× 50 mL) and dried (anhydrous sodium sulfate). After evaporating the solvent under reduced pressure, the residue was crystallized from a dichloromethane–methanol mixture to give white needles (59 mg, 96% yield): mp 63.0–63.5 °C; IR ($CHCl_3$) 2950, 1470, 1395, 1380, 1370, 1265 cm^{-1}; MS *m/e* (rel. intensity %) 280 (M^+, 0.27), 97 (28.0), 85 (23.5), 84 (30.5), 83 (62.5), 82 (30.0), 71 (29.0), 70 (29.0), 69 (100), 57 (67.5), 56 (80.5), 55 (80.0), 43 (60.0), 42 (21.5), 41 (95.0); ^1H NMR ($CDCl_3$) δ 0.83 (s, 3) and 1.37 (s, 2).

Oxidation of 3. A suspension of **3** (52.6 mg, 0.2 mmol) in aqueous potassium permanganate (828 mg, 5.2 mmol, in 50 mL) was heated at reflux for 20 h. After cooling to room temperature, the remaining permanganate was destroyed with sodium bisulfite. The reaction mixture was then acidified with sulfuric acid and extracted continuously with ether for 4 days. The ether extract was evaporated under reduced pressure to give an oil (24 mg), 95% by VPC, and was purified further by vacuum sublimation to give tetramethylsuccinic anhydride as a white gummy solid: mp sublimed without melting in a sealed tube; IR ($CHCl_3$) 2980, 1860, 1810, 1785, 1475, 1460, 1450, 1400, 1385, 1375, 1275, 1145, 970, 955, 920 cm^{-1}; MS *m/e* (rel. intensity %) 157 ($M^+ + 1$, 0.95), 156 (M^+, 0.13), 84 (100), 83 (21.0), 69 (100), 41 (71.5), 39 (41.5), 28 (32.0); ^1H NMR ($CDCl_3$) δ 1.24 (s).

Diethyl Tetramethylsuccinate. Diethyl tetramethylsuccinate was prepared from ethyl 2-methylpropanoate according the the method of T. J. Brocksom and co-workers.[13] The product so obtained was contaminated by an unknown compound [bp 77–78 °C (1 mm)]. Diethyl tetramethylsuccinate was separated from the contaminant by chromatography (silica gel, 1% ethyl acetate in hexane) followed by vacuum distillation: bp 79–80 °C (1 mm); IR ($CHCl_3$) 2990, 1725, 1470, 1445, 1400, 1385, 1370, 1270, 1170, 1125, 1025 cm^{-1}; MS *m/e* (rel. intensity %) 230 (M^+, 0.17), 185 (31.5), 157 (74.5), 116 (84.5), 115 (47.5), 111 (69.5), 88 (84.0), 87 (100.0), 85 (32.0), 84 (59.0), 83 (100.0), 73 (65.5), 70 (64.0), 69 (70.0), 59 (55.5), 57 (50.5), 55 (58.5), 43 (60.0), 42 (40.5), 41 (99.5), 39 (44.0), 29 (100.0), 28 (40.0), 27 (72.5); ^1H NMR ($CDCl_3$) δ 1.25 (s, 6), 1.25 (t, 3, J = 7 Hz), and 4.08 (q, 2, J = 7 Hz).

Tetramethylsuccinic Anhydride. Diethyl tetramethylsuccinate was hydrolyzed with aqueous ethanolic sodium hydroxide followed by acidification to give crude tetramethylsuccinic anhydride according to the procedure of D. J. Trecker and R. S. Foote.[8] The crude anhydride was purified by vacuum sublimation to give a gummy white solid with spectral properties identical to those mentioned above.

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Registry No.—1, 1111-97-3; 3, 61414-48-0; 1,1,2,2,7,7,8,8-octamethylcyclododecane, 61414-47-9; tetramethyl succinic anhydride, 35046-68-5; diethyl tetramethyl succinate, 33367-54-3.

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Addition of Diphenyldiazomethane to 7-Chloronorbornadiene. Implications for Orbital Control of 1,3-Dipolar Cycloadditions

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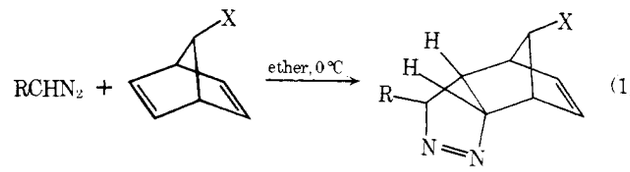
Theoretical treatment of the 1,3-dipolar cycloaddition reaction has shown remarkable sophistication, leading to a rather detailed knowledge of this fascinating process.[1] One aspect of the cycloaddition that still seems somewhat unclear is its exo–endo selectivity in norbornadienes. Although generally recognized as a typical exo-addition process on a wide variety of norbornenes, the reaction proceeds via both exo and endo pathways in a number of cases involving norbornadienes.[2] It is therefore startling that the addition of either diazomethane or (better) diazoethane to the 7-halonorbornadienes has been reported to occur *solely* via an endo,anti pathway (eq 1).[3] This specificity has been attributed to a



(1)

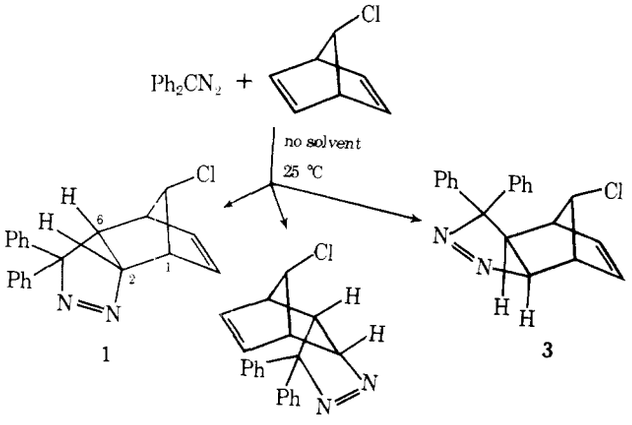
R = H, 35%
R = CH_3, 80%

contribution by the σ^* orbital of the C–X bond to the LUMO of the diene.[3] Because 1,3-dipolar cycloadditions of the present type are believed to be controlled by the interaction between the HOMO of the diazo component and the LUMO of the diene,[1] this σ^* contribution is considered to be significant, and to favor an endo,anti approach by the diazoalkane. However, such an interpretation seemingly places minor importance on the diazoalkane.

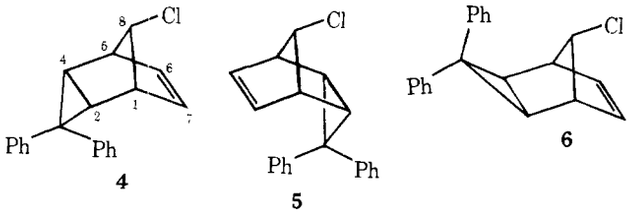
Because diphenyldiazomethane adds to 7-*tert*-butoxynorbornadiene to give all four possible monoadducts,[2a] we were curious about its addition to a 7-halonorbornadiene. In fact, its reaction with 7-chloronorbornadiene showed no such specificity as in eq 1. Three monoadducts were formed (Scheme I): the endo,anti (58%); the endo,syn (16%); and the exo,anti (26%) isomers, **1**, **2**, and **3**, respectively. The yield of isolated material was 47%.

The structures of the three adducts seem secure. The endo adducts **1** and **2** were differentiated from the exo adduct **3** by the value of the NMR coupling constant $J_{1,2} \sim 3.5$ Hz in the former pair and ~1 Hz in the latter compound. Further structural evidence was gained from their remarkably clean photolysis to the corresponding tricyclic chlorides. Adduct **1** was photolyzed in acetone at 366 nm[4] to the very labile chlo-

Scheme I



ride **4**, characterized by its symmetry-simplified NMR spectrum: δ (CCl_4) 6.9–7.5 (m, Ar-H), 5.07 (t, J = 2 Hz, H-6,7), 4.03 (shp m, H-8), 3.20 (six-line m, J = 2 Hz, H-1,5), 2.06 (t, J = 2 Hz, H-2,4). The syn nature of adduct **2** was demonstrated by its photolysis in benzene to chloride **5**, identical with that reported.[2a] Exo adduct **3** yielded chloride **6** upon photolysis in benzene, also readily characterized by its NMR spectrum: δ ($CDCl_3$) 7.0–7.4 (m, Ar-H), 6.37 (t, H-6,7), 3.58 (m, H-8), 3.10 (m, H-1,5), 1.75 (s, $W_{1/2}$ = 2 Hz, H-2,4).



The present results reaffirm the complexity inherent in such additions. It seems clear that the MO rationale[3] for eq 1 is not general and that it must somehow be modified to incorporate more features of the diazo component. A possible interpretation would involve a shift away from a type I cycloaddition (HOMO diazoalkane – LUMO diene control) in eq 1 toward a type II cycloaddition (all four frontier orbitals control) in Scheme I.[5] Such a shift would place less emphasis upon the LUMO of 7-chloronorbornadiene and thereby reduce the favorability of endo,anti approach. Alternatively, steric effects could be invoked, as in other comparisons of 1,3-dipolar cycloadditions of diphenyldiazomethane.[7] This seems unsatisfactory, however, in that the larger diazoethane was superior to the smaller diazomethane in its reaction in eq 1,[3] and in that the very crowded adduct **2** resulted as a significant product in Scheme I.

Experimental Section

Melting points were taken on a calibrated Fisher-Johns block. Infrared spectra were determined on a Perkin-Elmer Model 700 instrument. NMR spectra were recorded on a Varian A-60A spectrometer. Only significant absorptions for structural assignment are given for these spectra. Microanalyses were performed by Micro-Tech Laboratories, Skokie, Ill.

Addition of Diphenyldiazomethane to 7-Chloronorbornadiene. From the six additions carried out, a typical preparation is described. Diphenyldiazomethane (4.80 g, 24.7 mmol) was added to neat 7-chloronorbornadiene (used as received from Frinton Laboratories, 3.13 g, 24.7 mmol) and the homogeneous, liquid mixture was allowed to stand at room temperature for 12 weeks.[8] The dark, now solid mass was triturated with cold hexane, leaving adduct **1** [2.14 g, 27%, mp 161–162 °C dec from ether–hexane, IR ν (KBr) 1560 cm^{-1} (N=N), NMR δ ($CDCl_3$) 4.72 (dd, H-2, $J_{1,2}$ = 3.5 Hz). Anal. Calcd for $C_{20}H_{17}ClN_2$: C, 74.88; H, 5.34. Found: C, 74.68; H, 5.29]. Chromatography of the hexane-soluble material over alumina yielded upon elution (10% ether in hexane) benzophenone azine containing some adduct **2** [NMR δ ($CDCl_3$) 4.80 (dd, H-2, $J_{1,2}$ = 3.5 Hz)], followed by a mixture of **2** and **3** (Anal. Found: C, 74.83; H, 5.30), and finally pure adduct **3** [mp 164–166 °C dec from ether–hexane, NMR δ ($CDCl_3$) 5.22 (dd, H-2, $J_{1,2}$ = 1 Hz)]. Analysis of those fractions containing adducts **2** and **3** by NMR indicated a total weight of 0.61 g (8%) of the former and 0.97 g (12%) of the latter. Unidentified tarry material remained on the column.

Photolysis of the Adducts 1, 2, and 3. The appropriate adduct (200 mg) was dissolved in 5 mL of either acetone (adduct **1**) or benzene (adducts **2** and **3**) in a Pyrex test tube and irradiated at 366 nm in a small irradiation unit (Bradford Scientific, Inc., Marblehead, Mass.). After 2 h the photolyses were complete, as indicated by cessation of nitrogen evolution. The solvent was evaporated and the NMR spectrum of the crystalline residue was taken. The chlorides **4**, **5**, and **6** were fairly labile to chromatography on a variety of columns (alumina, Florisil, and silica gel), as well as thermally labile. Photolysis of **1** in benzene containing benzophenone gave only **4** also, exactly as did the use of acetone as solvent. Benzophenone appeared to be without effect in the photolyses of the other adducts.

Registry No.—**1**, 64011-10-5; **2**, 64044-01-5; **3**, 64044-02-6; **4**, 64044-03-7; **6**, 64044-04-8; diphenyldiazomethane; 883-40-9; 7-chlornorbornadiene, 1609-39-8.

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(5) In a Sustmann approach,[1] the frontier orbital energy levels of 7-chloronorbornadiene would be held constant. The variables would be the position of the frontier orbitals of diazomethane and diphenyldiazomethane relative to the diene. Unfortunately, the frontier orbital energies of diazomethane are only estimates as yet,[6] and those for diphenyldiazomethane appear to be unreported.
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(8) This is the most convenient method if time is not critical. Reaction in benzene solvent at 50 °C over 5 days gave similar results, but more tar was formed.

Thiol Addition to Crotepoxide and Dideacetylcrotepoxide[1a,b]

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In the course of our continuing research on tumor inhibitory compounds from plant sources, we have observed a marked difference between the reactions of crotepoxide (**1**), a tumor-inhibitory cyclohexane diepoxide previously isolated from the dried fruits of *Croton macrostachys* Hochst ex A. Rich. (Euphorbiaceae),[2] and dideacetylcrotepoxide (**2**) toward thiophenol. Since a large number of the plant-derived tumor inhibitory drugs isolated in these laboratories show reactivity toward sulfhydryl-containing compounds[3–5] as a potential mode of biological action, we felt that crotepoxide (**1**) might also exhibit this reactivity.

Thiophenol reacted with **1** in methanolic solution containing 10% pyridine at 25 °C to yield the thioethers **4** and **5** in approximately equal amounts. Hydrolysis of **1** under mild conditions[6] (triethylamine–water–methanol, 1:1:8, 30 min, 25 °C) gave both dideacetylcrotepoxide (**2**) and debenzoyldideacetylcrotepoxide (**3**). The reaction of thiophenol with **2** was carried out under the same conditions employed for **1** and gave thioether **6** exclusively. Hydrolysis of either **4** or **5** using