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A reinvestigation of the $Rh_2(OAc)_4$-catalysed decomposition of 1-diazo-4-(2-methoxyphenyl)alkan-2-ones: evidence for ionic 'ring-walk' rearrangement in norcaradiene derivatives

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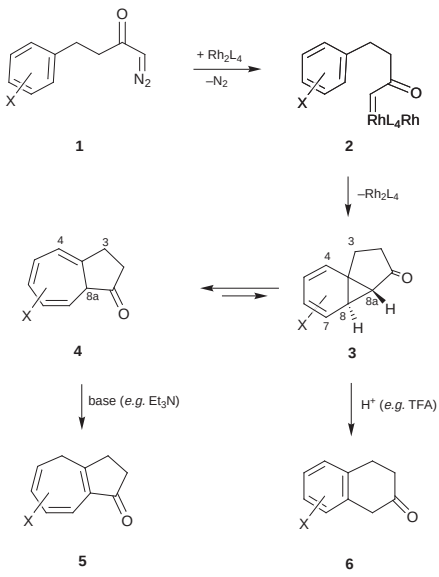
On $Rh_2(OAc)_4$-catalysed decomposition of 1-diazo-4-(2-methoxyphenyl)butan-2-one (9) and its methyl-substituted analogue (18), norcaradienones 10 and 19, respectively, were observed as the only regioisomers resulting from intramolecular cyclopropanation, indicative of attack by the metal carbene away from the methoxy group; to explain the transformation of 10 and 19 into dihydroazulenones 15 and 23, interconversion of 10 and 19 into their isomers 14 and 22 must be invoked, and an ionic 'ring-walk' rearrangement is suggested for such an isomerization.

The intramolecular Buchner reaction, (Scheme 1)† has emerged as a prominent synthetic method[1] after the discovery by Teyssié and co-workers[2] that rhodium(II) carboxylates strongly facilitate nitrogen loss from diazo compounds **1**, probably forming carbenoid species such as **2**. Thus, either 3,4-dihydroazulen-1(*2H*)-ones **5** or 2-tetralones **6** can be obtained in good yields from the equilibrium mixtures of norcaradienones (NCD) **3** and cycloheptatrienones (CHT) **4** by addition of a base or a protic acid, respectively.

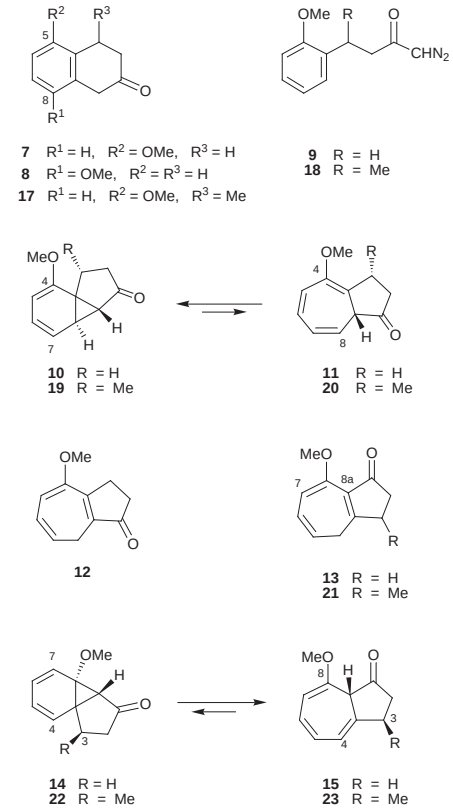
The fact that 5-methoxy-2-tetralone **7** results from 1-diazo-4-(2-methoxyphenyl)butan-2-one **9**,[3] instead of 8-methoxy-2-tetralone **8**,[1b] was explained by Cordi *et al.*[3] with the assumption that the tricyclic ketone **10** is formed through direct cyclopropanation of the benzene bond away from the methoxy group.

On the other hand, the trienone **13** could be envisaged as arising from the base-induced stabilisation of a reaction mixture consisting of the NCD/CHT couple **14**/**15**, *i.e.* of compounds formed by the attack of the carbenoid center on the 1,2-bond of the benzene ring. This direction of the intramolecular Buchner cyclisation had previously been suggested by McKervey and co-workers[1b] on the basis of the observation that the signal at *ca.* δ 5.0, which is characteristic of H-8 in 3,8a-dihydroazulen-1(*2H*)-one derivatives such as **4**,[4] was missing from the NMR spectrum of the crude product obtained by decomposition of **9**. Thus, structures **15** (instead of **11**) and **13** (instead of **12**) were assigned to the dihydroazulenone occurring in the reaction mixture and to its Et_3N-stabilised product, respectively.[1b]



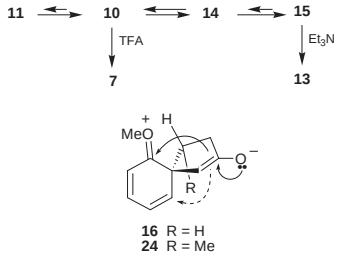
1 **2** **4** **3** **5** **6**

Scheme 1



We report here spectroscopic evidence proving structure **10** for the early reaction product in the decomposition of **9** under $Rh_2(OAc)_4$ catalysis and propose a reasonable explanation for its spontaneous conversion into **15** (giving rise to **13** by Et_3N treatment) and for the formation of **7** as the final product of the TFA-ended procedure.

The decomposition of **9**[1b] was performed in CH_2Cl_2 containing catalytic amounts of $Rh_2(OAc)_4$ at 0 °C for 1 h.[1a] After the usual work-up of the reaction mixture at 0 °C, the HPLC analysis‡ of the crude product revealed the presence of two main compounds showing different electronic absorptions: λ_{max} at 280 nm for the faster moving substance and at 260, 295sh, 315sh nm for the other. Such electronic absorptions appeared to be in agreement with those expected for a norcaradiene[5,6] and for a cycloheptatriene derivative,[6] respectively. The intensity ratio of the HPLC peaks was 2 : 1 in favour of that having the shorter retention time. However, after keeping the CH_2Cl_2 solution of the crude reaction product at



Scheme 2

room temperature overnight the peak of the faster moving substance disappeared completely. HPLC separation of the time-stabilised CH_2Cl_2 solution gave a pure compound (t_R = 11.2 min, yellowish oil, 75% yield)‡ to which the structure of 8-methoxy-3,8a-dihydroazulen-1(2*H*)-one (**15**)§ was assigned on the basis of its spectroscopic data.[1b,4] This structure was confirmed by NOE correlations (2.7 and 1.1% intensity enhancement of H-4 and H-3 by irradiation of H-3 and H-4).

Treatment of **15** with Et_3N in CH_2Cl_2 at room temperature furnished a compound (oil, 63% yield) whose spectroscopic data were consistent with the structure of a cross-conjugated dihydroazulenone,[1b,4] *i.e.* **13**.§ Thus, the occurrence of **14** as a precursor of **15** (and **13**) could be inferred. However, addition of a few drops of TFA to a CH_2Cl_2 solution of **15** or of the crude reaction product resulted in the rapid, quantitative formation of the tetralone **7**.[3]

All attempts to isolate the substance (t_R 8.7 min) accompanying **15** in the reaction mixture failed. Nevertheless, the ^{1}H NMR signals of that unstable component could be acquired by subtracting the spectra of **15** from those of the crude reaction mixture. The resulting congruent set of signals indicated a norcaradiene structure such as **10**§ having *three* olefinic hydrogens only. It must be pointed out that compound **10** does not correlate with the dihydroazulenone **15** through a direct electrocyclic reversion, but corresponds to an attack of the metal carbene on the benzene ring away from the methoxy group.

The above results can be interpreted in terms of a multiple equilibrium (Scheme 2) based on the following assumptions. The rhodium(II)-catalysed decomposition of **9** gives rise to the norcaradienone **10** (and possibly to **14,** to a lesser extent) through an intramolecular aromatic cycloaddition. Then compound **10** slowly converts into its isomer **14** (*vide infra*) which rapidly collapses to the much more stable dihydroazulenone **15**. By contrast, the NCD/CHT equilibrium[7] **10**/**11** must be assumed to be largely shifted toward the tricyclic form, *i.e* **10**. This seems plausible since it is known that hydroxy and trimethylsilyloxy groups at the 2- and/or 5-position of a cycloheptatriene ring have a strong stabilising effect on the tautomeric norcaradiene system.[8] The presence of **15** as the only final product in the reaction mixture is also consistent with the finding that among the four methoxycyclohepta-1,3,5-trienes the 1-methoxy isomer is the most stable.[9]

With regard to the possible mechanisms for the interconversion between **10** and **14** the intermediacy of a spiro derivative such as **16** (or its protonated form) seems the most likely explanation.

When 1-diazo-4-(2-methoxyphenyl)pentan-2-one **18** was decomposed by $Rh_2(OAc)_4$ in CH_2Cl_2 at 0 °C and the reaction mixture worked up in the usual manner, HPLC and ^{1}H NMR analysis revealed the presence of one reaction product. After purification by preparative HPLC this product (60% isolated yield) was shown to be the norcaradienone **19**,¶ which quickly furnished 5-methoxy-4-methyl-2-tetralone (**17**) by TFA treatment in almost quantitative yield. Compound **19** was found to be stable in CH_2Cl_2 at −20 °C for weeks; on the other hand, addition of catalytic amounts of Ph_3CBF_4 to a solution of **19** in CH_2Cl_2 caused rapid formation of the 8-methoxy-3-methyl-3,8a-dihydroazulen-1(2*H*)-one **23**,¶ which in turn gave rise to the cross-conjugated ketone **21**¶ when treated with Et_3N.

These results reinforce the above assumption concerning the occurrence of two NCD/CHT equilibria connected by ionic (cation-catalysed) interconversion of 4- and 8-methoxynorcaradienones. The fact that **19** appears to be more stable than **10** in respect to isomerization may be due to steric repulsion between the methyl group at the 3-position and the hydrogen atom at the 4-position in the spiranic intermediate **24** as well as in the tricyclic ketone **22**. In fact the methyl group in **19** was shown by NOE data¶ data to be oriented out of the plane of the six-membered ring thus minimizing its interaction with the methoxy group.

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Notes and references

† Throughout this paper azulene numbering is used for the tricyclic derivatives. A single enantiomer is depicted for all interrelated compounds.

‡ Analytical HPLC column: Merck LiChrospher 100 RP-18 (5 μm, 250 × 4 mm); eluent: MeOH–H_2O (58:42); flow rate: 1 ml min^{-1}.

§ *Selected data* for **15**: λ_{max}(MeOH)/nm (log ε) 258 (3.56), 294 (3.38), 315 (3.23); ν_{max}(film)/cm^{-1} 1752, 1707, 1610; δ_H(300 MHz, $CDCl_3$) 2.45–2.60 (2H, m, H_2-2), 2.64 (1H, br s, H-8a), 2.90 (2H, dt, *J* 2.0, 9.0, H_2-3), 3.58 (3H, s, OMe), 5.38 (1H, d, *J* 6.0, H-7), 6.18 (1H, dt, *J* 2.0, 5.5, H-4), 6.29 (1H, dd, *J* 5.5, 10.5, H-5), 6.36 (1H, dd, *J* 6.0, 10.5, H-6), assignment of the signal at δ 2.64 was confirmed by the ^{2}H NMR spectrum of a monodeuterated sample prepared from [1-^{2}H]-**9** which in turn was obtained by equilibration in CH_3OD in the presence of catalytic amount of TEA; δ_c(75 MHz, $CDCl_3$) 27.33 (t, C-3), 39.08 (t, C-2), 53.87 (d, C-8a), 56.63 (q, OCH_3), 97.06 (d, C-7), 120.58 (d, C-4), 124.42 (d, C-5), 126.66 (d, C-6), 132.81 (s, C-3a), 145.79 (s, C-8), 214.20 (s, C-1). For **13**: λ_{max}(MeOH)/nm (log ε) 232 (4.21), 266 (3.67), 323 (3.07); ν_{max}($CHCl_3$)/cm^{-1} 1698, 1612, 1554, 1439; δ_H(300 MHz, $CDCl_3$) 2.47–2.53 (2H, m, H_2-2), 2.67–2.74 (4H, m, H_2-3, H_2-4), 3.72 (3H, s, OMe), 5.50 (1H, dt, *J* 6.0, 9.5, H-5), 5.74 (1H, d, *J* 6.0, H-7), 6.09 (1H, dd, *J* 6.0, 9.5, H-6). For **10**: δ_H(300 MHz, $CDCl_3$ 1.35 (1H, br s, H-8a), 2.05–2.35 (2H, m, H_2-2), 2.80–2.90 (2H, m, H_2-3), 3.45 (1H, br d, *J* 6.5, H-8), 3.65 (3H, s, OMe), 5.51 (1H, d, *J* 8.5, H-5), 5.87 (1H, dd, *J* 6.5, 8.5, H-7), 6.14 (1H, t, *J* 8.5, H-6).

¶ *Selected data* for **19**: oil; λ_{max}(MeOH)/nm (log ε) 276 (3.70) (see ref. 6, 7); δ_H(300 MHz, $CDCl_3$), 0.95 (1H, br s, H-8a), 1.02 (3H, d, *J* 7.0, Me), 1.73 (1H, dd, *J* 9.0, 18.0, H_a-2), 2.31 (1H, dd, *J* 9.0, 18.0, H_b-2), 3.00 (1H, br d, *J* 5.0, H-8), 3.28 (1H, m, H-3), 3.67 (3H, s, OMe), 5.30 (1H, d, *J* 7.5, H-5), 5.85 (1H, dd, *J* 5.0, 9.0, H-7), 6.07 (1H, app t, *J* 8.5, H-6); selected NOE difference data: 1.02 → 3.00 (4.2%); 3.00 → 1.02 (0.5%). For **23**: yellowish oil, 51% after HPLC purification; δ_H(300 MHz, $CDCl_3$), 1.32 (3H, d, *J* 7.0, Me), 2.19 (1H, dd, *J* 7.0, 15.0, H_a-2), 2.70 (1H, br s, H-8a), 2.79 (1H, dd, *J* 7.0, 15.0, H_b-2), 3.08 (1H, m, H-3), 3.55 (3H, s, OMe), 5.40 (1H, d, *J* 5.0, H-7), 6.19 (1H, dd, *J* 2.5, 3.0, H-4), 6.32 (1H, dd, *J* 3.0, 11.0, H-5), 6.40 (1H, dd, *J* 5.0, 11.0, H-6). For **21**: oil, 35% yield after flash chromatography; δ_H(300 MHz, $CDCl_3$) 1.23 (3H, d, *J* 7.0, Me), 2.12 (1H, dd, *J* 2.0, 18.5, H_a-2), 2.76 (1H, dd, *J* 7.0, 18.5, H_b-2), 2.67 and 2.74 (2H, part AB of ABX system, J_{AB} 13.0, J_{AX} = J_{BX} 6.0, H_2-4), 2.93 (1H, m, H-3), 3.75 (3H, s, OMe), 5.29 (1H, ddd, part X of ABX system, *J* 6.0, 9.5, H-5), 5.78 (1H, d, *J* 6.5, H-7), 6.11 (1H, dd, *J* 6.5, 9.5, H-6).

1 (*a*) P. Manitto, D. Monti, S. Zanzola and G. Speranza, *J. Org. Chem.*, 1997, **62**, 6658; (*b*) M. Kennedy, M. A. McKervey, A. R. Maguire, S. M. Tuladhar and M. F. Twohig, *J. Chem. Soc., Perkin Trans. 1*, 1990, 1047.
2 A. J. Anciaux, A. Demonceau, A. F. Noels, A. J. Hubert, R. Warin and P. Teyssié, *J. Org. Chem.*, 1981, **46**, 873.
3 A. A. Cordi, J.-M. Lacoste and P. Hennig, *J. Chem. Soc., Perkin Trans. 1*, 1993, 3.
4 L. T. Scott, M. A. Minton and M. A. Kirms, *J. Am. Chem. Soc.*, 1980, **102**, 6311.
5 E. Wenkert and S. Liu, *Synthesis*, 1992, 323.
6 E. Ciganek, *J. Am. Chem. Soc.*, 1967, **89**, 1454; J. A. Berson, D. R. Hartter, H. Klinger and P. W. Grubb, *J. Org. Chem.*, 1968, **33**, 1669.
7 J. F. Liebman and A. Greenberg, *Chem. Rev.*, 1989, **89**, 1225.
8 C. S. Q. Lew, T.-H. Tang, I. G. Csizmadia and B. Capon, *J. Chem. Soc., Chem. Commun.*, 1995, 175.
9 W. H. Donovan and W. H. White, *J. Org. Chem.*, 1996, **61**, 969.

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