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CROWN COMPLEX AND AMMONIUM ION EFFECTS IN THE CANNIZZARO REACTION[1]

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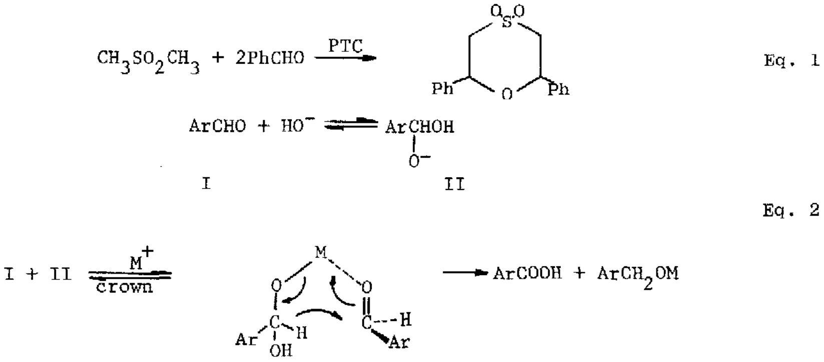
A number of recent publications involving both quaternary ion[2] and crown ether[3] mediated phase transfer (pt) catalysis, clearly imply the similarities inherent to these two methods.[4] Indeed, the common properties are manifest. Our interest in the scope of these methods has led us to an example of a clear contrast between these two methods and to a means by which at least one competing reaction can be suppressed.

The condensation of dimethyl sulfone with benzaldehyde under phase transfer conditions yields 3,5-diphenylthiadioxane-S,S-dioxide.[5] The product may be obtained in good yield (*ca.* 60%) using either benzyltriethylammonium chloride (TEBAC)[6] or 18-crown-6[7] as pt catalyst. When the catalyst is crown ether, however, the reaction is complicated by the production of benzoic acid, presumably *via* the Cannizzaro reaction.[8,9] Table I illustrates this difference for reactions conducted under similar conditions. This contrasting reactivity in terms of the Cannizzaro reaction caused us to undertake a study of this classical reaction, the preliminary results of which are reported herein.

Although the Cannizzaro reaction has been known for well over a hundred years,[8] the existence of a cation effect was not noted until just over two decades ago[10] and seems not to be widely recognized even today. We present evidence here that a Lewis acid is indeed involved in a coordinating role in this reaction and feel that the cyclic six-membered transition complex proposed by Pfeil (see Scheme) is a plausible intermediate. In Table II we present data which clearly implicate a Lewis acid.

Vigorous stirring of neat benzaldehyde at ambient temperature with 50% aqueous alkali (stand-

Scheme



ard Cannizzaro conditions) yields 90% each of benzoic acid and benzyl alcohol. Addition of a cosolvent like benzene or dichloromethane inhibits the reaction due to phase contact - ion solubility problems (Table II, entry 2). The reaction proceeds well using solid KOH as base with either benzene or dichloromethane as cosolvent (entries 6 and 7). When a macrocyclic polyether (in all cases herein reported: 18-crown-6[7]) is added to the reaction mixture, the yield is reduced apparently in accord with two factors: the amount of crown present and the ability of the solvent to stabilize the crown-cation complex. In the absence of crown, the yield of benzoic acid (in dichloromethane, entry 7) is 89%. In the presence of 1, 5 and 10 mole-percent added crown (entries 11-13) the yields of benzoic acid are 58%, 31% and 26% respectively. In benzene, which seems a less favorable solvent for crown complexation, the yield of benzoic acid is reduced less (yields 88%, 86% and 82% as above, entries 6, 8-10). The results presented in entries 3-5 also seem to accord with the above interpretation. Since ionic transport across the interfacial boundary is poor, the yield under standard conditions should be poor (entry 2). Addition of crown should increase the yield in proportion to the amount added, although the yield should not be high because of crown competition for the cation in the intermediate.

Under quaternary ion catalyzed pt conditions, the Lewis acid present in the bulk organic phase is the organic, rather than the inorganic, ion. An examination of space filling CPK models indicates that the "Makosza catalyst"[6] benzyltriethyl ammonium cation (TEBA) should be too sterically hindered to participate in a cyclic intermediate such as that formulated. On the other hand, it is not clear from model examination whether or not the nitrogen in the benzyltrimethyl ammonium (TMBA) ion can serve this purpose, although reports that Triton B successfully catalyzes the Cannizzaro[9] would seem to resolve the issue. Entries 14 and 15 in Table II indicate that in the absence of other cations, TMBA will coordinate, although apparently much less effectively than Na^+ of K^+. The TEBA ion will not catalyze the reaction and no benzoic acid is detected. The absence of benzoic acid (entry 14) should not be attributed to phase contact problems (entry 2) because the TEBA ion is well established as an efficient phase transfer catalyst.[2,3] Finally, we note (entries 16 and 17) that no change in mechanism is apparent under pt conditions.[11] Thus, α-deuterio benzaldehyde[12] yields α,α-dideuterio benzyl alcohol (>90% isotopic purity).

We have presented above essentially a steric argument to rationalize the differing behavior of ammonium versus alkali metal cations in the Cannizzaro reaction. Another factor which may account, at least in part, for this difference is the likelihood that electron flow through an ammonium ion should be less favorable than through a metal ion. Furthermore, the recent implication[13] that the Cannizzaro reaction may be a proton rather than a hydride transfer can be accommodated by these data and should not be overlooked.

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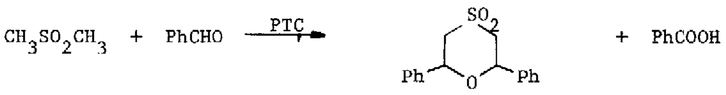
TABLE I[a]

Phase Transfer Condensation of Dimethyl Sulfone with Benzaldehyde



III IV

Catalyst	(M-%)	Solvent	Base	% III[b,c]	% IV
TEBAC	(1)	CH_2Cl_2	50% Aq NaOH	<5	trace
TEBAC	(5)	CH_2Cl_2	50% Aq NaOH	37	trace
TEBAC	(10)	CH_2Cl_2	50% Aq NaOH	48	trace
18-crown-6	(1)	CH_2Cl_2	solid KOH	10	17
18-crown-6	(5)	CH_2Cl_2	solid KOH	21	7
18-crown-6	(10)	CH_2Cl_2	solid KOH	48	0.4

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[a] Standard (non-optimal) conditions: 24 hours at ambient temperature 0.4 M in sulfone.

[b] Isolated yield of recrystallized material.[5]

[c] Using more concentrated, larger scale conditions the yield was 60%.[b]

TABLE II

Mixed Media Cannizzaro Reactions[a]

Entry	Base	Solvent	Catalyst	% PhCOOH[b]	% $PhCH_2OH$[c]	% PhCHO[c]
1	50% aq KOH	None	None	89 ± 1	88 ± 2	trace
2	50% aq KOH	CH_2Cl_2	None	1 ± 1[d]	0[e]	93
3	50% aq KOH	CH_2Cl_2	1M-% crown[f]	6 ± 1	4 ± 1	82 ± 1
4	50% aq KOH	CH_2Cl_2	5M-% crown[f]	11 ± 1	5 ± 1	68 ± 1
5	50% aq KOH	CH_2Cl_2	10M-% crown[f]	14 ± 1	7 ± 1	58 ± 1
6	solid KOH	C_6H_6	None	88 ± 1	62[g]	<5[g]
7	solid KOH	CH_2Cl_2	None	89 ± 3	73[g]	0[e]
8	solid KOH	C_6H_6	1M-% crown[f]	88 ± 2	71 ± 2	<5[g]
9	solid KOH	C_6H_6	5M-% crown[f]	86 ± 1	72 ± 7	8 ± 3
10	solid KOH	C_6H_6	10M-% crown[f]	81 ± 1	70 ± 2	<5
11	solid KOH	CH_2Cl_2	1M-% crown[f]	58 ± 1	<5[h]	11 ± 2
12	solid KOH	CH_2Cl_2	5M-% crown[f]	31 ± 3	<5[h]	30 ± 3
13	solid KOH	CH_2Cl_2	10M-% crown[f]	26 ± 2	<5[h]	31 ± 3
14	50% aq KOH	CH_2Cl_2	5M-% TEBAC	0[e,g]	trace	72[g]
15	50% aq KOH	CH_2Cl_2	5M-% TMBAC	11 ± 2	<5[h]	70[g]
16	solid KOH	CH_2Cl_2	1M-% crown[f]	54[g,i]	<5[g,j]	17[g,k]
17	solid KOH	CH_2Cl_2	1M-% crown[f]	87%	73%	3[g,k]

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[a] All reactions reported herein were conducted under N_2 for 24 hours at ambient temperature with vigorous magnetic stirring. The benzaldehyde was distilled prior to use, stored under nitrogen and delivered by syringe. Where an organic phase was used, the reaction was 1 M in benzaldehyde. [b] Yield obtained by isolation. Purity checked by mp, mmp, and/or spectral properties. [c] Yield determined by glpc analysis on 1/4" x 5', 10% SE-30 on 60/80 chromosorb-P. [d] The yield of benzoic acid depends on phase contact: if high speed stirring is used this value is 34% for a comparable time period. [e] None detected by glpc.[c] [f] 18-Crown-6 polyether.[7] [g] Yield determination performed on only one run. [h] Low yield of alcohol probably an artifact of the reaction of $PhCH_2O^-M^+$ with methylene chloride. [i] The yield difference between entries 11 and 16 is not significant. [j] Enough $PhCD_2OH$ to isolate and identify by gc, ms, nmr. [k] PhCDO.[12]