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A CONVENIENT SYNTHESIS OF 4-SUBSTITUTED PARACONIC ACIDS

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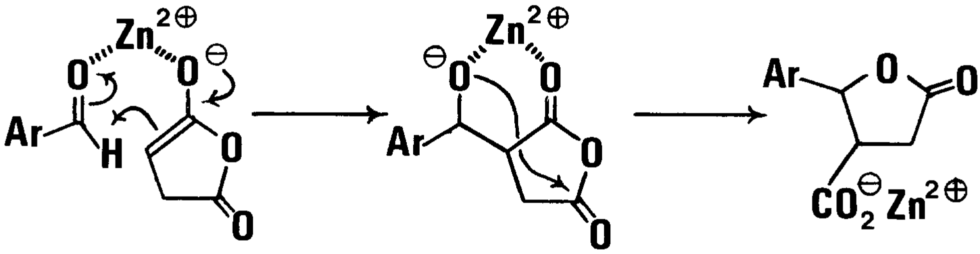
Abstract. *A mixture of zinc chloride and triethylamine effects the condensation of aryl aldehydes and of ketones with succinc anhydride to give paraconic acids.*

The Stobbe condensation is very general for aryl aldehydes but the yields of itaconic acid half-esters leave much to be desired[1]. The yields are commonly between 40% and 50% and seldom reach, let alone exceed, 60%. It is believed that much of the aldehyde is wasted by redox reactions (Cannizzaro, reduction by alkoxide ions or by the enolate ion of the succinic diester). A better way of condensing the succinic moiety with aryl aldehydes is desireable.

The combination of triethylamine and a catalytic quantity of zinc chloride is a well-established agent for the preparation of enol silyl ethers. An extreme example of this kind of silylation was the preparation of 2,5-bis(trimethylsiloxy)furan from succinic anhydride[2]. The use of an aldehyde instead of trimethylsilyl chloride to trap the zinc monoenolate of succinic anhydride was expected to give a zinc paraconate:-



This expectation was tested with a number of aryl aldehydes.

General procedure. Zinc chloride (20 to 22 mmole, dried in situ with thionyl chloride), succinic anhydride (15 mmole) and aryl aldehyde (10 mmole) were suspended in dry dichloromethane (12 cm^3). The stirred suspension was treated over a period of 5 minutes with triethylamine (20 mmole). The mixture became warm and nearly homogeneous ($ZnCl_2.Et_3N$ is soluble in CH_2Cl_2). The mixture was protected from moisture and was stirred gently for 20 to 24 hr. The solution was mixed with 2M hydrochloric acid (~ 20 cm^3) and ethyl acetate (~ 20 cm^3). After the organic phase had been washed with brine, the paraconic acids were isolated via extraction with aqueous $NaHCO_3$. The products were identified as paraconic acids by their neutralisation equivalents and by their ^{1}HMR spectra (which showed that they were E:Z mixtures). All the products gave satisfactory elemental analyses.

The yields of the paraconic acids obtained by this variation of the Perkin-Fittig condensation[3,4] are good (Table); much better than the yields of the Perkin-Fittig condensation itself and better than the yields of the corresponding Stobbe condensation products. Further advantages over the Stobbe procedure are the simplicity of the method and the ease of isolation of nearly pure products.

The yields of paraconic acids from ketones (Table) probably will be less satisfactory in general but the convenience of the method may compensate for moderate or poor yields when the ketone is cheap or easily recoverable. It is possible that more exotic Lewis acids, such as stannous triflate[6], may give better results. [The use of highly hindered, powerful bases at low temperature[7] gave results no better than those reported here.]

Table

Aldehyde or Ketone	Crude Paraconic Acid		
	yield (%)	n.e.	mp
Piperonal	88	249	135-143° (d)
Veratraldehyde	83	266	142-145° (d)
2,4-Dimethoxybenzaldehyde	88	264	85-115° (d)
2,4-Dimethoxy-5-methylbenzaldehyde	85	277	139-143° (d)
O-Benzylvanillin	87	341	112-119° (d)
4-Nitrobenzaldehyde	78	254	146-184°
Benzophenone	36	283	190-1° (d)
Fluorenone	98	282	187-190° (d)
Cyclohexanone	50	198	184-5° (d)[5]

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