Short Communication

On the Stereochemistry of Protonated, Aromatic Aldoximes

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From the classical experimental studies of aromatic aldoximes (Ar–CH = NOH) it is well known (1) that an aromatic E-aldoxime on treatment with a strong acid at a suitable temperature is rearranged to the salt of the corresponding Z-aldoxime,[1] (2) that in several of the cases studied, the isomeric E- and Z-hydrochlorides of an aromatic aldoxime were found to have approximately identical melting points,[2] and (3) that in some cases the same melting point also was observed from a mixture of the isomers.[2] The aim of the present work has been to account, in chemical terms, for these curious facts.

Experimental

4-Toluenesulfonic acid (TsOH). A commercial hydrate was dehydrated by azeotropic distillation with toluene; this procedure was performed twice.

(E)-Piperonal oxime. Oximation of piperonal[3] (3,4-methylenedioxybenzaldehyde) gave, upon crystallization from ethanol, snow-white, leafy crystals, m.p. (cap.) 110–111 °C (lit. 111 °C;[2] 112 °C[4]).

(Z)-Piperonal oximium tosylate. Solutions of 1 mmol of (E)-piperonal oxime in 5 ml dry ether and 1 mmol TsOH in 20 ml dry ether were mixed at room temperature. After a while crystals began to separate out. After one day a yield of 30% of the salt was obtained. Pale, yellow, thin needles, m.p. (cap.) 127–128 °C; the molten substance was yellow. The mother liquor gave, on slow evaporation, conglomerates of very thin, elongated crystals, of which one was selected for an X-ray crystal structure determination,[5] which proved the molecular configuration.

An attempt to obtain the (E)-piperonal oximium tosylate was performed by repeating the above procedure, but using 40 ml of dry ether, at -28 °C. After one day no precipitate had been formed, but after 3 days a tiny amount of a hard conglomerate of very small crystals was formed, from which the mother liquor was decanted and

immediately recooled to -28 °C. M.p. (cap.) at 126 °C, and mixed m.p. with the above Z-tosylate identified the crystals as one of the isomer piperonal tosylates. After a further 6 days the flask was placed at room temperature, and crystallization began after a short delay; after evaporation of the ether, the product was identified as (Z)-piperonal oximium tosylate.

(E)-Piperonal oximium tosylate. (E)-piperonal oxime (1.5 mmol) dissolved in 7 ml of dry ether and 1.5 mmol of TsOH dissolved in 30 ml of dry ether were mixed at -27 °C, and the solution was kept at -27 ± 3 °C. After one day slow precipitation began, and after four days six circular, hard conglomerates of small crystals were formed, weighing 0.25 g corresponding to 50% of the theoretical yield. 100 mg of this substance were crushed and subsequently neutralized with an aqueous solution of $NaHCO_3$. The solution obtained was extracted three times with small portions of ether. The ethereal solution obtained gave, after drying with sodium sulfate and subsequent evaporation of the ether, a yield of 0.04 g of a white precipitate, which was identified as (E)-piperonal oxime by m.p. (cap.) (104.5–107.5 °C) and a m.p. of 105.5–110 °C when mixed with the authentic E-oxime.

(E)-Piperonal oximium trifluoromethanesulfonate (triflate). Trifluoromethanesulfonic acid (0.2 ml, approximately 2.3 mmol), dissolved in 10 ml of dry ether, and 0.5 g (3 mmol) of (E)-piperonal oxime dissolved in 7 ml of dry ether were cooled to -26 °C. These solutions were then mixed, and the liquid immediately became opaque and a white precipitate was formed. After some days at -26 °C the colourless liquid was decanted, and the crystalline conglomerate was rinsed with cold ether. On evaporation of the ether 0.50 g of the product was left (approximately 71% of the theoretical yield from 2.3 mmol). m.p. (cap.) 125–126 °C. The crystals obtained were too small for an X-ray structure study, and a chemical analysis was undertaken: 0.20 g was shaken with ether and 10 ml of an approximately 3% solution of ammonia were added. This

solution was extracted twice with 5 ml of ether; the separated ethereal solution was dried and on evaporation left a white, crystalline compound with m.p. 106–108°C and mixed m.p. 105.5–108°C with authentic (E)-piperonal oxime, thus proving the E-form of the analysed oximium triflate.

(Z)-Piperonal oximium triflate. The mother-liquor from the above E-oxime triflate was kept at room temperature. After a few hours, well-developed crystals were formed on the walls of the flask, m.p. 126–127°C. Crystal structure determination proved the structure to be (Z)-piperonal oximium triflate.

Tosylations of anhydrous (E)-4-hydroxybenzaldehyde oxime. (Z)-4-Hydroxybenzaldehyde oximium tosylate was prepared in diethyl ether by analogy with the above tosylate using anhydrous 4-hydroxybenzaldehyde oxime[6] as the starting material; the product obtained at room temperature had m.p. (cap.) 145°C (m.p. for the authentic Z-form is given as 146°C[7]). At −26°C very slow crystallization took place, and after 3 days a yield of 60% of a crystalline product was obtained which had m.p. and mixed m.p. identical with the product obtained at room temperature. The very small crystals were pale yellow or nearly colourless, and the molten substance was yellow. By very slow evaporation of the mother liquor, larger, yellow, needle-shaped crystals were obtained.

Another attempt to obtain crystals of the tosylate from anhydrous (E)-4-hydroxybenzaldehyde oxime was made at room temperature. The oxime (0.10 g, 0.75 mmol) was dissolved in 5 ml of ether and the equivalent amount, 0.13 g, of 4-toluenesulfonic acid dissolved in 10 ml of ether was added at room temperature. The liquid immediately became opaque, and in a short time glittering, but small, flat crystals were precipitated. After about an hour the crystals were separated as quantatively as possible from the solvent, and dried on filter paper; weight: 0.07 g, m.p. (cap.) 138–140°C. An attempt to perform a crystal structure study failed, because the very thin crystals were found to be conglomerates, as indicated by the irregular shapes of the crystals and proved by the pattern of the X-ray reflections. In the liquid from which the plate-like crystals were separated, slow precipitation of tiny, needle-shaped crystals began after a short time. M.p. (cap.) 147–148°C. No melting point depression of a mixture of the plates and the needle-shaped crystals was observed; the m.p. (cap.) was 141.5–144°C.

Discussion

The salts of aromatic Z-aldoximes are — in contrast with the salts of the E-isomers — stable compounds. Brady and Dunn studied the hydrochlorides of a number of aldoximes[2] in the years up to 1923. They found that hydrochlorides of the E-aldoximes were very prone to rearrangement to the Z-forms, and that rapid preparation

and isolation of these salts was necessary to avoid this rearrangement. These authors also noted that for several oximes the E- and Z-hydrochlorides have identical melting points, and in some cases they found that a mixture of the two isomers melted at the same temperature. Antonowa and Hauptmann prepared and identified a number of tosylates of Z-oximes at room temperature.[7] Crystal structures have been published of the tosylates of (Z)-4-methoxybenzaldehyde oxime[8] and of (Z)-3,4-methylenedioxybenzaldehyde oxime[5]. For the present experiments high-boiling acids were selected, together with either (E)-piperonal oxime, which, according to Brady and Dunn[2], is relatively stable sterically, or a ring-hydroxylated oxime, (E)-4-hydroxybenzaldehyde oxime.[6]

The (Z)- and (E)-piperonal oximium tosylates had identical melting points both separately and when mixed together, at ca. 127°C. The identity of the E-salt was proved by the melting points of the isolated oxime and of a mixture with authentic (E)-piperonal oxime, the identity of the Z-isomer being proved by the X-ray structure determination.[8]

The (Z)- and (E)-piperonal oximium triflates had identical melting points, but a measurement of the mixed melting point was not performed. The identity of the Z-isomer was proved by an X-ray structure determination (to be published), and that of the E-isomer was proved by isolating the oxime and determining the melting point and the mixed melting point with authentic (E)-piperonal oxime as described in the Experimental section.

Tosylations of (E)-4-hydroxybenzaldehyde oxime at room temperature and at −26°C, respectively, gave salts with identical melting points and the same mixed m.p. for a mixture of the salts. No attempt to isolate the oxime was made, since ring-hydroxylated oximes are known only in the E-isomeric form.

The fact that a protonated aromatic oxime is more stable in the Z-form than in the E-form, in contrast with the unprotonated oxime, which is more stable as the E- than as the Z-isomer, has not been explained in the literature, whereas the fact that only E-isomers of ring-hydroxylated oximes are known has been discussed.[9]

As to the rearrangement of the non-ring-hydroxylated aromatic E-oximes, protonation of the oxime nitrogen atom may be considered the first step in an $E \rightarrow Z$ rearrangement; but the protonated E-oxime is severely destabilized owing to spatial interference of the N-hydrogen atom with an *ortho*-hydrogen atom. This is inferred from calculations of the expected molecular geometry based upon comparisons of the molecular dimensions found in crystal structures of aromatic aldoximes and of their derivatives.[8,10] The results obtained indicate that N-protonation of an aromatic E-aldoxime requires the angle between the plane of the oxime side chain and the plane of the benzene ring to be considerably larger than the corresponding angle observed in any of the structures considered. Thus delocalisation of π-electron density over the aromatic ring and the oxime moiety is sterically hindered, which results in the chemically important desta-

bilization of protonated aromatic *E*-aldoximes relative to the corresponding *Z*-isomers. A consequence of this result is that protonated aromatic *E*-oximes are very unstable and rearrange to the *Z*-isomer on being heated. This rearrangement takes place during melting-point determinations of the crystalline *E*-salt; the consequences are that protonated *E*- and *Z*-salts of an aromatic oxime apparently have the same melting point, and that the identical melting point is also found for a mixture of the isomers. However, in each case, it is in fact the melting point of the stable *Z*-isomer that is observed during melting-point determinations with gradual heating.

References

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