# Alumina sulfuric acid mediated solvent-free and one-step Beckmann rearrangement of ketones and aldehydes and a useful reagent for synthesis of keto- and ald-oximes

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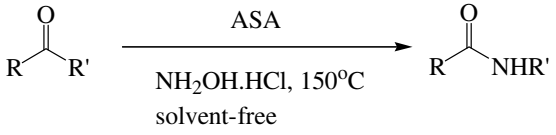
Under solvent-free conditions, one-step Beckmann rearrangement of a variety of ketones and aldehydes could proceed in the presence of alumina sulfuric acid (ASA). The ASA reagent can also be used for the preparation of keto- and ald-oximes.

**Keywords:** alumina sulfuric acid, one-step Beckmann rearrangement

Synthetic chemists continue to explore new methods of carrying out chemical transformations. One of these new methods is to run reactions on the surface of solids. As the surfaces have properties that are not duplicated in the solution or gas phase, entirely new chemistry may occur. Even in the absence of new chemistry, a surface reaction may be more desirable than a solution counterpart, because the reaction is more convenient to run, or a high yield of product is attained. For these reasons, synthetic surface organic chemistry is a rapidly growing field of study.

The rearrangement of oximes to the corresponding amides, known as the Beckmann rearrangement is an important reaction in organic chemistry.[1] The classical Beckmann rearrangement[2] requires an excess of strong protic acids such as sulfuric acid or phosphoric acid and this causes a large amount of by-products and serious corrosion problems.[1] Recently, this reaction has been studied using various modified reagents[3] and solid acid catalysts, such as metal oxides, clays[4] and zeolites.[5] However, most of these reactions are under vapour phase conditions and they proceed in rather a sluggish manner. The preparation procedure for these reagents often involves various tedious steps, such as precipitation, ion-exchange, hypothermal treatment and a prolonged activation time at a higher temperature. Reproducibility is another problem. Milder conditions were tried and several variants such as chloral,[6] solid metaboric acid,[7] $AlCl_3.6H_2O/KI/H_2O/CH_3CN$,[8] cyanuric chloride/DMF,[9] sulfamic acid,[10] anhydrous oxalic acid,[11] $B_2O_3/TiO_2–ZrO_2$,[12] chlorosulfonic acid,[13] Hβ zeolite and Hβ zeolite-supported boride[14] and vapour phase reactions[15] developed. Recently, Beckmann rearrangements in supercritical water[16] and ionic liquids[17] were also reported. However, the yield in supercritical water was very low and the ionic liquid catalyst system was very complicated. Also, few solid-phase methods have been developed,[18] and very few methods are available for one-step Beckmann rearrangement of aldehydes and ketones.[19, 20a,e] Therefore, there is still a need to develop a simple, highly efficient, highly selective and eco-friendly procedure for the preparation of amides from ketones and aldehydes.

In continuation of our studies on the development of novel synthetic methodologies in solvent-free conditions,[20] we have found that alumina sulfuric acid (ASA), which is an effective reagent for esterification reactions,[21] is a good inorganic acidic resin for Beckmann rearrangement reactions under simple and solvent free conditions (Scheme 1).




R, R' = H, alkyl, aryl, cycloalkyl

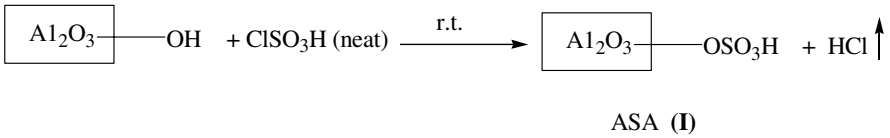
**Scheme 1**

Alumina sulfuric acid (ASA) (I) was formed by the reaction of alumina with chlorosulfonic acid (Scheme 2). It is interesting to note that the reaction is easy and clean without any workup procedure because the HCl gas is evolved from the reaction vessel immediately.

For each Beckmann rearrangement reaction, the ketone or aldehyde, hydroxylamine hydrochloride and ASA were mixed thoroughly. The mixture was then heated in an oil bath at 150 °C; there was no requirement for any additional solvent. The experimental results are summarised in Table 1.

According to Table 1, several aryl and alkyl ketones and aldehydes undergo one-step Beckmann rearrangement upon treatment with this reagent under solvent-free conditions to afford the corresponding amides with high selectivity. In all cases only one of the two possible amides were obtained. Generally, migration of an aryl group predominates over that of an alkyl group. Possibly the *E* and *Z* oximes interconverted under the reaction conditions as all oximes were prepared *in situ* in the presence of ASA.

Table 1 show that simple and electron-rich aldehydes and ketones require short reaction times but that electron-poor aldehydes and ketones took longer to undergo complete reaction. Cyclic ketones require longer reaction times than aryl ketones to give the corresponding lactams in good yields. This fact may be explained by steric or electronic factors, since it is known that substitution of an electron-donating group on the aromatic ring facilitates the reaction. Also, an attempt at the conversion of benzaldehyde into benzamide on a 100 mmol scale failed.




ASA **(I)**

**Scheme 1**

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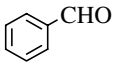
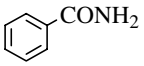
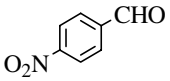
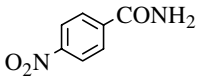
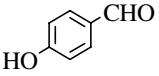
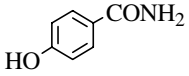
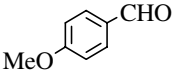
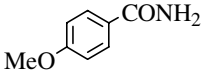
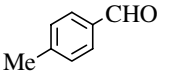
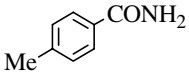
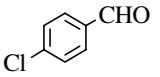
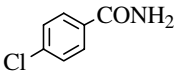
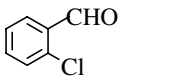
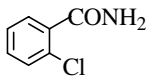
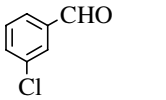
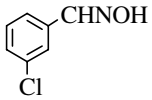
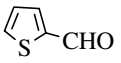
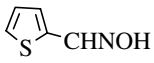
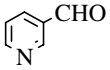
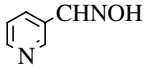
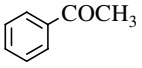
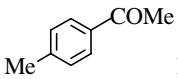
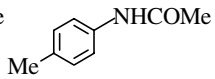
**Table 1** ASA-mediated conversion of ketones and aldehydes into amides

| Entry | Substrate | Product | Time/h | Yield[a]/% | M.p./°C (lit.) [22] | $^1$H NMR chemical shift of H amide (lit.) | IR (KBr) (lit.) |
|---|---|---|---|---|---|---|---|
| 1 |  |  | 5 | 87 | 130 (132) | 6.2 (6.26[19b] ) | 3385, 3190 ($NH_2$), 1665 (C=O) (3385, 3190, 1665[19b]) |
| 2 |  |  | 8 | 62 | 199 (201) | 7.2 (7.5[22]) | 3482, 3461 ($NH_2$), 1668 (C=O) (3479, 3420, 1678[24]) |
| 3 |  |  | 4 | 80 | 161 (162) | 5.85 (5.85[19b]) | 3140, 3210 ($NH_2$), 1650 (C=O) (3397, 3210, 1650[19b]) |
| 4 |  |  | 3 | 87 | 163 (165) | 6.8 ( 7.5[22]) | 3334, 3151 ($NH_2$), 1674 (C=O) (3343, 3161, 1670[22]) |
| 5 |  |  | 4 | 90 | 157 (160) | 6.12 (7.5[22])[b] | 3343, 3168 ($NH_2$), 1671 (C=O) ( 3343, 3168, 1670[24]) |
| 6 |  |  | 4 | 85 | 175 (179) | 5.97 (7.5[22])[b] | 3333, 3226, ($NH_2$), 1650 (C=O) (3333, 3226, 1667[22]) |
| 7 |  |  | 6 | 87 | 142 (142) | 6.45–6.49 (6.5[24]) | 3340, 3140 ($NH_2$), 1640 (C=O) (3369, 3191, 1638[24]) |
| 8 |  |  | 15 | 90 | 100 (100) | — | — |
| 9 |  |  | 5.5 | 83 | 130 (133) | — | — |
| 10 |  |  | 6 | 84 | 150 (153) | — | — |
| 11 | PhCOPh | PhCONHPh | 6 | 92 | 163 (163) | 8.1 (10.3[24])[b] | 3345 (NH), 1657 (C=O) (3346, 1657[24]) |
| 12 |  |  | 4 | 90 | 156 (157) | 7.79 (7.79[24]) | 3297 (NH), 1665 (C=O) (3294, 1665[24]) |
| 13 |  |  | 3.5 | 92 | 148 (150) | 6.12 (7.5[22])[b] | 3343, 3168, ($NH_2$), 1671 (C=O) (3343, 3168, 1671[24]) |
| 14 |  |  | 8 | 74 | 30.5 (30) | 7.4 (7.4[19b]) | 3212(NH), 1658 (C=O) (3231, 1663[24]) |
| 15 |  |  | 8 | 70 | 67 (69) | 6.9 (6.9[24]) | 3231 (NH), 1663 (C=O) (3231, 1663[24]) |

[a]Yields are the isolated compounds. [b]$^1$H NMR was obtained in DMSO-$d_6$.

Further, *meta* substituted aromatic aldehydes did not afford the corresponding rearranged products even after 12 h. Schofield and his co-workers [23] have shown that the rates of rearrangement for *meta* substituted aromatic oximes are lower than the *para* and *ortho* substituted compounds in 98.2% sulfuric acid at 80 °C.

We have also found that various types of aldehydes and ketones were cleanly and rapidly condensed with hydroxylamine hydrochloride at 80 °C in 5–20 min in the presence of ASA, giving the corresponding oximes in excellent yields. The results are summarised in Table 2. Therefore it seems clear that the preparation of oximes in the presence of ASA occurs first and the Beckmann rearrangement step follows.

In conclusion, the present procedure not only has the chemical, economical and environmental advantages of solvent-free reactions but also constitutes a method of preparing directly amides from the corresponding aldehydes and ketones without the need to prepare the aldo- and keto-oximes.

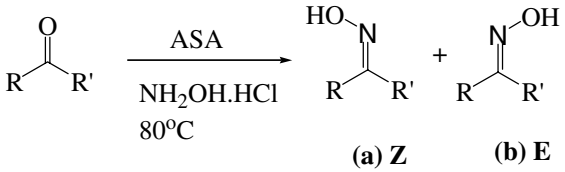
## Experimental

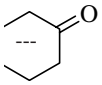
Starting materials were obtained from the Fluka company. Melting points were determined on a Buchi 510 apparatus and are uncorrected. IR spectra were recorded on Perkin–Elmer spectrometer. Proton NMR spectra were recorded on Bruker Advance DPX FT 250 MHz instrument, in $CDCl_3$. Acidic alumina ($Al_2O_3$ ) type 540 C was purchased from the Fluka company.

*Preparation of alumina sulfuric acid* (ASA)

A 500 ml suction flask was used. It was equipped with a constant pressure dropping funnel containing chlorosulfonic acid (14 ml, 210 mmol) and a gas inlet tube for conducting HCl gas over

**Table 2** Conversion of aldehydes and ketones into oximes using ASA.




| Entry | R | R′ | Time /min | Yields[a]/% | *Z/E* ratio/ %[b] | $^1$H NMR, δ, $H_a$(Z isomer)[20c] | M.p./°C of (a) (lit.) |
|---|---|---|---|---|---|---|---|
| 1 | $C_6H_5$ | H | 10 | 92 | 92/8 | 8.17 | 125(128[25]) |
| 4 | 4-$HOC_6H_4$ | H | 10 | 90 | 90/10 | 8.07 | 94 (72[22]) |
| 5 | 4-$MeOC_6H_4$ | H | 5 | 95 | >98/trace | 8.00 | 132 (133[25]) |
| 6 | 3-$MeC_6H_4$ | H | 20 | 93 | >98/trace | 8.13 | 56 (60[22]) |
| 7 | 4-$MeC_6H_4$ | H | 10 | 95 | >98/trace | 8.49 | 72 (80[22]) |
| 8 | 4-$NO_2C_6H_4$ | H | 20 | 87 | 80/20 | 8.21 | 100 (129[25]) |
| 9 | 3-$NO_2C_6H_4$ | H | 20 | 84 | 80/20 | 8.41 | |
| 10 | 2-$ClC_6H_4$ | H | 5 | 90 | >98/trace | 8.57 | 103 (100[26]) |
| 11 | 4-$ClC_6H_4$ | H | 5 | 92 | >98/trace | 8.12 | 146 (145[25]) |
| 12 |  | H | 10 | 83 | 73/27 | 7.73 | 130 (133[22]) |
| 13 |  | H | 10 | 84 | 70/30 | 8.47 | 150 (153[22]) |
| 14 | $CH_3CH_2CH_2$ | H | 5 | 92 | 90/10 | 7.43 | Liquid |
| 15 | $C_6H_5$ | $C_6H_5$ | 10 | 93 | --- | --- | --- |
| 16 | $C_6H_5$ | $CH_3$ | 10 | 91 | 90/10 | --- | --- |
| 17 | 4-$MeC_6H_4$ | $CH_3$ | 8 | 90 | 90/10 | --- | --- |
| 18 |  | 15 | 84 | --- | --- | --- | |

[a]Yields are isolated compounds. [b]Ratio of *Z/E* isomers were determined by $^1$H NMR.

the adsorbing solution *e.g.* water. Into it were charged (51 g, 510 mmol) of alumina. Chlorosulfonic acid was added dropwise over a period of 30 min at room temperature. HCl gas was evolved from the reaction vessel immediately (Scheme 2). After the addition was completed the mixture was shaken for 1 h. A white solid (ASA) (76.0 g) was obtained which could be stored for approximately two months without decrease of activity.

*Typical procedure for the Beckmann rearrangement:*
The ketone or aldehyde (1 mmol), hydroxylamine hydrochloride (0.3 g, 4.3 mmol) and ASA (0.2 g, 0.6 mmol) were mixed sufficiently. Then the mixture was charged into a test tube equipped with a magnetic stirrer and heated in an oil bath at 150 °C. There was no requirement for any additional solvent. At the end of the reaction (see Table 1) the resulting mixture was mixed with ethyl acetate (2 × 5 ml) and filtered to remove ASA. The filtrate was washed with water (2 × 10 ml), dried over $Na_2SO_4$ and the solvent removed under reduced pressure to give the product which was recrystallised from a suitable solvent or purified by column chromatography (ethyl acetate-hexane). All of the products are known and gave satisfactory physical data compared with those of authentic samples.

*Typical procedure for the preparation of oximes in the presence of ASA:*
Hydroxylamine hydrochloride (0.3 g, 4.3 mmol ) was added to a stirred mixture of ASA (0.2 g, 0.6 mmol ) and aldehydes or ketones (1 mmol ) at 80 °C in an oil bath. The progress of reaction was monitored by TLC. After complete disappearance of the starting material (see Table 2), the reaction mixture was washed with ethyl acetate (2 × 10 ml) and water (2 × 50 ml). The organic layer was dried over $Na_2SO_4$ and evaporated to give the oxime. The products were identified by comparison of their physical data with those prepared in accordance with the literature procedures.

We gratefully acknowledge the support of this work by the Shiraz University Research Council.

*Received 10 August 2005; accepted 28 October 2005*
*Paper 05/3245*

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