Stereoselective Cyclopropanation of 1-Azadienes with Fischer Carbene Complexes

José Barluenga,* Miguel Tomás, José A. López-Pelegrín and Eduardo Rubio

Instituto Universitario de Química Organometálica 'Enrique Moles', Universidad de Oviedo, Julián Clavería 8, 33071-Oviedo, Spain

1-Aza-1,3-dienes, including a 1-aza-1,3,5-triene, are cyclopropanated by pentacarbonyl(methoxy)phenylchromium to give *trans*-cyclopropaneimines stereoselectively; their transformation into cyclopropane aldehydes and five-membered heterocycles is also described.

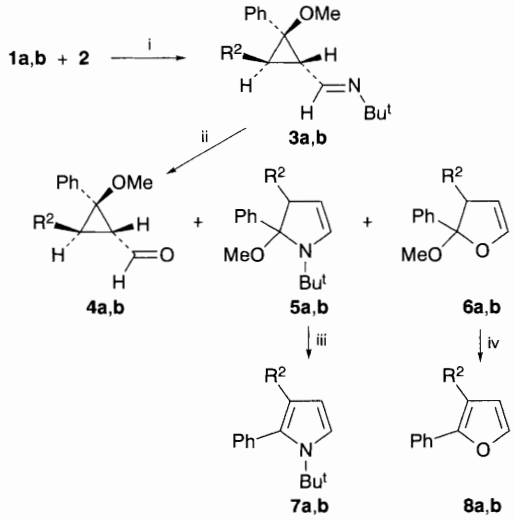
Among the reactions of Fischer carbene complexes, the cyclopropanation of alkenes has received much recent attention.[1] While neutral and electron-rich alkenes undergo cyclopropanation rather sluggishly, it is well known that electron-deficient alkenes are smoothly cyclopropanated with Fischer-type carbene complexes of chromium[2] and molybdenum.[3] However, major limitations are the low stereoselectivity of the process, in particular for phenylchromium Fischer carbene complexes, the formation of C–H insertion products and the fact that α,β-unsaturated aldehydes fail to react in this way, probably because of olefin polymerization.[2a] In order to overcome these drawbacks, we were intrigued by the use of 1-azadienes as masked aldehydes, since we recently observed that 4-*tert*-butylamino-1-azadienes display a relevant reactivity towards vinyl Fischer carbenes.[4] However, when this manuscript was in preparation, it was reported[5] that pentacarbonyl(ethoxy)phenylchromium reacts with 1-azadienes derived from cinnamaldehyde in refluxing toluene to give *N*-substituted 2,3-diphenylpyrroles in 50–60% yield; the authors point out that either a [2 + 1] cycloaddition/[1,3] rearrangement or a [4 + 1] cycloaddition might be responsible for the pyrrole formation. Therefore, we wish to disclose our preliminary results in this specific area; in this study azadienes **1a–e** and chromium carbene **2** were employed.†

First, **1a** and **2** (ratio 1 : 1) were heated at 80 °C for 3 h in THF to give cyclopropane **3a** in 75% yield after purification by column chromatography (silica gel; hexane–ethyl acetate 1 : 1). Interestingly, only the cyclopropane having the methoxy substituent *anti* to the imine group (*trans* isomer) was detected in the crude product (^{1}H NMR, 300 MHz), in contrast with the behaviour of electron-poor alkenes towards chromium carbenes which results, in general, in ratios close to 1 : 1.[2a] When **3a** was subjected to column chromatography using a less polar eluent (silica gel; hexane–ethyl acetate 6 : 1) the corresponding cyclopropane carboxaldehyde **4a** was isolated in 25% yield along with the rearranged heterocycles **5a** (20%) and **6a** (34%).‡ Acid treatment of **5a** and **6a** gave pyrrole **7a** and furan **8a**, respectively, in quantitative yield. Moreover, heating of **1a** and **2** for longer time (14 h) resulted in the formation of pyrrole **7a** (80%). Comparable results were achieved when azadiene **1b** and **2** were heated at 60 °C, furnishing **3b** in 70% yield and moderate purity after filtration through celite;§ in this case, the *cis* cyclopropaneimine was also detected (< 5%). As above, **3b** led to **4b** (20%), **5b** (17%) and **6b** (36%) (Scheme 1).¶

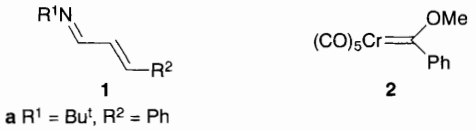
Electron-poor diene **1c** was then treated with **2** and we found the reaction to show total chemo- and peri-selectivity, as well as high stereoselectivity. The reaction takes place in THF at 60 °C for 14 h to give, after filtration through celite, cyclopropane **3c** and its stereoisomer **3c′** (60% yield, ratio 7 : 1). Further column chromatography (silica gel; hexane–ethyl acetate 4 : 1) allowed the isolation of cyclopropanecarboxaldehydes **4c** and **4c′** in 83% yield (50% overall yield from **1c**).‖ It should be noted that this reaction shows the opposite chemoselectivity to that found in the case of the analogous ester substituted dienes, which undergo cyclopropanation at the remote carbon–carbon double bond (Scheme 2).[6]

Azadiene **1d**, derived from aniline, also underwent cyclopropanation (80 °C, 4 h, 78%) but with much lower stereoselectivity (4 : 1). On the other hand, no face discrimination was observed when azadiene **1e** derived from (+)-Ph(Me)CHNH$_2$, was employed.

The cyclopropanation of 1-azadienes with Fischer carbenes has been demonstrated for the first time, with no C–H insertion products being formed. Contrary to previous belief, the elusive cyclopropane carboxaldehydes could be isolated and characterized. 1-Azatriene furnished a major cyclopropane isomer arising from participation of the internal carbon–carbon double bond. The [4 + 1] annulation of 1-azadienes to pyrroles involves tandem cyclopropanation and ring enlargement.



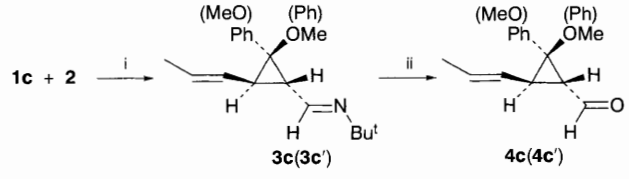
Scheme 1 *Reagents and conditions*: i, THF, 80 °C, 3 h for **3a**; THF, 60 °C, 8 h for **3b**; ii, SiO_2, hexane–EtOAc (6 : 1); iii, THF, 2 mol dm^{-3} HCl, 20 °C, 4 h; iv, THF, 2 mol dm^{-3} HCl, 40 °C, 6 h



1 **2**

a R^1 = Bu^t, R^2 = Ph
b R^1 = Bu^t, R^2 = Me
c R^1 = Bu^t, R^2 = CH=CHMe (*E*)
d R^1 = Ph, R^2 = Ph
e R^1 = (*R*)-CH(Me)Ph, R^2 = Ph

Fig. 1



Scheme 2 *Reagents and conditions*: i, THF, 60 °C, 14 h; ii, SiO_2, hexane–EtOAc (4 : 1)

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Footnotes

† We have found that 1-hydroxy-1-azadienes do not give cyclopropane derivatives (unpublished results). The reactivity of Fischer carbenes towards 1-amino-1-azadienes is currently being studied in our laboratory.

‡ Cyclopropane carboxaldehydes of this sort have been described as elusive species.[7]

§ Using higher temperatures resulted in pyrrole formation. Cyclopropane imine **3b** did not withstand column chromatography purification.

¶ Elemental analyses and spectroscopic data were in agreement with the structures assigned. The stereochemistries of **3** and **4** were ascertained by comparison of their NMR data with those previously reported for cyclopropanes.[2a,8] *Selected spectroscopic data* for **4a**: ^{1}H NMR ($DCCl_3$, 300 MHz) δ 2.90 (1H, dd, *J* 5.7, 7.0 Hz), 2.96 (3H s), 3.48 (1H, d, *J* 7.0 Hz), 7.23–7.56 (10H, m), 8.95 (1H, d, *J* 5.7 Hz). ^{13}C NMR ($DCCl_3$, 75 MHz) δ 35.6 (CH), 43.1 (CH), 54.5 (OMe), 75.1 (C), 125.9 (CH), 127.0 (CH), 128.2 (CH), 128.6 (CH), 128.9 (CH), 129.9 (CH), 133.9 (C), 135.0 (C), 198.0 (CH).

‖ The cyclopropanation of 1-carboxaldehyde-1,3-dienes is also unknown. No efforts have yet been made to separate **3c** and **4c** from their mixtures. For the utility of vinylcyclopropane carboxaldehydes as precursors of oxepines, see ref. 9.

References

1 H.-U. Reissig, *Top. Curr. Chem.*, 1988, **144**, 73; M. Brookhart and W. B. Studabaker, *Chem. Rev.*, 1987, **87**, 411; W. D. Wulff, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon, New York, 1991, vol. 5.

2 (*a*) A. Wienand and H.-U. Reissig, *Organometallics*, 1990, **9**, 3133; (*b*) A. Wienand and H.-U. Reissig, *Chem. Ber.*, 1991, **124**, 957; (*c*) J. W. Herndon and S. U. Tumer, *J. Org. Chem.*, 1991, **56**, 286.

3 D. F. Harvey and M. F. Brown, *Tetrahedron Lett.*, 1990, **31**, 2529.

4 J. Barluenga, M. Tomás, A. Ballesteros, J. Santamaría and F. López-Ortiz, *J. Chem. Soc., Chem. Commun.*, 1994, 321.

5 T. N. Danks and D. Velo-Rego, *Tetrahedron Lett.*, 1994, **35**, 9443.

6 R. Menicagli, C. Malanga and L. Lardicci, *J. Chem. Res. (S)*, 1985, 20.

7 I. Reichelt and H.-U. Reissig, *Chem. Ber.*, 1983, **116**, 3895.

8 R. K. Boeckman, Jr., M. D. Shair, J. R. Vargas and L. A. Stolz, *J. Org. Chem.*, 1993, **58**, 1295; B. Hofmann and H.-U. Reissig, *Synlett*, 1993, 27.

9 M. Buchert and H.-U. Reissig, *Chem. Ber.*, 1992, **125**, 2723.