

On the Preparation of Dibenzylidene-succinic Acid by the Stobbe Condensation

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The synthesis of dibenzylidenesuccinic acid (*1*) from benzaldehyde and diethyl succinate *via* the Stobbe condensation is a well-known procedure.¹ However, when the literature directions were followed, the crude product was invariably a dark-brown syrup from which it was difficult, and in some cases even impossible, to isolate the crystalline acid. Yields were low, less than 20 %, as was indeed noted previously.^{1,2}

The bases used in the early work were sodium alkoxides or sodium metal. The often superior base, sodium hydride, introduced by Johnson³ with excellent results in the condensation of ketones, had not been tried before in the synthesis of *1*. In the hope of finding a cleaner and higher-yielding synthetic procedure for *1*, needed for studies of the electrohydrocyclization reaction,⁴ a series of condensations under different conditions was undertaken with this base. The experiments were performed on a 0.01 molar scale in five solvents; hexane, toluene, diethyl ether, dimethylformamide (DMF) and dimethyl sulfoxide (DMSO). Sodium ethoxide in ethanol was included for a comparison with the conventional method. The results are summarized in Table 1, the most striking feature of which is that yields are the same and relatively high in the three nonpolar solvents and considerably lower in the two polar ones (DMF and DMSO) where substantial amounts of tar were formed. Only a small temperature effect is noticeable and in con-

trast to a previous report,⁴ higher temperatures seem to be favourable.

Table 1 further shows the relative product composition of the different runs. The main byproducts are monobenzylidenesuccinic acid (*2*) and benzoic acid (*3*). The run in refluxing toluene was performed twice, showing good interexperimental reproducibility.

Benzoic acid (*3*) is a prominent product in most cases which means that part of the aldehyde is removed from the reaction. It may be formed either by air oxidation or a Cannizzaro reaction, the latter possibility being suggested by Stobbe.^{5a} This was confirmed by the results obtained in a run carried out in a nitrogen atmosphere. Benzyl alcohol, the second product from the Cannizzaro reaction, was detected in this case too. The amount of *3* was similar to that formed in an air atmosphere (see entry 1, Table 2). One presumably has to accept *3* as an unavoidable byproduct since it is difficult to see how one could suppress the Cannizzaro reaction. There is obviously no need for an inert atmosphere as has been prescribed in some published procedures.^{3,6} The fact that ketones work so much better than aldehydes in the Stobbe condensation may depend on their lack of sensitivity to oxidative side-reactions.

The amount of *2* in the product mixture is usually between 15 and 20 %. One reason for the fact that *2* does not react further to give *1* might be the loss of aldehyde in the Cannizzaro reaction. Two experiments were therefore performed to see if a doubled molar ratio of base and aldehyde to ester would be advantageous (entries 2 and 3, Table 2). A consequence of the large amount of aldehyde used is then that the product mixture consists of predominantly *3*. The ratio of *1/2* is unchanged in the two cases. The yield of *1* has, however, been increased from 41 to 60 % when cold ether was used as a solvent. In refluxing toluene, the yield is the same (56 *vs.* 52 %).

The effect of doubling only the ratio of base

Table 1. Yield of products from the Stobbe condensation of benzaldehyde and diethyl succinate, using sodium hydride as the base.

Solvent	Absolute yield ^a of <i>1</i> /%		Relative product composition/%							
	Reflux temperature ^b	Low temperature ^c	Reflux temperature ^b				Low temperature ^c			
			<i>1</i>	<i>2</i>	<i>3</i>	Others	<i>1</i>	<i>2</i>	<i>3</i>	Others
Hexane	54	43	54	17	11	18	50	13	23	14
Toluene	52	44	52; 51	14; 17	5; 5	29; 27	55	12	20	13
Diethyl ether	50	41	55	16	13	16	41	15	30	14
Dimethyl sulfoxide	10	7 ^d	29	20	20	31	8	26	10	56
Dimethylformamide	22	5	48	14	16	22	6	23	31	40
Ethanol ^e	5	7	10	26	37	27	13	10	57	20

^a Determined by GLC after esterification with methanol. ^b Reflux time, 3 h. ^c Kept at 3 °C for 48 h and room temperature for 24 h. ^d Kept at room temperature for 72 h. ^e Sodium ethoxide as base.

Table 2. Yield of products from the Stobbe condensation of benzaldehyde and diethyl succinate using sodium hydride as the base, under different reaction conditions.

Entry No.	Reaction conditions (see also text)	Absolute yield of 1/%	Relative product composition/%			
			1	2	3	Others
1	Under N ₂ in ether at 3 °C	46	51	14	19	16
2	4.4 mol of PhCHO and NaH/2 mol of ester; in ether at 3 °C	60	34	8	49	9
3	Same as 2 but in refluxing toluene	56	40	10	31	19
4	4.4 mol of base/2 mol of ester in refluxing toluene	40	42	15	15	27
5	Normal addition of components; hexane, 20 °C	45	57	8	10	25
6	Inverse addition of components; hexane, 20 °C	14	19	1	13	67
7	NaH, 60 % in mineral oil, instead of 100 %; refluxing toluene	38	39	16	8	37
8	Crown ether added; refluxing toluene	38	44	19	11	26

to ester was also studied. The effect (entry 4, Table 2) was to lower the yield of 1 and increase the occurrence of side-reactions, while the amount of 2 was unaffected.

In normal practice, a mixture of the ester and aldehyde is added to the base. Therefore there is a large excess of base in the beginning of the reaction and, as just noted, such conditions are unfavorable. In another variation of the reaction conditions, inverse mixing of the reactants was employed. Solid sodium hydride was then added to a solution of diethyl succinate and benzaldehyde in hexane. A drastic reduction in the yield of 1 is noted (entries 5 and 6, Table 2) contrary to expectations.

As is seen from entry 7, Table 2, the use of 60 % sodium hydride in mineral oil instead of the 100 % powder lowers the yield of 1. The addition of dibenzo-6-crown-18 did not improve the yield of 1 (entry 8, Table 2).

Summarizing, the Stobbe condensation of benzaldehyde and diethyl succinate to give dibenzylidenesuccinic acid, using sodium hydride as the base, is favored in nonpolar solvents at higher temperatures. There is no need to use an inert atmosphere, since the process removing aldehyde from the Stobbe condensation is the Cannizzaro reaction.

Experimental. GLC analyses were performed on a Hewlett-Packard 5830A instrument equipped with a 2 m × 3 mm 3 % OV-17 on Chromosorb W column.

The standard procedure for performing the Stobbe reaction was as follows: Diethyl succinate (1.76 g, 10 mmol) and freshly distilled benzaldehyde (2.34 g, 22 mmol) were mixed and added to a slurry of 100 % sodium hydride (0.54 g, 22 mmol) in the appropriate solvent (20 ml). Absolute ethanol (ca. ten drops) was added. The solution was either refluxed for 3 h

or kept at 3 °C for 48 h and then at room temperature for 24 h. The solvent was evaporated, the residue refluxed with 10 ml of 0.1 M aqueous KOH for 1 h, and the resulting solution extracted twice with ether. After acidification of the aqueous layer, the organic material was extracted with three portions of ether. The combined ether extracts were dried, and the ether evaporated. The mixture of acids (1–3) was then esterified with methanol/sulfuric acid in the usual way.

Deviations from this procedure are indicated in Table 2. In the experiment with dibenzo-6-crown-18, this compound was added in an amount equimolar with sodium hydride.

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1. a. Stobbe, H. and Naoum, P. *Ber. Dtsch. Chem. Ges.* 37 (1904) 2240; b. Freudenberg, K. and Kempermann, T. *Justus Liebigs Ann. Chem.* 602 (1957) 184.
2. a. Baddar, F. G., El-Assal, L. S. and Gindy, M. J. *Chem. Soc.* (1948) 1270; b. Cordier, M. P. *Ann. Chim.* 15 (1931) 228.
3. Daub, G. H. and Johnson, W. S. *J. Am. Chem. Soc.* 72 (1950) 501.
4. Andersson, J. and Ebersson, L. *Submitted for publication.*
5. Johnson, W. S., McCloskey, A. L. and Cunnigan, D. A. *J. Am. Chem. Soc.* 72 (1950) 514.
6. Heller, H. G. and Swinney, B. *J. Chem. Soc. C* (1967) 2452.

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