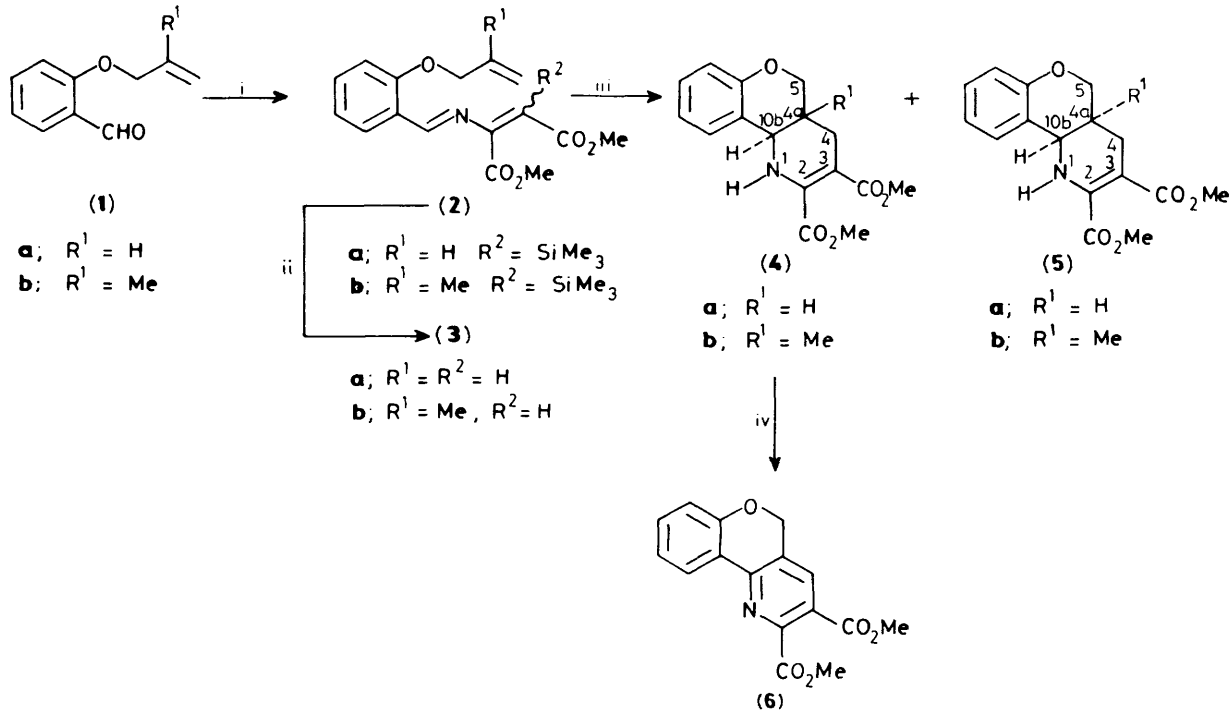
Cycloaddition Reactions of 3,4-Bismethoxycarbonyl-2-aza-1,3-dienes. The First Example of an Intramolecular [4 + 2] Cycloaddition of Simple 2-Azadienes

José Barluenga,* Miguel Tomás, Alfredo Ballesteros, and Vicente Gotor

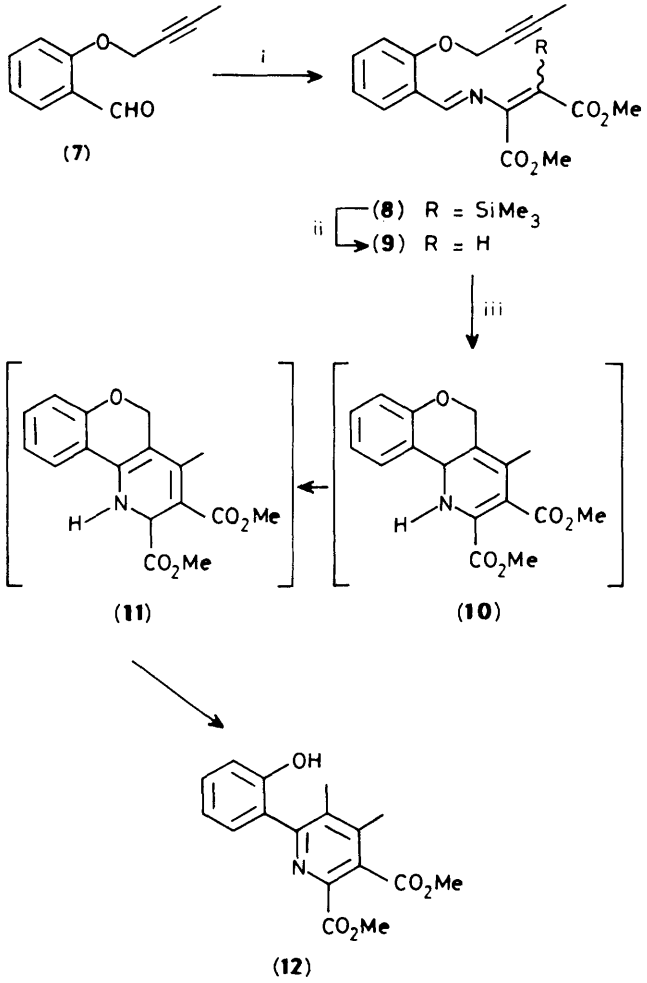
Departamento de Química Organometálica, Facultad de Química, Universidad de Oviedo, 33071 Oviedo, Spain

Electron-poor 2-aza-1,3-dienes undergo intramolecular [4 + 2] cycloadditions to unactivated carbon–carbon double and triple bonds in high yields.

The [4 + 2] cycloadditions of aza-1,3-dienes have recently been reviewed and a number of reactions of 1- and 2-azadienes are known;[1] moreover, we have described the preparation of 2-azadienes containing electron-withdrawing groups and their cycloaddition to enamines.[2] However, in spite of this important role in organic synthesis the corresponding intramolecular version has been much less investigated; in fact, while a few relevant examples involving 1-azadienes have been reported, there have been no reports dealing with simple 2-azadienes, to the best of our knowledge.[1,3] Here, we report the intramol-



Scheme 1. *Reagents*: i, see ref. 2; ii, (a) CsF–MeOH, 25 °C, 15 h; (b) toluene, 110 °C, 4 h; iii, sealed tube, 125—150 °C, 30—48 h; iv, DDQ, benzene, reflux, 15 h.



Scheme 2. *Reagents*: i, ii, see Scheme 1; iii, sealed tube, toluene, 150 °C, 48 h.

ecular [4 + 2] cycloaddition reaction involving 3,4-bismethoxycarbonyl-2-aza-1,3-dienes and unactivated dienophiles, such as simple alkenes and alkynes.†

The starting materials (**3**) containing diene and dienophile units were readily synthesized from *O*-substituted salicylaldehydes (**1**). Thus, dienes (**2**) were prepared as reported previously[2] and purified by distillation [(**2a**), 86%, b.p. 138—142 °C at 10^{-5} torr; (**2b**), 85%, b.p. 149—152 °C at 10^{-5} torr]; compounds (**2**) were then desilylated by treatment with CsF–MeOH followed by heating in toluene to give (**3**).‡ When

† The intermolecular reaction of 3,4-bismethoxycarbonyl-1-phenyl-2-azabuta-1,3-diene with *trans*-stilbene (sealed tube, toluene, 160 °C, 4 days) led to diene decomposition and recovery of the alkene.

‡ Compound (**3b**) was isolated as a single stereoisomer in quantitative yield: ^{13}C n.m.r. (75 MHz; $CDCl_3$) δ 165.12(s), 163.90(s), 160.01(d), 158.85(s), 152.85(s), 140.03(s), 133.37(d), 128.00(d), 123.52(s), 120.76(d), 120.62(t), 120.23(d), 108.43(d), 71.73(t), 52.65(q), 51.15(q), and 19.04(q).

Compound (**4a**) ^{1}H n.m.r. (300 MHz; $CDCl_3$) δ 2.0 (m, 2H, 4-, 4a-H), 2.6 (dd, 1H, *J* 15.7 and 3.8 Hz, 4-H), 3.6 (s, 3H), 3.7 (m, 1H, 5-H), 3.8 (s, 3H), 4.1 (d, 1H, *J* 10 Hz, 10b-H), 4.3 (dd, 1H, *J* 11 and 3.2 Hz, 5-H), 4.75 (br. s, NH), 6.85 (m, 2H, Ar), and 7.1 (m, 2H, Ar). ^{13}C n.m.r. (75 MHz; $CDCl_3$) δ 167.29(s), 166.92(s), 153.78(s), 145.30(s), 128.91(d), 124.50(d), 120.59(d), 123.53(s), 116.95(d), 97.36(s), 68.18(t), 52.83(q), 51.63(d), 51.24(q), 32.41(d), and 24.47(t). The proton resonances were assigned completely from 2D ^{1}H–^{13}C heteronuclear shift correlation.

Compound (**6**) ^{13}C n.m.r. (75 MHz; $CDCl_3$) δ 167.11(s), 164.91(s), 156.97(s), 151.88(s), 151.46(s), 133.74(d), 132.92(d), 126.52(s), 125.92(d), 122.86(s), 122.54(d), 121.45(s), 117.04(d), 67.23(t), 52.88(q), and 52.70(q).

Compound (**8**) ^{1}H n.m.r. (300 MHz; $CDCl_3$) δ 0.1 (s, 9H), 1.7 (t, 3H, *J* 2.3 Hz), 3.6 (s, 3H), 3.65 (s, 3H), 4.55 (q, 2H, *J* 2.3 Hz), 6.9 (m, 2H, Ar), 7.3 (t, *J* 8.2 Hz, 1H, Ar), 7.9 (d, *J* 8.2 Hz, 1H, Ar), and 8.75 (s, 1H).

Compound (**12**) ^{13}C n.m.r. (75 MHz; $CDCl_3$) δ 167.98(s), 164.36(s), 157.20(s), 156.30(s), 147.20(s), 139.02(s), 134.83(s), 131.10(d), 130.27(d), 121.14(s), 118.81(d), 118.36(d), 53.11(q), 52.95(q), 18.13(q), and 17.40(q).

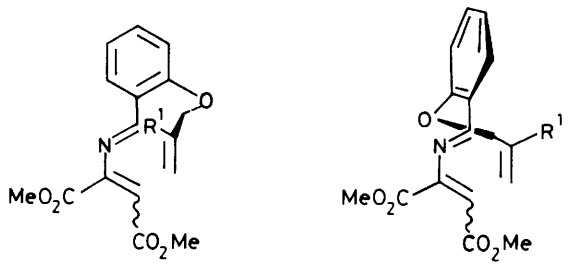


Figure 1. *exo*- and *endo*-Transition states.

a toluene solution of (**3a**) was heated at 125 °C for 30 h the tricyclic adduct (**4a**) [90% from (**2a**)] was obtained as a solid, in almost pure form, and recrystallized from hexane–chloroform (m.p. 168—170 °C); interestingly, solely the *trans*-fused stereoisomer (**4a**) [*J*(4a-H–10b-H) 10 Hz][4] was formed, the *cis*-fused isomer (**5a**) not being detectable in the crude mixture (^{1}H n.m.r., 300 MHz) (Scheme 1). Dehydrogenation of (**4a**) with dichlorodicyanobenzoquinone (DDQ) led to compound (**6**) (90%, m.p. 137—139 °C).‡

Compound (**3b**; R = Me) underwent cyclization at 150 °C to furnish, after 48 h, an oil identified as a *ca.* 1 : 1 mixture of *trans*- (**4b**) and *cis*-fused (**5b**) isomers in 88% yield (Scheme 1).§ The stereochemical results can be explained by assuming that an *exo*-transition state is favoured for (**3a**) because diene–aryl coplanarity is achieved, while in the case of (**3b**) (R^1 = Me) the *endo*-transition state competes owing to non-bonding interactions in the *exo*-transition state (Figure 1).

The azadiene–alkyne system (**8**) was prepared from (**7**) (83%, b.p. 152—155 °C at 10^{-5} torr),‡ and desilylated to give (**9**), which was identified by ^{1}H n.m.r. spectroscopy, and heated in a sealed tube at 150 °C; after 48 h the pyridine (**12**) [91% from (**8**), m.p. 144—146 °C]‡ was obtained (Scheme 2). The formation of (**12**) can be explained if initially intramolecular cycloaddition leading to (**10**) takes place; this cycloadduct is not isolated, but presumably under the reaction conditions undergoes a [1,5]H shift and electrocyclic ring opening of the resulting 2*H*-1-benzopyran structure (**11**)[5] to afford (**12**), after aromatization.¶

In conclusion, this work shows for the first time that easily available electron-poor 2-azabutadienes cleanly undergo intramolecular [4 + 2] cycloadditions; this process should be useful for the construction of structurally complex nitrogen heterocyclic systems. The geometry of the transition state seems to depend strongly on non-bonding interactions.‖

Received, 5th August 1988; Com. 8/03216E

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§ Compound (**2a**) does not undergo cycloaddition; it was recovered unalterated after prolonged heating (toluene, 160 °C, 7 days).

¶ Although, in the chrom-3-ene ⇌ *o*-quinoneallide equilibrium, the acyclic valence tautomer is thermally unstable,[5] in our case the aromatization of both phenyl and pyridine rings must be responsible for the electrocyclic ring opening.

‖ All new compounds isolated gave satisfactory elemental analytical figures and were characterized by spectroscopic means (i.r., mass, ^{1}H and ^{13}C n.m.r.).