# Heterocycles from Ketenimines XI. Oxindoles (1)

*Marvin W. Barker and Hsiu-Sun Sung*

Department of Chemistry, Mississippi State University, Mississippi State, Mississippi 39762

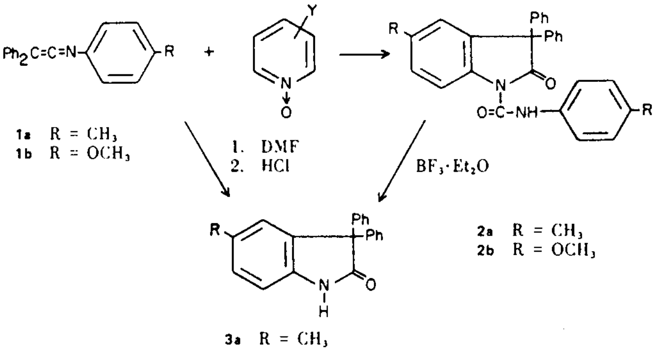
Received March 1, 1977

The reaction of ketenimines with heterocyclic *N*-oxides yields *N*-substituted oxindoles. Hydrolysis of these adducts or acid work-up of the original reaction mixtures leads directly to oxindoles in which the nitrogen atom is unsubstituted.

*J. Heterocyclic Chem.*, 14, 693 (1977).

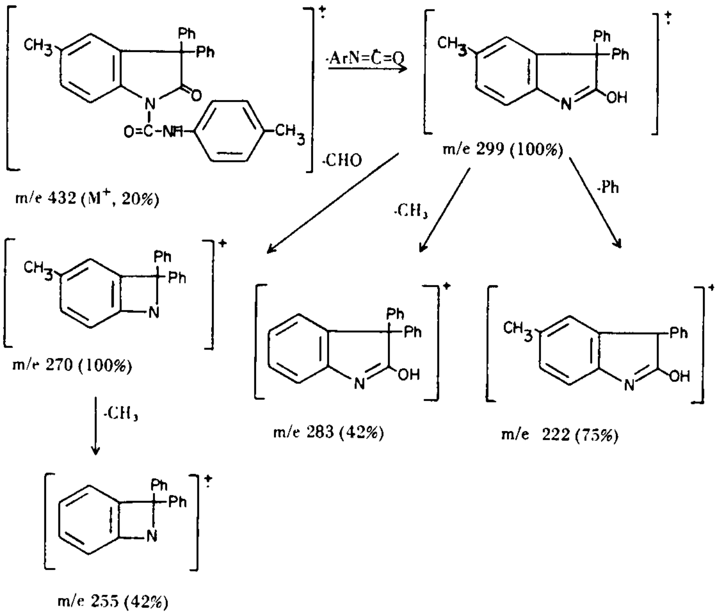
The heterocyclic *N*-oxides have been shown to function either as 1,3-dipoles or as oxygenating agents for heterocumulenes. For example, the *N*-oxides of pyridine, isoquinoline, and phenanthridine behave as nitrones would toward phenyl isocyanate and phenyl isothiocyanate. In these reactions the heterocyclic *N*-oxide adds across the N=C bond of each of the two heterocumulenes and the 1:1 adducts formed subsubsequently rearrange (2) and decompose to yield amino substituted heterocycles (3). Conversely, Koenig has observed that pyridine *N*-oxide transfers oxygen to the ketene moiety of diphenylketene producing carbon dioxide and benzophenone (4). Other literature reports attest to the dual behavior of the heterocyclic *N*-oxides toward unsaturated centers (5). Since the ketenimine heterocumulene system has been shown to be receptive to cycloaddition reactions (6) and to oxidation (7), we felt it would be of interest to investigate the behavior of this system toward heterocyclic *N*-oxides.

When diphenykentene *N*-*p*-tolylimine (**1a**) is treated with the *N*-oxide of pyridine, α-picoline, γ-picoline, or quinoline in dimethylformamide (DMF) heated to reflux, the ir absorption for ketenimine at 2000 cm$^{-1}$ disappears in 6 hours. Work-up of each reaction mixture affords **2a** in about 25% yield (eq.). The product was identified by elemental analysis, ir (absorptions for C=O at 1740 and 1715 cm$^{-1}$), nmr (absorptions for the methyl protons at δ 2.34 and absorptions for the aromatic protons and the amide proton from δ 6.9 to 7.4), and mass spectral data (Scheme). An additional product was isolated from the reaction mixture; however, an unequivocal structure has not been assigned to this compound (8).



Compound **2a** was hydrolyzed to 5-methyl-3,3-diphenyloxindole (52% yield), identical with an authentic sample (9), with boron trifluoride etherate. Indeed, hydrolysis of the original reaction mixture with 6*N* hydrochloric acid without prior isolation of **2a** gave **3a** in good yield, and this is a novel and useful preparative route to substituted oxindoles.

Scheme



## EXPERIMENTAL

Melting points were determined on a Mel Temp apparatus and are corrected. Infrared spectra were determined on a Perkin-Elmer Infracord (potassium bromide wafers). Mass spectra were recorded on a Du Pont model 490 spectrometer while nmr spectra were determined on a Jeolco Minimar with deuteriochloroform as the solvent. Elemental analyses were performed by the Heterocyclic Chemical Corporation of Harrisonville, Missouri.

### The Reaction of Diphenylketene *N*-*p*-Tolylimine (**1a**) with Pyridine *N*-Oxide: Preparation of **2a**.

To a solution of 1.41 g. (5 mmoles) of **1a** in 30 ml. of DMF was added 5 mmoles of pyridine *N*-oxide dissolved in 40 ml. of DMF. The resulting mixture was heated to reflux until the ir absorption for ketenimine at 2000 cm$^{-1}$ disappeared (6 hours). The reaction mixture was then added to 400 ml. of cold water whereupon precipitation occurred. The precipitate was collected, dissolved in 100 ml. of benzene, and the benzene solution was dried over anhydrous magnesium sulfate. The dried benzene solution was diluted with 200 ml. of petroleum ether, and the resultant precipitate was collected to give 0.67 g. of material. A sample of this material purified by column chromatography gave the following properties: m.p. 245°; ir: 1730 (s) and 1620 cm$^{-1}$ (s); nmr: δ 2.15 (s, 3H), 2.20 (s, 3H), 6.6-7.4 (m, 28H); ms: m/e (relative abundance), 446 (12%), 354 (22%), 296 (49%), 282 (17%), 281 (22%), 263 (34%), and 262 (100%). Satisfactory elemental analyses were not obtained (8).

The benzene-petroleum ether mother liquor from above was allowed to stand at room temperature for one week. The precipitated material was collected and recrystallized from acetone to give 0.45 g. (25%) of **2a**, m.p. 221-222°; ir: 1740 (s) and 1715 cm$^{-1}$ (s); nmr: δ 2.34 (s, 2 $CH_3$) and 6.9-7.4 (complex of 18H, aromatic protons plus the N-H proton); ms: m/e (relative abundance), 432 ($M^+$, 22%), 341 ($M^+$-*p*-tolyl, 6%), 299 (100%), 283 (41%), and 270 (99%).

*Anal.* Calcd. for $C_{29}H_{24}N_2O_2$: C, 80.55; H, 5.55; N, 6.48. Found: C, 80.72; H, 5.81; N, 6.39.

Similar results were obtained with **1a** and α-picoline *N*-oxide, γ-picoline *N*-oxide, and quinoline *N*-oxide.

5-Methyl-3,3-diphenyloxindole (**3a**).

(A) From **1a**, α-Picoline *N*-Oxide, and the Hydrochloride.

To a solution of 1.41 g. (5 mmoles) of diphenylketene-*N*-*p*-tolylimine (**1a**) in 30 ml. of DMF was added a solution of 5 mmoles of α-picoline *N*-oxide in 30 ml. of DMF. The mixture was heated to reflux for 6 hours (time necessary for the disappearance of the ketenimine absorption in the ir). The reaction mixture was cooled and then added to 300 ml. of 6 *N* hydrochloric acid while the total mixture was stirred vigorously. The precipitate was collected and crystallized from ethyl acetate to give 0.52 g. (35%) of **3a**. The m.p. ir, and nmr agreed with those of an authentic sample prepared by the method of Sheehan and Beeson (9).

When the reaction mixture was added to 300 ml. of dilute sodium hydroxide instead of hydrochloric acid, a 50% yield of **3a** was obtained.

(B) From the Hydrolysis of **2a**.

A solution of 108 mg. (0.25 mmole) of **2a** and 15 ml. of boron trifluoride etherate was heated to reflux for 1 hour. The solution was poured into water and the product was extracted with 50 ml. of dichloromethane. Removal of the dichloromethane solvent left 47 mg. (62%) of 5-methyl-3,3-diphenyloxindole, m.p. 282-283°.

5-Methoxy-3,3-diphenyloxindole.

Diphenylketene-*N*-*p*-anisylimine (**1b**, 1.49 g., 5 mmoles) and γ-picoline *N*-oxide (0.55 g., 5 mmoles) were treated as described for **3a** with the hydrochloric acid work-up. From the reaction was obtained 1.10 g. (70% yield) of product, m.p. 251-252°; ir: 1710(s), 1670(s), 1600(s), and 1490 cm$^{-1}$(s); nmr: δ 4.03 (s, 3H), 7.02 (m, 3H), 7.40 (s, 11H).

*Anal.* Calcd. for $C_{21}H_{17}NO_2$: C, 80.00; H, 5.30; H, 4.44. Found: C, 80.18; H, 5.41; N, 4.72.

## REFERENCES AND NOTES

(1) Part X. M. W. Barker and C. J. Wierengo, *J. Heterocyclic Chem.*, **12**, 175 (1975).

(2) R. A. Abramovitch, I. Shinkai, and R. Van Dahm, *ibid.*, **13**, 171 (1976).

(3) R. Huisgen, *Angew. Chem., Int. Ed. Engl.*, **2**, 565 (1963).

(4) T. Koenig, *Tetrahedron Letters*, 3127 (1965).

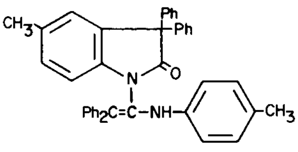
(5) G. R. Didpeirre and M. Lamchen, *J. Chem. Soc.*, 4693 (1963); B. G. Murray and A. F. Turner, *ibid.*, 1338 (1966); R. N. Pratt and G. A. Taylor, *ibid.*, 1653 (1968); and T. Cohen, I. H. Song, J. H. Fager, and G. L. Deets, *J. Am. Chem. Soc.*, **89**, 4968 (1967).

(6) M. W. Barker and C. J. Wierengo, *J. Heterocyclic Chem.*, **12**, 175 (1975) and references cited therein.

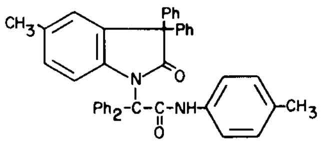
(7) H. Staudinger and E. Hauser, *Helv. Chim. Acta*, **4**, 887 (1921); H. Kagen and I. Lillien, *J. Org. Chem.*, **31**, 3728 (1966); J. K. Crandall and L. C. Crawley, *ibid.*, **39**, 489 (1974); and M. W. Barker and S. I. Perumal, *Tetrahedron Letters*, 349 (1976).

(8) This compound (for which structure **4** is tentatively proposed) is very similar in its properties to **5** which was prepared by Sheehan (9) from the reaction of *N*-*p*-totyl-α-chloro-α,α-diphenylacetamide with sodium hydride. Neither adduct gave a parent ion in its mass spectrum and neither gave a good elemental analysis. However, **4** and **5** cannot be identical since **4** yields *N*-*p*-tolyldiphenylacetamide upon hydrolysis whereas **5** yields *N*-*p*-tolyl-α-hydroxydiphenylacetamide upon hydrolysis. Structure **4** is tentatively proposed by us based on these observations plus the observed presence of only one carbonyl and one double bond in the ir spectrum.[

(9) J. C. Sheehan and J. H. Beeson, *J. Org. Chem.*, **31**, 1637 (1966) and J. C. Sheehan and J. W. Frankenfeld, *J. Am. Chem. Soc.*, **83**, 4792 (1961).



**4**



**5**