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METALATED CARBOXYLIC ACIDS V. THERMAL CONDENSATION OF SILYLATED KETENE ACETALS WITH AROMATIC ALDEHYDES

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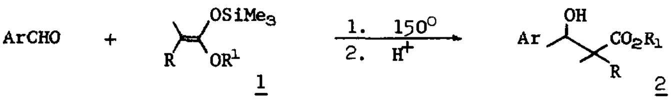
Metalated carboxylic acids react with carbonyl compounds with varying success depending upon steric effects in each of the reaction partners.[1] Given a delocalized structure for the metalated intermediate,[2] addition to a carbonyl group is the result of a reorganization of the double bonds in the reactants. The reaction can be more formally represented by use of silylated ketene acetals,[3] 1, where the product of the bond reorganization would be trapped by intermolecular transfer of the mobile trimethylsilyl substituent. Hydrolysis to the hydroxy acid (ester), in this case, may be accomplished in neutral or mildly acidic conditions which could be expected to avoid product dissociation as reported for base hydrolysis of Reformatsky products.[3]



Despite related reports[5,6] which anticipated the general design of the reaction shown, the present sequence derives importance from the stability and availability of 1 with a range of substituents.[2,4] Model examples studied are summarized in the Table.

The course of the thermal reorganization was established with a model probe using benzaldehyde and 1 ($R = Me$, $R_1 = SiMe_3$) in a sealed nmr tube. Only traces of product were detected after 16 hr at 100°, and the reaction was ca. 50% complete after 6 hr at 150°. Long reaction times (72 hr, 150°) showed no adverse effect. Yields illustrated in the Table on a 50 mmol scale resulted from exposure of the reactants to standard conditions (150°, 18 hr) adopted for benzaldehyde as an average case.

The thermal condensation appeared to be potentially capable of near quantitative conversion to product based on the nmr probe experiments. However, use of the standard conditions on a preparative scale revealed unreacted aldehyde in cases with electron contributing substituents (Examples 5, 6). Example 8 (Table) was obtained as a mixture of isomers which was not separated.

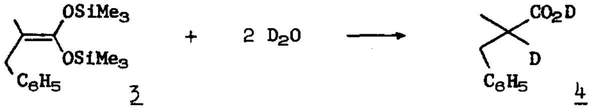
Thermal Condensation Products, 2, from 1 and Aromatic Aldehydes

Example	Ar	R	R_1	Yield	m. p. [b. p.]
1	C_6H_5	Me	H	68	131-132°
2	C_6H_5	Me	Me	81	[100-3°(0.50mm)]
3	m-$O_2NC_6H_4$	Me	H	86	142-4°
4	p-$O_2NC_6H_4$	Me	Me	78	114-6°
5	p-$MeOC_6H_4$	Me	Me	62	79-81°
6	a	Me	Me	65	[129-132°(.01mm)]
7	b	Me	H	61	[133-135°(.02mm)]
8	C_6H_5	$C_6H_5CH_2$	H	63	114-140°

a = Piperonyl b = 1-Naphthyl

Cyclopentanone failed to react with 1 ($R = R_1 = Me$) at reflux (130°). Phenylacetaldehyde suggested multiple outcomes and acetophenone failed to react completely at 200°. Preparative scale experiments, therefore, were not attempted. Thus, without an added catalyst,[5,6] the reaction may be restricted to aromatic aldehydes.

Silylated ketene acetals, 1, are remarkably stable thermally and hydrolytically which permits simple storage. Hydrolytic stability was determined by treating a THF solution of 3 with D_2O. After 12 hrs at ambient temperature, 55-60% of 3 remained, and, after another 4 hr at reflux, 2% of silicon bound methyl was detected in the nmr spectrum of 4.



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