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A Novel Entry to the Bicyclo[4.2.2]decatriene and Tetraene Systems: The Unexpected 1,4-Cycloaddition of 2-(Methylthio)acrylonitrile to Cyclooctatetraene

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Various cycloaddition reactions of captodative olefins to dienes have been reported,[2] and the so-formed adducts have been used in a number of useful transformations.[3] The structure of the Diels−Alder adducts have shed light on the respective role of steric and electronic factors on the stereoselectivity of the cycloaddition.[4] Kinetic studies revealed that with 2-(methylthio)acrylonitrile (**3**), the captodative substitution accelerates the Diels−Alder reaction with cyclohexadiene by stabilizing the transition state in which contribution of biradical configurations should be important.[5] As captodative substitution provides stability to a radical center,[6] it is no surprise that captodative olefins are good partners in [2 + 2] cycloadditions.[7] So, the long-known spontaneous head-to-head cyclodimerization of 2-(methylthio)acrylonitrile (**3**) appears to result from the stabilization of the 1,4-biradical intermediate by a *bis*-captodative effect.[8] However, as far as one can tell, *captodative olefins do not convert the normally concerted, although asynchronous, [4+2] cycloadditions into stepwise processes*.[9] We wish to report that 2-(methylthio)acrylonitrile (**3**) provides one of the very few examples[10] of formal all-carbon Diels−Alder cycloaddition to cyclooctatetraene (COT). The original structure of the product could be interpreted as the result of a typical behavior of the bicyclo[4.2.0] valence tautomer of COT, followed by a homolytic rearrangement.

Over the past three decades, the chemistry of COT has received considerable attention.[11] In contrast to its easy 1,3-dipole cycloaddition reactions,[12] monocyclic COT is reluctant to act as the diene in Diels−Alder-type cycloadditions against electron-deficient 2π components. The tub conformation[13] of the COT ring precludes the requisite coplanarity of two neighboring double bonds. As a result, the disrotatory ring closure to bicyclo[4.2.0]octatriene **2** generally precedes intermolecular $[_{\pi}4_s + _{\pi}2_s]$ cycloaddition (*i.e.*, $k_2 > k_1$), despite the 28.1 kcal/mol energy barrier.[14] This preference occurs because the bicyclic intermediate **2** affords a quasi-planar diene system that greatly facilitates the capture by the dienophile (*cf.* k_3). The elegant work from Huisgen has shown that the rate-controlling step in the later process is related to the reactivity of the dienophile.[15] With sluggish dienophiles, the bimolecular addition is rate-limiting (*i.e.*, $k_2 > k_3$). If the Diels−Alder reaction is very fast, then the ease of valence isomerism determines the rate (*i.e.*, $k_2 < k_3$).

There are very few reports on the direct concerted cycloaddition of COT itself with unsaturated compounds (*i.e.*, $k_1 > k_2$).[10] As a rare example, *N*-phenyltriazolinedione (PTAD) exhibits a predilection for 1,4-cycloaddition to the monocyclic ring system of COT.[16] The presumed electrophilicity of PTAD has led Huisgen to suggest that the transformation proceeds through a zwitterionic homotropylium intermediate,[16b] but the solvent independence of the reaction rate (k_1) argues for a concerted $[_{\pi}4_s + _{\pi}2_s]$ cycloaddition.[17] On the other hand, chlorosulfonyl isocyanate,[18] sulfur monoxide,[19] and singlet oxygen,[20] like α-cyanoisopropyl radicals,[21] difluoroaminyl radicals,[22]

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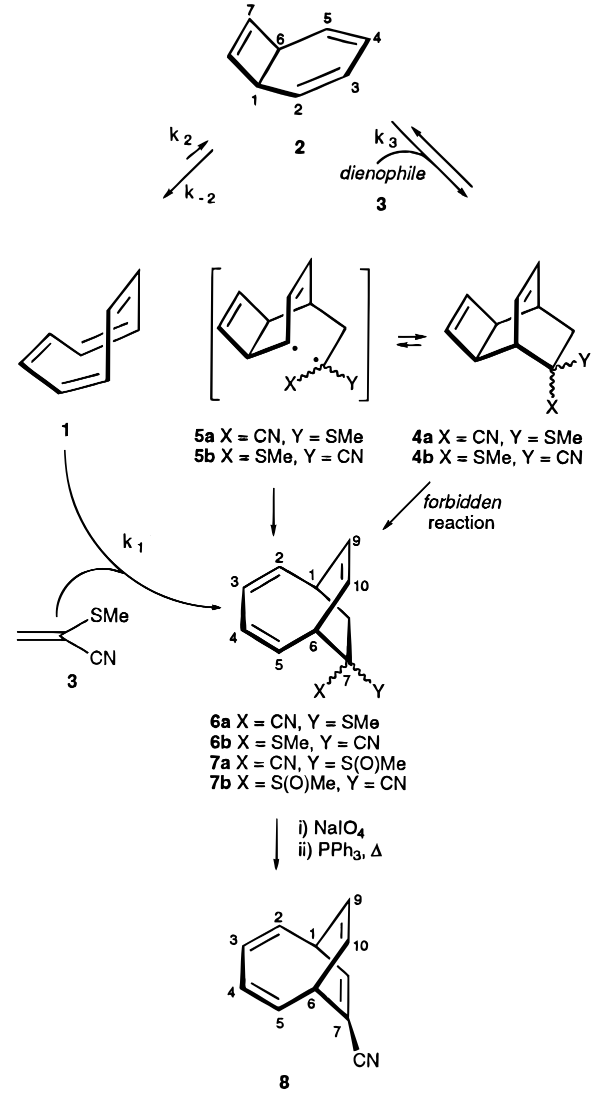
cyanonitrene,[23] dicyanocarbene,[24] and dinitrogen tetraoxide[25] (five examples, all radical in nature), also add to COT in a 1,4-manner, while 1,1-dichloro-2,2-difluoroethylene (a typical partner for biradical cycloaddition) gives only the [2 + 2] cycloadduct.[26]

Heating a mixture of **3** and **1** (1.3 equiv) in mesitylene, at 160 °C for 10 h, resulted in the formation of a 60:20:20 mixture of three components: two 1:1 cycloadducts **6**, together with a 2:1 adduct, respectively. The 1:1 and 2:1 nature of the cycloadducts was established by capillary GC/MS analysis. The structures of **6a** and **6b** were unambiguously deduced from the structure of the unique product **8** obtained *via* a subsequent oxidation–elimination sequence.[27] The mixture of sulfides **6a** and **6b,** which was isolated in 52% yield, was oxidized with sodium metaperiodate in aqueous methanol, to the mixture of sulfoxides **7a** and **7b** (97% yield). The latest smoothly eliminated sulfenic acid, in refluxing benzene, to afford the bicyclic tetraene **8** (60% yield). The structure of **8** was assigned on the basis of ^{1}H and ^{13}C NMR spectra. The presence of seven ethylenic protons (δ 6.42–5.54 ppm) and two bridgehead bis-allylic protons (δ 3.44–3.36 ppm) as well as seven sp^2 methine carbons (δ 139.31–106.29 ppm) and two sp^3 methine carbons (δ 36.37 and 35.06 ppm) excludes the possibility of structure **4**. Furthermore, extensive analyses of ^{1}H, ^{13}C, COSY gradient and HMQC gradient data unambiguously allowed the assignment of all the carbon and hydrogen atoms. However, the H_2, H_3, H_4, and H_5 atoms exhibited second-order signals, even at 400 MHz, and thus demanded LAOCOON program simulation.[28] The initial parameters were determined from the experimental spectra based on several double resonance experiments. Good agreement was obtained between observed and calculated spectra (Supporting Information).

This work provides a rare example of formal all-carbon Diels–Alder cycloaddition to COT. As illustrated in Scheme 1, the mechanism of formation of the cycloadducts **6** must be consistent with the $k_1 < k_2$ reaction rate order. The easy disrotatory ring closure of COT to bicyclo[4.2.0]octatriene should be followed by the classic Diels–Alder cycloaddition leading to **4**. The stereospecific, conrotatory nature of the cyclobutene electrocyclic ring-opening has been clearly demonstrated.[29] Then, the *cis*-disubstituted cyclobutene in **4** should give rise to the formation of butadienyl moiety having *E,Z*- and/or *Z/E*-geometries (since formation of *E,E*- and *Z,Z*-isomers is *forbidden* by orbital symmetry rules).[30] Structurally constrained molecules, such as **4**, undergo ring-opening with activation energies much higher than would otherwise be predicted.[30] The thermal rearrangement of tricycle **4** to bicycle **6** should be the consequence of an homolytic breaking of the σ-bond between captodative and allylic positions. Then, the incipient diradical **5** can rearrange *via* a cyclobutenylmethyl radical opening.[31]

Scheme 1



In summary, the 1,4-cycloaddition of 2-(methylthio)-acrylonitrile to COT synthetically represents an exceptional example of an all-carbon Diels–Alder reaction involving this special tetraenic partner and provides a novel entry into the original bicyclo[4.2.2]decatriene and tetraene structures.[32]

Experimental Section

General Methods. NMR spectra were recorded at 200 or 400 MHz (^{1}H) and 50 or 100 MHz (^{13}C), in $CDCl_3$, and are reported in ppm downfield from TMS; signal multiplicities were established by DEPT or ATP experiments, and extensive analysis of **8** was performed by COSY gradient and HMQC gradient experiments. ^{1}H NMR spectra of **8** were analyzed with the LAOCOON-3 computer program (Supporting Information). The maximum errors for the chemical shifts and coupling constants (*J*, Hz) of calculated spectra are 0.35 and 0.07 Hz, respectively. GC–MS analyses were performed at an ionizing voltage of 70 eV. Thin-layer chromatography was carried out on Merck silica gel 60 F_{254} analytical plates,

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visualized by using iodine vapor or UV light or by means of a 5% ethanolic solution of molybdophosphoric acid. Column chromatography was performed using Merck silica gel 60 (230−400 mesh). Elemental analysis were performed by the Service Central d'Analyses, CNRS, Solaize, France.

Cycloaddition Reaction of Cyclooctatetraene with 2-(methylthio)acrylonitrile (3). A mixture of **1** (2.70 g, 26.0 mmol), **3**[8a] (1.98 g, 20.0 mmol), and 1,3,5-trimethylbenzene (0.30 g) was heated at 160 °C for 10 h under Ar. Trimethylbenzene and **1** in excess were evaporated under reduced pressure (45 °C/0.02 Torr), and the residue was chromatographed on silica gel (80 g), using first petroleum ether (150 mL) then methylene chloride. GC−MS analysis showed a 3:1:1 mixture of two cycloadducts **6** and of a heavier compound: *m/z* 309 (1.2), 308 (4.3), 307, $M^+ = [2 \times 104] + 99$ (18.2), 260 (2.1), 208 (7.9), 193 (6.7), 178 (6.1), 165 (10.3), 154 (10.8), 141 (15.6), 129 (100), 115 (93.2), 91 (99.5), 77 (36.8). Kugelrohr distillation gave the isomeric cycloadducts **6** (2.102 g, 52%) as a viscous oil: $bp_{(0.02\ Torr)}$ 95−100 °C; R_f 0.65 (SiO_2, CH_2Cl_2); IR (film) 3030, 2930, 2870, 2230, 1640, 1460, 1380, 1270, 1090, 1020, 960, 910, 880, 810, 780, 760, 740, 710 cm^{-1}; GC−MS analysis confirmed the relative amounts of the two cycloadducts to be 75:25; major *m/z* 203 M^+ (3.6), 202 (2.2), 155 (32.9), 140 (7.4), 128 (20.4), 104 (100), 91 (42.6), 78 (38.2); minor *m/z* 203 M^+ (6.1), 202 (3.4), 188 (2.6), 155 (46.6), 140 (10.6), 128 (35.2), 104 (100), 91 (63.7), 78 (60.3); ^1H NMR (200 MHz) major 5.95 and 5.63 (m, $J = 7.8, 2.6$, 4H), 5.75 (m, six lines, $J = 7.0, 6.8$, 2H), 3.91 (m, 1H), 3.59 (m, 1H), 2.97 (m, 1H), 2.67 (m, 1H), 2.59 (dd, $J = 13.8, 1.6$, 1H), 2.26 (s, 3H), 1.48 (dd, $J = 13.8, 3.2$, 1H); minor (partial) 6.35 (m, six lines, $J = 7.2$, 2H), 6.04 (m, 2H), 3.12 (m, 1H), 2.78 (m, 1H), 2.37 (dd, $J = 13.8, 1.8$, 1H), 2.25 (s, 3H). Anal. Calcd for $C_{12}H_{13}NS$: C, 70.90; H, 6.45; N, 6.89; S, 15.77. Found: C, 71.10; H, 6.65; N, 6.78; S, 15.57.

Oxidation of Sulfides 6 to Sulfoxides 7. Sulfides **6** (1.36 g, 6.7 mmol) were dissolved in 20 mL of methanol and cooled in an ice bath prior to the dropwise addition of a solution of sodium metaperiodate (1.52 g, 7.1 mmol) in 5 mL of water. After the addition was completed, the ice bath was removed, and the reaction was stirred at room temperature for 15 h. The reaction mixture was filtered, and the precipitate was washed several times with methanol. The combined filtrate and washings were concentrated in vacuo to yield an oil, which was dissolved in ethyl acetate (30 mL), washed with water (2 × 10 mL), and dried (Na_2SO_4). Concentration of the organic layer in vacuo gave an oily mixture of sulfoxides **7** (1.42 g, 97%) that slowly solidified and turned brown in few hours: IR (film) 3030, 2930, 2870, 2230, 1640, 1460, 1380, 1280, 1050 (MeSO), 920, 870, 820, 780, 760, 740, 700 cm^{-1}. The crude mixture of sulfoxides **7** was utilized directly in the elimination step.

Elimination of Sulfoxides 7. Preparation of 7-Cyanobicyclo[4.2.2]deca-2,4,7,9-tetraene (8). A benzene solution (10 mL) of the crude oily sulfoxides **7** (1.42 g, 6.47 mmol) and triphenylphosphine (470 mg, 1.8 mmol) was refluxed for 10 h under a positive pressure of dry nitrogen. Benzene was removed in vacuo and the residue chromatographed on silica gel (15 g), eluting with diethyl ether−hexane (1:3) R_f 0.21. Kugelrohr distillation gave 614 mg (60%) of a colorless oil, which slowly solidified at room temperature, $bp_{(0.4 Torr)}$ 75−80 °C. Analysis of this material by GC−MS revealed the presence of one single compound **8**: *m/z* 156 (5.2), 155 M^+ (48.5), 154 (100), 153 (18.7), 140 (56.8), 127 (65.1), 115 (44.6), 102 (7.6), 77 (25.8), 63 (35.0), 51 (51.4); IR (film) 3050, 3040, 2950, 2220, 1610, 1440, 1400, 1310, 1290, 1110, 990, 930, 900, 870, 840, 820, 790, 740, 720, 700 cm^{-1}; ^1H NMR (400 MHz) 6.42 (dt, $J_{1,8} = 6.3$, $J_{6,8} = J_{8,9} = 0.8$, 1H, H_8), 6.23 (m, $J_{2,5} = 1.1$, $J_{3,5} = 0.7$, $J_{4,5} = 11.8$, $J_{5,6} = 8.6$, 1H, H_5), 6.14 (m, $J_{1,2} = 8.9$, $J_{2,3} = 11.6$, $J_{2,4} = 0.75$, $J_{2,5} = 1.1$, $J_{2,6} = 0.1$, 1H, H_2), 5.93 (m, $J_{1,3} = 0.15$, $J_{2,3} = 11.6$, $J_{3,4} = 8.6$, $J_{3,5} = 0.7$, 1H, H_3), 5.92 (m, $J_{2,4} = 0.75$, $J_{3,4} = 8.6$, $J_{4,5} = 11.8$, $J_{4,6} = 0.15$, 1H, H_4), 5.63 (dd, $J_{6,10} = 6.1$, $J_{9,10} = 8.9$, 1H, H_{10}), 5.54 (ddd, $J_{1,9} = 5.9$, $J_{8,9} = 0.8$, $J_{9,10} = 8.9$, 1H, H_9), 3.44 (m, $J_{1,6} = 0.2$, $J_{4,6} = 0.15$, $J_{5,6} = 8.6$, $J_{6,8} = 0.8$, $J_{6,10} = 6.1$, 1H, H_6), 3.36 (m, $J_{1,2} = 8.9$, $J_{1,3} = 0.15$, $J_{1,6} = 0.2$, $J_{1,8} = 6.3$, $J_{1,9} = 5.9$, 1H, H_1); ^{13}C NMR (100 MHz) 139.31 (C_5), 138.60 (C_2), 136.7 (C_8), 125.93 (C_3), 126.42 (C_4), 119.48 (C_9), 119.90 (C_{10}), 118.15 (CN), 106.29 (C_7), 36.37 (C_6), 35.06 (C_1). Anal. Calcd for $C_{11}H_9N$: C, 85.13; H, 5.85; N, 9.02. Found: C, 84.89; H, 5.88; N, 8.91.

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Supporting Information Available: Copies of experimental and calculated ^1H NMR, ^{13}C NMR, HMQC gradient, and COSY gradient spectra for **8** (22 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information

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