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ACID-CATALYZED REARRANGEMENT OF O-(2-ARYLPHENYL)HYDROXYLAMINES TO ARYLDIHYDROAZEPINONES

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Summary: Acid-catalyzed rearrangement of O-(2-arylphenyl)hydroxylamines followed by ring enlargement affords 7-aryl-2,3-dihydro-1H-azepin-2-ones. 2-Amino-2-phenyl-3,5-cyclohexadienone, an intermediate of the reaction, was trapped as the N-trifluoroacetamide.

The Bamberger rearrangement of N-phenylhydroxylamine to 4-aminophenol is a well-known aromatic rearrangement found at the end of the last century. On the other hand, O-arylhydroxylamines was first prepared in 1962.[1] The reactivity of O-arylhydroxylamine has been examined in connection with the rearrangement of O-aryloximes to benzofurans[2] (the O-analog of the Fischer indole synthesis). However, the N-O bond cleavage of the O-arylhydroxylamines initiates several new reactions. For example, we have reported on the introduction of a nucleophile onto the aromatic nucleus of O-aryl-N-tosylhydroxylamines as applied to a synthesis of hydroxylbiphenyls,[3] and the introduction of an oxygen, nitrogen or carbon functional group onto the aromatic nucleus of O-arylhydroxylamine derivatives by [3,3] or [5,5] rearrangements.[4] The acid-catalyzed conversion of O-phenyloximes and O-phenylhydroxylamine hydrochloride into 2-aminophenol was presented by Carter and Robinson,[5] though the details of the rearrangement have not been examined. In this paper, we describe an acid-catalyzed rearrangement followed by a ring enlargement reaction of O-(2-arylphenyl)hydroxylamines.[6]

O-2-(Biphenylyl)hydroxylamine (**1a**), prepared from 2-hydroxylbiphenyl (**2a**) by the method described previously,[4a] was treated with 10 eq of trifluoroacetic acid at the concentration of 2.5 x 10^{-2} mol/l at -10 °C for 1 h and the mixture was refluxed for 1 h to give 7-phenyl-2,3-dihydro-1H-azepin-2-one[7] (**3a**, 63 %) and 2,5-dihydroxybiphenyl (**5a**, 14 %) as major products. Trace amounts of 2-hydroxybiphenyl (**2a**) and 2-hydroxy-3-aminobiphenyl (**4a**) were also obtained (Scheme 1). No product aminated at the para position was obtained. By analogy with the formation of dihydroazepinones reported by Paquette in the reaction of 2,6-dialkylphenols and sodium metal with chloramine,[8] the intermediate of the present rearrangement seems to be 2-amino-2-phenyl-3,5-cyclohexadienone (**6a**) (Scheme

2). The intermediate was detected by TLC and by ^{1}H-NMR in CF_3COOD-$CDCl_3$,[9] and **6a** was stable in the solution at room temperature for at least 10 days. At elevated temperature, intramolecular addition of the amino group to the carbonyl group of **6a** occurred to give the hydroxyaziridine (**7a**), which was converted to the dihydroazepinone (**3a**). After treatment of **1a** with TFA at -10 °C for 1 h, the mixture was worked up below room temperature to give the dimeric Diels-Alder adduct (**8a**) in a yield of 51 %.[10] When the dimer was heated at reflux in xylene, it was reverted to **6a** and rearranged to the dihydroazepinone (**3a**) in 69 % yield. Finally, **6a** was trapped as its N-trifluoroacetamide (**9a**) in 63 % yield, by treatment of the reaction mixture with trifluoroacetic anhydride before heating.

Scheme 1

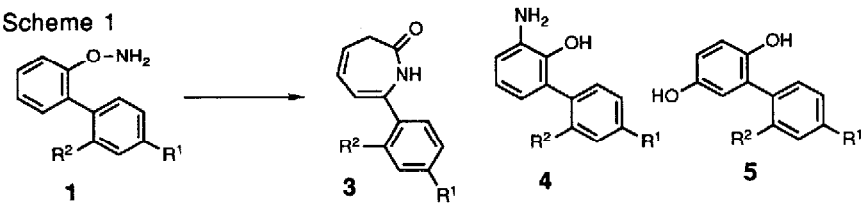
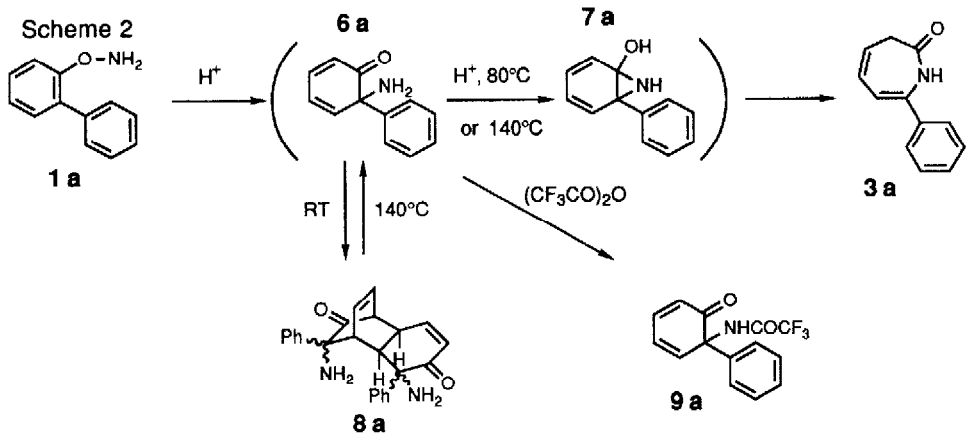


Table 1. Rearrangement of O-(2-Arylphenyl)hydroxylamines

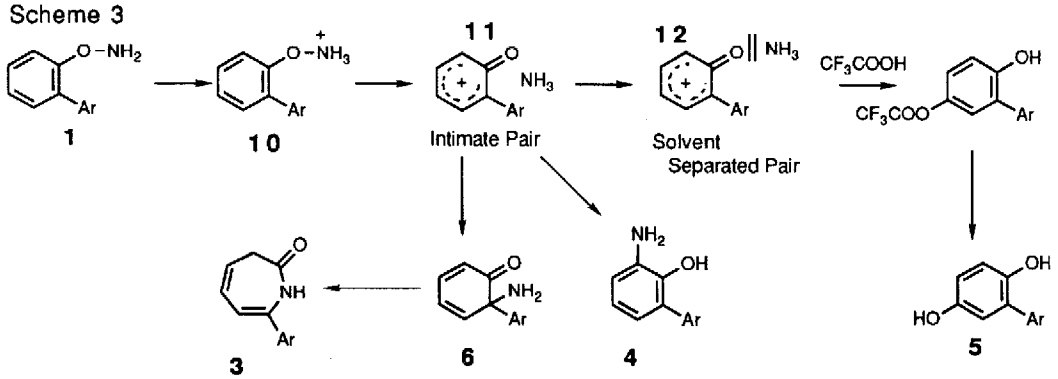
			Yield (%)		
	R^1	R^2	**3**	**4**	**5**
1a	H	H	63	<1	14
1b	CH_3	H	43	0	13
1c	NO_2	H	58	13	2
1d	NO_2	NO_2	0	20	45

Scheme 2



The direction of the initial amino migration is affected by the electron density on the phenyl group. The rearrangement of the compound substituted at the 4-position by a methyl group (**1b**) smoothly proceeded at -30 °C, and the mixture was refluxed for 30 min to give **3b** (43%). The rearrangement of **1c**, which required 25 °C for 1.5 h and reflux for 1 h, afforded a considerable amount of the *ortho*-aminated product (**4c**, 13 %) together with **3c** (58 %) and **5c** (13 %). Further, the 2,4-dinitro derivative (**1d**) did not give the *ipso*-aminated product (**3d**) but the *ortho*-aminated product (**4d**, 20 %) accompanied with **5d** (45 %). These results suggest that an active species in the amino migration is positively charged, and the *ipso*-amination is more favorable when the aryl group is electron-rich.

Scheme 3



In the previous report,[3b] we showed that the reaction of aryloxenium ion with carboxylic acid predominantly gave the *para*-substituted product. In the case of reaction of **1**, the heterolytic cleavage of a protonated hydroxylamine (**10**) gives an aryloxenium ion (**12**), which might plausibly react with trifluoroacetate anion followed by hydrolysis during the work-up to give **5**. The formation of amino-migrated products (**6** and **4**) is explicable by the rearrangement of an intimate ion pair such as **11**, because the *ortho* rearrangement of the amino group of O-arylhydroxylamines proceeds completely through intramolecular processes.[11]

The rearrangements described here seem to be of theoretical interest in connection with the N-O bond cleavage of O-arylhydroxylamines and the chemistry of aryloxenium ions. A detailed examination of the amino migration mechanism is in progress.

References and Notes

1) Bangardner, C. L., Lilly, R. L., *Chem. and Ind.*, **1962**, 559; Nicholson, D. S., Peak, D. A., *Chem. and Ind.*, **1962**, 1244

2) Sheradsky, T., *J.Heterocycl.Chem.*, **1967**, *4*, 413; Mooradian, A., *Tetrahedron Lett.*, **1967**, *8*, 407; Mooradian, A., Dupont, P. E., *Tetrahedron Lett.*, **1967**, *8*, 2867; Kaminsky, D., Shavel, J., Meltzer, R. I., *Tetrahedron Lett.*, **1967**, *8*, 859; Mooradian, A., Dupont, P. E., *J.Heterocycl.Chem.*, **1967**, *4*, 441; Sheradsky, T., Salemnick, G., *J.Org.Chem.*, **1971**, *36*, 1061; Cattanach, C. J., Rees, R. G., *J.Chem.Soc.*, **1971**, 53; Sharkova, L. M., Aksanova, I. F., Zagorevski, V. A., *Khim.Geterotsikl.Soedin.*, **1971**, 762; Grandberg, D. R., Sorokin, V. I., *Khim.Geterotsikl.Soedin.*, **1973**, 31; Bender, D. R., Hearst, J. E., Rapoport, H., *J.Org.Chem.*, **1979**, *44*, 2176; Moron, J., Nguyen, C. H., Bisagni, E., *J.Chem.Soc. Perkin Trans. 1*, **1983**, 225; Castellino, A. J., Rapoport, H., *J.Org.Chem.* **1984**, *49*, 4399.

3) a) Endo, Y., Shudo, K., Okamoto, T., *J.Am.Chem.Soc.*, **1977**, **99**, 7721. b) Endo, Y., Shudo, K., Okamoto, T., *J.Am.Chem.Soc.*, **1982**, *104*, 6399. c) Iijima, H., Endo, Y., Shudo, K., *Tetrahedron*, **1984**, *40*, 4981.

4) a) Endo, Y., Shudo, K., Okamoto, T., *Synthesis*, **1980**, 461. b) Endo, Y., Shudo, K., Okamoto, T., *Synthesis*, **1983**, 471. c) Endo, Y., Terashima, T., Shudo, K., *Tetrahedron Lett.*, **1984**, *25*, 5537. d) Endo, Y., Namikawa, K., Shudo, K., *Tetrahedron Lett.*, **1986**, *27*, 4209.

5) Carter, M. A., Robinson, B., *Chem. and Ind.*, **1974**, 304.

6) Acceptable microanalyses and appropriate infrared and NMR spectral data were secured for all of the new compounds mentioned in this paper.

7) **3a**: pale yellow needles (CH_2Cl_2-n-hexane) mp 161°C; ^{1}H-NMR ($CDCl_3$, 400 MHz) 3.01 (d, 2H,J=8.0 Hz), 5.70 (m, 1H), 6.30 (m, 2H), 7.2-7.4 (m, 3H), 7.5-7.6 (m, 2H)

8) Paquette, L. A., *J.Am.Chem.Soc.*, **1963**, *85*, 3288; Paquette, L. A., Farley, W. C., *J.Org.Chem.*, **1967**, *32*, 2725.

9) **6a**: ^{1}H-NMR (CF_3COOD-$CDCl_3$, 400 MHz) 6.40 (d, 1H, J=9.8 Hz), 6.84 (dd, 1H, J=4.9, 8.8 Hz), 7.03 (d, 1H, J=8.8 Hz), 7.31 (dd, 1H, J=4.9 Hz)

10) The structure of **8a** was determined based on the detailed NMR experiments, especially on the two-dimensional C-H shift-correlated spectra and long-range C-H shift-correlated spectra. **8a**: pale yellow needles (benzene) mp 184-187°C; ^{1}H-NMR ($CDCl_3$, 400 MHz) 1.95 (s, 4H), 3.37 (ddd, 1H, J=5.9, 2.6, 1.5 Hz), 3.49 (dddd, 1H, J=8.4 ,4.0, 2.6, 1.7 Hz), 4.10 (ddd, 1H, J=6.4, 1.5, 1.5 Hz), 4.29 (dd, 1H, J=8.4, 1.5 Hz), 5.80 (ddd, 1H, 8.2, 5.9, 1.5 Hz), 5.99 (dd, 1H, J=10.0, 1.7 Hz), 6.19 (dd, 1H, 10.0, 4.0 Hz), 6.21 (ddd, 1H, J=8.2, 6.4, 1.5 Hz), 7.18-7.38 (m, 10H).

11) Cross-coupling experiments of the O-arylhydroxylamine employing stable isotope-labelled hydroxylamines will be reported in the near future.

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