Tetrahedron Letters,Vol.28,No.42,pp 4929-4932,1987 0040-4039/87 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

INTRAMOLECULAR REACTIONS OF 2-(AZIDOBUTYL)-1,4-BENZOQUINONES. UNEXPECTED REARRANGEMENT TO A FURO[3,4-b]INDOLIZIDINE-2-ONE

Arthur G. Schultz,* Wayne G. McMahon, and Ronald R. Staib
Department of Chemistry, Rensselaer Polytechnic Institute, Troy, New York 12180-3590

Rudolph K. Kullnig
Sterling-Winthrop Research Institute, Rensselaer, New York 12144

Summary: Thermal rearrangements of 2-(azidobutyl)-1,4-benzoquinone 1 give 3 and 4, while that of 10 produces ring-contracted 12; thermolysis of 12 gives ring-expanded 15.

We have previously reported the first study of thermal rearrangements of 2-(azidopropyl)-1,4-benzo- and 1,4-naphthoquinones.[1] Based on the earlier study, we expected products of benzoquinone ring expansion, 3, and contraction, 5, to be generated from thermolysis of the homologous 2-(azidobutyl)-1,4-benzoquinone 1 (Scheme 1). However, as a consequence of the increased connecting chain length, 1 required more forcing conditions for complete consumption of starting material (refluxing toluene, 24 h). Flash chromatography of the resulting complex mixture of products on silica gel gave the expected azepine-1,5-dione 3 (light yellow oil, 6.8%),[2] but none of the ring-contracted 4-cyclopentene-1,3-dione 5. Instead, a bright yellow crystalline solid (mp 137-137.5°C) was obtained in 12% yield; e.g., 4.[2] An assignment of structure for 4 was made by single crystal X-ray studies (Figure 1).

Triazoline 2 is suggested to be an intermediate in the conversion of 1 into 3. The rearrangement of 2 to 3 presumably occurs by 1,2-acyl migration to the piperidine nitrogen atom with concomitant loss of N_2. Tricyclic lactone 4 may originate from the ring-contracted imine 5 (Scheme 2), in which tautomerization of the type suggested in the earlier study[1] cannot operate. A 1-aza-Cope rearrangement[3] of 5 would give the ketene enamide 7 (path a), from which cyclization would give zwitterion 8. Hydrogen atom rearrangement in 8 would give the pyrrole 9 (or a

double bond isomer); dehydrogenation of 9 by the starting quinone, 1, completes one mechanistic hypothesis. Alternatively, zwitterion 8 might be generated from 5 by a nucleophile-induced acyl group cleavage to give 6a (path b), followed by an intramolecular Michael-like addition (a 5-exo-trig closure)[4] to give 6b; intramolecular enamide acylation would then deliver 8 (Scheme 2).

Scheme 1

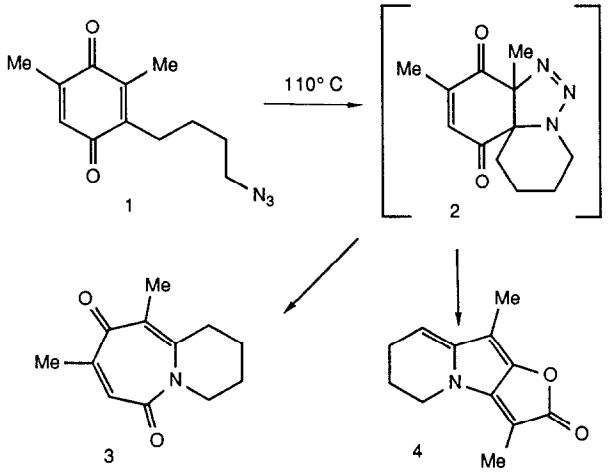
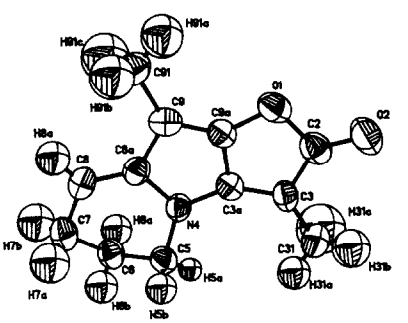


Figure 1

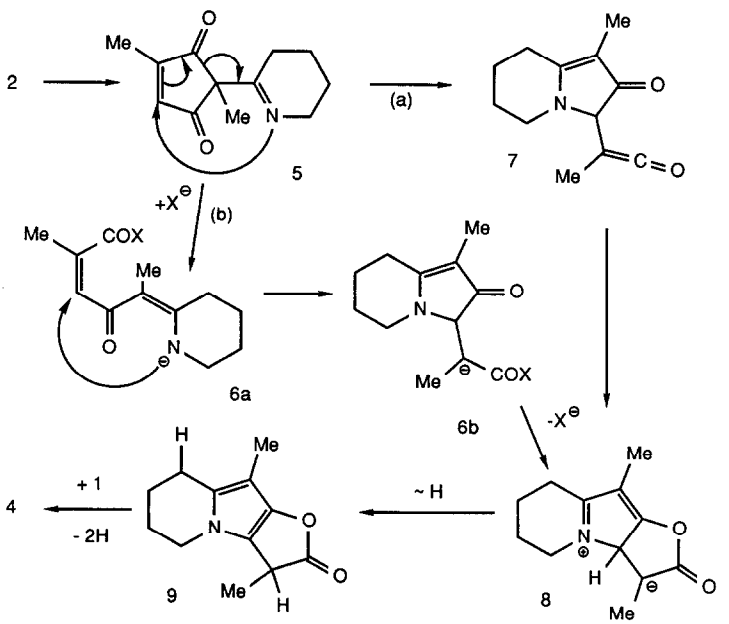


Azidoquinone 10 was expected to undergo cycloaddition under milder reaction conditions than did azidoquinone 1. In fact, thermolysis of 10 in refluxing methylene chloride solution (Scheme 3) gives dihydroisoquinoline 12 (50% isolated yield), isoquinoline 13, and hydroquinone 14. The formation of hydroquinone 14 together with isoquinoline 13 suggested that the starting quinone was involved in the dehydrogenation of 12. We subsequently found that dihydroisoquinoline 12 is converted to 13 in quantitative yield on reaction with dichlorodicyanobenzoquinone (DDQ) and that when 10 is heated in refluxing methylene chloride solution in the presence of DDQ, isoquinoline 13 is formed in 83% isolated yield.

Dihydroisoquinoline 12 does not undergo thermal rearrangement to the analogue of tricyclic lactone 4. Instead, thermolysis of 12 in refluxing toluene gave the ring-expanded 15, 16 (the product of dehydrogenation of 15 as determined by the conversion of 15 to 16 in ~ quantitative yield with DDQ), and another material of unassigned structure. A photochemical variant of the 1,3-acyl shift 12 → 15 was observed in the earlier study;[1] however, photolysis of 12 at 366 nm (THF solution) gave no reaction, while irradiation through Pyrex glassware gave extensive photodecomposition.

With regard to the hypothetical conversion of 5 into 6a via nucleophile-induced acyl group cleavage (Scheme 2, path b), we have found that analogue 12 is stable in triethylamine solution at room temperature and even at reflux (2 h).[5] Thus, despite the rather distorted transition state required for a 1-aza-Cope rearrangement of 5, path (a) seems to be the more reasonable mechanistic alternative. The opportunity for delocalization of the electron pair on the nitrogen atom in the enamide group of 7 (or zwitterion 8) may provide sufficient driving force for the 3,3-sigmatropic process.[3]

Scheme 2

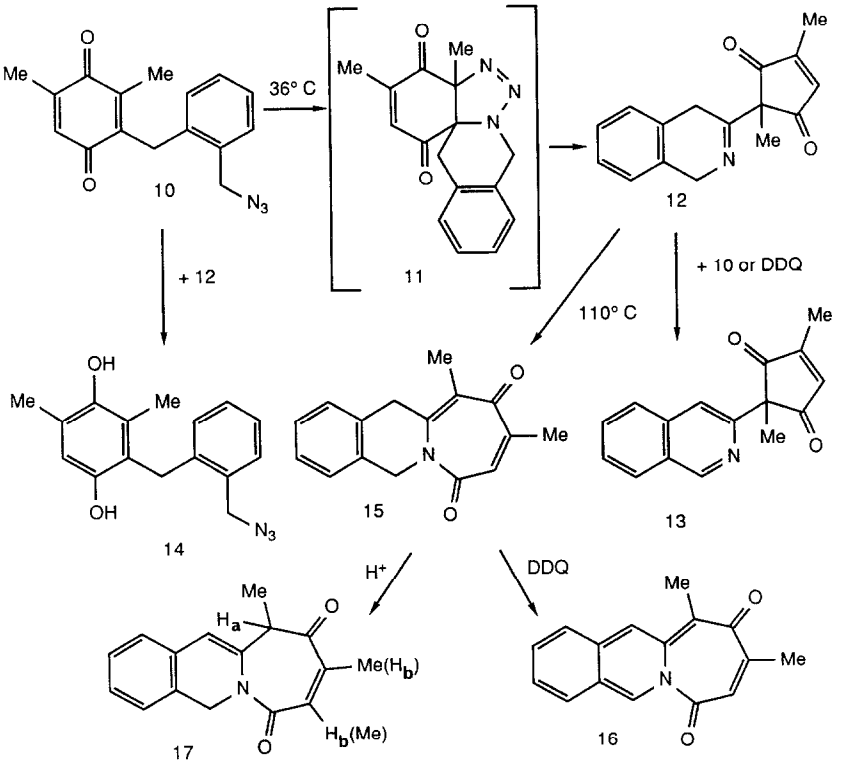


Attempted purification of 15 by chromatography on silica gel or reaction of 15 with p-toluenesulfonic acid in THF solution resulted in double bond migration to give dihydroisoquinoline 17 (97% yield isolated from the preparative reaction). The ^1H NMR spectrum (200 MHz) obtained for 17 shows no coupling between H_a and H_b. Had the other possible regioisomer indicated in the drawing been obtained, then a coupling of 1-2 MHz for $J_{a,b}$ would have been expected.[1] The regioselectivity of the rearrangement 12 → 15 presumably results from stabilization of the transition state for acyl group rearrangement by the electron-donating vinyl methyl substituent.

The striking difference in reactivity between 12 and the hypothetic reaction intermediate 5 (Scheme 2) cannot be fully explained at present. It may be that 5 also undergoes ring expansion

(to give 3), but labeling studies which would address this point are not available.

Scheme 3



Acknowledgment. This work was supported by the National Institutes of Health (GM 26568). We thank the National Science Foundation and Rensselaer Polytechnic Institute for funds for the purchase of the Nicolet R3m X-ray Diffractometer.

References and Notes

1. Schultz, A. G.; McMahon, W. G. J. Org. Chem. 1984, 49, 1676.

2. Combustion analyses. 3: Anal. Calcd. for $C_{12}H_{15}NO_2$: C, 70.21; H, 7.38; N, 6.82. Found: C, 70.34; H, 7.25; N, 6.66. 4: Anal. Calcd. for $C_{12}H_{13}NO_2$: C, 70.90; H, 6.46; N, 6.89. Found: C, 70.75; H, 6.39; N, 6.78. 13: Anal. Calcd. for $C_{16}H_{13}NO_2$: C, 76.47; H, 5.22; N, 5.58. Found: C, 76.36; H, 5.40; N, 5.45.

3. For examples of the 1-aza-Cope rearrangement, see: Chu, M.; Wu, P.-L.; Givre, S.; Fowler, F. W. Tetrahedron Lett. 1986, 27, 461 and references cited therein.

4. Baldwin, J. E.; Cutting, J.; Dupont, W.; Kruse, L.; Silberman, L.; Thomas, R. C. J. Chem. Soc., Chem. Commun. 1976, 736.

5. In contrast to the nonenolizable diketo imine 12 in the earlier study[1] that fragmented to 2-methyl-4,5-benzocyclopentene-1,3-dione on attempted chromatography, 12 in this study is stable to flash chromatography on silica gel. The enhanced stability of 12 may be a reflection of the relatively poor leaving group, 2,4-dimethyl-3-hydroxycyclopentadiene-1-one.

(Received in USA 28 April 1987)