

One Step Synthesis of 3,4-Dihydro-2H-1,3-oxazines

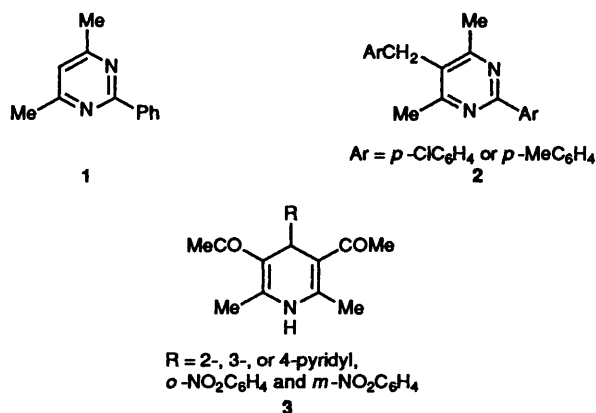
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2,4,5,6-Tetrasubstituted-3,4-dihydro-2H-1,3-oxazines 4–9 have been synthesized by condensing acetylacetone or ω -phenylsulfonylacetophenone with aryl aldehydes and ammonium acetate.

Among the four possible dihydro-1,3-oxazines, quite a large number of studies have been undertaken on three systems *viz.* 5,6-dihydro-4H-1,3-oxazines, 5,6-dihydro-2H-1,3-oxazines and 3,6-dihydro-2H-1,3-oxazines. These oxazine derivatives have been widely used as herbicides,¹ gasoline antioxidants,² and in the preparation of non-ionic polymer surfactants.³ However, very little work has been reported on 3,4-dihydro-2H-1,3-oxazines due to the lack of synthetic methods for this system. So far, only two methods involving many steps have been reported for the synthesis of 3,4-dihydro-2H-1,3-oxazines;⁴ in this communication we report a one step synthesis of such compounds by condensing compounds possessing an active methylene group adjoining a carbonyl group with aryl aldehydes and ammonia. We have employed acetylacetone and ω -phenylsulfonylacetophenone for this condensation.

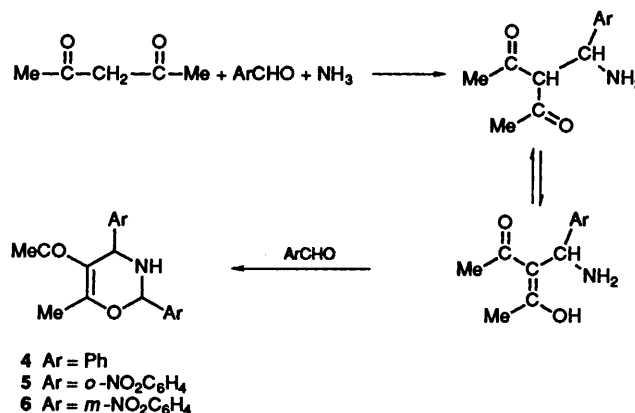
Although the condensation of acetylacetone with aryl aldehyde and ammonia has been reported previously, only 2,4,6-trisubstituted pyrimidines 1,⁵ 2,4,5,6-tetrasubstituted pyrimidines 2⁶ and 1,4-dihydropyridines 3⁷ were obtained.



We have obtained 5-acetyl-2,4-diaryl-6-methyl-3,4-dihydro-2H-1,3-oxazines 4–6 with yields greater than 90% by condensing acetylacetone with aryl aldehyde and ammonium acetate in the mole ratio 1:2:1 in 95% ethanol. A possible mechanism for this condensation is given in Scheme 1. Under similar conditions, *p*-chloro- and *p*-nitro-benzaldehydes did not give oxazines; prolonged refluxing of the reaction mixture yielded only 2.

Since formation of 1 and 2 require two carbonyl groups whereas the formation of 4–6 require only one carbonyl group, we tried similar condensations employing PhSO₂CH₂COPh instead of acetylacetone and obtained 2,4-diaryl-6-phenyl-5-phenylsulfonyl-3,4-dihydro-2H-1,3-oxazines 7–9 in good yields, after refluxing the reaction mixture for about 8 h.

The structure of compounds 4–7 were elucidated by C,H analysis and IR and ¹H and ¹³C NMR spectroscopy. Structures of compounds 8 and 9 were confirmed by C,H analysis and IR spectra. The physical data for compounds 4–9 are given in



Scheme 1

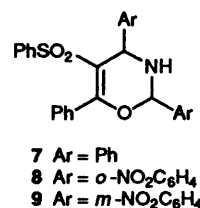


Table 1. The spectroscopic data for compounds 4–7 are available from the British Library as a Supplementary Publication† (SUP. PUBL. NO. 56889).

Experimental

5-Acetyl-2,4-diaryl-6-methyl-3,4-dihydro-2H-1,3-oxazines 4–6.—A mixture of acetylacetone (5 g, 0.05 mol), aryl aldehyde (0.1 mol) (Ar = Ph, *o*-NO₂C₆H₄ and *m*-NO₂C₆H₄), and ammonium acetate (3.9 g, 0.05 mol) in 95% ethanol (40 cm³) was refluxed until the reaction mixture turned orange (about 15–30 min). The reaction mixture was cooled to room temp. The separated product was recrystallized from ethanol.

Under similar conditions, *p*-chloro- and *p*-nitro-benzaldehydes did not give any solid product. However, on refluxing the reaction mixture for about 8 h and cooling the reaction mixture to room temp. they gave compound 2.

2,4-Diaryl-6-phenyl-5-phenylsulfonyl-3,4-dihydro-2H-1,3-oxazines 7–9.—A mixture of ω -phenylsulfonylacetophenone⁸ (12.9 g, 0.05 mol), aryl aldehyde (0.1 mol) (Ar = Ph, *o*-NO₂C₆H₄ and *m*-NO₂C₆H₄) in 95% ethanol (50 cm³) was refluxed for about 8–10 h. The reaction mixture was cooled to

† For details of the British Library Supplementary Publication Deposition Scheme see 'Instructions for Authors,' *J. Chem. Soc., Perkin Trans. 1*, 1992, Issue 1.

Table 1 Physical data for compounds 4-9

Compound	Yield (%)	M.p. ($T/^{\circ}\text{C}$)	Molecular formula	Found (%)		Calculated (%)	
				C	H	C	H
4	92	173	$\text{C}_{19}\text{H}_{19}\text{O}_2\text{N}$	77.7	6.6	77.78	6.53
5	90	190	$\text{C}_{19}\text{H}_{17}\text{O}_6\text{N}_3$	59.4	4.6	59.52	4.47
6	95	183	$\text{C}_{19}\text{H}_{17}\text{O}_6\text{N}_3$	59.7	4.6	59.52	4.47
7	80	160	$\text{C}_{28}\text{H}_{23}\text{NO}_3\text{S}$	73.9	5.2	73.48	5.11
8	80	132	$\text{C}_{28}\text{H}_{21}\text{N}_3\text{O}_7\text{S}$	62.5	3.8	61.66	3.92
9	65	153	$\text{C}_{28}\text{H}_{21}\text{N}_3\text{O}_7\text{S}$	62.9	3.8	61.66	3.92

room temp. The separated product was recrystallized from ethanol.

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