Alumina in Methanesulfonic Acid (AMA) as a New Efficient Reagent for Direct Acylation of Phenol Derivatives and Fries Rearrangement. A Convenient Synthesis of *o*-Hydroxyarylketones

J. Chem. Research (S), 1998, 628–629
J. Chem. Research (M), 1998, 2678–2693

Hashem Sharghi* and Babak Kaboudin

Department of Chemistry, Shiraz University, Shiraz 71454, Iran

Alumina in methanesulfonic acid is used to prepare *o*-hydroxyarylketones, by acylation of phenol and naphthol derivatives with carboxylic acids and Fries rearrangement of phenolic esters.

The Friedel–Crafts acylation is one of the most popular reactions for the synthesis of aromatic ketones,[8] and direct acylation of phenol derivatives, using $AlCl_3$ or $TiCl_4$ as a promoter, also provides useful synthetic methods for the preparation of *o*-hydroxyarylketone derivatives.[9–11] However, treatment of the aluminium residue has, sometimes, induced environmental problems and the drastic reaction conditions have caused some severe side reactions. On the other hand, acid chlorides or acid anhydrides are commonly used as acylating reagents in these reactions. These reagents are usually prepared from carboxylic acids, and, therefore, it would be useful if the acylations could be carried out by using carboxylic acids as acylating reagents.[12–14] An alternative method is the Fries rearrangement of acyloxy benzenes or naphthalenes which provides useful routes to these compounds.[15] The acid–base properties of metal oxide supports have a significant role in the selectivity exhibited by heterogeneous catalysts.[19a–d] One of the most common solid supports in heterogeneous catalysis is alumina, which has been used as a dehydrating agent in aromatic cyclodehydration.[20a,b] We herein present work that describes the direct acylation of phenol derivatives with carboxylic acids by a mixture of acidic alumina (type 504C) in methanesulfonic acid (AMA). We have also noticed that AMA catalyses the Fries rearrangement of acyloxybenzenes for the preparation of *o*-hydroxyarylketones (Scheme 2).

The reaction of **1d** with **2d** at 100 °C for 12 h in methanesulfonic acid afforded **3d** in 15% yield. Unfortunately, the extension of the reaction time, and the increase of the reaction temperature, decomposed the reaction mixture,[18] and a darkened solid, which would dissolve in organic solvents, was obtained. Reaction of **1d** with *m*-cresol in the presence of alumina failed in chlorobenzene, toluene and 1,2-dichloroethane when boiled under reflux for 24 h. In nitrobenzene, however, compound **5d** was obtained in 20% yield. Since attempts to prepare **3d** were unsuccessful, attention was turned to methanesulfonic acid/alumina mixtures, which have not yet been used for this purpose. The reaction of **1d** (2 mmol) with **2d** (2 mmol) in methanesulfonic acid (1 mL) and acidic alumina (0.2–0.3 g) at 100 °C for 12 h produced **3d** in 50% yield. When the reaction was carried out at 140 °C, **3d** was produced in 85% yield after 1 h. The extension of this new reagent to the Fries rearrangement of **5d** was also successful and **3d** was produced in 70% yield after 2 h (Table 2).

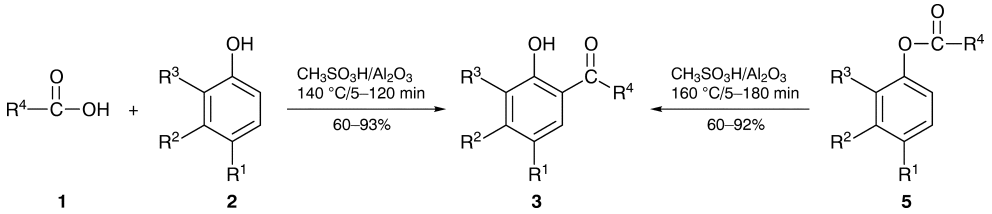
The reaction of benzoic acid derivatives with *m*-cresol and Fries rearrangement of *m*-tolylbenzoate derivatives in the presence of AMA afford 2-hydroxyarylketones in high yields (Table 2). The results clearly show that the reactions seem to be faster when the aromatic part of the acid carries electron-donating groups. Acetic acid, cyclohexylcarboxylic acid, phenylacetic acid, hexanoic acid and 11-bromoundecanoic acid were also employed as acylating reagents. Fries rearrangement of *m*-tolylalkanoates also occurs in the presence of AMA and affords the desired products in excellent yields. Upon reaction of *o*-cresol with benzoic acid and Fries rearrangement of corresponding ester, the *para* isomer was obtained in high yield. With a

Table 2 Comparison of results obtained from the reaction of phenol derivatives with carboxylic acids and Fries rearrangements of phenolic esters in the presence of AMA

Entry	Product **3** and ester **5**	R^1	R^2	R^3	R^4	A[a] Time (*t*/min)	A[a] Yield (%)[c]	B[b] Time (*t*/min)	B[b] Yield (%)[c]
1	**a**	H	CH_3	H	Ph	10	86	120	60
2	**b**	H	CH_3	H	*o*-ClC_6H_4	25	82	60	81
3	**c**	H	CH_3	H	*m*-$CH_3C_6H_4$	5	90	60	80
4	**d**	H	CH_3	H	*m*-BrC_6H_4	60	85	120	70
9	**i**	H	CH_3	H	CH_3	5	85[d]	15	80
13	**m**	H	CH_3	H	Br-$(CH_2)_{10}$	5	80	30	80
14	**n**	H	F	H	CH_3	120	63[d]	180	60
15	**o**	H	OH	H	CH_3	30	82[d]	–	–
18	**r**	OH	H	H	Ph	60	83	–	–
22	**v**	H	H	CH_3	Ph	20	10(90)[e]	50	15(85)[e]
23	**w**	H	H	Cl	Ph	60	13(87)[e]	90	15(85)[e]
24	**x**	H	OH	H	Ph	30	85	–	–
25	**y**	H	H	CH_3	$PhCH_2$	5	12(88)[e]	10	15(85)[e]
26	**z**	H	H	CH_3	CH_3	5	8(92)[e]	10	15(85)[e]
28	**b′**	α-Naphthol			$CH_3(CH_2)_4$	20	91	15	60
29	**c′**	Pyrogallol			CH_3	20	83[d]	–	–
30	**d′**	NO_2	H	H	Ph	720[f]	–	720	–
31	**e′**	H	CH_3	H	*p*-NO_2-C_6H_4	720	–	720	–

[a]Direct acylation method. [b]Fries rearrangement phenolic esters. [c]Yields refer to isolated yield. [d]Reaction was carried out at 120 °C. [e]Values in parentheses are referred to the yield of 4-acylated product. [f]In this case 15% ester was produced.

*To receive any correspondence.



Scheme 2

fluorine group at the *meta* and *para* positions, acylation and Fries rearrangement give the corresponding 2-hydroxy isomer in good yields.

Three mechanistic pathways are proposed in the literature for the Fries rearrangement: (a) intramolecular,[23–25] (b) intermolecular[26–28] and (c) bimolecular.[29–34] Mechanistic studies show that the acylation reaction in AMA occurs through a prior esterification, followed by a Fries rearrangement of the phenolic ester by an intermolecular mechanism.

In summary, AMA is introduced as an efficient reagent in the direct acylation reactions of phenol and naphthol derivatives with carboxylic acids, and in Fries rearrangements of acyloxy benzene and naphthalene derivatives. The present methods have the following advantages: (a) the reagent is readily available, safe to handle and inexpensive; (b) the procedure is simple; (c) the reaction times are very short, and the reaction can be performed with a wide range of carboxylic acids and phenol derivatives; and (d) workup is easy. Further investigations to develop other synthetic reactions using AMA are now in progress.

Techniques used: ^{1}H NMR, IR and mass spectrometry

References: 38

Schemes: 4

Table 1: Reaction of *m*-bromobenzoic acid (**1d**) with *m*-cresol (**2d**) in the presence of some Lewis and some protic acids

Table 3: The reaction of *o*-chlorobenzoic acid (**1b**) with *m*-cresol (**2b**) in AMA

Table 4: Progress of the Fries rearrangement of the ester **5b**

Received, 5th January 1998; Accepted, 16th June 1998
Paper E/8/00158H

References cited in this synopsis

8 G. A. Olah, *Friedel–Crafts Chemistry*, Wiley-Interscience, New York, 1973.
9 (*a*) B. M. Trost and M. G. Saulnier, *Tetrahedron Lett*., 1985, **26**, 123; (*b*) L. Crombie, R. C. F. Jones and C. J. Palmer, *Tetrahedron Lett*., 1985, **26**, 2933.
10 G. N. Dorofeenko and V. V. Tkachenko, *Khim. Geterotsikl. Soedin*., 1971, **7**, 1703; *Chem. Abstr*., 1972, **76**, 153503k.
11 G. Sartori, G. Casnati and F. Bigi, *J. Org. Chem*., 1990, **55**, 4371.
12 G. Fodor, J. Kiss and M. Szekerke, *J. Org. Chem*., 1950, **15**, 227.
13 (*a*) R. M. G. Roberts and A. R. Sadri, *Tetrahedron*, 1983, **39**, 137; (*b*) M. Hino and K. Arata, *J. Chem. Soc., Chem. Commun*., 1985, 112; (*c*) B. Chiche, A. Finiels, C. Gauthier and P. Geneste, *J. Org. Chem*., 1986, **51**, 2128; (*d*) T. Keumi, K. Yoshimura, M. Shimada and H. Kitajima, *Bull. Chem. Soc. Jpn*., 1988, **61**, 455.
14 S. Kobayashi, M. Moriwaki and I. Hachiya, *Tetrahedron Lett*., 1996, **12**, 2053.
15 R. Martin, *Org. Prep. Proced. Int*., 1992, **24**, 369.
19 (*a*) K. Tanabe, *Solid Acids and Bases*, Academic Press, New York, 1970; (*b*) M. C. Kung and H. H. Kung, *Catal. Rev. Sci. Eng*., 1985, **27**, 425; (*c*) K. Tanabe, *Catalysis by Acids and Bases*, Elsevier, Amsterdam, 1985; (*d*) K. Tanabe, M. Misono, Y. Ono and H. Hattori, *New Solid Acids and Bases*, Elsevier, Amsterdam, 1989.
20 (*a*) F. A. Vingiello and A. Borkovec, *J. Am. Chem. Soc*., 1956, **78**, 3205; (*b*) G. H. Posner, *Angew. Chem., Int. Ed. Engl*., 1978, **17**, 487.
23 Y. Ogata and H. Tabuchi, *Tetrahedron*, 1964, **20**, 1661.
24 N. M. Gullinane and B. F. R. Edwards, *J. Chem. Soc*., 1958, 2926.
25 A. Furka and T. Szell, *J. Chem. Soc*., 1960, 2312 and 2321.
26 J. L. Gibson and L. S. Hart, *J. Chem. Soc., Perkin Trans 2*, 1991, 1343.
27 (*a*) I. M. Dawson, J. L. Gibson, L. S. Hart and J. S. Littler, *J. Chem. Soc., Perkin. Trans 2*, 1985, 1601.
28 M. R. Banks, *J. Chem. Soc., Perkin Trans 1*, 1986, 507.
29 J. R. Norell, *J. Org. Chem*., 1973, **38**, 1924.
30 E. H. Cox, *J. Am. Chem. Soc*., 1930, **52**, 352.
31 A. M. El-Abbady, F. G. Baddar and A. Labib, *J. Chem. Soc*., 1961, 1083.
32 C. R. Hauser and E. H. Man, *J. Org. Chem*., 1952, **17**, 390.
33 A. Schonberg and A. Mustafa, *J. Chem. Soc*., 1943, 642.
34 D. S. Tarbell and P. E. Fanta, *J. Am. Chem. Soc*., 1943, **65**, 2169.