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Reisert Compound Studies. VI. The Condensation of Aldehydes With 2-Benzoyl-1,2-dihydroisoquinaldonitrile (1,2)

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In 1958 McEwan and coworkers (4) reported the condensation of the lithium salts of 1-benzoyl-1,2-dihydroquinaldonitrile and 2-benzoyl-1,2-dihydroisoquinaldonitrile (I) with aldehydes to form esters of secondary alcohols containing the 2-quinoyl or 1-isoquinoyl (II) group bonded to the carbinol carbon atom. This method was used to devise from appropriate Reissert compounds a convenient synthesis of papaverinol (5) and some attractive intermediates for eventual conversion to the ipecac alkaloids (6).

If the appropriate aldehydes could be caused to react with the lithium salt of I, this synthesis could play an important part in synthetic sequences leading to a number of alkaloids and alkaloid-like compounds. In particular the use of benzaldehydes containing nitro-, bromo-, and hydroxy- groups would be necessary. None of these substituents were reported in the previous study (4) of this reaction. Since 4-chloro- and 2,6-dichlorobenzaldehyde were successfully used (4), no problems were anticipated in the case of the bromobenzaldehydes. The hydroxybenzaldehydes, however, could be expected to cause difficulty since the presence of the strongly electron donating dimethylamino- group in the 4-position of benzladehyde caused the yield to drop to zero (4).

The results of this study on the condensation of aldehydes with the anion of I to yield esters (II) are included in Table I. While the benzaldehydes with nitro- and bromo- substituents did not lead to any trouble, both 4-hydroxybenzaldehyde and vanillin failed to react. It was felt that if the electron donating power of the hydroxy-group on the aromatic ring could be reduced by some group that could be removed at a later point in a synthetic sequence that the reaction might be useful. Conversion of 4-hydroxybenzaldehyde to its benzoate ester gave an aldehyde which condensed with the anion of I to give the desired ester. The yield in this condensation was quite low and the product was difficult to purify. The conversion of the hydroxy-group to a benzyloxy- group proved to be of much greater value. The benzyloxybenzaldehydes were all converted to the expected esters (II) in good yields.

EXPERIMENTAL

Preparation of Aryl-1-isoquinolylcarbinyl benzoates.

To a solution of 0.04 mole of 2-benzoyl-1,2-dihydroisoquinaldonitrile in 150 ml. of anhydrous ether and 75 ml. of anhydrous dioxane maintained at -30° in a nitrogen atmosphere was added with stirring an ether solution of a slight excess of phenyl lithium. To the resulting red solution was added dropwise with stirring a solution of 0.04 mole of an aldehyde in ether. The mixture was stirred in the cold for an hr. and then at room temperature for 12 hrs. Ether was added and the mixture was washed with water, 0.5 N hydrochloric acid, and water. Removal of the solvent gave the product which was recrystallized to give the substances listed in Table I.

REFERENCES

(1) Part V, F. D. Popp and A. Soto, *J. Chem. Soc.*, 1760 (1963).

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(3) N. D. E. A. Fellow.

(4) L. R. Walters, N. T. Iyer, and W. E. McEwen, *J. Am. Chem. Soc.*, 80, 1177 (1958).

(5) F. D. Popp and W. E. McEwen, *ibid.*, 79, 3773 (1957).

(6) F. D. Popp and W. E. McEwen, *ibid.*, 80, 1181 (1958).

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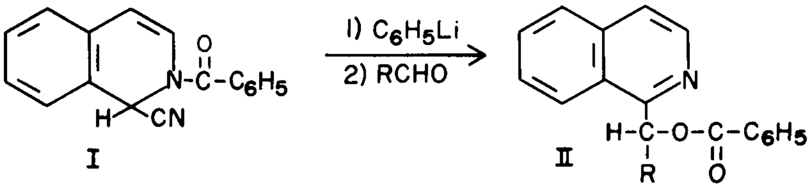
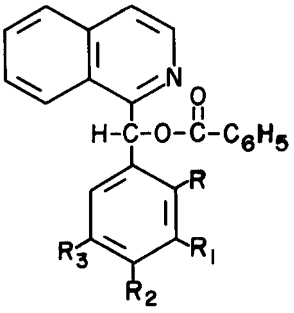


Table I

Aryl-1-isoquinolylcarbinyl benzoates



R	R_1	R_2	R_3	Yield, %	M.p.	Analysis (a) Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
-	-	OH	-	0	-						
-	-	$OCO\phi$	-	11	138-140 (b)	78.42	4.61	3.05	77.98	4.21	2.82
-	-	$OCH_2\phi$	-	40	151-153 (c)	80.88	5.20	3.14	80.78	5.25	2.78
-	OCH_3	OH	-	0	-						
-	OCH_3	$OCH_2\phi$	-	50	148-149 (c)	78.30	5.30	2.95	78.03	5.44	2.97
-	Br	$OCH_2\phi$	-	59	171-173 (d)	68.71	4.23	2.67	68.47	4.12	2.72
-	OCH_3	$OCH_2\phi$	Br	66	144-145 (e)	67.15	4.36	2.53	67.18	4.22	2.39
$OCH_2\phi$	OCH_3	-	-	54	141-144 (c)	78.30	5.30	2.95	77.82	5.18	3.03
OCH_3	OCH_3	-	-	74	188-190 (e)	75.17	5.30	3.51	74.92	5.13	3.40
-	OCH_3	-	-	66	141-142 (c)	78.03	5.18	3.79	77.73	5.07	3.90
-	$-C-CH_2-O-$		-	81	158-159 (c)	75.18	4.47	3.65	74.85	4.36	3.45
-	Cl	Cl	-	70	156-158 (e)	67.66	3.70	3.43	67.66	3.70	3.42
-	-	NO_2	-	54	202-203 (e)	71.87	4.20	7.29	71.82	4.01	7.38
-	NO_2	-	-	37	130-132 (f)	71.87	4.20	7.29	71.68	3.98	7.15
NO_2	-	-	-	48	200-201 (d)	71.87	4.20	7.29	71.42	4.00	7.55
NO_2	-	OCH_3	OCH_3	26	199-200 (g)	67.56	4.54	6.30	67.27	4.33	6.51
-	-	Br	-	91	162-163 (e)	66.04	3.86	3.35	65.89	3.90	3.52
-	Br	OCH_3	-	89	147-148 (e)	64.30	4.05	3.12	63.92	4.37	3.17
Br	-	OCH_3	OCH_3	82	154-155 (c)	62.77	4.21	2.93	62.33	3.96	3.04

(a) Analyses by Spang Microanalytical Laboratory, Ann Arbor, Mich. and Drs. Weiler and Strauss, Oxford, England. (b) recrystallized from ethanol-dioxane-water. (c) recrystallized from ethanol. (d) recrystallized from dioxane. (e) recrystallized from ethanol-dioxane. (f) recrystallized from benzene. (g) recrystallized from ethanol-benzene.