

Graphite as an effective catalyst for Friedel–Crafts acylation

Mitsuo Kodomari,* Yoshitada Suzuki and Kouji Yoshida

Department of Industrial Chemistry, Faculty of Engineering, Shibaura Institute of Technology, Shibaura, Minato-ku, Tokyo 108, Japan

Graphite is found to promote Friedel–Crafts acylation of aromatic compounds such as anisole, toluene and *o*-xylene with acyl halides to give the corresponding acylated products in high yields.

Friedel–Crafts acylation of aromatic compounds is one of the most important syntheses of aryl ketones. In contrast to Friedel–Crafts alkylation, which proceeds readily in the presence of catalytic amounts of Lewis acid, acylation requires more than one equivalent, *e.g.* of AlCl₃. This is due to the complexation of AlCl₃ by the ketone product. The catalyst used cannot easily be recovered and recycled; therefore, a large amount of toxic waste is generated. In order to solve this problem, some catalytic Friedel–Crafts acylations have recently been developed. Ln(OTf)₃–LiClO₄,¹ TiCl(OTf)₃–TfOH² and ReBr(CO)₅³ have been reported as catalysts for Friedel–Crafts acylation. In addition, the use of inorganic solid supported reagents⁴ or solid acids⁵ as catalysts, resulting in higher selectivity, easier work-up and environmentally safe reactions, has been reported. For instance, HZSM-5 zeolite has been reported to promote the liquid-phase acylation of anisole with carboxylic acid.^{5b}

Table 1 Acylation of anisole using the various inorganic solids^a

Inorganic solid	Yield (%) ^b
None	0
Graphite	89
Active charcoal	trace
Molecular sieves (5 Å)	41
Al ₂ O ₃ (neutral)	9
Silica gel	0

^a A mixture of anisole (2 mmol), benzoyl bromide (3 mmol) and inorganic solid (1 g) in benzene (5 ml) was refluxed for 8 h. ^b Yields were determined by GLC.

Table 2 Acylation of anisole with acyl chlorides^a

R	<i>t</i> /h	Yield (%) ^b
Ph ^c	8	85
Cyclohexyl	8	84
Pr ⁱ	3	89
C ₅ H ₁₁	8	66
C ₁₂ H ₂₅	8	63
PhCH ₂	8	61

^a Conditions: anisole (2 mmol), acyl chloride (3 mmol), graphite (1 g), ClCH₂CH₂Cl (5 ml). ^b Yields were determined by GLC. ^c The reaction was carried out at 120 °C in chlorobenzene.

However, it has limitations with regard to generality and efficiency. Recently, it has also shown that alumina promotes the acylation of reactive aromatics such as anisole and

Table 3 Graphite catalysed Friedel–Crafts acylation^a

Run	ArH	<i>t</i> /h	Product	Yield (%) ^b
1		8		89
2 ^c		16		70
3		8		92
4		8		60
5		8		93
6 ^d		24		86 (<i>o</i> : <i>p</i> = 1:4)
7 ^e		24		97
8		3		84
9		3		85
10		3		83

^a ArH (2 mmol), benzoyl bromide (3 mmol), graphite (1 g) and benzene (5 ml). ^b Yields were determined by the internal standard method *via* GLC. ^c Addition of sodium carbonate (6 mmol). ^d Solvent: toluene (5 ml). ^e Solvent: *o*-xylene (5 ml).

thiophene with carboxylic acid in the presence of trifluoroacetic anhydride.⁶ During the course of our studies aimed at developing supported reagents as catalysts for Friedel–Crafts reaction,⁷ we found that graphite, without any treatment, promotes the Friedel–Crafts acylation of aromatic compounds with acyl halides to afford the corresponding acylated products in high yields.

Graphite was shown to have a remarkably high activity for the acylation of active aromatic compounds such as anisoles and polymethylbenzenes with acyl halide to give the corresponding acylated compounds in high yields, without any of the environmental disadvantages of using toxic homogeneous reagents such as AlCl₃. In a typical experiment, graphite† was added to a mixture of anisole (2 mmol) and benzoyl bromide (3 mmol) in benzene. The mixture was heated under reflux for 8 h. Graphite was removed by filtration, and the filtrate was washed with aqueous sodium hydrogen carbonate, to remove the excess benzoyl bromide, and concentrated under reduced pressure. The crude product was chromatographed on silica gel to afford *p*-methoxybenzophenone (80%). The products obtained were analysed by GLC, IR and NMR spectroscopy. The amount of graphite used relative to benzoyl bromide was between 0.5 and 2 g. The optimum yield of *p*-methoxybenzophenone was obtained with 1 g of graphite, whereas 2 g gave a slightly lower yield. When a large amount of graphite was used, the yields were decreased due to absorption of an appreciable amount of the product and starting material on the graphite. Empirical testing of five inorganic solids revealed that graphite was most effective in promoting the reaction. MS-5A, though less effective than graphite, was also effective, whereas active charcoal, silica gel and alumina were entirely ineffective (see Table 1). Alkanoyl and cycloalkanecarbonyl chlorides could be used as acylating reagents in the reactions, and the corresponding acylated products were obtained in good yield (Table 2). The reaction of anisole with isobutyl chloride and with cyclohexanecarbonyl chloride gave isopropyl 4-methoxyphenyl ketone and cyclohexyl 4-methoxyphenyl ketone, respectively, in high yields. However, the acylation of anisole with acetyl chloride gave *p*-methylacetophenone in low yield. This is probably due to evaporation (low boiling point of acetyl chloride). Benzoylation of several anisoles and polymethylbenzenes with benzoyl bromide in the presence of graphite was carried out and the results are summarised in Table 3. Anisole, veratrole and α -methoxynaphthalene reacted with benzoyl bromide to give the corresponding benzoylated prod-

ucts in high yields. In the present reactions, benzoyl bromide was a better acylating reagent than benzoyl chloride. For example, anisole reacted with benzoyl bromide to afford *p*-methoxybenzophenone in 89% yield, whereas a 50% yield was obtained in the reaction with benzoyl chloride under the same conditions; the yield was improved to 85% when the reaction was carried out at 120 °C in chlorobenzene. These graphite-promoted acylations proceeded even after addition of sodium carbonate, which traps hydrogen bromide generated during the reaction, although the rate of the reaction was slower than that in the reaction without sodium carbonate (Table 3, run 2). Polymethylbenzenes such as mesitylene, 1,2,3,5-tetramethylbenzene and pentamethylbenzene gave the corresponding benzoylated products in high yields. However, benzoylation of toluene and *o*-xylene was very slow in refluxing benzene, giving methylbenzophenone (a mixture of *o*- and *p*-isomers) and 3,4-dimethylbenzophenone in low yield, respectively; the yields were improved when the reaction was performed using toluene and *o*-xylene as both substrate and solvent. Benzene was hardly benzoylated under similar conditions. The reaction of benzene with benzoyl bromide was heated to reflux for 24 h to give benzophenone in 20% yield.

Further understanding of the catalysis by graphite and the application of graphite to other synthetic reactions are now under investigation.

Footnotes and References

* E-mail: kodomari@sic.shibaura-it.ar.jp

† Graphite powder was from Aldrich (Catalogue no. 28, 286-3) and was employed without further purification.

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