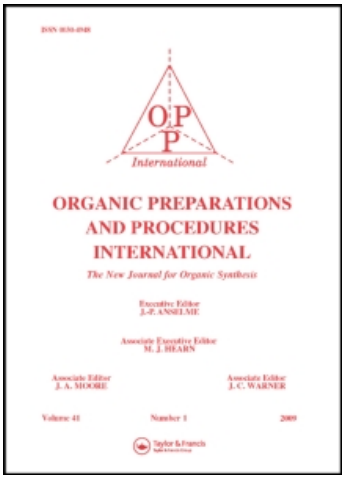

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REGIOSELECTIVE BECKMANN REARRANGEMENT

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REGIOSELECTIVE BECKMANN REARRANGEMENT

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Beckmann rearrangements normally yield mixtures of two amides, the ratios of which reflect the syn-anti isomer composition of the starting oximes. In our work on insect hormone analogs, we found it possible to control the course of the Beckmann rearrangement of the oxime tosylates of two representative methyl ketones so that the products were almost exclusively that of higher alkyl migration. A recent publication by Fleming and Woodward[2] on the effect of acid-catalyzed equilibration of oxime tosylates on the Beckmann rearrangement prompts us to report our findings.

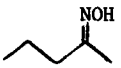
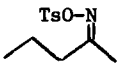
Two ketones, 2-pentanone and 3-methyl-2-butanone, were used for this study. Syn-anti isomer compositions of the oximes of these two ketones (syn referring to the hydroxyl and methyl on the same side) are known.[3] We have determined the amide ratios by integrating the proton signals for N-C-H[5] and by gas chromatography.[6]

The preparation of the oxime tosylates and their rearrangement to amides were carried out, stepwise, in one reaction vessel. A two-phase system containing p-toluenesulfonyl chloride and the oxime in THF and 10% aqueous potassium hydroxide was stirred at room temperature for one hour; one equivalent of p-toluenesulfonic acid monohydrate was then added and stirring was continued overnight. The products were isolated by removal of the solvent under reduced pressure, and dissolution of the residue in water. After filtration, the solution was made basic and continuously

extracted with ether. Distillation afforded the amides in 45-60% yields.

Amides prepared by this method were mainly derived from the migration of the non-methyl group. Specifically, 2-pentanone oxime gave exclusively N-n-propylacetamide, and 3-methyl-2-butanone oxime gave a 93:7 ratio of N-isopropylacetamide to N-methylisobutyramide. On the other hand, if the oxime tosylates, prepared as described above, were not treated with p-toluenesulfonic acid but instead, were rearranged on a column of alumina, according to Craig's method,[7] the ratios of amides obtained reflected the syn-anti composition of the starting oximes. These results are summarized in Table I together with the results obtained by the method of Fleming and Woodward which uses a 2:1 mixture of acetic acid and concentrated hydrochloric acid for the isomerization and rearrangement. The yields obtained by the latter method and by ours were comparable (45-60%) while Craig's method gave somewhat higher yields (65-80%). The high water solubilities of these amides appear to be a factor in these unimpressive yields. The yield of the less water soluble amide from 2-octanone oxime was higher (70-90%).

Table I. Percentage Composition of Products

		Method of Rearrangement					
	Syn-anti ratio of oximes[3]	Alumina		p-TsOH		HCl/HOAc	
		RNHAc	$RCONHCH_3$	RNHAc	$RCONHCH_3$	RNHAc	$RCONHCH_3$
	73:27	75	25	100	0*	100	0*
	86:14	88	12	93	7	93	7
	Pure anti	0*	100	100	0*	--	--

R = n-propyl or isopropyl; *Undetectable by glpc and nmr.

That the selectivity of our procedure was due to the pre-equilibration of the oxime tosylates followed by preferential rearrangement of the syn isomer and not to some selectivity either in the formation, decomposition, or extraction of products was demonstrated as follows. When excess potassium hydroxide was used to prepare 2-pentanone oxime tosylate in a two-phase THF-KOH(aq.) system and the reaction allowed to proceed overnight, the syn-oxime tosylate rearranged completely to N-n-propylacetamide whereas the anti-oxime tosylate had not rearranged to any significant extent. Apparently, oxime tosylates are configurationally stable in basic solution. Column chromatography on silica gel afforded pure anti-2-pentanone oxime tosylate. Rearrangement of this material on a column of alumina gave only N-methylbutyramide; treatment with p-toluenesulfonic acid in THF-water gave only N-n-propylacetamide (see Table I).

Proper manipulation of methyl ketone oxime tosylates by our procedure thus allows control of this Beckmann rearrangements under much milder conditions than here-to-fore.[8] Although kinetic control of the Beckmann rearrangement is not new,[8,9] our method allows separate production of the two amides in a ratio reflecting oxime composition or the entire reaction may be steered toward the amide derived from the syn-oxime.

REFERENCES

* To whom inquiries should be directed.

1. Mention of a commercial or proprietary product in this paper does not constitute an endorsement of this product by the U.S. Department of Agriculture.

2. I. Fleming and R. B. Woodward, J. Chem. Soc. Perkin I, 1653 (1973).

3. K. D. Berlin and S. Rengaraju, J. Org. Chem., 35, 2912 (1971). An opposite assignment has been proposed by Wolkowski, Tetrahedron Letters, 825 (1971), we favor the assignment of Berlin and Rengaraju because of their Beckmann rearrangement results and because the magnitude (ca. 40 ppm) of the $Eu(DPM)_3$ induced oximino hydroxyl hydrogen shift[5] (extrapolated to equimolar[3] concentration) compared unfavorably with that for ROH (ca. 80 ppm).[4] Unfortunately, we could not accurately determine the isomer composition of the oxime tosylates by the method of Berlin and Rengaraju which utilized the paramagnetic shift induced by $Eu(DPM)_3$. The methyl peaks shifted slightly and in tandem so that they were barely resolvable. We suspect that the shift reagent is complexing with those oxygen atoms of the tosylate not bonded to the oxime nitrogen, thereby greatly increasing the distance to the methyl group in question. For instance, we find shift values of 3 ppm [extrapolated to equimolar concentration of $Eu(DPM)_3$] for the methoxyl tosylate as compared to 25 ppm for methyl benzyl ether .

4. P. V. Demarco, T. K. Elzey, R. B. Lewis, and E. Wenkert, J. Am. Chem. Soc., 92, 5734 (1970).

5. Shift values for the N-C-H protons were (Varian T-60[1]);

N-Methylbutyramide and N-methylisobutyramide	δ = 2.73 (d, J=7)
N-Propylacetamide	δ = 3.11 (q, J=6)
N-Isopropylacetamide	δ = 3.98 (sextuplet, J=7)

6. Gas chromatographic analysis on 122 cm x 3.2 mm ID 5% carbowax 20M-TPA on base-washed Chromosorb W column.

7. J. C. Craig and A. R. Naik, J. Am. Chem. Soc., 84, 3410 (1962).

8. A. D. McLaren and R. E. Schachat, J. Org. Chem., 14, 254 (1949).

9. L. Donaruma and W. Z. Heldt, the Beckmann Rearrangement, Vol. 11, pp. 54-55 (and references therein), Organic Reactions, J. Wiley and Sons, New York, N. Y., 1960.

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