SHORT PAPER

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Deacetylation of activated acetophenones with tin(IV) chloride†

Mohamed Hadjeri, Anne-Marie Mariotte and Ahcène Boumendjel*

Département de Pharmacochimie Moléculaire UMR-CNRS 5063. UFR de Pharmacie de Grenoble, 38706 La Tronche, France

Activated acetophenones were deacetylated by treatment with an excess of tin(IV) chloride in 1,2-dichloroethane.

Keywords: activated acetophenones, deacetylation, tin(iv)chloride

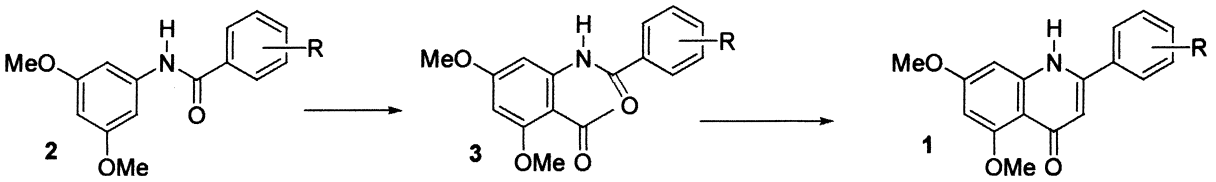
2-Acetyl-3,5-dimethoxyaniline derivatives are key and valuable intermediates largely used for the preparation of biologically active 2-phenyl-4-quinolones bearing a 5,7-dimethoxy groups which are frequently required for good activity.[1–3] 5,7-Dimethoxy-2-phenyl-4-quinolones **1** (Scheme 1) can be prepared by cyclisation of *N*-(2-acetyl-3,5-dimethoxyphenyl) benzamide **3** which was obtained from 3,5-dimethoxyaniline by *N*-benzoylation of 3,5-dimethoxyaniline and acetylation under Friedel–Crafts conditions ($CH_3COCl/SnCl_4$).[2]

In executing Scheme 1, we have come across an unusual reactivity of **3** in the presence of tin(IV) chloride which was used as the Friedel–Crafts catalyst. Treatment of **3** with an excess of $SnCl_4$ gave the deacetylated compound (compound **2**) in excellent yield (Scheme 2).

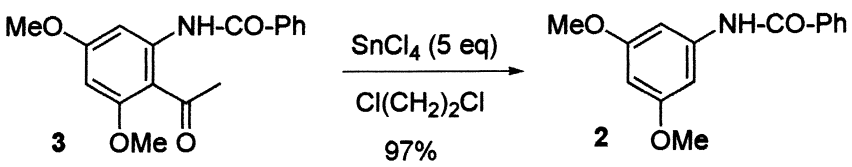
We then found out that the reaction works well with activated acetophenones (Table 1). Under such conditions, we have found that only removal of the acetyl function occurs and transacetylation is not a competing process. The reaction is chemospecific; for example, *N*-acetyl or *O*-acetyl groups were not cleaved under these conditions. The presence of substituents in *ortho* positions to the acetyl group is required for the success of this reaction. The favourable *ortho* steric interaction with the methyl ketone seems to provide the driving force for the deacetylation as the reaction failed to proceed in the case of many *N*-(4-acetyl-3,5-dimethoxyphenyl) benzamides. Finally, it should be mentioned that the deacetylation reaction does not proceed when other Lewis acids ($AlCl_3$, $ZnCl_2$, $SnCl_2$) are used.

In the literature, reversible Friedel–Crafts methodology has been reported. Schubert has reported that deacetylation of activated acetophenones occurs with strong sulfuric acid.[4–9] The isomerisation of aromatic ketones by a deacetylation/acetylation sequence under Friedel–Crafts conditions has been also reported. More recently, Olah observed that Nafion-H perfluorinated resin sulfonic acid catalyses the deacetylation of activated aromatics.[10] The mechanism of deacetylation with either protic acids or Lewis acids has been studied.[11] However, up to now, most of the reported deacetylations have been conducted on aromatic ketones bearing only methyl groups (in *ortho* and *para* positions to the acetyl group) which are resistant to the reaction conditions which can be drastic.

In conclusion, this is the first time that deacetylation of acetophenones has been accomplished with tin(IV) chloride in the presence of fragile functions and without transacetylation. The utility of the present method can be found in using the acetyl as a reaction directing group. We can presume that the acetyl group can be occasionally introduced into a ring, used to direct another group, and then removed as we do with sulfonic acid and tertiary alkyl groups which are widely used as reaction directing groups.



Scheme 1

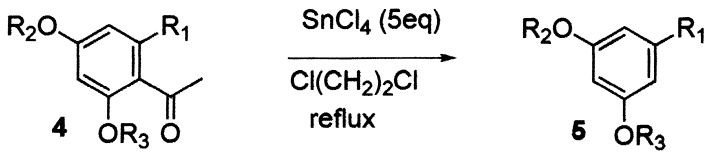


Scheme 2

* To receive any correspondence. E-mail: Ahcene.Boumendjel@ujf-grenoble.fr

† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M)*.

Table 1 Deacetylation of activated acetophenones with $SnCl_4$



Entry	R_1	R_2	R_3	Yield, physical and spectral data of deacetylated compounds (**5**)
1	OH	H	H	95%. m.p. 210–212°C; ^{1}H NMR (CD_3OD): δ 5.63 (s, 3H). m.p. and NMR agree with those of phloroglucinol (m.p. 215–218°C).[12]
2	OCH_3	CH_3	CH_3	90%. m.p. 53–55°C. ^{1}H NMR ($CDCl_3$): δ 6.09 (s, 3H); 3.76 (s, 9H). m.p. and NMR data were agree with those of 1,3,5-trimethoxybenzene (51–53°C).[12]
3	OAc	Ac	H	92%. amorphous. ^{1}H NMR ($CDCl_3$): δ 7.23 (t, *J* = 2.1 Hz, 1H); 6.46 (d, *J* = 2.1 Hz, 2H), 2.53 (s, 6H). MS *m/z*: 210 [M^+]. Anal. Calcd. for $C_{10}H_{10}O_5$: C, 57.14; H, 4,80. Found. C, 57.06; H, 4.77.
4	NH-Ac	CH_3	CH_3	93%. white solid. m.p. 134–136°C; ^{1}H NMR ($CDCl_3$): δ .7.35 (bs, 1H); 6.7 (bs, 2H); 6.23 (bs, 1H); 3.76 (s, 6H); 2.15 (s, 3H). MS *m/z*: 195 [M^+]. Anal. Calcd. for $C_{10}H_{13}NO_3$: C, 61,53; H, 6,71; N, 7,18. Found. C, 61.50; H, 6.69; N, 7.14.
5	NH-CO-Ph	CH_3	CH_3	97%. white powder. m.p. 143–145°C; ^{1}H NMR (CD_3OD): δ 7.84–7.89 (dd, J_1 = 1.27 Hz, J_2 = 7.6 Hz, 2H); 7.49–7.52 (m, 3H); 6.92 (d, *J* = 2.3 Hz, 2H); 6.35 (t, *J* = 2.3 Hz, 1H); 3.90 (s, 6H). MS *m/z*: 257 [M^+]. Anal. Calcd. For $C_{15}H_{15}NO_3$: 70,02; H, 5.88; N, 5.44. Found: C, 69.98; H, 5.83; N, 5.36.
6	NH-CO-(3-Cl-Ph)	CH_3	CH_3	89%. white powder. m.p. 101–103°C; ^{1}H NMR (CD_3OD): δ 7.85 (m, 2H); 7.69 (m, 1H); 7.48 (m, 1H); 6.88 (d, *J* = 2.2 Hz, 2H); 6.29 (d, *J* = 2.2 Hz, 1H); 3.79 (s, 6H). MS *m/z*: 291 [M+H]$^+$. Anal. Calcd. For $C_{15}H_{14}ClNO_3$: C, 61.76; H, 4.84; Cl, 12.15; N, 4.80. Found. C, 61.71; H, 4.80; Cl, 12.08; N, 4.79.
7	NH-CO-(3-OMe-Ph)	CH_3	CH_3	86%. white powder. m.p. 131–133°C; ^{1}H NMR (CD_3OD): δ 7.35–7.42 (m, 3H); 7.10–7.03 (m, 1H); 6.89 (d, *J* = 2.2 Hz, 2H); 6.28 (t, *J* = 2.2 Hz, 1H); 3.91 (s, 3H); 3.89 (s, 6H). MS *m/z*: 288 [M+H]$^+$. Anal. Calcd. For $C_{16}H_{17}NO_4$: C, 66.89; H, 5.96; N, 4.88. Found. C, 66.86; H, 5.93; N, 4.85.

Experimental

Acetophenones used in this study were either commercially available (entries 1 and 2) or prepared according to ref. 2 (entries 4, 5, 6 and 7). 2′,4′-Diacetate-6′-hydroxy acetophenone (entry 3) was prepared by acetylation of 2′,4′,6′-trihydroxyacetophenone (Ac_2O/pyridine).

To an ice cold solution of the acetophenone in anhydrous 1,2-dichloroethane (5 ml/mmol) was added tin(IV) chloride (5 eq) in a dropwise manner. The ice bath was removed and the solution was refluxed overnight. The solution was hydrolysed by adding water and was extracted with dichloromethane. The organic layer was separated, washed with brine, dried and evaporated to yield pure deacetylated compound (Table 1).

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12 Phloroglucinol (1,3,5-trihydroxybenzene) and 1,3,5-trimethoxybenzene are commercially available compounds.