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IMPROVED ORGANIC-INORGANIC CONTACT IN THE BENZOIN CONDENSATION

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The successful completion of synthetic organic reactions involving an inorganic reactant hinges upon proper intimate contact between the inorganic, often water-soluble, species and the organic, often water-insoluble, species. To achieve a proper degree of organic-inorganic contact, chemists often resort to techniques such as mixed solvents, high temperatures or both. However, these techniques can generate other problems such as multiple reaction pathways, rearrangements, solvent interaction, etc.

As Brändström has indicated,[1] most organic chemists have ignored the use of tetraalkylammonium salts in planning syntheses. Indeed, except for the synthetic work of Brändström,[1] and Reinheimer and Hostetler,[2a] nucleophilic aromatic substitution studies of Grunwald,[2b] borohydride reductions by Sullivan and Hinckley,[2c] and findings of Baizer[2d] and others[2e] on different reaction paths offered by use of alkali metals vs. tetraalkylammonium cations, little can be found in the literature on this subject.

We wish to report that dramatic results can be achieved by substituting tetraalkylammonium ions for the alkali metal ions in the benzoin condensation, a reaction which is known to require contact of organic benzaldehyde with inorganic cyanide.[3] Although sodium cyanide is an excellent catalyst for this reaction when run at 90° in 50% aqueous methanol,[4] it is fairly ineffective when run in water alone at room temperature. Tetrabutylammonium cyanide, on the other hand, affords a 70% yield of benzoin when the reaction is run at room temperature in water. (Table)

The success of this reaction is probably due to the well known "salting-in" effect which aqueous solutions of tetraalkylammonium ions have toward aromatic compounds,[5] thus greatly increasing the amount of benzaldehyde actually dissolved in the same phase as the catalyst.[6]

It would appear that there are many synthetic procedures which could benefit from the approach used here.

Table - Benzoin Yield[a]

Cation	Time	Moles of cyanide added 0.033	0.053	0.10
Sodium	20-21 hrs.	no product		2.83 g
Tetraethylammonium	21-24 hrs.	3.32 g	8.76 g	
Tetrabutylammonium	1-1/4 hr.	17.31 g		

(a) Obtained by mixing 25 ml benzaldehyde, 100 ml water and the cyanide. Stir, filter product, wash, dry at 70° overnight.

References:

1. A. Brändström, et al, Acta. Chem. Scand. 23 2202, 2203, 2204 (1969).
2. a) J. D. Reinheimer and W. Hostetler, Ohio J. Sci. 64 275 (1964).
   b) E. F. J. Duynstee and E. Grunwald, Tetrahedron 21 2401 (1965).
   c) E. A. Sullivan and A. A. Hinckley, J. Org. Chem. 27 3731 (1962).
   d) M. M. Baizer and J. P. Petrovich, J. Electrochem. Soc. 114 1023 (1967).
   e) R. D. Guthrie, Abstr. 158th Am. Chem. Soc. Natl. Meeting, Org. Div. 138.
3. E. S. Gould, "Mechanism and Structure in Organic Chemistry" p. 394, Holt, Rinehart and Winston, 1959.
4. Organic Syntheses, Coll. Vol. 1, 94 (1941).
5. J. E. Desnoyers, G. E. Pelletier, C. Jolicoeur, Can. J. Chem. 43 3232 (1965).
6. The effect of "salting-in" in the benzoin condensation is speculative at present. Note that Brändström's work (ref. 1) and Sullivan's (ref. 2c) both involve a different effect in that tetraalkylammonium ions are used to dissolve an otherwise insoluble ionic reagent in an organic solvent.