A Reinvestigation of the Intramolecular Buchner Reaction of 1-Diazo-4-phenylbutan-2-ones Leading to 2-Tetralones

Alex A. Cordi,* Jean-Michel Lacoste and Philippe Hennig
Institut de Recherches Servier, 11 rue des Moulineaux, F-92150 Suresnes, France

Rhodium acetate-catalysed decomposition of 1-diazo-4-(2-methoxyphenyl)butan-2-one **8** leads, after rearrangement under acidic conditions, to 5-methoxy-2-tetralone **13** and not to 8-methoxy-2-tetralone **10** as reported.

In the course of our synthetic effort directed towards the discovery of biologically active molecules, we were interested in the synthesis of 2-tetralones **3** bearing various substituents in diverse positions. Our attention was attracted by the recent finding that an intramolecular Buchner reaction of 1-diazo-4-phenylbutan-2-ones **1** could lead, after isomerization, to the target molecules.[1] In an attempt to rationalize the position of the tetralone substituents from the position of the respective substituents on the 1-diazo-4-phenylbutan-2-ones **1**, we postulated a mechanism (Fig. 1) which implies that the cyclopropanated tricyclic intermediate **2** is in equilibrium with the 3,8a-dihydroazulen-1(2*H*)-one **4**, as has been demonstrated in the original paper[1] for some substituent patterns. Under acidic conditions, this tricyclic intermediate **2** can be protonated leading to a formal cyclopropyl carbenium ion which rearranges[2] by the opening of a C–C bond to allow rearomatization. A similar mechanism was proposed to explain the occurrence of 6-oxo-3-isopropylcyclohexene[3] from a cyclopropyl ketone derivative.[4] Under basic conditions, the 3,8-dihydroazulen-1(2*H*)-one **2** tautomerizes to the thermodynamically more stable isomer **5**, **6** or **7**.

This mechanism could explain the fate of all 1-diazo-4-phenylbutan-2-ones reported except one. Indeed, 1-diazo-4-(2-methoxyphenyl)butan-2-one **8** is reported to cyclize to the 8-methoxy-3,8a-dihydroazulen-1(2*H*)-one **9** which in turn is said to isomerize either to 8-methoxy-3,4-dihydroazulen-1(2*H*)-one **11** or 8-methoxy-2-tetralone **10** under basic or acidic conditions, respectively (Fig. 2).

According to the mechanism we put forth, the rearrangement of **9** would have required a methoxonium ion as leaving group in the cyclopropyl carbenium rearrangement leading to the tetralone. To verify this mechanism, we reinvestigated the reaction by reproducing exactly the experimental procedures reported in the literature,[1] as well as synthesizing an authentic sample of **10** by an independent route.[5] In routine characterisation (200 MHz NMR) the two samples were, at first glance, identical, except by TLC (Merck F_{254} SiO_2, eluted with hexane–ethyl acetate 9:1) when although their R_f values were the same (0.2), after iodine visualisation, the reference compound became yellow while the compound from the Buchner reaction became red. On careful examination very slight differences showed up in the high field NMR (400 MHz) of the two compounds (Table 1).

NOE experiments clearly demonstrated that the product of the Buchner reaction, after rearrangement in the presence of CF_3CO_2H, was in fact the 5-methoxytetralone **13** arising from addition of the ketocarbenoid on the position of the phenyl ring most distant from the methoxy substituent (Fig. 2). This result was confirmed by the isomerisation, in basic conditions (triethylamine) of **12** which gave the 4-methoxy-3,8-dihydroazulen-1(2*H*)-one **14** as shown by the NMR analysis (Table 1).

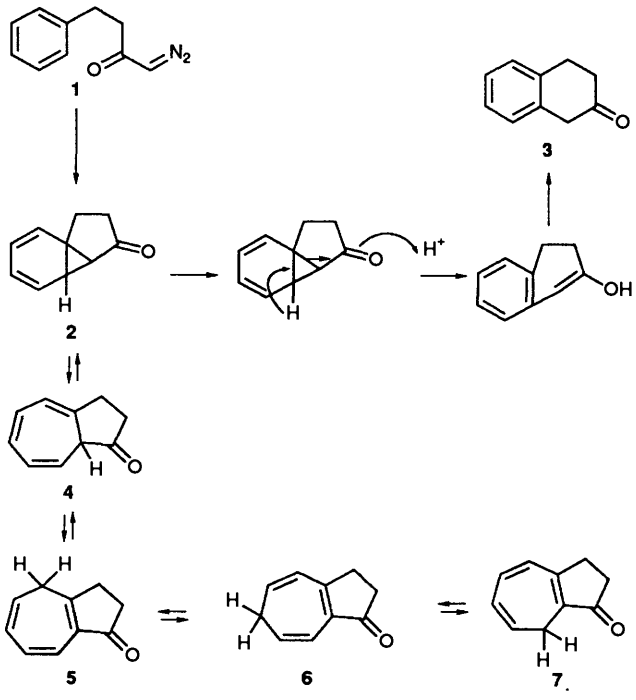

Fig. 1

This result is in accord with the outcome of the intermolecular reaction catalysed by rhodium(II) trifluoroacetate, between anisole and ethyl diazoacetate, which yielded no product arising from addition of the keto carbenoid on the most hindered site of the anisole.[6] This fact has already been pointed out by Maas in a review he devoted to the transition metal-catalysed decomposition of aliphatic diazo compounds.[7] Finally, in contrast to what is mentioned in Kennedy's paper,[1] the outcome of the rhodium(II) catalysed decomposition of 1-diazo-4-phenylbutan-2-ones could not be compared with the result of the trifluoroacetic acid decomposition of 1-diazo-4-phenylbutan-2-ones because it is the 1-diazo-4-(3-methoxyphenyl)butan-2-one and not the 1-diazo-4-(2-methoxyphenyl)-butan-2-one **8** which leads to the 8-methoxy-2-tetralone **10** through an electrophilic substitution mechanism.[8]

Experimental

Decomposition of the Diazoketone **8**.—A solution of the crude diazoketone **8** (2 g, 10 mmol) prepared according to ref. 1, in dichloromethane (50 cm^3), was added dropwise to a boiling solution of rhodium acetate (20 mg) in dichloromethane (500 cm^3). After evolution of gas has ceased, the solution was cooled,

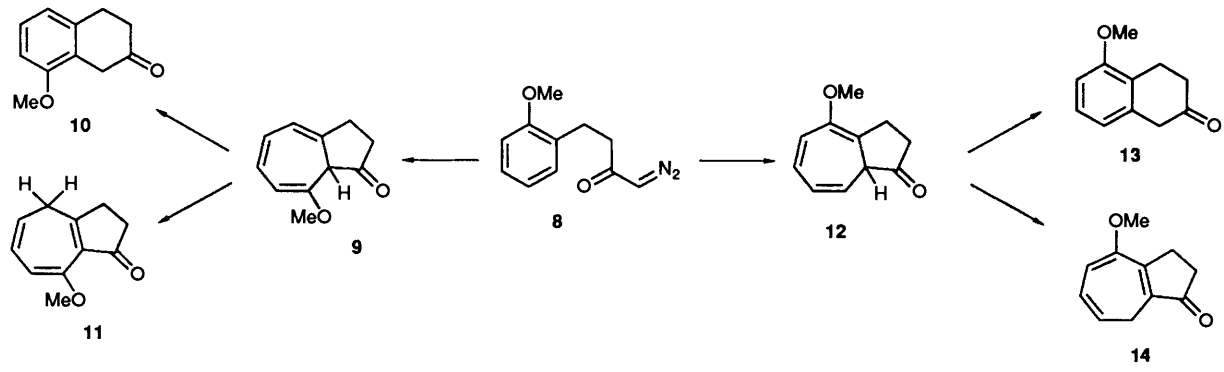

Fig. 2

Table 1 Chemical shift [δ, $(CH_3)_4Si$ as internal standard] and multiplicity of signals found in the 400 MHz NMR spectra of **10**, **13** and **14**, recorded in $CDCl_3$ at room temp. Assignments were made following NOE experiments.

Compound	δ_H						
10	2.58 (t, 2 × H^3)	3.05 (t, 2 × H^4)	3.53 (s, 2 × H^1)	3.83 (s, 3-OCH_3)	6.77 (H^7)	6.83 (H^5)	7.19 (H^6)
13	2.51 (t, 2 × H^3)	3.08 (t, 2 × H^4)	3.55 (s, 2 × H^1)	3.84 (s, 3-OCH_3)	6.77 (H^6)	6.72 (H^8)	7.17 (H^7)
14	2.53 (t, 2 × H^2)	2.72 (t, 2 × H^3)	2.76 (d, 2 × H^6)	3.77 (s, 3-OCH_3)	5.33 (dt, H^7)	5.78 (d,H^5)	6.13 (dd, H^6)

washed with water (2 × 100 cm^3) and saturated aqueous sodium hydrogen carbonate (100 cm^3), dried ($MgSO_4$) and evaporated to dryness. The brownish oil (1.65 g, 94%) is identified as the 4-methoxy-3,8a-dihydroazulen-1(2*H*)-one **12** by NMR spectroscopy.

Rearrangement of the Dihydroazulenone **12** *Under Acidic Conditions.*—A solution of the crude dihydroazulenone **12** (800 mg, 4.5 mmol) in dichloromethane (100 cm^3) was acidified by addition of trifluoroacetic acid (1 cm^3); the solution became intensely coloured. After stirring at room temp. for 30 min, the solution was washed with saturated aqueous sodium hydrogen carbonate (3 × 50 cm^3), dried ($MgSO_4$) and evaporated to dryness. The oil was purified by column chromatography on silicagel (100 g, Merck 60, particle size 0.040–0.063 mm, hexane–ethyl acetate, 9:1). The core of the main peak was isolated, the solvants evaporated to dryness and the oil (500 mg, 63%) identified as the tetralone **13** by NMR analysis.

Rearrangement of the Dihydroazulenone **12** *Under Basic Conditions.*—A solution of the crude dihydroazulenone **12** (600 mg, 3.2 mmol) in dichloromethane (100 cm^3) was basified by addition of triethylamine (1 cm^3). After stirring at room temp. for 30 min, the solution was washed with 1 mol dm^{-3} hydrochloric acid (2 × 10 cm^3), dried ($MgSO_4$) and evaporated to dryness. The oil (410 mg, 68%) was purified by column chromatography on silica gel (100 g, Merck 60, particle size 0.040–0.063 mm, hexane–ethyl acetate, 9:1) and is identified as the dihydroazulenone **14** by NMR analysis.

References

1 M. Kennedy, M. A. McKervey, A. R. Maguire, S. M. Tuladhar and M. F. Twohig, *J. Chem. Soc., Perkin Trans. 1*, 1990, 1047; M. A. McKervey, S. M. Tuladhar and M. F. Twohig, *J. Chem. Soc., Chem. Commun.*, 1984, 129.
2 S. Sarel, J. Yovell and M. Sarel-Imber, *Angew. Chem., Int. Ed. Engl.*, 1968, **7**, 577.
3 O. Wallach, *Liebigs Ann. Chem.*, 1908, **359**, 265.
4 D. Wendisch; *Houben-Weyl*, 1971, *Band IV/3*, 652.
5 P. K. Oommen, *Aust. J. Chem.*, 1976, **29**, 1393.
6 A. J. Anciaux, A. Demonceau, A. F. Noels, A. J. Hubert, R. Warin and P. Teyssié, *J. Org. Chem.*, 1981, **46**, 873.
7 G. Maas, *Top. Curr. Chem.*, 1987, **137**, 77.
8 D. W. Johnson and L. M. Mander, *Aust. J. Chem.*, 1974, **27**, 1277.

Paper 2/05871E
Received 2*nd November* 1992
Accepted 13*th November* 1992