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Iodine-Induced Transannular Coupling of 1,6-Cyclodecadiyne

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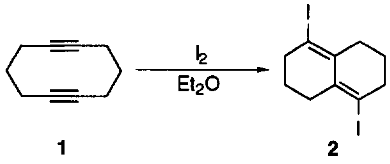
Abstract: Treatment of 1,6-cyclodecadiyne (**1**) with one equivalent of iodine in ether leads to regioselective transannular coupling, producing 1,5-diiodo-2,3,4,6,7,8-hexahydronaphthalene (**2**) in excellent yield. Solvent-incorporation products are observed in addition to **2** when the reaction is done in benzene, chlorobenzene, or methanol. Bromination of **1** gives analogous products, but the reaction is not as clean.

Our group has been exploring the nature of conjugative interactions in dinuclear transition metal complexes with 1,3-butadienediyl bridges,[1] and we wished to prepare for comparison complexes whose bridges are conformationally constrained. In this communication, we present the high-yield synthesis of a functionalized and conformationally constrained *s-trans*-butadiene derivative, 1,5-diiodo-2,3,4,6,7,8-hexahydronaphthalene (**2**). This potentially useful synthetic intermediate was prepared through the iodine-induced transannular coupling of 1,6-cyclodecadiyne (**1**, eq 1).[2] Related transannular alkyne coupling reactions from the literature are shown in equations 2[3] and 3,[4] the first related by ring system and the second by reagent.



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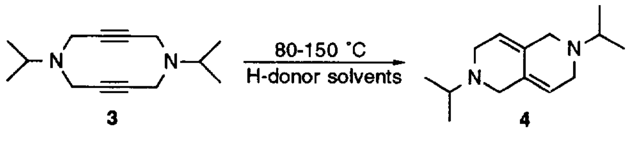

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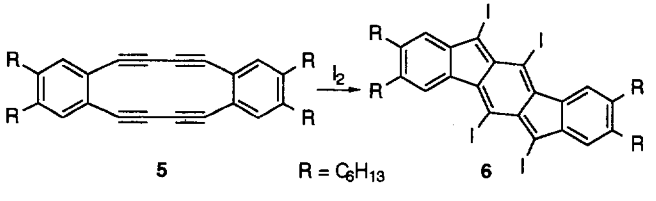
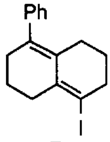


(3)

The preparation of diiodide **2** in our laboratory was quite simple: an ether solution of diyne **1** (10^{-3} M) was added to an equimolar amount of iodine in ether (10^{-3} M) under argon at 0°C. After 2 h, **2**[5] was obtained as the sole product in 94% isolated yield. When the reaction was done in benzene at 10-18°C under argon, the yield of **2** was 88%, and a minor product, the 1-iodo-5-phenyl derivative **7**,[6] was obtained in 7% yield. In neither case were bicyclo[5.3.0]decane derivatives or any other significant products formed according to GC and NMR analysis. Solvent incorporation (<10%) was also observed with chlorobenzene as solvent.[7]



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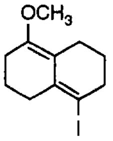
The product distribution was sensitive to concentration and mixing procedure. The slow addition of diyne **1** at higher dilution in benzene (10^{-4} M, each component) gave compound **7** as the major product (50%). Higher concentrations (≥0.1 M) led to more complicated mixtures, and an exothermic reaction even occurred when the solid reactants were mixed (in air), giving a black, sticky, insoluble material. A similar material was obtained when compounds **2** or **7** were exposed to air for several hours in the solid state or in concentrated solution (>0.1 M). In dilute solution, both compounds were stable in air.

3-Hexyne was found to be unreactive under the conditions employed for diyne **1**. Literature reports of iodine addition to internal alkynes have involved activated iodine reagents such as bis(pyridine)iodonium tetrafluoroborate[8] or aluminum oxide/I_2.[9,10] These observations are consistent with experimental studies of **1** that show an enhanced reactivity of this diyne to in-plane attack of electrophiles.[11] Theoretical studies suggest that the increased reactivity is caused by both through-space and through-bond interactions between the alkyne units.[2,12]

Mechanistic experiments done to date, though incomplete, have been informative. The solvent-incorporation product **7** could be explained by either ionic (iodonium) or free-radical chain mechanisms. However, a significant product (17%) from the reaction in methanol, tentatively assigned as structure **8**,[13] is inconsistent with a radical mechanism. The same product was also formed at a faster rate (in 59% yield)[14] in the presence of silver nitrate, which should promote an ionic mechanism. This result is different from Heasley's findings for iodination of terminal alkynes, in which methanol is incorporated only in the presence of silver nitrate.[10] Addition of BHT (2,6-di-*t*-butyl-4-methylphenol), a known inhibitor of carbon-based free-radicals, had no effect on the rate or product distribution in benzene. The rate was, however, sensitive to solvent: the reaction took about 40 times longer in methanol (without silver nitrate) than it did in benzene. These results are suggestive of an ionic mechanism in which the reactants (or a complex between the reactants) are stabilized by polar solvation more than the transition state. More complete mechanistic experiments are in progress.[15]

Enedione **9**[16] was observed as a variable-yield product (3-20%) of the iodination of **1** (in benzene) when the reaction mixture was not rigorously deoxygenated. In control experiments, compounds **1** and **2** were both found to be stable to O_2 and H_2O in dilute solution. The fact that the formation of **9** could be avoided by excluding oxygen from the reaction mixture suggests that oxidation of a reaction intermediate led to **9**. After the reaction was quenched with sodium thiosulfate, exposure to oxygen had no effect. In contrast, tetraiodide **6** was reported by Swager to readily undergo oxidation in air to produce diketone **10**.[4] Efficient conversion of **2** to **9** was achieved by using the more powerful oxidant *m*-CPBA at room temperature.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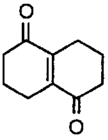
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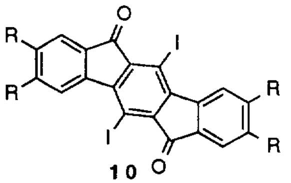
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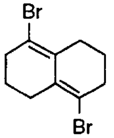
R = C_6H_{13}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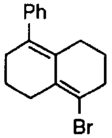
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Bromination of diyne **1** has also been accomplished in ether at -78°C, and the transannular coupling product, 1,5-dibromo-2,3,4,6,7,8-hexahydronaphthalene (**11**) was similarly obtained, though in much lower yield (21%).[17] The 1-bromo-5-phenyl derivative **12**[18] was also observed by NMR when benzene was used as the solvent. Enedione **9** was not formed in the bromination reaction, even in the presence of oxygen. Dibromide **11** is air-stable, even in concentrated solution and in the solid state. Several other products were observed in the bromination reaction, and we are currently characterizing them.

In summary, iodine adds readily and regioselectively to diyne **1** to produce diiodide **2**, a functionalized, conformationally constrained, *s-trans*-butadiene. Further work on the transannular coupling reactions of diyne **1** and the synthetic elaboration of **2** is in progress.

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Chem. Soc. **1960**, 3614-3625. For a related base-induced cyclization, see Mayer, J.; Sondheimer, F. *J. Am. Chem. Soc.* **1966**, *88*, 603-604.

5. After the reaction was completed, 20% aqueous NaS_2O_3 was added to consume the unreacted I_2. The organic layer was then washed with saturated NaCl solution and dried over $MgSO_4$. After evaporating the solvent, the residue was subjected to silica flash column chromatography. Compound **2**: mp 60.5-61.0 °C (dec); ^1H NMR (300 MHz, $CDCl_3$) δ 2.79 (4H, t, 6 Hz), 2.50 (4H, t, 6 Hz), 1.73 (4H, quintet, 6 Hz); ^{13}C NMR (76 MHz, $CDCl_3$) δ 136.7, 103.6, 43.2, 36.9, 25.4; IR (KBr, cm-1): 2914, 2821, 1586, 1414, 1319, 1112, 617. MS (EI): 386 (M+).
6. Compound **7**: mp 59.5-61.5°C; ^1H NMR ($CDCl_3$) δ 7.20 (5H, m), 2.65 (2H, t, 6 Hz), 2.50 (2H, t, 6 Hz), 2.18 (2H, t, 6 Hz), 2.12 (2H, t, 6 Hz), 1.82 (2H, quintet, 6 Hz), 1.62 (2H, quintet, 6 Hz); ^{13}C NMR (acetone-d_6) 145.2, 143.4, 138.0, 136.6, 129.8, 128.8, 127.4, 102.2, 43.5, 37.9, 34.1, 28.5, 26.4, 23.8; IR (KBr, cm^{-1}) 3058, 2939, 1648, 1581, 1429, 1327, 760, 695; MS (EI): 336 (M+).
7. Peaks were overlapped in the ^1H NMR, precluding unambiguous assignment, but the spectrum was consistent with roughly equal amounts of the *p*- and *o*-chlorophenyl derivatives.
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12. Gleiter, R.; Karcher, M.; Jahn, R.; Irngartinger, H. *Chem. Ber.* **1988**, *121*, 735-740.
13. Compound **8**: ^1H NMR ($CDCl_3$) δ 3.09 (3H, s), 2.70 (4H, m), 1.60-2.40 (8H, m); ^{13}C NMR ($CDCl_3$) δ 173.4, 130.8, 128.8, 114.3, 66.8, aliphatic (6C). Compound **8** apparently does not arise from a secondary solvolysis reaction of **2**, since **2** was unchanged after several days in methanol solution.
14. The relatively low yield of **8** observed in the absence of silver nitrate may be due to slow oxidation of **8** to **9**, perhaps by iodine, as suggested by a reviewer. Indeed, **9** was the primary product of this reaction.
15. A preliminary result from the reaction of **1** and HCl in methanol/water shows that ionic transannular coupling of **1** can be achieved. The coupling product 3,4,5,6,7,8-hexahydronaphthalen-1(2H)-one was obtained in 89% yield. The same compound was reported to come from the related transannular coupling of 5-cyclodecynone with HCl. See Wempe, M. F.; Grunwell, J. R. *J. Org. Chem.* **1995**, *60*, 2714-2720, and references cited therein.
16. Compound **9**: all spectroscopic data (^1H, ^{13}C, IR, MS) are consistent with the structure and the literature: (a) Peet, N. P.; Cargill, R. L. *J. Org. Chem.* **1973**, *38*, 4281-4285. (b) Hamon, D. P. G.; Richards, K. R. *Aust. J. Chem.* **1983**, *36*, 2243-2259.
17. Compound **11**: ^1H NMR ($CDCl_3$) δ 2.64 (4H, t, 6 Hz), 2.51 (4H, t, 6 Hz), 1.78 (4H, quintet, 6 Hz); ^{13}C NMR ($CDCl_3$) 123.2, 105.0, 37.4, 29.7, 23.6; MS (EI) 294, 292, 290 (M^+).
18. Compound **12**: ^1H NMR ($CDCl_3$) δ 7.20 (5H, m), 2.42 (2H, t, 6 Hz), 2.37 (2H, t, 6 Hz), 2.26 (2H, t, 6 Hz), 2.19 (2H, t, 6 Hz), 1.80 (2H, quintet, 6 Hz), 1.65 (2H, quintet, 6 Hz).

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