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Inversion of the Relative Reactivities of Mesitylene and Toluene in Clay-Catalyzed Friedel-Crafts Alkylations

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Abstract : *Whereas toluene is more reactive than mesitylene when these substrates are benzylated separately by benzyl chloride, one-pot reactions in the presence of "clayzic" conversely favor mesitylene, with high intermolecular selectivity (a factor 6-15).*

Coexistence with benzene (as a co-reactant) accelerates in spectacular manner alkylation of an aromatic hydrocarbon by benzyl chloride, when performed in the presence of clay-impregnated zinc chloride ("clayzic")[1]. This is not a fluke but integral part of an array of novel and intriguing phenomena. They bear on the design of micro-reactors capable of molecular recognition. One deals with the seemingly paradoxical proposition that, besides achieving high intermolecular selectivities on mixtures, the reaction of the thus favored component is greatly sped-up ; which generalizes and extends the earlier observations of such synergism[1].

We have examined the effect of the presence of toluene on the benzylation of mesitylene. For this purpose, "clayzic"[2-4] (0.25 g) is added in one shot to a mixture (pre-heated to 40° C) of benzyl chloride (10 mmol) and of the aromatic substrate(s) in excess (100 mmol total). Conversion of the benzyl chloride reactant is monitored by GC, with *n*-hexadecane as internal standard for determination of the yields in monobenzylation products. We did not observe, in a more sophisticated reactor with high-speed stirring, any overheating of the reaction mixture.

Table 1 Results of Competition Experiments Between Mesitylene and Toluene[a] for Benzylation by Benzyl Chloride. (Only mesitylene gives rise to polybenzylation products).

Run	Substrate(s)	Conversion time [b], mn	Overall yield[c], ±5%	**M'/T'**
1	Toluene (**T**)	60	95	-
2	Mesitylene (**M**)	75	70	-
3	**T+M** 4:1	20	90	1.5
4	**T+M** 1:1	20	80	15.0
5	**T+M** 1:4	20	83	40
6	**T+M** 1:9	90	80	∞

[a] the product distribution is near-invariant at o : m : p = 40 : 5 : 55.
[b] total disappearance of benzyl chloride. - [c] monobenzylation products.

The results in Table 1 show both substantial acceleration of the conversion and a switch in the relative reactivities. As separate substrates, toluene is the more reactive (Runs 1 and 2). As mixed substrates, mesitylene is the more reactive (Runs 3-6). Furthermore, benzylmesitylene **M'** dominates the product distribution[5]. The ratio **M'** / **T'** measured by GC ± 10% (where **T'** denotes the total molar amounts of *o*-, *m*- and *p*-benzyltoluene) points to an intermolecular selectivity favoring mesitylene by a factor 6-15, after correcting for the molar ratios of the reactants (Runs 3-5). The extrapolation was tempting : indeed, at a molar ratio of 1 : 9 (Run 6), toluene is left unscathed ; its presence only translates into a small decrease of the conversion time for the mesitylene co-reactant. With other, less active samples of catalyst (conversion times of 180 mn), the selectivity is yet more spectacular : at **T** + **M** 1 : 4 toluene remains unreacted[6].

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4 - Prepared by dissolving 1 g of zinc chloride in 100 mL of warm (60° C) acetonitrile and addition with vigorous stirring of 20 g of K10 montmorillonite (Süd Chemie, München).
5 - The result of run 4 is temperature-invariant, a factor 15 at 60° C also.
6 - Independent experiments by Michèle Davister in this laboratory.

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