Formal [(2+2)+2] and [(2+2)+(2+2)] Nonconjugated Dienediyne Cascade Cycloadditions

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ABSTRACT



Fluoranthene 2 and heptacycle 3 are easily accessible from the reaction of diyne 1 and norbornadiene (NBD) in the presence of the rhodium catalyst. The unusual [(2+2)+(2+2)] adduct 3 was confirmed by the X-ray crystal structure analysis.

Through-space interaction between proximal olefins, as in norbornadiene (NBD), leads to reactivity analogous with conjugated dienes.1 NBD reacts directly with tetracyanoethylene to give a homo-Diels-Alder [(2+2)+2] adduct.² In the presence of transition-metal catalysts, NBD and acetylenes generate homo-Diels-Alder products among other coupling products, depending on the catalyst.³ Similar perturbations of reactivity could be anticipated for functional groups in the peri (i.e., 1,8)-positions of naphthalene. Therefore, reactivity of 1,8-dialkynylnaphthalenes should be a good test of this hypothesis. We report a general variant of the reaction in which 1,8-dialkynylnaphthalenes and NBD undergo metal-catalyzed [(2+2)+2] and [(2+2)+(2+2)]cycloadditions. In the latter case, four new bonds form in a one-pot transformation, and three-, five-, and sevenmembered rings are formed at once.

Several complexes are known to effect transformations A-D (Scheme 1). Pauson-Khand conditions, formally a



[2+2+1] cycloaddition of NBD, an alkyne and CO, generate cyclopentenones **A**.⁴ Reaction of NBD and 1 equiv of alkyne

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⁽⁴⁾ Selected examples: (a) Marchueta, I.; Montenegro, E.; Panov, D.; Poch, M.; Verdaguer, X.; Moyano, A.; Pericas, M. A.; Riera, A. J. Org. Chem. 2001, 66, 6400–9. (b) Lee, B. Y.; Moon, H.; Chung, Y. K.; Jeong, N. J. Am. Chem. Soc. 1994, 116, 2163. (c) Verdaguer, X.; Moyano, A.; Pericas, M. A.; Riera, A.; Bernardes, V.; Greene, A. E.; Alvarez-Larena, A.; Piniella, J. F. J. Am. Chem. Soc. 1994, 116, 2153.

 Table 1.
 Preparation of Fluoranthenes 2 and [(2+2)+(2+2)]

 Adducts 3 from Divnes 1 and NBD



a: $R^1 = R^2 = Ph$. **b**: $R^1 = R^2 = 4 \cdot tBu-C_6H_4$. **c**: $R^1 = R^2 = 2-Br-C_6H_4$. **d**: $R^1 = Ph$, $R^2 = C_6F_5$. **e**: $R^1 = R^2 = 4-CO_2Me-C_6H_4$.

diyne	$catalyst^a$	$T\left(^{\circ}\mathrm{C}\right)$	2^{b}	3^{b}	yield ^{c} (%)
1a	А	130	77	23	99
1a	В	80	100	0	96
1a	С	80	100	0	96
1b	Α	130	81	19	95
1b	В	90	100	0	92
1c	Α	110	98	2	78^d
1d	Α	130	51	49	83
1e	А	80	63	37	93
1e	В	90	100	0	99

^{*a*} A = 5 mol % of RhCl(PPh₃)₃, B = 2.5 mol % of [RhCl(COD)₂]₂, C = 2.5 mol % of Rh₂(OAc)₄·2H₂O. ^{*b*} The ratio was according to the ¹H NMR spectrum of the crude product. ^{*c*} Isolated yields. ^{*d*} Thermolytic cyclization (ca. 2%) of **1c** was also observed.

affords a homo-Diels–Alder product \mathbf{B}^5 or a formal [2+2] adduct \mathbf{C} ,⁶ depending on the catalysts and alkynes used.

In the special case of a nickel catalyst, NBD, and acetylene gas, a trace of the unusual tetracycle **D** formed;⁷ however, with internal alkynes, even this system produced **B** and **C**. The reaction to form **D** represents a formal [(2+2)+2+2] cycloaddition of NBD and two acetylene moieties. NBD's role as a "proalkyne" raises the question of whether the [(2+2)+2+2] product is from NBD and two molecules of acetylene or from oligo-adducts of NBD with thermal eliminations of cyclopentadiene.⁸

In our parallel study, 7,8,9,10-substituted fluoranthenes are easily accessible from 1,8-bis(arylethynyl)naphthalene and alkynes in the presence of the Wilkinson catalyst (5 mol %) with good to excellent yields.⁹ To prepare 7, 10-disubstituted fluoranthene **2** in the same manner, NBD

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was used instead of inconvenient acetylene gas.¹⁰ As expected, fluoranthene **2** was generated from the corresponding diyne **1** and NBD (Table 1 with legend),¹¹ but besides the desired product **2**, the byproduct **3** was also observed. The heptacycle **3a** was confirmed by an X-ray crystal structure analysis (Figure 1).¹² To our knowledge, this



Figure 1. The molecular structure of 3a in the crystal.

unusual heptacycle **3** is the first example of [(2+2)+(2+2)] cycloaddition of alkynes and NBD.¹³ It also explains that this [(2+2)+(2+2)] cycloadduct **3** and the [(2+2)+2+2] product **D** (cf. Scheme 1) can be formed only at the short distance between two alkyne moieties.¹⁴

This protocol indicates that intermolecular reactions of **1a** and NBD are much faster than the intramolecular cyclization of **1a** alone.¹⁵ On the other hand, this reaction is performed under neutral conditions with some functional group tolerance (cf. Table 1). Though the full scope of the reaction remains to be investigated, there are advantages over the traditional Knoevenagel condensation, which is well-used to prepare cyclopentadienones, important precursors of fluor-

(13) Similar [4+(2+2)] cycloadducts come from 1,3-butadienes and NBD. See: (a) Lautens, M.; Tam, W.; Sood, C. J. Org. Chem. **1993**, 58, 4513–15. (b) Chen, Y.; Snyder, J. K. J. Org. Chem. **1998**, 63, 2060.

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⁽⁷⁾ From over 37 g of NBD and an excess of acetylene gas, 2.5–2.8 g of **D** was isolated. See: Schrauzer, G. N.; Glockner, P. *Chem. Ber.* **1964**, *97*, 2451.

⁽⁸⁾ Neat NBD was used as the solvent in the presence of various rhodium complexes to generate different dimers and trimers of NBD. See: Acton, N.; Roth, R. J.; Katz, T. J.; Frank, J. K.; Maier, C. A.; Paul, I. C. J. Am. Chem. Soc. **1972**, *94*, 5446.

⁽⁹⁾ This method has been also applied to prepare indenocorannulenes. See: Wu, Y.-T.; Hayama, T.; Baldridge, K. K.; Linden, A.; Siegel, J. S. Submitted to *J. Am. Chem. Soc.* 2005.

⁽¹⁰⁾ It was also observed that NBD as a "proalkyne" participates in the [2+2+2] cycloaddition with two alkynes to generate 1,3-disubstituted benzenes as byproducts; see ref 6c.

⁽¹¹⁾ Only the reaction products from 1 are isolated and characterized. Yields are based on 1 as the limiting reagent. Dimers coming from NBD were also formed but neglected.

⁽¹²⁾ Crystal data for $\mathbf{\tilde{3a}}$: crystals from CH₂Cl₂/MeOH, Nonius Kappa-CCD diffractometer, C₃₃H₂₄, M = 420.55, monoclinic, a = 15.6716(7), b = 9.0731(4), c = 16.7091(7) Å, $\beta = 113.433(3)^\circ$, V = 2179.9(2) Å³, T = 160(1) K, space group $P2_1/n$, Z = 4, μ (Mo K α) = 0.072 mm⁻¹, 33 181 reflections measured, 3834 unique reflections ($R_{int} = 0.077$), which were used in all calculations (SHELXL-97), 2860 reflections with $I > 2\sigma(I)$, R(F) = 0.0554 ($I > 2\sigma(I)$ data), $wR(F^2) = 0.1344$ (all data). The "polycyclic alkane" part of the molecule is disordered over two conformations (0.7:0.3 occupation ratio), which are inverted images of one another.

⁽¹⁴⁾ A mixture of 1,2-diphenylethyne, NBD, and Wilkinson catalyst was employed at 130 °C as a blank experiment. According to the HPLC and GC analyses, only the starting materials were obtained. Thus, the key intermediate of this reaction, the 1-rhodacyclopentadiene derivative **6**, is confirmed. The same reason can also explain how **D** is formed only in high-pressure conditions.

⁽¹⁵⁾ Intramolecular cyclizations of **1a** at 100 °C to form 7-phenylbenzo-[*k*]fluoranthene. See: Bossenbroek, B.; Sanders, D. C.; Curry, H. M.; Shechter, H. J. Am. Chem. Soc. **1969**, *91*, 371.

anthenes. Additionally, fluoranthene **2c** has been applied to prepare dibenzo[a,g]corannulene.¹⁶

To understand the factors controlling the distribution of products, a limited systematic study was undertaken. The choice of catalyst had a demonstrable effect. Wilkinson catalyst provided a ratio of ca. 77:23 between **2a** and **3a** in this reaction. [RhCl(COD)]₂ and Rh₂(OAc)₄ led exclusively to the formation of fluoranthene **2a** (cf. Table 1). It was found that not only the catalyst utilized but also the substituents (R¹ and R²) of diyne **1** play important roles in the chemoselectivity between **2** and **3**. Electron-donating and/or bulky groups (R¹ and R²) on diyne **1** enhanced the formation of **2** (cf. Table 1). However, an electron-withdrawing moiety on the diyne **1** slightly increased the ratio of **3** (cf. Table 1). Reaction temperature does not appear to have a serious influence on product ratios.

A working mechanism for the formation of 2 and 3 can be formulated by analogy with literature processes (Scheme 2).^{3a} Initially, 1-rhodacyclopentadiene 6 is formed and subsequent coordination of NBD partitions between an η^4 -complex 5 or an η^2 -complex 8. Complex 5 can easily rearrange to the deltacyclane derivative 4. Heptacycle 3 is produced from the intermediate 4 after a reductive elimination of the Rh complex. In contrast, complex 8 inserts NBD





from its ligand sphere to afford σ -complex 7. A reductive elimination of the Rh catalyst gives a transient dihydrofluoranthene that thermally eliminates cyclopentadiene to produce fluoranthene 2.

In conclusion, NBD can act as an acetylene equivalent or a conjugated diene mimic in this rhodium-catalyzed protocol.¹⁷ The former role produces fluoranthenes formally by a [(2+2)+2] reaction with excellent chemoselectivity in very good yield and purity. The latter role for NBD results in a formal [(2+2)+(2+2)] reaction, wherein the diene and diyne fragments owe their special "conjugated-like" properties to proximal through-space orbital interactions. This reactivity exemplifies one of very few ways that three different rings can be formed in a single reaction sequence.

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Supporting Information Available: Crystal structure data for **3a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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⁽¹⁶⁾ Reisch, H. A.; Bratcher, M. S.; Scott, L. T. Org. Lett. 2000, 2, 1427. (17) Preparative procedure: a mixture of diyne 1a (164 mg, 0.5 mmol), NBD (1 mL, 9.22 mmol), Wilkinson catalyst (23 mg, 25.0 µmol), and p-xylene (20 mL) in a Schlenk tube at ambient temperature was passed through nitrogen for 5 min. The mixture was kept in an oil bath under nitrogen at 130 °C for 41 h. After cooling to room temperature and removal of the solvent, the residue was subjected to chromatography on SiO2. Elution with hexane/CH₂Cl₂ (from 4:1 to 3:1) afforded 16 mg of pure 2a and 168 mg of a mixture of 2a and 3a. Pure 3a was obtained by further chromatography on alumina eluting with hexane. 2a: a pale yellow crystal, mp 167 °C. IR (KBr): ν cm⁻¹ = 3053, 3013, 1598, 1475, 1447, 1427, 825, 776, 759, 701. ¹H NMR (300 MHz, CDCl₃): δ ppm = 7.24 (d, J = 7.2 Hz, 2 H), 7.35 (d, J = 8.1 Hz, 2 H), 7.38 (d, J = 7.2 Hz, 2 H), 7.49– 7.62 (m, 6 H), 7.64–7.69 (m, 4 H), 7.75 (d, J = 8.1 Hz, 2 H). ¹³C NMR (75.5 MHz, CDCl₃, plus DEPT): δ ppm = 122.9, 126.6, 127.4, 127.6, 128.5, 129.0 × 2 (all +), 129.7, 132.7, 136.2, 136.7, 137.9, 140.9 (all C_{qual}). MS (70 eV), m/z (%): 354 (100) [M⁺], 328 (40), 149 (20). Elemental analysis calcd (%) for C₂₈H₁₈ (354.4): C 94.88, H 5.12; found, C 94.64, H 5.16. HRMS (EI) calcd for $C_{28}H_{18}$: 354.1409; found, 354.1410. **3a**: a pale yellow crystal, mp 327–329 °C. IR (KBr): ν cm⁻¹ = 3051, 1577, 1487, 778, 753, 698. ¹H NMR (300 MHz, CDCl₃): δ ppm = 0.86 (t, J = 5.4 Hz, 1 H), 1.47 (s, 2 H), 1.79 (d, J = 5.4 Hz, 2 H), 2.59 (s, 2 H), 2.61 (s, 1 H), 5.76 (d, J = 7.2 Hz, 2 H), 6.93 (d, J = 7.2 Hz, 2 H), 7.16-7.50 (m, 12 H). ¹³C NMR (75.5 MHz, CDCl₃, plus DEPT): δ ppm = 8.4, 20.1, 33.2, 55.0 (all +), 35.3 (-), 119.9, 123.0, 127.0, 127.3, 127.8, 129.3, 129.6 (all +), 130.7, 132.9, 137.5, 139.1, 142.7, 146.5 (all C_{quat}). MS (70 eV), m/z (%): 420 (100) [M⁺]. Elemental analysis calcd (%) for C₃₃H₂₄ (420.5): C 94.25, H 5.75; found, C 93.96, H 5.78. HRMS (EI) calcd for C₃₃H₂₄: 420.1878; found, 420,1871.