Intramolecular [3+2] Cycloaddition of 2-Alkenyloxy-1-naphthaldehyde Oximes

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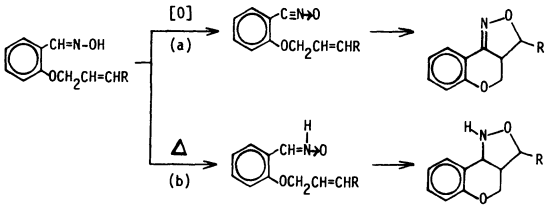
(Received August 11, 1984)

Synopsis. The thermal treatment of the mixture of 2-alkenyloxy-1-naphthaldehydes and hydroxylamine hydrochloride in ethanol gave intramolecular [3+2] cycloadducts, 1,3a,4,11c-tetrahydro-3*H*-naphtho[1',2':5,6]pyrano-[4,3-*c*]isoxazole hydrochlorides.

We have reported several intramolecular 1,3-dipolar cycloadditions of 2-(alkenyloxy)benzaldehyde (or 1-naphthaldehyde) arylhydrazones.[1] From the studies, it was found that the acid-catalyzed [3+2] cycloaddition was the most effective method for the preparation of cycloadducts.[1d] Several cycloadditions of analogous oximes have been reported; routes (a)[2] and (b)[3], respectively, consist of the intramolecular 1,3-dipolar cycloaddition of nitrile oxide or nitrone intermediates which were prepared from the oxidation or the thermal isomerization of aldehyde oximes. We report here the intramolecular [3+2] cycloaddition of 2-(alkenyloxy)-1-naphthaldehyde oximes.



Results and Discussion

After the treatment of 2-(alkenyloxy)-1-naphthaldehyde (**1a—e**) with an excess amount of hydroxyamine hydrochloride in refluxing ethanol for 20 h, the intramolecular [3+2] cycloadducts, 1,3a,4,11c-tetrahydro-3*H*-naphtho[1',2':5,6]pyrano[4,3-*c*]isoxazole hydrochlorides (**2**), were obtained in the yields shown in Table 1. The treatment of **2** with triethylamine gave the free bases (**3**). The structures of **2** and **3** were established on the basis of elemental analyses and spectral data. The methine proton at 4-position of the isoxazolidine ring of **2** and **3** was observed as a multiplet at about δ 3 in ^{1}H NMR. An ambigous doublet at about δ 4.5 in the NMR spectra of **3** was assigned to be a proton at 3-position and it was converted into a simple doublet after adding D_2O. On the other hand, the proton of compounds **2** was observed as a doublet at about δ 5.6 because of the presence of the neighboring quaternary ammonium group. The observed coupling constants (6—7.5 Hz) of the bridgehead proton at 3-position suggest *cis* relationship with the bridgehead proton at 4-position and coupling constants (6—8 Hz) observed for the proton at 5-position suggest *trans* relationship with the proton at 4-position.[4]

Compounds **2** were also obtained after refluxing an ethanol solution containing 8% hydrogen chloride

Table 1. Yields of the reaction products (**2** and **3**)

Adduct	Yield/%	Adduct	Yield/%	Mp θ_m/°C
2a	10	**3a**	72	135—137
2b	33	**3b**	70	121—123
2c	14	**3c**[a]		
2d	8	**3d**	70	221—224
2e	60	**3e**	70	204—205

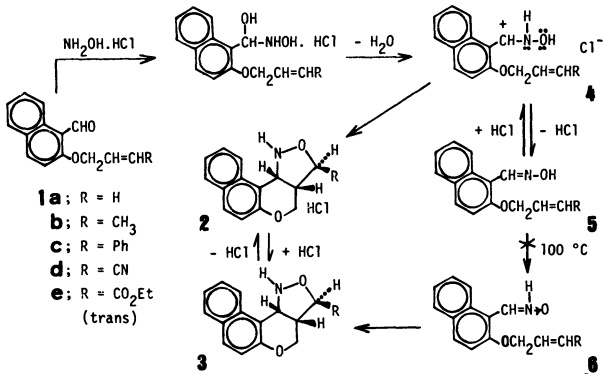
a) Not isolated.

Table 2. Spectral data of **2** and **3**

Compound	IR ν/cm^{-1}	NMR[a] (δ)
2a	2470 (N+H)	3.0—3.6 (m, 1H), 3.9 (t, 1H, J=11), 4.2—4.8 (m, 3H), 5.57 (d, 1H, J=6), 7.05—8.05 (m, 5H), 8.1—8.4 (m, 1H), 10.5 (br, 2H)[b]
2b	2500 (N+H)	1.5 (d, 3H, J=6), 2.7—3.2 (m, 1H), 4.0 (t, 1H, J=11), 4.3—4.8 (m, 2H), 5.5 (d, 1H, J=7), 7.0—8.1 (m, 5H), 8.3—8.6 (m, 1H), 10.8 (br, 2H)[b]
2c	2450 (N+H)	3.1—3.7 (m, 1H), 3.9—4.8 (m, 2H), 5.48 (d, 1H, J=6), 5.65 (d, 1H, J=7), 7.1—8.1 (m, 10H), 8.2—8.6 (m, 1H), 10.5 (br, 2H)[b]
2e	2450 (N+H)	1.27 (t, 3H, J=7), 3.1—3.7 (m, 1H), 3.9—4.9 (m, 5H), 5.1 (d, 1H, J=6) 7.05—8.3 (m, 6H), 10.5 (br, 2H)[b]
3a	3210 (NH)	2.5—3.2 (m, 1H), 3.4—4.4 (m, 5H), 4.48 (d, 1H, J=6), 4.9—5.4 (br, 1H)[b], 6.9—7.8 (m, 5H), 8.1—8.4 (m, 1H).
3b	3200 (NH)	1.4 (d, 3H, J=6), 2.2—2.7 (m, 1H), 3.75 (quintet, 1H, J=6), 3.8 (dd, 1H, J=2 and 11), 4.2 (dd, 1H, J=5 and 11), 4.68 (d, 1H, J=7.5), 5.0—5.4 (br, 1H)[b], 6.85—7.8 (m, 5H), 8.0—8.3 (m, 1H).
3d	3200 (NH) 2230 (CN)	3.0—3.6 (m, 1H), 4.0—4.5 (m, 2H), 4.65 (d, 1H, J=6), 4.5 (br, 1H)[b], 5.4 (d, 1H, J=8), 7.0—8.0 (m, 5H), 8.0—8.3 (m, 1H).

a) **2** were dissolved in DMSO-d_6 and **3** in $CDCl_3$. Coupling constants (J) are shown in hertz (Hz). b) This peak was disappeared by adding D_2O.

of 2-alkenyloxy-1-naphthaldehyde oximes (**5**). From the fact that **5** was stable for the thermal treatment in ethanol and recovered quantitatively, the formation of **2** can not be explained by the reaction *via* a nitrone intermediate (**6**), but a cationic intermediate (**4**).



No cycloadducts could be obtained from the reaction mixture of 2-(alkenyloxy)benzaldehydes (**7a**—**7e**) and hydroxylamine hydrochloride, and only isolable compounds were salicylaldehyde oxime hydrochloride (**8**) (in 40—60% yields from **7a**—**c**) and 2-(alkenyloxy)benzaldehyde oximes (**9**) (in 90 and 10% yields from **7d** and **7e**, respectively). Phenol could not be detected after refluxing allyl phenyl ether in ethanol containing 8% HCl for 24 h, thus, the formation of **8** may be interpreted in terms of an acid-catalyzed intramolecular hydrolysis of **9**.

The results that **7** gave no cycloadduct (**10**) in the reaction may be explained by the comparison of the frontier molecular orbitals of the cationic intermediates (**4** and **11**). It is well-known[5] that the introduction of conjugated substituents (phenyl or naphthyl group) at the dipole increase in the HOMO energy and decrease in the LUMO energy and these effects of naphthyl group may be larger than those of phenyl group. While the intramolecular cycloaddition of **4** is only slightly more favorable than the other competitive reactions, the similar cycloaddition of **11** would be more unfavorable than the other competitive reactions, thus, **8** and **9** were formed.

Experimental

Measurements. All melting points are uncorrected. Satisfactory analytical data were obtained for the cycloadducts (**2a—c**, **3a**, **3b**, and **3d**)(±0.3% for C, H, and N).

Materials. The 2-(alkenyloxy)benzaldehydes (or -1-naphthaldehydes)(**7** or **1**)[1b] and those oximes (**9** and **5**)[2a] were prepared according to the method in the literature.

Reaction of 2-(Alkenyloxy)-1-naphthaldehydes (I) with Hydroxylamine Hydrochloride. A mixture of **1** (5 mmol) and hydroxylamine hydrochloride (1.0 g, 14 mmol) was refluxed in ethanol (50 ml) for 20 h with stirring. Evaporation of the solvent from the reaction mixture gave crystals, which were mixed well with benzene (30 ml) and filtered off, and the residue was washed with water and then dried *in vacuo* to give **2** in the yields shown in Table 1. The NMR spectra of **2** were shown in Table 2. The compounds **2** obtained above generally showed the broad melting points ranges (*ca.* 140—180 °C). In the case of **1a**, 2-allyloxy-1-naphthonitrile was also obtained in 80% yield from the filtrate by evaporation of the solvent (benzene); mp 64—65 °C (from ethanol), IR (Nujol): 2220 cm^{-1}, NMR ($CDCl_3$) δ: 4.73 (d, 2H, J=4 Hz), 5.1—5.6 (m, 2H), 5.7—6.4 (m, 1H), and 7.0—8.1 (m, 6H), Calcd for $C_{14}H_{11}NO$: C, 80.36; H, 5.30; N, 6.69%. Found: C, 80.25; H, 5.29; N, 6.71%. In the other cases, we could not isolate any by-products.

The Treatment of 2 with Triethylamine. Into a suspension of **2** in chloroform was added an excess mol of triethylamine, after which the mixture was stirred for 30 min at room temperature. The reaction mixture was then washed with water several times, and the organic layer was dried over anhydrous sodium sulfate. Evaporation of the solvent yielded crude naphthopyranoisoxazoles (**3**), which were recrystallized from ethanol to give pure materials in the yields shown in Table 1.

References

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