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# Efficient Beckmann rearrangement and dehydration of oximes via phosphonate intermediates

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**Abstract**—Under mild conditions, conversion of a variety of ketoximes and aldoximes to their corresponding amides and nitriles proceeded in the presence of diethyl chlorophosphate with excellent yields.


Amides and nitriles are of particular interest in preparative organic chemistry.[1] Great efforts have been made to prepare amides and nitriles from their corresponding ketoximes and aldoximes by Beckmann rearrangement and dehydration, respectively.

The Beckmann rearrangement of ketoximes is a well-known transformation of ketoximes to N-substituted amides and is a topic of current interest of organic chemists.[2,3] In general, it requires a strong acid, a relatively high reaction temperature and harsh reaction conditions, and generates a large amount of waste.[3,4] Thus, milder conditions have been sought and until now mild conditions were essentially related to forming activated oxime derivatives which were found to rearrange under the mild conditions, for example using chlorosulfonic acid,[5] sulfamic acid,[6] cyanuric chloride/DMF,[7] chloral,[8] anhydrous oxalic acid,[9] *O*-alkyl-*N*,*N*-dimethylformamidium salt,[10] and ethyl chloroformate/boron trifluoride etherate.[11] Recently, the Beckmann rearrangement was reported in ionic liquids at room temperature[12] and supercritical water.[13] The drawbacks in such methods are (a) the use of toxic solvents, (b) expensive reagents, (c) production of considerable amounts of by-products, (d) long reaction times, and (e) low yields. Therefore, the development of a simple, clean, highly efficient and selective Beckmann rearrangement is still in demand.

Dehydration of aldoximes to nitriles is also an important transformation in organic synthesis. A number of methods have been introduced,[14] which have their own disadvantages, for example: (a) the use of anhydrous reaction conditions, (b) toxic and hazardous chemicals, (c) tedious and cumbersome work-up procedures, (d) the need to prepare the reagent prior to the reaction, and (e) long reaction times.[15–19] Therefore, the search for a more convenient method is ongoing.

Herein we report a simple and efficient process for the Beckmann rearrangement of ketoximes to amides and the dehydration of aldoximes to nitriles using diethyl chlorophosphate in toluene where the molar ratio of diethyl chlorophosphate and oxime is 1:1. The method is simple, isolation of the product from reaction mixture is easy and the yields are high.

The Beckmann rearrangement of a series of aryl and alkyl ketoximes to the corresponding amides has been studied (Scheme 1).

As shown in Table 1, good to excellent yields were obtained for the Beckmann rearrangement of cyclopentanone oxime, 1-phenyl-propan-2-one oxime and 1,3-diphenyl-propan-2-one oxime (entries 4–6) without any by-product or parent ketone formation. For entry 4, the Beckmann rearrangement occurred at room temperature after one hour with 100% conversion. The best results were obtained when the aryl ketoximes (entries 1, 2, 3, and 8) were applied in the Beckmann rearrangement. In the case of 4-chlorobenzophenone oxime (entry 7), *ρ*-chloro-benzanilide was obtained in 58% yield in 2 h.

All the product amides were separated from the reaction mixture by neutralization with an aqueous solution of sodium hydroxide (5%) and then extraction with ether.

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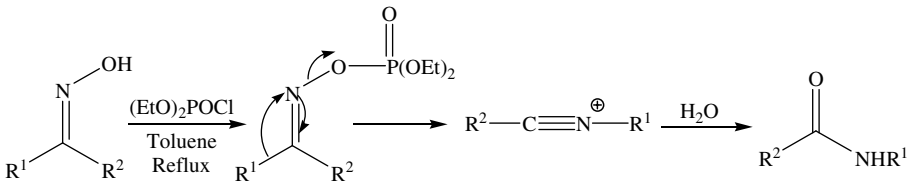
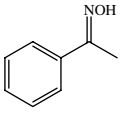
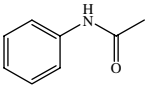
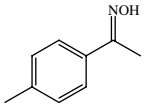
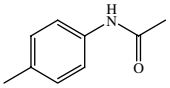
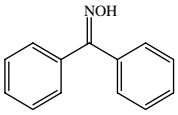
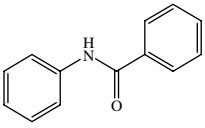
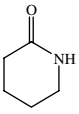
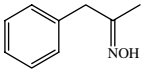
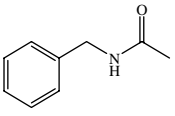
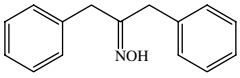
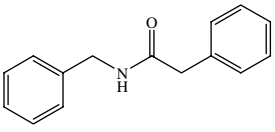
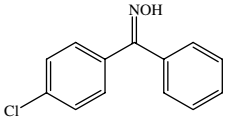
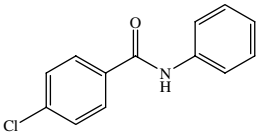
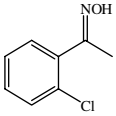
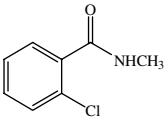



**Scheme 1.**

**Table 1.** Rearrangement of ketoximes to amides in the presence of diethyl chlorophosphate

| Entry | Ketoxime | Amide[a] | Mp (Lit.) | Yield[b] (%) | Reaction time (min) |
|---|---|---|---|---|---|
| 1 |  |  | 113 (114–15)[20] | 91 | 30 |
| 2 |  |  | 151 (152)[20] | 92 | 25 |
| 3 |  |  | 162 (162–5)[20] | 91 | 20 |
| 4 |  |  | 40 (39.5)[20] | 87 | 60 |
| 5 |  |  | 59 (61)[20] | 82 | 5 |
| 6 |  |  | 68 (68)[20] | 90 | 5 |
| 7 |  |  | 166–7 | 58 | 120 |
| 8 |  |  | 134 | 94 | 30 |

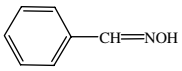
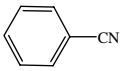
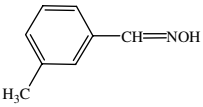
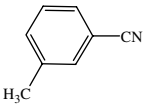
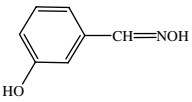
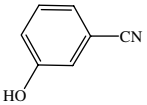
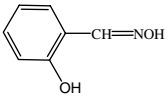
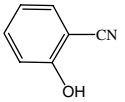
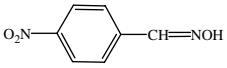
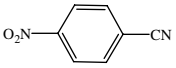
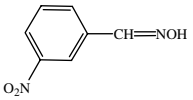
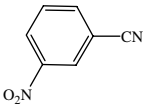
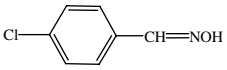
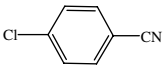
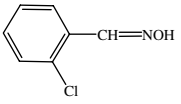
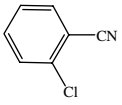
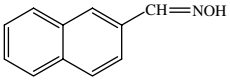
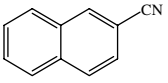
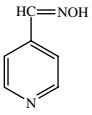
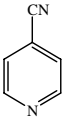
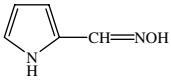
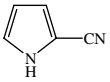
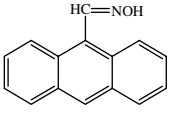
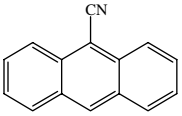
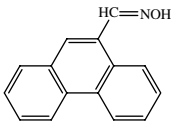
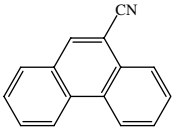
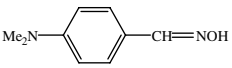
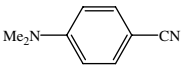
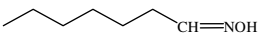
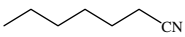
[a] All the products are known.[21]
[b] Isolated yield.

Evaporation of ether and column chromatography provided the pure amides. The amides could also be purified by short column chromatography without neutralization of the produced acid. According to Table 1, in most cases, the selectivity was high.

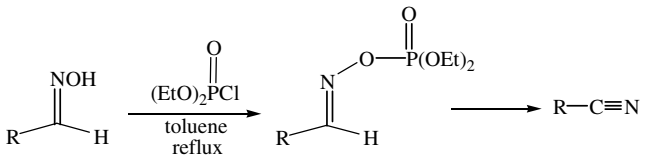
Diethyl chlorophosphate in toluene also proved to be an efficient, versatile and rapid system for the dehydration of aldoximes to nitriles in excellent yields, Table 2 (Scheme 2).

All the nitriles were purified using the same procedure as used for the purification of the amides. According to Table 2, excellent yields were obtained from benzaldoximes with different substituents (hydroxyl, methyl, chloro, nitro, and dimethylamino groups in *ortho*-,

**Table 2.** Dehydration of aldoximes to nitriles in the presence of diethyl chlorophosphate

| Entry | Aldoxime | Nitrile[a] | Mp (Lit.) | Yield[b] (%) | Reaction time (min) |
|---|---|---|---|---|---|
| 1 |  |  | 70 (70–1)[20] | 90 | 60 |
| 2 |  |  | 210 (210–12)[20] | 94 | 30 |
| 3 |  |  | 79 (79–80)[20] | 90 | 30 |
| 4 |  |  | 94 (93–6)[20] | 93 | 60 |
| 5 |  |  | 149 (147)[20] | 92 | 35 |
| 6 |  |  | 115 (114–17)[20] | 93 | 20 |
| 7 |  |  | 92 (90–3)[20] | 89 | 40 |
| 8 |  |  | 42 (43–5)[20] | 27 | 180 |
| 9 |  |  | 65 (66)[20] | 88 | 30 |
| 10 |  |  | 77–8 (76–9)[20] | 94 | 240 |
| 11 |  |  | 186[c] | 98 | 5 |
| 12 |  |  | 170–1 (170–2)[20] | 94 | 15 |
| 13 |  |  | 109 (110–112)[20] | 97 | 5 |
| 14 |  |  | 74–5 (69–71)[22] | 98 | 5 |
| 15 |  |  | 181 (183)[22] | 95 | 120 |

[a] All the products are known.[23]
[b] Isolated yield.
[c] Boiling point.




**Scheme 2.**

*para*-, and *meta*-positions, entries 1–7 and 14) in less than one hour, except for 2-chlorobenzaldoxime (entry 8) which even after 3 h refluxing in toluene gave only a 27% yield of the desired product.

Pyridine-4-carbaldoxime did not undergo dehydration under the same conditions. When triethylamine was added to the reaction mixture to neutralize the produced hydrochloric acid from the reaction of the oxime with diethyl chlorophosphate, dehydration occurred but the yield of the reaction was only 37% after 4 h. Further addition of triethylamine did not increase the yield but when the initial reaction mixture, including the same equivalent of the oxime, diethyl chlorophosphate, and triethylamine, was heated at 160–165 °C, all of the oxime was consumed and the corresponding nitrile was obtained in 94% yield. Pyrrole-2-carbaldoxime (entry 11), which is a weaker base than pyridine-4-carbaldoxime, was dehydrated quantitatively to the corresponding nitrile after five minutes in boiling toluene without using triethylamine. Polynuclear aromatic aldoximes (entries 9, 12, and 13) were converted easily and rapidly to the desired nitriles in excellent yields.

In conclusion, a simple and efficient technique for direct conversion of ketoximes and aldoximes via Beckmann rearrangement and dehydration to the corresponding amides and nitriles, respectively, has been presented which has advantages over the previously reported methods.

*General procedure*: For each reaction, the oxime (5 mmol) and toluene (1 ml) were charged into a 50 ml two necked round-bottom flask equipped with a magnetic stirrer and condenser. The reaction was heated to reflux and diethyl chlorophosphate (5 mmol) was added to the mixture. The reaction was heated for 20–120 minutes and then cooled to room temperature. The crude mixture was neutralized with 10 ml of an aqueous solution of sodium hydroxide (5%) and then extracted with diethyl ether (10 ml). Drying the ethereal layer over anhydrous sodium sulfate and then filtration and evaporation of the solvent gave the crude product, which was purified by short column chromatography over silica gel using *n*-hexane and ethyl acetate (9:1–5:5) as eluent.

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*N*-benzylacetamide: 588-46-5, *N*-benzyl-2-phenyl-acetamide: 7500-45-0, 4-chloro-*N*-phenylbenzamide: 6833-15-4, 2-chloro-*N*-methylbenzamide: 3400-31-5.

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