

## Sonochemical Switching of Reaction Pathways in Solid-Liquid Two-phase Reactions

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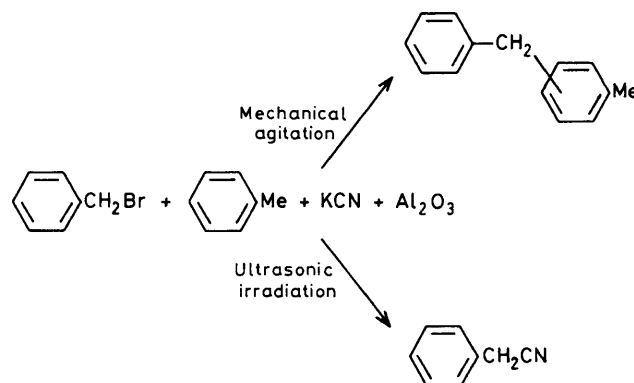
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Ultrasonic irradiation of a mixture of benzyl bromide, potassium cyanide, and alumina in an aromatic solvent yields benzyl cyanide, whereas mechanical agitation gives the Friedel-Crafts type product; sonication changes the main reaction pathway from aromatic electrophilic to aliphatic nucleophilic substitution.

Organic synthesis using inorganic supports as reagents or reaction media has attracted much attention in recent years,<sup>1</sup> and ultrasound has been successfully applied to a number of heterogeneous reactions, particularly in the field of organo-metallic chemistry.<sup>2</sup> Here we report the first example of ultrasonic irradiation dramatically changing the course of an alumina-promoted reaction.

Inorganic supports such as alumina, silica gel, and zeolites have been reported to promote nucleophilic substitution with alkali cyanides in organic solvents in the same way as a solid-liquid phase transfer catalyst.<sup>3</sup> However, when benzyl bromide was treated with potassium cyanide and alumina in toluene under mechanical agitation at 50 °C, only a mixture of *o*- and *p*-benzyltoluene was obtained in 75% yield. Unexpectedly, alumina had not promoted the cyanide substitution reaction but had promoted the Friedel-Crafts reaction of benzyl bromide with toluene. This is an interesting example of Lewis-acid sites on the surface of the alumina acting as a solid catalyst.<sup>4</sup> In contrast, when the same reaction mixture was irradiated by ultrasound (Branson laboratory cleaner, 200 W,

45 kHz) at 50 °C, the substitution did take place to afford benzyl cyanide in 71% yield. Thus, ultrasound completely switched the reaction course from the Friedel-Crafts reaction to nucleophilic substitution as shown in Scheme 1.



Scheme 1

**Table 1.** The effect of ultrasound on the Friedel-Crafts reaction and cyanide substitution.<sup>a</sup>

Entry	ArH	<i>p</i> -XC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Br	Conditions <sup>b</sup>	Time/h	Product yield/% <sup>c</sup>	
					<i>p</i> -XC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Ar	<i>p</i> -XC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> CN
1	Benzene	H	M	24	9	0
			U	24	1	70
2	Benzene	Br	M	24	22	0
			U	48	60	0
3	Benzene	Me	U	24	1	67 (54)
			M	24	(75) <sup>d</sup>	0
4	Toluene	H	U	24	1	77 (73)
			M	5	83 (75)	0
5	Toluene	Br	U	24	0	76 (71)
			U*-M	24	14	0
6	Toluene	Me	M	5	87 (80)	0
			U	24	10	69
7	<i>p</i> -Xylene	H	M	5	80	0
			U	5	84 (84) <sup>e</sup>	0
8	<i>p</i> -Xylene	Br	U*-U	3	77	9
			M	2	76	0
9	Anisole	H	U	2	76	0
			U*-U	24	6	76
10	<i>p</i> -Xylene	Br	M	5	83	0
			U	24	52	40
11	Anisole	H	U*-U	24	8	70
			M	24	61	0
12	Anisole	H	U	48	72	0
			U*-U	24	14	50
13	Anisole	H	U	24	3	73
			U*-U	24	3	73

<sup>a</sup> The reaction of the *para*-substituted benzyl bromide (3.2 mmol), the aromatic component (5 cm<sup>3</sup>), potassium cyanide powder (1.0 g, 16 mmol), and alumina (1.6 g, Merck, Type 90 for column chromatography, neutral, activity I, 70–230 mesh) was carried out at 50 °C. <sup>b</sup> M, Mechanical agitation using a vibration apparatus (Tokyo Rikakikai Mini Vapour S-10); U, ultrasonic irradiation using a thermostated ultrasonic cleaner (Branson, 200 W, 45 kHz); U\*, ultrasonic pretreatment for 3 h before the addition of benzyl bromide. <sup>c</sup> Isolated yields after purification are shown in parentheses, and the others are those determined by g.l.c. using internal standards. <sup>d</sup> The total yield of mono-, di-, and tri-substituted products. <sup>e</sup> The total yields of mono- and di-substituted products.

This unusual effect of ultrasound to switch the reaction course was observed for several combinations of substituted benzyl bromides and aromatic compounds (entries 1–5, Table 1). In these cases substituted benzyl cyanides were obtained under ultrasonic irradiation, whereas diphenylmethane derivatives were obtained under mechanical agitation.

With *p*-xylene or anisole as the aromatic component (entries 7–9), the Friedel-Crafts reaction occurred in competition with the cyanide substitution under ultrasonic irradiation. For example, sonication of a mixture of *p*-bromobenzyl bromide, *p*-xylene, and inorganic reagents gave the diphenylmethane derivative in 49% yield together with the corresponding cyanide in 32% yield (entry 8, U). However, when the mixture of *p*-xylene and inorganic reagents was previously irradiated by ultrasound for 3 h before the addition of the bromide and then the reaction carried out under continued sonication, the cyanide was obtained in 70% yield with a minor amount of the diphenylmethane derivative (entry 8, U\*-U). A similar effect of ultrasound pretreatment was also observed in other cases (entries 7 and 9). With substrates as reactive as *p*-methylbenzyl bromide and toluene, however, ultrasound had no effect; the Friedel-Crafts reaction was the main reaction pathway even with ultrasonic pretreatment (entry 6, U\*-U). Thus, in most combinations of substituted benzyl bromides and aromatic compounds studied, ultrasound was found to switch the reaction course from alumina-catalysed electrophilic substitution of the aromatic compounds to alumina-assisted nucleophilic substitution by the cyanide anion.

It is interesting that both cyanide substitution and the

Friedel-Crafts reaction were retarded when the reaction mixture was mechanically agitated after ultrasonic pretreatment for 3 h; only a 14% yield of the Friedel-Crafts type product was formed from benzyl bromide and toluene after 24 h (entry 4, U\*-M). Thus, ultrasound is essential for nucleophilic substitution to take place. On the other hand, in the absence of potassium cyanide the mixture of benzyl bromide, toluene, and alumina gave smoothly the Friedel-Crafts type products not only under the mechanical agitation conditions (83%; 3 h) but also under the sonication conditions (79%; 3 h). These results indicate that ultrasound assists the contact of potassium cyanide with alumina to decrease the catalytic ability of alumina for the Friedel-Crafts reaction and to enhance nucleophilic attack by the cyanide ion at the alumina surface.

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