double bond of 2, the exact structure of products among four possible stereo- and regioisomers could not be determined. Therefore, the structure of the major product 9 was unequivocally determined by X-ray diffraction analysis as depicted in Figure 1,[10] in which



9 (exo)   10 (endo)

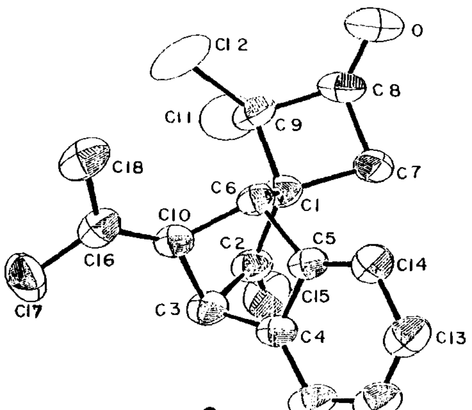
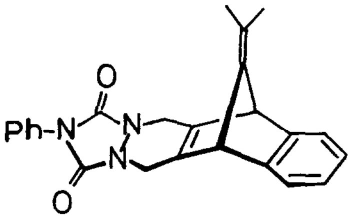


Figure 1 9

the characteristic bond elongation of C_1-C_7 (1.572 Å) and C_1-C_9 (1.596 Å) due to through-bond interaction with the carbonyl group was observed. With the precise structure of 9 in hand, the structure of 10 was determined by comparison of their spectra. In the ^{13}C NMR spectra, the chemical shifts of cyclobutanone carbons (C-1,7,8,9) of 9 and 10 are very similar (for 9 δ 56.81, 52.46, 192.58, 91.87; for 10 δ 56.16, 55.19, 191.54, 90.77), suggesting the same regiochemistry of both adducts. Furthermore, in the ^{1}H NMR spectra, the upfield shift of cyclobutanone methylene signal of 9 compared with 10 can be attributed to the anisotropic effect of the aromatic ring. Thus, 10 was concluded to be the endo-stereoisomer. These results are sharp contrast to the case of 1 which reacted with dichloroketene both at C_7=C_8 and C_5=C_6 double bonds.[2] It is also interesting to note the regioselective formation of 9 and 10, which are sterically less favorable compared with their regioisomers. This indicated the importance of electronic factors for regioselection in the reaction of 2.

Compound 2 also reacted with N-phenyl-1,2,4-triazoline-3,5-dione to give [4+2] cycloadduct 11[11] in a quantitative yield, whereas the similar reaction of 3 led to a mixture of ene-adducts 12[11] (syn:anti = 64:36). Compound 2 underwent the Diels-Alder reactions with other dienophiles such as TCNE, DMAD, N-phenylmaleimide, and diethyl azodicarboxylate to give the corresponding adducts in high yields. In order to clarify the origin of regio- and stereocontrol, further cycloaddition reactions of 2 and 3 with other electrophiles are now under examination.



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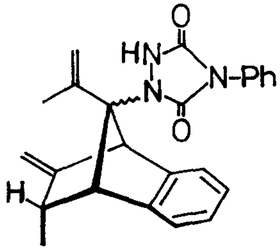

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References and Notes

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5. Satisfactory analytical and spectral data were obtained for all new compounds.
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7. Compound 2: mp 155-157 °C; IR (KBr) 3067, 2980, 2920, 1620, 700 cm^{-1}; UV (EtOH) 253 nm (log ε 4.04), 329 (3.53), 322 (3.46); ^1H NMR (δ $CDCl_3$) 1.64 (6H, s; Me x 2), 4.14 (2H, s;bridgehead-H), 4.92 (2H, s; vinyl-H), 5.01 (2H, s; vinyl-H), 6.8-7.3 (4H, m; ArH); ^{13}C NMR (δ $CDCl_3$) 19.56 q, 53.57 d, 100.76 t, 112.12 s, 119.88 d, 125.48 d, 145.40 s, 147.11 s, 147.38 s; MS m/e 208 (M^+ 26.5%), 193 (100%).

   Compound 3: mp 95-97 °C; IR (KBr) 3080, 2990, 2940, 2880, 1652, 1446, 727 cm^{-1}; UV (EtOH) 260 nm (log ε 3.37), 267 (3.43), 273 (3.40); ^1H NMR (δ $CDCl_3$) 0.71 (3H, d, J = 6.75 Hz; Me), 1.63 (6H, s; Me x 2), 2.57 (1H, m; H-2), 3.68 (1H, d, J = 3.75 Hz; H-1), 4.14 (1H, s; H-4), 4.58, 5.02 (2H, each d, J = 2.7 Hz; vinyl-H), 6.9-7.4 (4H, m; ArH); ^{13}C NMR (δ $CDCl_3$) 17.53 q, 19.67 q, 19.80 q, 40.71 d, 50.52 d, 54.48 d, 102.65 t, 112.20 s, 119.60 d, 122.59 d, 125.19 d, 126.03 d, 143.89 s, 145.77 s, 148.17 s, 155.18 s; MS m/e 210 (M^+).
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9. Compound 9: mp 184-184.5 °C; IR (KBr) 1793, 1440, 1372, 1090, 740 cm^{-1}; ^1H NMR (δ $CDCl_3$) 1.68 (3H, s; Me), 1.75 (3H, s; Me), 2.70, 3.25 (2H, ABq, J = 18.0 Hz; cyclobutanone-CH_2), 4.31 (2H, s; bridgehead-H), 4.75 (1H, br s; vinyl-H), 5.29 (1H, br s; vinyl-H), 6.9-7.4 (4H, m; ArH); ^{13}C NMR (δ $CDCl_3$) 20.06 q, 20.91 q, 52.46 t, 52.98 d, 54.61 d, 56.81 s, 91.87s, 108.30 t, 116.68 s, 119.86 d, 122.00 d, 125.97 d, 127.26 d, 143.24 s, 144.15 s, 147.72 s, 153.82 s, 192.58 s.

   Compound 10: mp 168-172 °C; IR (nujol) 1800 cm^{-1}; ^1H NMR (δ $CDCl_3$) 1.68 (6H, s; Me x 2), 3.06, 3.77 (2H, ABq, J = 17.25 Hz; cyclobutanone-CH_2), 4.23 (1H, s; bridgehead-H), 4.28 (1H, s; bridgehead-H), 4.55 (1H, br s; vinyl-H), 5.17 (1H, br s; vinyl-H), 7.0-7.4 (4H, m; ArH); ^{13}C NMR (δ $CDCl_3$) 19.99 q, 20.91 q, 54.08 d, 55.19 t, 55.58 d, 56.16 s, 90.77 s, 106.68 t, 115.45 s, 120.31 d, 123.89 d, 125.90 d, 126.86 d, 142.39 s, 144.67 s, 147.65 s, 154.47 s, 191.54 s.
10. The compound 9, $C_{18}H_{18}OCl_2$, forms triclinic crystals belonging to the space group P $\bar{1}$, with a = 8.582(7), b = 9.903(14), c = 10.615(12) Å; α = 115.17(9), β = 103.64(8), γ =85.30(10)°; Z = 2. Final R-value 8.6%. Total reflections 2795.
11. Compound 11: mp 280-283 °C; IR (KBr) 3480, 2930, 2860, 1780, 1767, 1697 cm^{-1}; ^1H NMR (δ $CDCl_3$) 1.57 (6H, s; Me x 2), 3.9-4.8 (4H, m; CH_2 x 2), 4.32 (2H, s; bridgehead-H), 6.8-7.5 (9H, m; ArH).

    Compound 12-syn: mp 195-197 °C; IR (KBr) 3460, 1773, 1687, 1510, 1430, 740 cm^{-1}; ^1H NMR (δ $CDCl_3$) 0.67 (3H, d, J = 6.9 Hz; Me), 1.93 (3H, br s; Me), 2.86 (1H, m; methine-H), 3.65 (1H, br d; bridgehead-H), 4.4-5.4 (5H, m; bridgehead-H and vinyl-H), 7.0-7.7 (9H, m; ArH), 9.50 (1H, br s, D_2O-exchangeable; NH).

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