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A CONVENIENT SYNTHESIS OF 1-AROYLISOQUINOLINES

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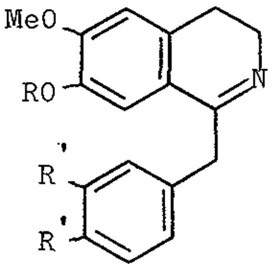
1-Aroylisoquinolines could be conveniently prepared by the oxidation of 1-benzyl-3,4-dihydroisoquinolines or 1-benzylisoquinolines with oxygen and triton B in pyridine.

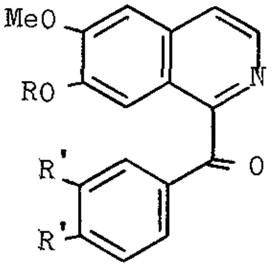
During our study[1] of the model for the synthesis of cancentrine we have found that the carbanion at the benzylic position of 1-benzyl-3,4-dihydroisoquinoline can be effectively generated by the action of triton B in pyridine. From this finding, we have developed a convenient synthesis of 1-aroylisoquinolines.

When a stream of oxygen was passed through a refluxing solution of 1-benzyl-3,4-dihydroisoquinolines (Ia-Ic) in pyridine together with triton B[2] for 26-60 hrs., 1-aroylisoquinolines[3] were isolated in yields shown below after purification by silica gel column chromatography. The generality of the reaction is exemplified by the successful oxidation of compounds (Ia-Ic) to compounds (IIa-IIc). The overall transformation[4] of oxidation and dehydrogenation of 1-benzyl-3,4-dihydroisoquinolines to the corresponding 1-aroylisoquinolines have been previously carried out in two steps with lower overall yields. It is noteworthy that the reaction condition employed allows the required oxidation while the protecting benzyloxy group remains unaffected (Ic to IIc) This is very useful because the normally used oxidation of 1-benzyl isoquinoline with sodium dichromate in acetic acid, competitive oxidation at the methylene carbon of the benzyloxy group is a severe problem[4b].

The same transformation could also be effected by using potassium t-butoxide in anhydrous butanol instead of triton B in pyridine, however the reaction gave lower yield and the inconvenience caused by the requirement of anhydrous condition.



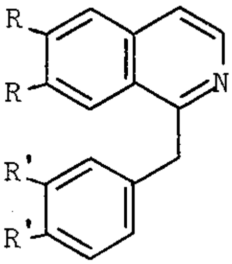
(I)



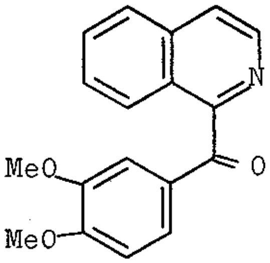
(II)

							yield(%)
a)	R	=	Me,	R'	=	OMe	68.5
b)	R	=	Me,	R'	=	H	66.0
c)	R	=	Bz,	R'	=	OMe	63.6

Triton B in pyridine/oxygen system could also be applied successfully to the oxidation of 1-benzylisoquinoline. For example, oxidation of papaverine (IIIa) with the above system at room temperature for 48 hrs., gave papaveraldine[5] (IIa) in 89% yield. Similar treatment of compound (IIIb) gave compound[6] (IV) in 86% yield.



(III)



(IV)

a) R = R' = OMe

R = H, R' = OMe

When triton B was replaced with cetyltrimethyl ammonium hydroxide (prepared <u>in situ</u> from cetyltrimethylammonium bromide and 50% aqueous sodium hydroxide solution) the same oxidation could be performed in comparable yield, for example papaveraldine could be prepared in 90% yield from papaverine.

Since 1-benzyl-3,4-dihydroisoquinoline with oxygenation substitution at positions 6 and 7 can be easily prepared by the Bischler-Napieralski reaction[7] and 1-benzylisoquinoline (with or without the oxygenation substitution in ring A) can be conveniently prepared from the Reissert compounds[8], our findings have made possible a convenient access to 1-aroylisoquinoline derivatives[9].

References and Footnotes

1 S. Ruchirawat and V. Somchitman, Tetrahedron Lett., in press

2 Triton B was prepared *in situ* from benzyltrimethylammonium chloride and 50% aqueous sodium hydroxide solution.

3 The physical data of all compounds are in full accord with the assigned structure.

4 For example, see T. Kametani, R. Nitadori, H. Terasawa, K. Takahashi and M. Ihara, Heterocycles 1975, 3, 821; b. M. P. Cava and I. Noguchi, J. Org. Chem., 1973, 38, 2291.

5 R.Pschorr, Chem. Ber. 1904, 37, 1926.

6 J. L. Neumeyer and C. B. Boyce, J. Org. Chem. 1973, 38, 2291.

7 For a review, see W. M. Whalley and T. R. Govindachari, Org. React. 1951, 6, 74.

8 For a review, see F. D. Popp in Advances in Heterocyclic Chem. eds. by A. R. Katritzky and A. J. Boulton, Academic Press, 1968 v. 9, p. 1.

9. For the previous syntheses and synthetic utilities of 1-aroylisoquinolines, see refs. 4, 5, 6 and J. Knabe and A. Frie, Arch. Pharm. 1973, 306, 648; H. Reimlinger, J. J. M. Vandewalle, W. R. F. Lingier and E. de Ruiter, Chem. Ber. 1975, 108, 3771; H. Reimlinger, W. R. F. Lingier and R. Merenyi, Chem. Ber. 1975, 108, 3794; and references cited therein.

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