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# Rhodium-Catalyzed Beckmann Rearrangement

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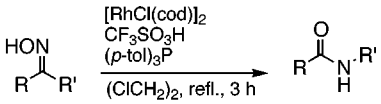
## ABSTRACT




**Beckmann rearrangement of oxime is catalyzed by [RhCl(cod)]$_2$, trifluoromethanesulfonic acid, and tris(*p*-tolyl)phosphine in refluxing dichloroethane, giving the corresponding amide in good yield. Product/acid ratios of 10:20 can be attained in the reaction of benzophenone oximes.**

The rearrangement of a ketoxime to the corresponding amide is a powerful method in organic synthesis[1] and is known as the Beckmann rearrangement. This reaction, however, generally requires a large amount of a strong Brønsted acid such as sulfuric acid and forms ammonium sulfate as a byproduct. Development of this important process promoted by a catalytic amount of active species has been strongly desired for a long time. In the vapor-phase process, a few examples of the Beckmann rearrangement catalyzed by activators such as boria-hydroxyapatite are reported.[2] The Beckmann rearrangement in the supercritical water is also reported.[3] As for the liquid-phase process, the catalytic methods have been developed by using *O*-alkyl-*N*,*N*-dimethylformamidium salt[4] or tetrabutylammonium perrhenate.[5] Antimony(V) salt was reported to catalyze the reaction of silylated oximes.[6] The efficiency of the liquid-phase process, however, is not very high, and turn over number (TON) based on the acid is generally less than 5. Formation of the parent ketone often is a serious problem. As an extension of our recent investigations on the use of transition metal complexes and sulfuric acid derivatives in organic synthesis,[7] we examined the Beckmann rearrangement. A small amount of rhodium complex was found to promote the reaction of ketoxime and trifluoromethanesulfonic acid.

When propiophenone oxime is treated with [RhCl(cod)]$_2$ (cod = 1,5-cyclooctadiene) (2.5 mol %), (*p*-tol)$_3$P (15 mol %), and trifluoromethanesulfonic acid (25 mol %) in refluxing dichloroethane for 3 h, *N*-propionylaniline **2** is obtained in 78% yield (Table 1, entry 1), which is accompanied by a small amount of ethyl migrated *N*-ethylbenzamide **3** (2%). Ketone is recovered in 7% yield. The rhodium complex and the phosphine are essential for the rearrangement, and no reaction occurs in the absence of either of the reagents (entries 2 and 3). This reaction is effectively promoted by trifluoromethanesulfonic acid, while the yield of product decreases when methanesulfonic acid, *p*-toluenesulfonic acid, or fluorosulfonic acid is used (entries 4−6). The reaction is relatively insensitive to the substituent on the triarylphosphine (entries 7−10). Alkyl phosphines (entries 11−13) and a bidentate phosphine (entry 14) are not very effective except for dppf (entry 15). The trifluoromethanesulfonic acid/rhodium ratio of more than 5 is critical. Otherwise, the yield of amide decreases, and a considerable amount of ketone is formed. The catalytic activities of several metal complexes are compared employing benzophenone oxime for the substrate: while RhCl(PPh$_3$)$_3$ and [RhCl(cod)]$_2$ + PPh$_3$ are

(1) Gawly, R. E. *Org. React.* **1988**, *35*, 1 and references therein.
(2) Izumi, Y.; Sato, S.; Urabe, K. *Chem. Lett.* **1983**, 1649.
(3) Ikushima, Y.; Hatakeda, K.; Sato, O.; Yokoyama,T.; Arai, M. *J. Am. Chem. Soc.* **2000**, *122*, 1908. Sato, O.; Ikushima,Y.; Yokoyama, T. *J. Org. Chem.* **1998**, *63*, 9100.
(4) Izumi, Y. *Chem. Lett.* **1990**, 2171.
(5) Kusama, H.; Yamashita, Y.; Narasaka, K. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 373. Narasaka, K.; Kusama, H.; Yamashita, Y.; Sato, H. *Chem. Lett.* **1993**, 489.
(6) Mukaiyama, T.; Harada, T. *Chem. Lett.* **1991**, 1653. Harada, T.; Ohno, T.; Kobayashi, S.; Mukaiyama, T. *Synthesis* **1991**, 1216.
(7) Arisawa, M.; Yamaguchi, M. *J. Am. Chem. Soc.* **2000**, *122*, 2387. Arisawa, M.; Yamaguchi, M. *Adv. Synth. Cat.* **2001**, in press.

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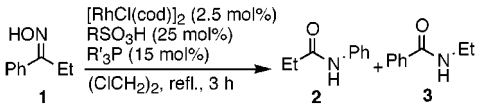
**Table 1.** Effect of Sulfonic Acid and Phosphine on the Rh-Catalyzed Beckmann Rearrangement



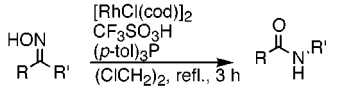

| | | | yield (%) | |
|---|---|---|---|---|
| entry | R | R′$_3$P | **2** | **3** |
| 1 | $CF_3$ | ($p$-tol)$_3$P | 78 | 2 |
| 2[a] | $CF_3$ | ($p$-tol)$_3$P | – | – |
| 3 | $CF_3$ | none | – | – |
| 4 | $CH_3$ | ($p$-tol)$_3$P | 13 | – |
| 5 | $p$-tol | ($p$-tol)$_3$P | 16 | – |
| 6 | F | ($p$-tol)$_3$P | 23 | – |
| 7 | $CF_3$ | ($p$-MeOC$_6$H$_4$)$_3$P | 68 | 5 |
| 8 | $CF_3$ | (C$_6$H$_5$)$_3$P | 58 | 3 |
| 9 | $CF_3$ | ($p$-ClC$_6$H$_4$)$_3$P | 59 | 3 |
| 10 | $CF_3$ | (C$_6$F$_5$)$_3$P | 40 | – |
| 11 | $CF_3$ | (C$_6$H$_5$)Me$_2$P | 39 | – |
| 12 | $CF_3$ | ($n$-C$_4$H$_9$)$_3$P | – | – |
| 13 | $CF_3$ | (cycloC$_6$H$_{13}$)$_3$P | 24 | – |
| 14 | $CF_3$ | dppe[b] | 13 | – |
| 15 | $CF_3$ | dppf[c] | 52 | 2 |

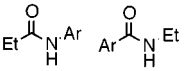
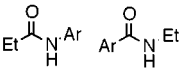
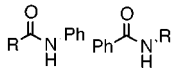
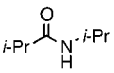
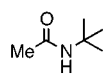
[a] In the absence of Rh catalysis. [b] 1,2-Diphenylphosphinoethane. [c] 1,1′-Bis(diphenylphosphino)ferrocene.

active, $RhH(PPh_3)_4$, $RhH(CO)(PPh_3)_3$, $RuCl(CO)(PPh_3)_3$, $RuH(OAc)(PPh_3)_3$, $Pd_2(dba)_3$, and $Pd(PPh_3)_4$ are inactive. Use of dichloroethane, chlorobenzene, toluene, or hexane as the solvent gives better result than use of dichloromethane or THF.

The catalytic Beckmann rearrangements of several oximes are summarized in Table 2.[8] When derivatives of benzophenone oxime are used, product/acid ratios of 10 to 20 can be attained, and the ratio of product/Rh approaches 100. The stereochemistry as shown in the case of *p*-fluoropropiophenone oxime is unimportant. Facile isomerization of oxime in the presence of trifluoromethanesulfonic acid is known.[5]

**Table 2.** Rh-Catalyzed Beckmann Rearrangement of Oximes[a]




| substrate | Rh[b] (mol%) | product / yield (%) | |
|---|---|---|---|
|  | |  | |
| Ar = $p$-MeC$_6$H$_4$ | 1.0 | 99 | |
| Ar = C$_6$H$_5$ | 1.0 | 93 | |
| Ar = $p$-FC$_6$H$_4$ | 2.0 | 91 | |
| Ar = $p$-ClC$_6$H$_4$ | 2.0 | 95 | |
|  | |  | |
| Ar = $p$-MeOC$_6$H$_4$ | 2.5 | 88 | 6 |
| Ar = $p$-MeC$_6$H$_4$ | 2.5 | 66 | 4 |
| Ar = C$_6$H$_4$ | 5.0 | 78 | 2 |
| Ar = $p$-FC$_6$H$_4$ | 5.0 | 56 | 5 |
|  | |  | |
| Ar = $p$-FC$_6$H$_4$ | 5.0 | 55 | 6 |
|  | |  | |
| R = $n$-Bu | 5.0 | 70 | 2 |
| R = $i$-Bu | 5.0 | 72 | 2 |
| R = $i$-Pr | 5.0 | 52 | 12 |
| R = 1-ethylpentyl | 5.0 | 65 | 18 |
| R = $t$-Bu | 5.0 | 68 | 13 |
|  | |  | |
| | 5.0 | 71 | |
|  | |  | |
| | 5.0 | 30 | |

[a] The reaction is carried out using Rh metal/($p$-tol)$_3$P/$CF_3SO_3H$ in the ratio of 1/3/5. [b] The amount of Rh metal.

As in the conventional Beckmann rearrangement, electron-donating groups on the aromatic ring facilitate the reaction, and electron-withdrawing groups retard it. Migration of an aryl group predominates over that of an alkyl group. The yield of the product decreases with unbranched aliphatic ketone oximes; for example, 6-undecanone oxime gives the product in 18%, which is accompanied by the regeneration of the ketone (18%) and the recovery of the oxime (27%).

Although the mechanism of the present reaction is not clear, the first step probably is the oxidative addition of oxime to a low valent rhodium complex at the nitrogen−oxygen bond.[9] Then, the alkyl migration and the reductive elimination take place, resulting in the amide.

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(8) The rearrangement reaction of benzophenone oxime is representative. In a one-necked flask were placed [RhCl(cod)]$_2$ (0.5 mol %, 12.3 mg), tris(*p*-tolyl)phosphine (3 mol %, 45.7 mg), benzophenone oxime (5.0 mmol, 985 mg), and trifluoromethanesulfonic acid (5 mol %, 0.022 mL) in dichloroethane (4 mL) under an argon atmosphere, and the solution was heated at reflux for 3 h. Then, water was added, and the organic materials were extracted twice with ether. The combined organic layers were washed with brine, dried over magnesium sulfate, and concentrated. The residue was purified by flash column chromatography to give benzanilide (916 mg, 93%).

(9) Tsutsui, H.; Narasaka, K. *Chem. Lett*. **1999**, 45. Ferreira, C. M. P.; Guedes de Silva, M. F. C.; Kukushkin, V. Y.; Fraústo da Silva, J. J. R.; Pombeiro, A. J. L. *J. Chem. Soc., Dalton Trans*. **1998**, 325. Deeming, A. J.; Owen, D. W.; Powell, N. I. *J. Organomet. Chem*. **1990**, *398*, 299. Hosokawa, T.; Shimo, N.; Maeda, K.; Sonoda, A.; Murahashi, S. *Tetrahedron Lett*. **1976**, 383.