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ENOLATES OF o-HYDROXYACETOPHENONES: NOVEL SYNTHESIS OF 2, 2-DIALKYL-4-CHROMANONES

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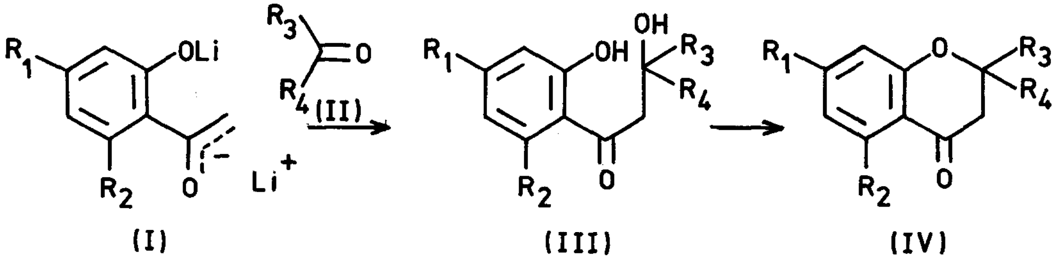
The reactions between anions derived from substituted o-hydroxyacetophenones with electrophilic carbons of ketones, aldehydes and esters are of great importance in syntheses of oxygen-heterocycles wherein a wide variety of bases under different experimental conditions have been utilised.[1] In recent years, strong bases with low nucleophilicity have been extensively used for the preparation of enolates from carbonyl compounds.[2] We have found that lithium enolates (I) of o-hydroxyacetophenones can be generated under mild conditions using lithium diisopropylamide and their reactions with different electrophiles have been studied. In this communication the reactions of enolates (I) with different ketones (II) are reported. The cross aldol condensation products (III) thus obtained, undergo facile cyclodehydration to give 2, 2-dialkyl-4-chromanones (IV) in high yields.



The lithium enolate (I) was obtained by addition[3] of appropriate o-hydroxyacetophenone (2 mmol) to a solution of lithium diisopropylamide[4] (5 mmol) in THF at -25°. After stirring for 1 hr, the temperature was lowered to - 40° and the ketone (II) (2.5 mmol) was added and the mixture was stirred for another 1.5 hr. The reaction mixture was acidified to pH 3 by cautious addition of 1:1 aqueous HCl and worked up in the usual way. The reaction product (III) was isolated either by column chromatography (SiO_2) or by short path distillation and characterised.[5] The cross condensation products (III) underwent facile cyclodehydration on refluxing (2 hr) with methanolic HCl (10%) to give 2, 2-dialkyl-4-chromanones (IV) in high yields.[5] Some representative results are shown in the Table.

TABLE

				III			IV		
R_1	R_2	R_3	R_4	% Yield	b.p.	m.p.	% yield;	b.p.	m.p.
H	H	CH_3	CH_3	95	156°/15mm		90		86°-88°
H	H	CH_3	C_2H_5	85	142°/6 mm		77	120°/5mm	
H	H	CH_3	i-C_4H_9	65	156°/6 mm		68	134°/6mm	
H	H	CH_3	n-C_3H_7	92	136°/5 mm		82	128°/6mm	
H	H	n-C_3H_7	n-C_3H_7	67	166°/6 mm		78	146°/6mm	
OCH_3	OCH_3	CH_3	CH_3	80		71°	80		105°
OCH_3	H	CH_3	CH_3	80	162°-4°/6mm		80		78°

As can be seen from the Table, this method is of general applicability for the synthesis of 2, 2-disubstituted 4-chromanones. These are synthons for the preparation of chromans and chrom-3-enes which show interesting photochromic[6] and biological activities.[1, 7] Further, the starting materials are easily accessible and the low temperature employed, precludes self condensation giving neat reaction products.

REFERENCES AND NOTES

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3. Flame dried glasswares were used. THF was freshly distilled over LAH. Reactions were carried out in oxygen-free dry argon atmosphere. All solution transfers were carried out using hypodermic syringes via septum caps. The pregress of the reactions were monitored by TLC.
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5. All the compounds gave satisfactory microanalytical values. The spectral data (MS, PMR, IR, UV) were consistent with the assigned structures.
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7. e.g. W.S. Bowers, T. Ohta, J.S. Cleere and P.A. Marsella, Science, 193, 542 (1976); R.K. Razdan, in "Progress in Organic Chemistry", (J. Cook and W. Carruthers, eds.) Vol. 8, Butterworths, London, 1973, p. 78.

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