“Formal” Ruthenium-Catalyzed [4+2+2] Cycloaddition of 1,6-Diynes to 1,3-Dienes: Formation of Cyclooctatrienes vs Vinylcyclohexadienes

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Supporting Information

I. General

Dry DMF (Fluka) was used as received. All other solvents and reagents were used as received, unless otherwise noted. All reactions were carried out under an atmosphere of argon in flame-dried glassware with magnetic stirring, unless otherwise indicated.

II. Preparation of starting materials and catalysts

2,2-Diprop-2-ynyl malonic acid dimethyl ester (**1a**), 2,2-dibut-2-ynyl malonic acid dimethyl ester (**1b**) and 2-allyl-2-prop-2-ynyl malonic acid dimethyl ester (**1c**) were prepared following published procedures.¹ *Cis,cis*-**2e**² and *trans,trans*-**2e**³ were prepared following the methods described in the literature.

Catalysts [CpRu(CH₃CN)₃]PF₆ and [Cp*Ru(CH₃CN)₃]PF₆ were also prepared following published procedures.^{4,5}

III. General procedure for the “formal” Ru-catalyzed [4+2+2] cycloadditions:

5,8-Dimethyl-1,3,4,5-tetrahydrocyclopentacyclooctene-2,2-dicarboxylic acid dimethyl ester (**3e**). *Conditions A:* In a 25 mL round-bottomed flask was prepared, under vacuum, a solution of [Cp*Ru(CH₃CN)₃]PF₆ (25 mg, 10%) and Et₄NCl (8 mg, 10%) in DMF (4 mL). After stirring for 10 minutes at room temperature the diene **2e** (123 mg, 0.17 mL, 1.5 mmol, 3eq.) and then, after stirring for another 10 minutes, the diyne **1a** (104 mg, 0.5 mmol, 1 eq.) were added to the solution. Stirring was continued for 1 hour and the reaction was quenched with saturated aqueous solution of NH₄Cl (10 mL) and extracted with ethyl ether (3 x 10 mL). The organic layers were collected, dried over anhydrous Na₂SO₄ and evaporated under vacuum. Column chromatography of the residue on silica gel using ethyl acetate/hexane (2:8) as eluents afforded 1,3,5-cyclooctatriene **3e** in 21% yield.

Conditions B: Identical conditions as A, but the diyne **1a** was solved in DMF (2 mL) and added to the solution over 2 or 4 hours via syringe pump. After chromatography of the residue 1,3,5-cyclooctatriene **3e** was obtained in 47% yield (addition of **1a**, 2 h) and 58% yield (addition of **1a**, 4 h).

Conditions C: Identical conditions as B, but heating at 80°C during the slow addition of the diyne **1a** to the reaction flask. 1,3,5-Cyclooctatriene **3e** was obtained in 65% isolated yield.

1,3,4,5-Tetrahydrocyclopentacyclooctene-2,2-dicarboxylic acid dimethyl ester (**3a**) and 6-vinyl-1,3,4,5-tetrahydroindene-2,2-dicarboxylic acid dimethyl ester (**4a**)

A stream of 1,3-butadiene was bubbled over 15 min into a solution of [Cp*Ru(CH₃CN)₃]PF₆ (25 mg, 10%) and Et₄NCl (8 mg, 10%) in DMF (4 mL). Then, a solution of the diyne **1a** (104 mg, 0.5 mmol, 1 eq.) in DMF (2 mL) was added and the reaction mixture was kept at room temperature for 72 h under a balloon of 1,3-butadiene. After workup and purification as above, a 1:2.4 mixture of cyclooctatriene **3a** and hexadiene **4a** was obtained in 60% combined yield.

1,3,4,5-Tetrahydrocyclopentacyclooctene-2,2-dicarboxylic acid dimethyl ester (3a)

¹H-NMR (250 MHz, CDCl₃) δ (ppm): 5.97-5.82 (m, 2H), 5.76-5.59 (m, 2H), 3.70 (s, 6H), 3.08 (m, 4H), 2.44-2.36 (m, 2H), 2.31-2.26 (m, 2H). ¹³C-NMR, DEPT (63 MHz, CDCl₃) δ (ppm): 171.5 (2 x C), 137.1 (C), 136.3 (CH), 128.2 (C), 127.9 (CH), 125.8 (CH), 125.2 (CH), 56.2 (C), 52.7 (2 x CH₃), 47.0 (2 x CH₂), 30.3 (CH₂), 25.7 (CH₂). MS, m/z (% relative intensity) 263 (M⁺ +1, 19), 231 (29), 203 (100).

6-Methyl-1,3,4,5-tetrahydrocyclopentacyclooctene-2,2-dicarboxylic acid dimethyl ester (3b)

¹H-NMR (250 MHz, CDCl₃) δ (ppm): 5.79-5.72 (m, 2H), 5.62 (d, *J* = 12.8 Hz, 1H), 3.70 (s, 6H), 3.05 (m, 4H), 2.46 (t, *J* = 10.1 Hz, 2H), 2.22 (t, *J* = 10.1 Hz, 2H), 1.76 (s, 3H). ¹³C-NMR, DEPT (63 MHz, CDCl₃) δ (ppm): 172.2 (2 x C), 144.5 (C), 135.6 (C), 127.7 (C), 126.8 (CH), 123.9 (CH), 123.2 (CH), 56.1 (C), 52.7 (2 x CH₃), 47.4 (CH₂), 47.3 (CH₂), 30.2 (CH₂), 29.8 (CH₂), 24.1 (CH₃). MS, m/z (% relative intensity) 277 (M⁺ +1, 22), 245 (100), 217 (74).

5-Methyl-1,3,4,5-tetrahydrocyclopentacyclooctene-2,2-dicarboxylic acid dimethyl ester (3c)

¹H-NMR (250 MHz, CDCl₃) δ (ppm): 5.82-5.51 (m, 4H), 3.66 (s, 6H), 3.00 (m, 5H), 2.19 (m, 2H), 1.00 (d, *J* = 6.8 Hz, 3H). ¹³C-NMR, DEPT (63 MHz, CDCl₃) δ (ppm): 172.5 (2 x C), 142.2 (CH), 136.3 (C), 128.3 (C), 126.5 (CH), 125.7 (CH), 125.5 (CH), 56.3 (C), 52.6 (2 x CH₃), 47.0 (CH₂), 46.7 (CH₂), 38.8 (CH₂), 31.0 (CH), 21.7 (CH₃). MS, m/z (% relative intensity) 277 (M⁺ +1, 32), 245 (43), 217 (100).

8-Methyl-1,3,4,5-tetrahydrocyclopentacyclooctene-2,2-dicarboxylic acid dimethyl ester (3d)

¹H-NMR (250 MHz, CDCl₃) δ (ppm): 5.9-5.4 (m, 3H), 3.71 (s, 6H), 3.08-3.00 (m, 4H), 2.41 (t, *J* = 9.8 Hz, 2H), 2.18 (t, *J* = 9.8 Hz, 2H), 1.77 (s, 3H). ¹³C-NMR, DEPT (63 MHz, CDCl₃) δ (ppm): 172.0 (2 x C), 134.5 (CH), 133.8 (C), 133.1 (C), 131.3 (CH), 127.6 (C), 121.7 (CH), 56.2 (C), 52.7 (2 x CH₃), 47.3 (CH₂), 47.0 (CH₂), 30.2 (CH₂), 25.7 (CH₂), 24.0 (CH₃). MS, m/z (% relative intensity) 277 (M⁺ +1, 40), 245 (48), 217 (100).

5,8-Dimethyl-1,3,4,5-tetrahydrocyclopentacyclooctene-2,2-dicarboxylic acid dimethyl ester (3e)

¹H-NMR (250 MHz, CDCl₃) δ (ppm): 5.73 (d, *J* = 10.7 Hz, 1H), 5.45 (dd, *J* = 10.7, 7.8 Hz, 1H), 5.41 (s, 1H), 3.68 (s, 3H), 3.66 (s, 3H), 3.04-2.86 (m, 5H), 2.26-1.93 (m, 2H), 1.75 (s, 3H), 0.98 (d, *J* = 6.6 Hz, 3H). ¹³C-NMR, DEPT (63 MHz, CDCl₃) δ (ppm): 172.7 (C), 172.4 (C), 140.6 (CH), 134.7 (C), 134.0 (C), 129.1 (CH), 128.6 (C), 121.5 (CH), 56.3 (C), 52.7 (CH₃), 52.6 (CH₃), 47.1 (CH₂), 46.9 (CH₂), 38.9 (CH₂), 30.9 (CH), 23.9 (CH₃), 21.6 (CH₃). MS, m/z (% relative intensity) 291 (M⁺ +1, 47), 259 (84), 231 (100).

5,8-Dimethyl-2-(toluene-4-sulfonyl)-2,3,4,5-tetrahydro-1H-cycloocta[c]pyrrole (3'e)

¹H-NMR (250 MHz, CDCl₃) δ (ppm): 7.70 (d, *J* = 8.2 Hz, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 5.75 (d, *J* = 11.0 Hz, 1H), 5.47 (dd, *J* = 11.0, 8.2 Hz), 5.30 (s, 1H), 4.00 (m, 4H), 2.92 (m, 1H), 2.42 (s, 3H), 2.00 (m, 2H), 1.77 (s, 3H), 1.01 (d, *J* = 6.7 Hz, 3H). ¹³C-NMR, DEPT (63 MHz, CDCl₃) δ (ppm): 143.3 (C), 137.2 (C), 134.0 (C), 131.4 (C), 126.9 (C), 140.9 (CH), 129.7 (CH), 129.2 (CH), 127.5 (CH), 118.4 (CH), 59.9 (CH₂), 59.7 (CH₂), 36.7 (CH₂), 30.7 (CH), 24.0 (CH₃), 21.5 (CH₃), 21.5 (CH₃). MS, m/z (% relative intensity) 316 (M⁺ +1, 100), 160 (33), 125 (20).

5,8-Dimethyl-1,3,4,5-tetrahydro-cycloocta[c]furan (3''e)

¹H-NMR (250 MHz, CDCl₃) δ (ppm): 5.85 (d, *J* = 11.0 Hz, 1H), δ = 5.54 (dd, *J* = 11.0, 8.4 Hz, 1H), 5.41 (s, 1H), 4.67-4.36 (m, 4H), 3.08-2.93 (m, 1H), 2.25-1.92 (m, 2H), 1.82 (s, 3H), 1.07 (d, *J* = 6.6 Hz, 3H). MS, m/z (% relative intensity) 177 (M⁺ +1, 79), 175 (89), 159 (100), 147 (28), 133 (24).

6-Vinyl-1,3,4,5-tetrahydroindene-2,2-dicarboxylic acid dimethyl ester (4a)

¹H-NMR (250 MHz, CDCl₃) δ (ppm): 6.37 (dd, *J* = 17.6, 10.6 Hz, 1H), 5.80 (s, 1H), 5.16 (d, *J* = 17.6 Hz, 1H), 4.99 (d, *J* = 10.6 Hz, 1H), 3.71 (s, 6H), 3.06-3.03 (m, 4H), 2.44-2.33 (m, 2H), 2.26-2.18 (m, 2H). ¹³C-NMR, DEPT (63 MHz, CDCl₃) δ (ppm): 172.5 (C), 138.3 (CH), 135.0 (C), 133.9 (C), 130.8 (C), 122.9 (CH), 111.7 (CH₂), 58.4 (C), 52.7 (2 x CH₃), 43.3 (CH₂), 41.1 (CH₂), 23.2 (CH₂), 22.1 (CH₂). MS, *m/z* (% relative intensity) 263 (*M*⁺ +1, 27), 231 (16), 203 (100).

6-Isopropenyl-1,3,4,5-tetrahydroindene-2,2-dicarboxylic acid dimethyl ester (4b)

¹H-NMR (250 MHz, CDCl₃) δ (ppm): 5.94 (s, 1H), 5.06 (s, 1H), 4.92 (s, 1H), 3.72 (s, 6H), 3.05 (m, 4H), 2.46 (t, *J* = 10.1 Hz, 2H), 2.22 (t, *J* = 10.1 Hz, 2H), 1.90 (s, 3H). ¹³C-NMR, DEPT (63 MHz, CDCl₃) δ (ppm): 172.7 (2 x C), 142.3 (C), 135.8 (C), 133.3 (C), 131.0 (C), 118.6 (CH), 111.5 (CH₂), 58.5 (C), 52.7 (2 x CH₃), 43.2 (CH₂), 41.4 (CH₂), 24.0 (CH₂), 23.6 (CH₂), 20.4 (CH₃). MS, *m/z* (% relative intensity) 277 (*M*⁺ +1, 48), 245 (24), 217 (100).

6-Trans-propenyl-1,3,4,5-tetrahydroindene-2,2-dicarboxylic acid dimethyl ester (4c)

¹H-NMR (250 MHz, CDCl₃) δ (ppm): 6.05 (d, *J* = 15.8 Hz, 1H), 5.66 (s, 1H), 5.82-5.51 (m, 1H), 3.68 (s, 6H), 3.00 (m, 4H), 2.35 (t, *J* = 9.8 Hz, 2H), 2.18 (t, *J* = 9.8 Hz, 2H), 1.7 (d, *J* = 6.4 Hz, 3H). ¹³C-NMR, DEPT (63 MHz, CDCl₃) δ (ppm): 172.5 (2 x C), 134.9 (C), 133.1 (CH), 132.1 (C), 130.9 (C), 123.6 (CH), 120.1 (CH), 58.4 (C), 52.6 (2CH₃), 43.2 (CH₂), 41.1 (CH₂), 23.2 (CH₂), 23.0 (CH₂), 18.3 (CH₃). MS, *m/z* (% relative intensity) 277 (*M*⁺ +1, 68), 245 (37), 217 (100).

6-Cis-propenyl-1,3,4,5-tetrahydroindene-2,2-dicarboxylic acid dimethyl ester (4d)

¹H-NMR (250 MHz, CDCl₃) δ (ppm): 5.9-5.4 (m, 3H), 3.70 (s, 6H), 3.08-3.00 (m, 4H), 2.42 (t, *J* = 9.8 Hz, 2H), 2.18 (t, *J* = 9.8 Hz, 2H), 1.80 (d, *J* = 7.3 Hz, 3H). ¹³C-NMR, DEPT (63 MHz, CDCl₃) δ (ppm): 172.5 (2 x C), 134.6 (C), 131.4 (C), 130.9 (C + CH), 124.9 (CH), 121.5 (CH), 58.4 (C), 52.7 (2 x CH₃), 43.2 (CH₂), 41.3 (CH₂), 27.6 (CH₂), 23.5 (CH₂), 15.4 (CH₃). MS, *m/z* (% relative intensity) 277 (*M*⁺ +1, 48), 245 (38), 217 (100).

3-Methylene-4-(3-methyl-2-methylene-3-butenylidene)cyclopentane-1,1-dicarboxylic acid dimethyl ester VI

¹H-NMR (250 MHz, CDCl₃) δ (ppm): 6.10 (s, 1H), 5.44 (s, 1H), 5.24 (s, 1H), 5.10 (s, 2H), 4.99 (s, 1H), 4.94 (s, 1H), 3.72 (s, 6H), 3.06-3.02 (m, 4H), 1.91 (s, 3H). ¹³C-NMR, DEPT (63 MHz, CDCl₃) δ (ppm): 171.6 (2 x C), 145.3 (C), 142.0 (C), 140.6 (C), 136.7 (C), 124.9 (CH), 114.1 (CH₂), 113.7 (CH₂), 111.3 (CH₂), 57.2 (C), 52.7 (2 x CH₃), 42.9 (CH₂), 42.7 (CH₂), 19.9 (CH₃). MS, *m/z* (% relative intensity) 276 (*M*⁺ +1, 32), 245 (51), 217 (100).

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VIb