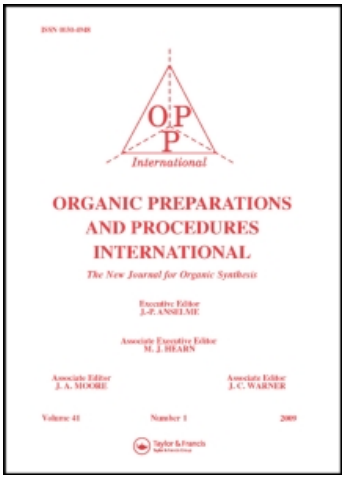

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STUDIES ON DIHYDROISOCOUMARIN (II).
A NOVEL STOBBE-LIKE CONDENSATION CATALYZED BY 1,8-DIAZABICYCLO[5.4.0]-UNDECENE-7 (DBU)

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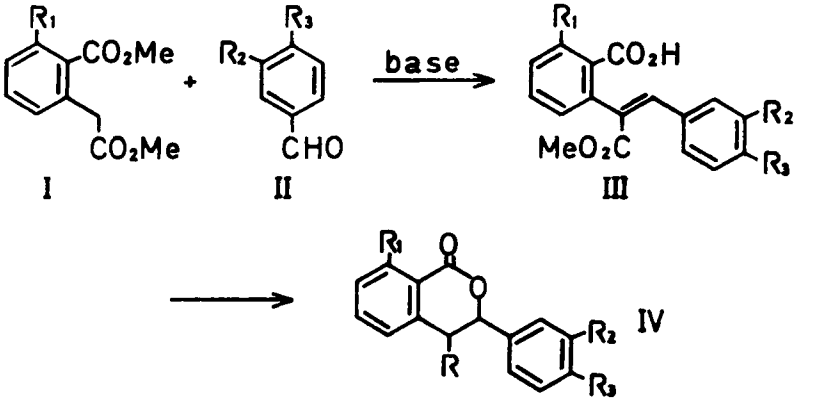
The condensation of diesters of homophthalic acid with aromatic aldehydes followed by cyclization, has provided a convenient route to 3-aryldihydroisocoumarin derivatives (IV). Thus, the reaction of dimethyl homophthalate (I, R_1 = H) with benzaldehyde[1] and piperonal[2] gave excellent yields



of the cinnamic esters (III) which were subsequently cyclized to the dihydroisocoumarins (IV). However, an

attempted condensation of dimethyl homophthalate with 3-hydroxy-4-methoxybenzaldehyde (II, R_2 = OH and R_3 = OCH_3) and 3-benzyloxy-4-methoxybenzaldehyde (II, R_2 = OCH_2Ph, R_3 = OCH_3) gave practically none of the corresponding cinnamates when common bases such as sodium hydride, alkoxide, etc. were used. Yamato et al.[3] were able to obtain a 15 % yield of IV (R_1 = H, R_2 = OH, R_3 = OCH_3) by carring the condensation of dimethyl homophthalate with 3-hydroxy-4-methoxybenzaldehyde in the presence of potassium acetate at elevated temperatures. In view of its mild and highly specific proton accepting ability[4], 1,8-diazabicyclo [5.4.0]-undecene-7 (DBU) was tried as a condensation catalyst and the results were completely satisfying as shown in Table I.

Table I. DBU-catalyzed Condensation of I with II.

	R_1	R_2	R_3	Mole ratio of DBU	Reaction time (hrs)	Reaction temp.[a]	Yield of III (%)
(a)	H	OCH_2Ph	OCH_3	1	6	reflux	70
(b)	H	$-OCH_2O-$		1	6	reflux	75
(c)	OH	OCH_2Ph	OCH_3	2	10	60°	80[b]
(d)	OCH_3	OCH_2Ph	OCH_3	1	6	reflux	57

a) Benzene is used as solvent; b) Isolated as the dicarboxylic acid after alkaline hydrolysis of IIIc.

Table II. Mps and Elemental Analyses

Compound	mp. (from MeOH)	Elemental Analysis Calculated	Found
IIIa	152-153°	C, 71.76	72.08
		H, 5.30	5.55
IIIb	Identical to product reported in ref.[2]		
IIIc	202-203°	C, 67.12	67.52
		H, 4.93	5.13
IIId	176-177°	C, 69.63	70.08
		H, 5.39	5.18

Table III. Spectral Data of Cinnamic Acid Derivatives.

Compound	IR (cm^{-1}) $\nu_{C=O}$	NMR (τ Value) other	ArH	vinyl	CH_2	CH_3 (ether)	CH_3 (ester)
IIIa	1680	0.5	1.7-3.3	3.7	5.7	6.25	6.34[a]
	1700	(1,COOH)	(12)	(1)	(2)	(3)	(3)
IIIc	1675	5.4	2.2-3.3	3.5	6.3	6.85	——[b]
		(1,ArOH)	(11)	(1)	(2)	(3)	
IIId	1690	——	2.3-3.2	3.3	5.4	6.2 6.3	6.4[b]
			(11)	(1)	(2)	(3,3)	(3)

a) In $CDCl_3$; b) In d_6-DMSO

EXPERIMENTAL

The IR spectra were taken on a Nippon Bunko model IR-G-spectrometer; The nmr spectra were obtained on a Hitachi-Perkin Elmer R-20A spectrometer, and the elemental analyses were determined on a Perkin Elmer 240 Analyzer.

General procedure; 2-Carboxy-3'-benzyloxy-4'-methoxy-α-carbomethoxy stilbene (IIIa). - To a solution of 208 g. (1

mole) of dimethyl homophthalate and 152 g. (1 mole) of DBU in 600 ml. of dry benzene was added 160 g. (0.66 mole) of 3-benzyloxy-4-methoxybenzaldehyde (benzylisovaniline) dissolved in 500 ml. of dry benzene and then the mixture was refluxed for 4 hrs. After cooling, the reaction mixture was cautiously acidified to pH 5 with glacial acetic acid, then washed with 100 ml. of water. The organic layer was extracted with 5 % aqueous sodium carbonate. The aqueous extract was washed with ether, then acidified with glacial acetic acid. Compound IIIa (193 g. 70 %) precipitated as white crystalline powder. This powder was recrystallized from methanol to give 165 g. (60 %), mp. 152-153°.

2-Carboxy-3'-benzyloxy-4'-methoxy-α-carboxy stilbene. - A solution of 64 g. (0.15 mole) of IIIa in 600 ml. of 2N NaOH was boiled under reflux for 4 hrs. After cooling, the reaction mixture was acidified with conc. hydrochloric acid. The precipitate was recrystallized from methanol to yield 62 g. (100 %), mp. 202-203° (dec.).

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* To whom inquiries should be directed.

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