An Expeditious Stereoselective Synthesis of Functionalized Seven-membered Carbocycles by Reaction of 2-Aminobuta-1,3-dienes with Vinylchromium Fischer Type Carbenes

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The reaction between 2-aminobuta-1,3-dienes and pentacarbonyl-[1-methoxy-*trans*-3-(2-furyl)-prop-2-enylidene]-chromium(0) takes place at room temperature leading with total regio- and stereo-selectivity to functionalized seven-membered carbocycles with good yields.

Recently, we have been engaged in the study of the behaviour and synthetic applications of 2-aminobuta-1,3-dienes, which are readily prepared *via* the catalytic amination of alk-3-en-1-ynes.[1] The initial results have shown that they can act either as enamines or as 1,3-butadienes in [4 + 2] cycloaddition processes.[2]

On the other hand, stable Fischer carbene complexes have been increasingly used in organic synthesis.[3] In this context, the cyclopropanation reaction of alkenes has been one of the most extensively studied, not only because of its potential synthetic applications, but also because of its relationship to alkene metathesis.[4] However, only moderate yields of cyclopropanes, formed in an intermolecular fashion, have been reported in the case of olefins containing either strong electron-withdrawing[5] or -donating[6] groups. In most cases quite vigorous reaction conditions were required, *e.g.* elevated temperture and/or pressure of carbon monoxide, and only moderate levels of stereoselectivity were achieved. To the best of our knowledge, only one example of the intermolecular cyclopropanation of electron-rich 1,3-dienes involving a chromium vinyl carbene complex has been described.[7] Thus, Wulff and coworkers reported that the cyclopropanation reaction of Danishefsky's diene with chromium cyclohexenyl methoxymethylene complex takes place at the most electron-rich carbon–carbon double bond affording a mixture of a seven-membered ring compound (23%) and a *trans*-divinylcyclopropane derivative (40%), which in turn can be converted into the seven-membered ring by heating.

We report here preliminary results obtained in the reaction of 2-aminobuta-1,3-dienes with pentacarbonyl [1-methoxy-*trans*-3-(2-furyl)-2-propenylidene]chromium(0). Thus, the reaction of dienes **1** with the chromium carbene complex **2** (molar ratio 1:1; room temp.) in acetonitrile led in almost quantitative yields to a mixture of cycloheptadiene derivatives **3**, as the major compounds, and cyclohexenylchromium carbene complexes **4**, arising from the [4 + 2] cycloaddition reaction (Scheme 1, Table 1).

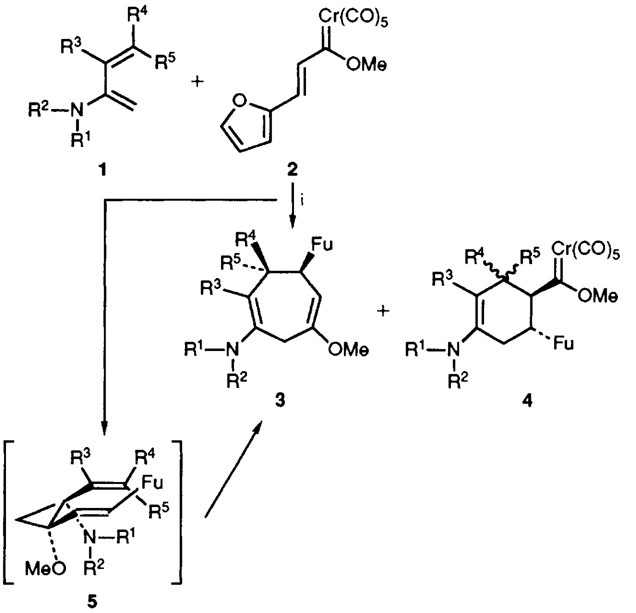
Compounds **3** were formed as sole stereoisomers according to the ^{1}H NMR (300 MHz) data, and the stereochemical assignment was ascertained from their hydrolysis derivatives (see below).

The formation of the seven-membered carbocycles **3** is

Table 1 Compounds **3** and **4** obtained from **1**[a]

Compound 1	R^1	R^2	R^3	R^4	R^5	Ratio **3**:**4**[b]	Solvent
a	Ph	Me	Me	CH_2OMe	H	10:1	Acetonitrile
a	Ph	Me	Me	CH_2OMe	H	7:1	Toluene
b	Ph	Me	Me	H	CH_2OMe	7:1	Acetonitrile
c	Ph	Me	$-(CH_2)_4-$		H	11:1	Acetonitrile
d	$(CH_2)_2O(CH_2)_2$		Me	CH_2OMe	H	3:1	Acetonitrile
d	$(CH_2)_2O(CH_2)_2$		Me	CH_2OMe	H	2:1	THF
d	$(CH_2)_2O(CH_2)_2$		Me	CH_2OMe	H	5:1	THF + 1 equiv. pyridine

[a] Yields are, in all cases, higher than 95%. [b] Deduced from ^{13}C NMR (75 MHz) of crude reaction product.

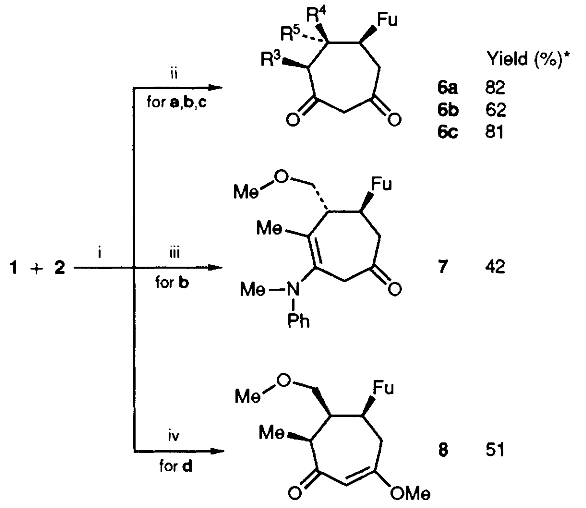


Scheme 1 *Reagents and conditions*: i, MeCN, 25 °C, 2 h **1c** or 48 h **1a, b, d**

understood in terms of a total chemo- and *cis*-stereo-selective carbene ligand transfer from **2** to the enamine carbon–carbon double bond of **1** giving rise to the cyclopropane derivatives **5**. Further Cope rearrangement of these *cis*-divinyl cyclopropanes occurs under the reaction conditions to yield **3** (Scheme 1).†

The molar ratio of **3**:**4** depends on the solvent nature as well as on the basicity of the amine substituent in the diene (Table 1). Thus, the ratio of **3**:**4** increases in going from toluene (**3**:**4** = 7:1) to acetonitrile (**3**:**4** = 10:1) (see entry **a**). On the other hand, the higher **3**:**4** ratios are reached when less basic amine are used. This can be seen by viewing the first entries for both **a** (R^1, R^2 = Ph, Me; **3**:**4** = 10:1) and **d** (R^1, R^2 = $(CH_2)_2$-O-$(CH_2)_2$; **3**:**4** = 3:1).

The hydrolysis of **3** was carried out *in situ* after completion of the reaction between **1** and **2** and allowed the isolation of cycloheptanedione and cycloheptenone derivatives. Thus, dienes **1a–c** were converted into diketones **6** in 62–82% overall yield by reaction with **2** followed by treatment with 3 mol dm^{-3} HCl–THF (tetrahydrofuran) and column chromatography (silica gel; ethyl acetate:hexane, 1:3). In the same way, **1b** led to the cycloheptenone **7** in 41% overall yield, after column chromatography (silica gel; ethyl acetate:hexane, 1:6) when the reaction mixture was hydrolysed with 1 mol dm^{-3} HCl–THF. On the other hand, diene **3d** was found to undergo hydrolysis by SiO_2; thus, treating of **1d** with **2**



Scheme 2 *Reagents and conditions*: i, MeCN, 25 °C, 2 h **1c** or 48 h **1a, b, d**; ii, 3 mol dm^{-3} HCl, THF, 25 °C, 2 h; iii, 1 mol dm^{-3} HCl, THF, 25 °C, 1 h; iv, SiO_2. * Based on the carbene complex **2**.

followed by column chromatography on SiO_2 (ethyl acetate:hexane, 1:3) gave cycloheptenone **8** in 51% yield (Scheme 2).‡

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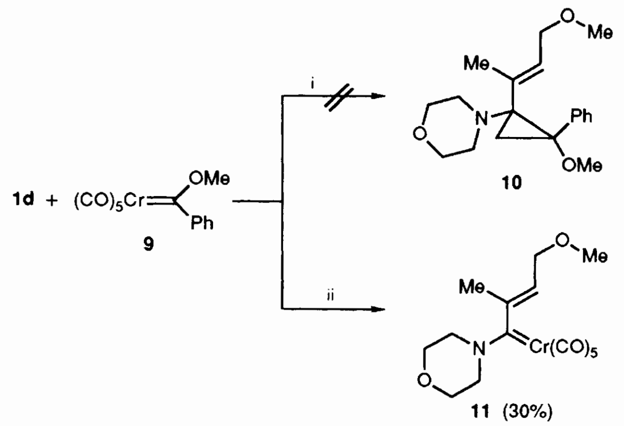
† It is known that *cis*-divinylcyclopropanes undergo Cope rearrangement below room temperature and they are not usually isolated.[8]

‡ Elemental analyses and spectroscopic data were in agreement with the structures assigned. [*E.g.* **6a**; m.p. 101–102 °C. ^1H NMR ($DCCl_3$, 300 MHz) δ 1.18 (d, *J* 6.7 Hz, 3H), 2.41–2.51 (m, 1H), 2.75–2.90 (m, 2H), 3.09 (s, 3H), 3.15 (d,d, *J* 15.5, 13.5 Hz, 1H), 3.33 (d,d, *J* 10.1, 1.9 Hz, 1H), 3.40 (d,d, *J* 10.1, 3.7 Hz, 1H), 3.61 (d, *J* 13.0 Hz, 1H), 3.78 (m, 1H), 3.85 (d, *J* 13.0 Hz, 1H), 6.09 (d, *J* 3.3 Hz, 1H), 6.32 (d, d, *J* 3.3, 1.8 Hz, 1H), 7.35 (d, *J* 1.8 Hz, 1H). ^{13}C NMR ($DCCl_3$): δ 14.3(q), 39.6(d), 43.5(t) 45.7(d), 50.1(d), 57.9(q), 60.6(t), 67.6(t), 105.4(d), 110.1(d), 141.5(d), 155.9(s), 201.1(s), 202.4(s).

7; yellowish oil. ^1H NMR ($DCCl_3$): δ 1.78 (s, 3H), 2.75 (d,d, *J* 16.5, 3.8 Hz, 1H), 2.87–3.00 (s + m, 5H), 3.07 (d,d, *J* 16.5, 8.9 Hz, 1H), 3.45 (s, 3H), 3.51–3.64 (m, 2H), 3.70 (d,d, *J* 8.9, 3.8 Hz, 1H), 3.76 (d,d, *J* 8.9, 3.8 Hz, 1H), 6.17 (d, *J* 3.2 Hz, 1H), 6.37 (d,d, *J* 3.2, 1.9 Hz, 1H), 6.63–6.80 (m, 3H), 7.18–7.31 (m, 2H), 7.39 (d, *J* 1.9 Hz, 1H). ^{13}C NMR ($DCCl_3$): δ 19.1(q), 35.0(d), 36.3(q), 44.1(t), 45.7(t), 48.5(d), 55.8(q), 71.8(t), 105.3(d), 109.9(d). 112.4(d), 116.9(d), 129.0(d), 133.4(s), 133.5(s), 141.2(d), 148.5(s). 156.6(s), 208.2(s).

8; m.p. 41–43 °C. ^1H NMR ($DCCl_3$): δ 1.18 (d, *J* 7.0 Hz, 3H), 2.52–2.59 (m, 1H), 2.79 (d,d, *J* 17.5, 4.3 Hz, 1H), 2.83 (q,d, *J* 7.0, 3.8 Hz, 1H), 2.97 (d,d, *J* 17.5, 10.7 Hz, 1H), 3.15 (s, 3H), 3.32 (d,d, *J* 9.9, 4.3 Hz, 1H), 3.39 (d,d, *J* 9.9, 5.6 Hz, 1H), 3.52–3.61 (m, 1H), 3.62 (s, 3H), 5.51 (s, 1H), 6.09 (d, *J* 3.3 Hz, 1H), 6.63 (d,d, *J* 3.3, 1.9 Hz, 1H), 7.36 (d, *J* 1.9 Hz, 1H). ^{13}C NMR ($DCCl_3$): δ 15.4(q), 34.9(t), 38.9(d), 43.6(d), 49.2(d), 55.2(q), 58.4(q), 69.6(t), 104.9(d), 105.7(d), 109.9(d), 140.8(d), 156.8(s), 169.5(s), 201.1(s).

11; yellowish oil. ^1H NMR ($DCCl_3$): δ 1.78 (s, 3H), 3.39 (s, 3H), 3.65–3.72 (m, 4H), 3.91–4.12 (m, 4H), 4.30–4.50 (m, 2H), 5.01 (t, *J* 6.7 Hz, 1H). ^{13}C NMR ($DCCl_3$): δ 14.7(q), 54.2(t), 58.0(q), 59.7(t), 67.6(t), 68.0(t), 115.4(d), 147.9(s), 217.2(s), 222.9(s), 273.5(s). IR ν/cm^{-1} (film): 1935, 1971, 2055].



Scheme 3 *Reagents and conditions*: i, Toluene, 25 °C, 5 d; ii, toluene, 110 °C, 2 d

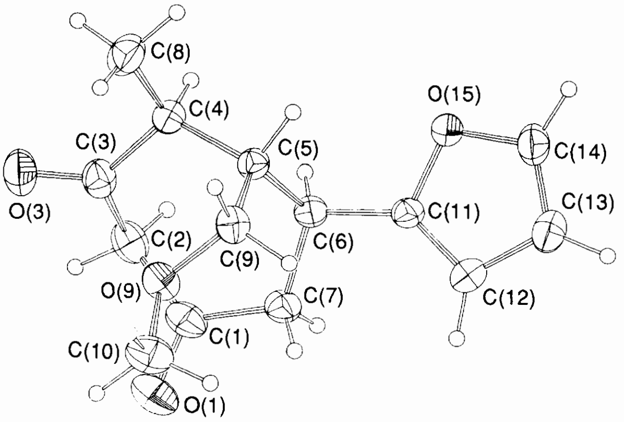


Fig. 1 Perspective view of compound **6a** with the numbering scheme. Selected bond lengths (Å) and torsion angles (°): O(15)–C(11) 1.375 (3), O(15)–C(14) 1.378(3), C(11)–C(12) 1.344(4), C(11)–C(6) 1.501(3), C(12)–C(13) 1.425(4), C(13)–C(14) 1.324(5), C(6)–C(7) 1.534(4), C(6)–C(5) 1.549(3), C(7)–C(1) 1.507(4), C(1)–C(2) 1.510(4), C(1)–O(1) 1.217(3), C(2)–C(3) 1.517(4), C(3)–O(3) 1.212(3), C(3)–C(4) 1.523(4), C(4)–C(5) 1.547(4), C(4)–C(8) 1.527(4), C(5)–C(9) 1.520(3), C(9)–O(9) 1.419(3), O(9)–C(10) 1.417(3); O(15)–C(11)–C(6)–C(7) −168.9(2), O(15)–C(11)–C(6)–C(5) 63.9(3), C(11)–C(6)–C(5)–C(4) −150.5(2), C(1)–C(6)–C(7)–C(1) −178.5(2), C(7)–C(6)–C(5)–C(9) −43.5(3), C(7)–C(6)–C(5)–C(4) 86.2(3), C(5)–C(6)–C(7)–C(1) −54.5(3), C(6)–C(7)–C(1)–C(2) −18.0(4), C(6)–C(7)–C(1)–O(1) 165.2(3), C(7)–C(1)–C(2)–C(3) 74.2(4), O(1)–C(1)–C(2)–C(3) −109.1(3), C(1)–C(2)–C(3)–O(3) 113.1(3), C(1)–C(2)–C(3)–C(4) −72.9(3), C(2)–C(3)–C(4)–C(5) 53.4(3), C(2)–C(3)–C(4)–C(8) −176.9(3), O(3)–C(3)–C(4)–C(5) −132.7(3), O(3)–C(3)–C(4)–C(8) − 3.0(4), C(3)–C(4)–C(5)–C(6) −69.5(3), C(3)–C(4)–C(5)–C(9) 66.4(3), C(8)–C(4)–C(5)–C(6) 167.0(2), C(8)–C(4)–C(5)–C(9) −63.1 (3), C(4)–C(5)–C(9)–O(9) −51.0(3), C(6)–C(5)–C(9)–O(9) 79.6(3), C(5)–C(9)–O(9)–C(10) −164.5(3).

The stereochemistry of compounds **6**, and, therefore, that of their precursors **3**, was deduced from ^{1}H NMR (300 MHz) data, including NOE (nuclear Overhauser effect) and NOESY [(two-dimensional) NOE enhanced spectroscopy] experiments. This structure was confirmed by an X-ray determination performed on **6a** (Fig. 1).§

Investigation of the scope of this cyclopropanation reaction of 2-aminobuta-1,3-dienes using Fischer metal carbenes showed that the vinyl function of the chromium carbene complex was essential. Thus, when the phenyl carbene complex **9** was treated with diene **1d** in toluene at room temp., the cyclopropanation reaction to furnish **10** did not take place, but the starting materials were recovered unaltered after 5 days; however, heating the mixture at 110 °C for two days resulted in the formation of the metathesis compound **11** in 30% yield. This reaction appears to be a straightforward entry into aminovinylcarbene complexes.

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§ *Crystal data*: $C_{14}H_{18}O_4$, $M_r = 282.34$, colourless prisms, orthorhombic, space group *Pbca*, $a = 8.235\ (4)$, $b = 19.461\ (6)$, $c = 16.571\ (6)$ Å, $V = 2656\ (2)$ Å^3, $Z = 8$, $D = 1.41$ g cm^{-3}, $T = 293$ K; crystal dimensions $0.49 \times 0.46 \times 0.20$ mm^3. 2668 reflections measured, range $0 < \theta < 25$ and $0 < h < 9$, $0 < k < 23$, $0 < l < 19$; 2311 unique reflections ($R_{int} = 0.040$, averaging double measured) and 1456 observed with $I > 3\sigma (I)$; $\mu = 0.98$ cm^{-1} final $R = 0.045$, $R_w = 0.050$. (236 parameters and $\omega = 1/(\sigma^2 (F_o) + 0.001 F_o^2)$; maximum shift/error 0.002, $\rho_{max} = 0.15$, $\rho_{min} = -0.21$ e Å^{-3}, ρ = residual electron density. X-Ray experimental procedures: Mo-Kα radiation ($\lambda = 0.71073$ Å) graphite monochromated; Enraf-Nonius CAD4 (ω-2θ scan technique). Semiempirical and empirical absorption corrections were applied. The structure was solved by direct methods (SHELXS86) and anisotropically refined (SHELX76, local version). Drawing made using the EUCLID package. All calculations made on a MicroVax-3400 at the Scientific Computer Center of the University of Oviedo. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data centre. See Notice to Authors, Issue No. 1.