

Oxindoles from α -Acyloxyamides

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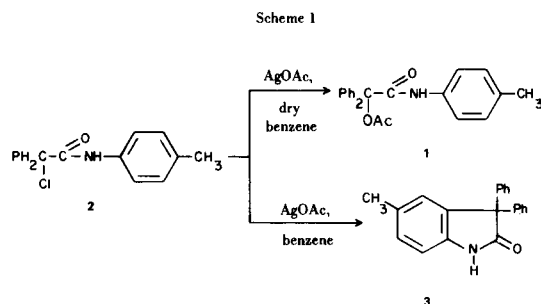
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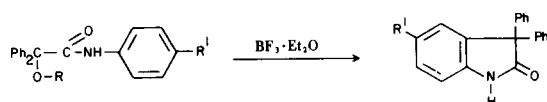
Oxindoles have been obtained in good yields from the reaction of several α -acyloxy- α,α -diphenylacetanilides and boron trifluoride etherate. The reaction probably occurs by hydrolysis of the ester followed by electrophilic substitution of the resultant carbonium ion on the anilide ring.

J. Heterocyclic Chem., 14, 521 (1977).

While attempting to prepare *N*-(*p*-tolyl)- α -acetoxy- α,α -diphenylacetamide (**1**) from *N*-(*p*-tolyl)- α -chloro- α,α -diphenylacetamide (**2**) by a modification of the process of Kagan and Lillien (1) in which the α -chloroamide is treated with silver acetate in anhydrous benzene, we neglected to dry the benzene sufficiently. The major product of the reaction was not the expected α -acetoxyamide but rather it was 5-methyl-3,3-diphenyloxindole (**3**). When the reaction was repeated with anhydrous benzene as solvent, only the α -acetoxyamide was isolated (Scheme 1).



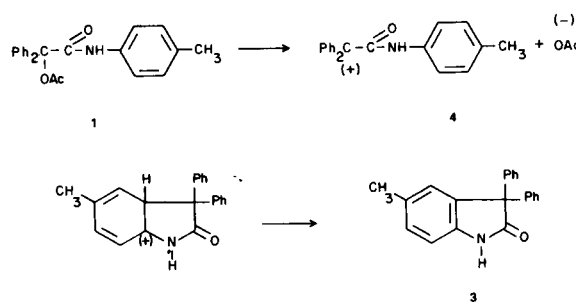
The Reaction of α -Acyloxyamides and Boron Trifluoride Etherate



R	R ¹	% yield
CH ₃ C=O	CH ₃	91
PhC=O	CH ₃	89
CH ₃ C=O	OCH ₃	85
CH ₃ C=O	Br	64
Ph ₂ CHC=O	CH ₃	81

One possible rationale for this observation is that in benzene the α -chloroamide is undergoing dissociation or the α -acyloxyamide is undergoing hydrolysis to give the tertiary carbonium ion **4** which affects an electrophilic attack upon the tolyl ring *ortho* to the amide nitrogen (Scheme 2). However, since we observed that neither *N*-*p*-anisyl nor *N*-*p*-bromo- α -chloro- α,α -diphenylacetamide yielded an oxindole when treated with silver acetate in benzene, the α -acyloxyamide appears to be the substrate leading to oxindole.

Scheme 2



Since several α -acyloxy analogs of **1** are readily available (1,2), a study in which these analogs of **1** were treated with boron trifluoride etherate was initiated. If the Lewis acid catalyzes hydrolysis of these analogs to yield carbonium ions similar to **4**, then cyclization of the carbonium ions should occur to produce oxindoles. The Table shows the results of this study.

The data in the Table shows that, indeed, treatment of α -acyloxydiphenylacetanilides with boron trifluoride etherate produces oxindoles in good yields. This reaction appears to be a novel and a significant route to oxindoles.

EXPERIMENTAL

All melting point determinations were made with a Mel-Temp

apparatus and are corrected. Infrared spectra were determined on a Perkin-Elmer Model 137 instrument in potassium bromide wafers and elemental analyses were performed by the Heterocyclic Chemical Corporation of Harrisonville, Missouri. The mass spectrum was determined on a DuPont Model 490.

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

From *N*-(*p*-tolyl)- α -chloro- α,α -diphenylacetamide.

To a solution of 3.3 g. (0.01 mole) of α -chloro- α,α -diphenyl-*N*-*p*-tolylacetamide in 50 ml. of benzene was added 3.34 g. (0.02 mole) of silver acetate. The flask was protected from the light. The contents were stirred vigorously for 24 hours at room temperature. The benzene solution was filtered, was washed repeatedly with dilute ammonium hydroxide and water, and was dried over sodium sulfate. Concentration of the benzene solution and dilution of the concentrate with petroleum ether caused the precipitation of 5-methyl-3,3-diphenyloxindole, 2.5 g. (84%), m.p. 282-283° (recrystallized from ethyl acetate). The mixture melting point with authentic material (1) was not depressed, and the infrared spectra of an authentic sample and this material were superimposable.

From *N*-(*p*-Tolyl)- α -acetoxy- α,α -diphenylacetamide.

Boron trifluoride etherate (30 ml.) was added to 1.8 g. (5 mmoles) of *N*-(*p*-tolyl)- α -acetoxy- α,α -diphenylacetamide (4) and the resulting mixture was heated to reflux for one hour. The solution was then poured into water, and the product was extracted with methylene chloride. Evaporation of the methylene chloride solution gave 1.36 g. (91%) of 5-methyl-3,3-diphenyloxindole which was recrystallized from ethyl acetate, m.p. 282-283°. The infrared spectrum and melting point were identical with those of an authentic sample.

From *N*-(*p*-Tolyl)- α -benzoy- α,α -diphenylacetamide.

Boron trifluoride etherate (30 ml.) was added to 2.11 g. (5 mmoles) of *N*-(*p*-tolyl)- α -benzoy- α,α -diphenylacetamide (4), and the resulting solution was heated to reflux for one hour. The solution was then poured into water, and the product was extracted with methylene chloride. Evaporation of the methylene chloride solution gave 1.33 g. (89%) of 5-methyl-3,3-diphenyloxindole, m.p. 282-283°. The infrared spectrum and melting point were identical with those of an authentic sample.

From *N*-(*p*-Tolyl)- α -diphenylacetoxy- α,α -diphenylacetamide.

Boron trifluoride etherate (30 ml.) was added to 2.56 g. of

N-(*p*-tolyl)- α -diphenylacetoxy- α,α -diphenylacetamide (4). The resulting solution was heated to reflux for one hour and then poured into water. The product was extracted with methylene chloride. Evaporation of methylene chloride gave 1.21 g. (81%) of 5-methyl-3,3-diphenyloxindole which was recrystallized from ethyl acetate, m.p. 282-283°. The infrared spectrum and melting point were identical with those of an authentic sample.

5-Methoxy-3,3-diphenyloxindole.

Boron trifluoride etherate (30 ml.) was added to 1.87 g. (5 mmoles) of *N*-(*p*-anisyl)- α -acetoxy- α,α -diphenylacetamide (4), and the resulting mixture was heated to reflux for one hour. The solution was then poured into water, and the product was extracted with methylene chloride. Evaporation of the methylene chloride solution gave 1.34 g. (85%) of 5-methoxy-3,3-diphenyloxindole which was recrystallized from ethyl acetate, m.p. 251-252°. Absorptions for the carbonyl groups were at 1710 and 1670 cm^{-1} and the mass spectrum exhibited the parent ion at $m/e = 315$.

Anal. Calcd. for $\text{C}_{21}\text{H}_{17}\text{NO}_2$: C, 80.00; H, 5.39; N, 4.44. Found: C, 80.18; H, 5.41; N, 4.72.

5-Bromo-3,3-diphenyloxindole.

Boron trifluoride etherate (30 ml.) was added to 2.12 g. (5 mmoles) of *N*-(*p*-bromophenyl)- α -acetoxy- α,α -diphenylacetamide, and the resulting mixture was heated to reflux for one hour. The solution was then poured into water, and the product was extracted with methylene chloride. Evaporation of the methylene chloride solution gave 1.16 g. (65%) of 5-bromo-3,3-diphenyloxindole which was recrystallized from ethyl acetate, m.p. 284-285° (lit. m.p. 284° (3)). The ir spectrum and melting point were identical with those of an authentic sample (3).

REFERENCES AND NOTES

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- (2) M. W. Barker and H. Sung, *J. Heterocyclic Chem.*, **13**, 1351 (1976).
- (3) D. A. Petyunin, I. S. Berdinskii and N. G. Panferova, *Ah. Obshch. Khim.*, **27**, 1901 (1957); *Chem. Abstr.*, **52**, 4647h (1958).
- (4) All α -acyloxyamides were made by the reaction of the appropriate ketenimine with pyridine *N*-oxide and the corresponding carboxylic acid (see reference 2) or by the method given in reference 1.