

# SILICA GEL INDUCED ISOMERISATION OF ALDOXIMES TO AMIDES

## A GENERAL METHOD\*

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**Abstract**—Aldoximes have been isomerised to corresponding amides, using silica gel as catalyst. This method is found to be much better than other methods for simplicity and high conversions. Unlike acid-catalysed isomerisation, the nitrile is not an intermediate in this isomerisation.

In an attempt to dehydrate aldoximes to the corresponding nitriles with silica gel (TLC grade prepared by the Fine Chemicals Division of this Laboratory; a 50% aqueous suspension showed pH 6.6–6.7), benzaldoxime was adsorbed on silica gel in 1:5 portions respectively (w/w) and heated at 100–10° in an oven for a period of 60 h. The product on working up was found to be benzamide (73%) and no traces of benzonitrile were detected. From this it was clear that benzaldoxime was isomerised to benzamide under substantially neutral conditions. Earlier, various catalysts have been tried to isomerise benzaldoxime to benzamide and found that nickel acetate was most suitable.<sup>1</sup> In an effort to make this method more general, the reaction was carried out in xylene. Thus, benzaldoxime (5 g) was refluxed in dry xylene (25 ml) with activated silica gel of TLC grade (activated at 130–40°; 0.24 g, 10% of the weight of the oxime) until the solution showed the absence of aldoxime on TLC plates (69 h). The product was found to be benzamide isolated in 90% yield.

Adopting the above method, various oximes have been isomerised to the corresponding amides and we find that in all cases the yields are very high and the method is much better than all the methods known so far for its simplicity and high conversions. The list of aldoximes that have been isomerised by this method are given in Table 1. The reaction occurred satisfactorily even in compounds having an *o*-hydroxyl group which normally interferes in methods of isomerisation, such as the nickel acetate method, by forming an intermediary nickel-coordinated compound. Thus, salicylaldoxime was converted to salicylamide in over 83% yield. Boron trifluoride in acetic acid produced salicylamide in 47% yield.<sup>2</sup> Similarly 2,4-dihydroxybenzaldoxime gave 2,4-dihydroxybenzamide in over 60% yield and the rest was recovered on refluxing for a period of 68 h, while

nickel acetate "gave only an intractable mixture".<sup>1</sup> Further, a conjugated double bond with the oxime, as in the case of cinnamaldehyde oxime did not interfere in the smooth conversion to the amide. Electron donating or electron withdrawing substituents on the aromatic aldoximes have not effected the yields and in all cases the conversions are much better when silica gel was employed as catalyst compared with nickel acetate. The silica gel induced isomerisation appears to be a promising means of converting oximes to amides under substantially neutral conditions. Such neutral isomerisation reactions will be of much theoretical interest and are useful for synthesis and characterisation.

When silica gel was replaced by neutral alumina (TLC grade), the isomerisation did occur, although the yields were somewhat lower for the same amount of the catalyst used in the silica gel experiment. Thus when benzaldoxime was treated with neutral alumina (10% of the weight of aldoxime) in xylene for 80 h, the conversion was around 40–50%. An additional amount of alumina (50% w/w) did not improve the yields.

The mechanism of this isomerisation is not clearly understood. The possibility of a nitrile intermediate, as in all acid-catalysed isomerisation,<sup>2,4</sup> is ruled out because at no stage of the reaction could the presence of nitrile be detected. In a parallel experiment, benzaldoxime (5 g), silica gel (0.24 g), benzonitrile (2 ml) were refluxed in xylene (20 ml) for 62 h and at the end of the reaction the nitrile was recovered unchanged. Similarly, when benzonitrile was refluxed with silica gel in dry xylene for 48 h, no traces of benzamide were detected on TLC silica gel plates.

This reaction is only useful for converting aldoximes to the corresponding amides and not applicable for the conversion of ketoximes. Thus acetophenone oxime, when submitted to this isomerisation reaction for the same length of time, was recovered quantitatively. Similarly, acetaldoxime gave exclusively acetamide and no traces of *N*-methylformamide.

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Table 1

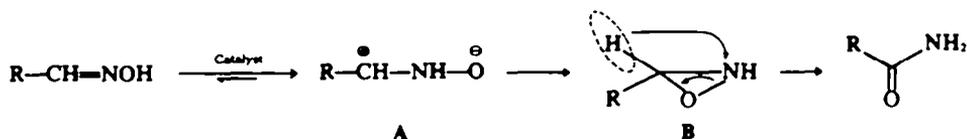
Aldoxime from	m.p. (°C) of oxime	Yield <sup>c</sup> %	Amide m.p. (°C)	Amide lit. <sup>a</sup> m.p. (°C)	Time (h)
1 Benzaldehyde	29-31	92	128 <sup>a</sup>	128	69
2 <i>p</i> -Chlorobenzaldehyde	110	91	178-79 <sup>b</sup>	179	59
3 <i>p</i> -Hydroxybenzaldehyde	74-75	84	162 <sup>b</sup>	162	61
4 <i>p</i> -Methoxybenzaldehyde	131-3	81	162-3 <sup>a</sup>	163	52
5 Piperonal	105-7	93	169 <sup>a</sup>	169	64
6 Cinnamaldehyde	138	79	146-7 <sup>a</sup>	147	66
7 Salicylaldehyde	60-61	83	139-40 <sup>b</sup>	140	73
8 2,4-Dihydroxybenzaldehyde	191-2	61 <sup>c</sup>	227-8 <sup>b</sup>	229	68
9 Acetaldehyde	47	89	81-2 <sup>a</sup>	83	57

<sup>a</sup>Crystallised from benzene.

<sup>b</sup>Crystallised from benzene-alcohol mixture.

<sup>c</sup>Conversions are quantitative, the yield denoted here is the actual amount isolated.

<sup>d</sup>Unconverted oxime has been recovered.



SCHEME 1.

The exact role of silica gel in bringing about this isomerisation is not clear. Silica gel activated at 130-40° does not contain more than 1% of moisture and is known to have bonded with the hydroxyl group of the silica gel, which is a polymer of silicic acid. The chemistry of silica gel has been reviewed by Mitchell.<sup>1</sup>

Field *et al.*<sup>1</sup> have suggested that a nickel-oxime complex brings about the isomerisation directly. The mechanism of isomerisation may or may not be the same with silica gel. One possibility is of intramolecular cyclisation through a transitional intermediate B, that might have arisen from a nitronium-type tautomer A which possibly becomes dominant in the presence of the catalyst, as indicated in the Scheme.\*

#### EXPERIMENTAL

##### Isomerisation of oximes with silica gel in xylene

**General Procedure.** A mixture of the aldoxime (1 to 8) (0.02 mole) TLC grade silica gel (pH of the silica gel aqueous suspension 6.5 to 7) activated at 130-40° (0.24 g, 10% of the oxime weight, w/w) in anhydrous xylene (25 ml) was heated at reflux for a period of 52 to 73 h. The solution was filtered hot and part of the solvent was distilled from the filtrate. On cooling, crude amide sepa-

rated out, and was crystallised from an appropriate solvent.

##### Isomerisation of the benzaldoximes with neutral alumina in xylene

A mixture of the benzaldoxime (2.42 g, 0.02 mole), neutral alumina (Brockman activity I, 0.48 g, 20% of the oxime weight, w/w) in anhydrous xylene (25 ml) was heated to reflux for a period of 80 h. The soln was filtered hot and part of the solvent was distilled from the filtrate. On cooling the contents, crude benzamide (m.p. 126-28°; 0.96 g; 40%) separated out and was crystallised from benzene in flakes, m.p. 128-29°. On removal of the solvent from the mother liquor a thick oil (1.1 g) was isolated which was found to be unconverted benzaldoxime on comparison with the authentic sample of benzaldoxime.

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#### REFERENCES

1. L. Field, P. B. Hughmark, S. H. Shumaker and W. S. Marshall, *J. Am. Chem. Soc.* **83**, 1983 (1961)
2. D. S. Hoffenberg and C. R. Hauser, *J. Org. Chem.* **20**, 1496 (1955)
3. E. C. Horning and V. L. Stromberg, *J. Am. Chem. Soc.* **74**, 5151 (1952)
4. W. R. Dunstan and T. S. Dymond, *J. Chem. Soc.* 206 (1894)
5. S. A. Mitchell, *Chem. and Ind.* 924 (1966)
6. *Dictionary of organic compounds*, (Edited by I. Heilborn). Eyre and Spottiswoode, London (1965)

\*The possibility of an intramolecular cyclisation involving a six-membered cyclic intermediate cannot be ruled out.