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Trialkylamine Controlled Phenol–Formaldehyde Reaction over Clay Catalysts: Selective and Environmentally Benign Synthesis of Salicylic Aldehydes

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Abstract—Substituted salicylic aldehydes **6** are synthesised in good yields and excellent selectivities by reaction of phenols **1** with formaldehyde **2** over montmorillonite KSF–Et_3N as a heterogeneous and reusable catalyst. © 2000 Elsevier Science Ltd. All rights reserved.

Introduction

Salicylic aldehydes are excellent precursors for the preparation of important classes of organic compounds such as coumarins,[1] benzofurans,[2] salen derivatives[3] and industrially useful metal extractants.[4]

Different reagents and catalysts have been utilised to perform formylation of aromatic substrates including phenols.[5] Among them, formaldehyde–tin tetrachloride–tributylamine mixtures are reported to produce salicylic aldehydes with high yield and selectivity.[6] Other methods utilise a range of alternative formaldehyde equivalents such as $HC^+{=}NH$ (from $HCN/AlCl_3$), $Me_2N^+{=}CHCl$ (from $DMF/POCl_3$), ClC^+HOMe (from $MeOCHCl_2/TiCl_4$) and $:CCl_2$ (from $CHCl_3/NaOH$).[7]

Unfortunately, all these reactions are encumbered with the general limitations due to the use of large amounts of Lewis acids and/or dangerous reagents. On the other hand, there is a general need for more environmentally friendly synthetic methodologies.

The explosive development of heterogeneous catalysis over the past several years has led to a detailed re-examination of the most important synthetic processes by organic chemists.[8] In fact, the use of heterogeneous catalytic systems shows undoubted advantages from both economic and environmental points of view.[9]

Recently, as a part of our continuing efforts in the application of solid acid catalysis for fine chemical preparation,[10] we have re-investigated the phenol–formaldehyde reaction over acid clays. Here we report our preliminary results of these studies with particular emphasis on the synthesis of salicylic aldehydes over montmorillonite KSF as a heterogeneous catalyst.

Results and Discussion

Preliminary reactions were carried out in toluene (5 ml) using 2-*tert*-butyl-4-methylphenol **1a** as the model substrate (10 mmol) and paraformaldehyde powder **2** (40 mmol); the montmorillonite KSF catalyst (1.5 g) was heated at 130°C for 10 h before use. The slurry was heated at 100°C for 1 h under efficient stirring in a small autoclave.[11]

Since the phenol–formaldehyde reaction is essentially an acid–base controlled process, the catalytic activity and product selectivity were expected to strongly depend on the acid–base properties of the catalyst and reaction medium. In fact, two different modes of reaction were observed depending on the presence or not of a suitable basic additive such as Et_3N.

In all cases, phenol **1a** was firstly converted into the alcoholic intermediate **3a**, which in the absence of Et_3N afforded the acetal **4a** in 48% yield accompanied by diphenylmethane **5a** in 35% yield, due to the acid-promoted reaction of **3a** with a second molecule of formaldehyde **2** (acetalisation process)[12] or phenol **1a** (condensation process).[13] Minor amounts (~10%) of partly and/or completely de-*tert*-butylated diphenylmethanes were also detected. The phenol conversion was 97% (Scheme 1, route a). When Et_3N was added in a stoichiometric amount with respect to the phenol **1a**, the reaction took a quite different course. Under these conditions the acidity of the catalyst was reduced to such a point to prevent both

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Keywords: heterogeneous catalysis; clay; salicylic aldehydes.

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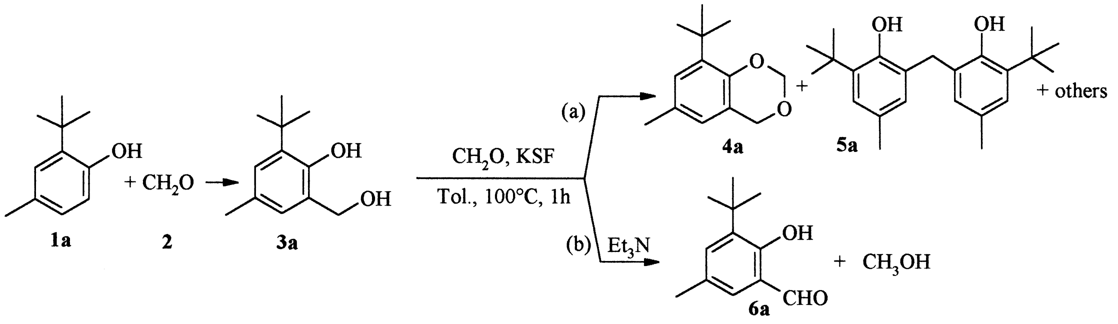


Scheme 1. Reaction between 2-*tert*butyl-4-methylphenol and formaldehyde in the presence or not of triethylamine.

acetalisation and condensation processes and to allow the production of the alcoholic intermediate **3a** (15%) accompanied by the salicylic aldehyde **6a** (32%) and methanol resulting from the Oppenauer oxidation of **3a.**[14] As expected, the system was less reactive and 50% phenol conversion was detected (Scheme 1, route b).

Successively, the amount of alcohol **3a** and aldehyde **6a** formed and phenol **1a** consumed were checked as a function of the reaction time (see Fig. 1).

The rates of phenol **1a** consumption and aldehyde **6a** production mildly decreased from 1 to 3 h. The kinetic curve of the primarily formed alcohol **3a** exhibits an initial increase with a maximum of 20% yield after 0.5 h, accompanied by an increase in the yield of salicylic aldehyde **6a** which reached the maximum after 4 h (67% yield, 72% conversion).

To confirm the Oppenauer-type oxidation step (**3a**→**6a**), an equimolecular amount of **3a** and formaldehyde **2** was reacted in the presence of KSF–Et_3N mixture at 100°C for 5 h, leading to the production of **6a** and methanol in 75% yield, whereas only trace amount of **6a** (~5%) was detected in a control experiment without formaldehyde. Moreover, the fundamental requirement for the oxidation step is that the hydride donor CH_2OH group occupies the position *ortho* to the phenolic OH group. In fact, under the above conditions, 2-hydroxybenzyl alcohol was converted into salicylic aldehyde in 65% yield while a complex mixture of tar materials was obtained with 4-hydroxybenzyl alcohol; moreover, benzyl alcohol as well as 2-methoxybenzyl alcohol were recovered unchanged.

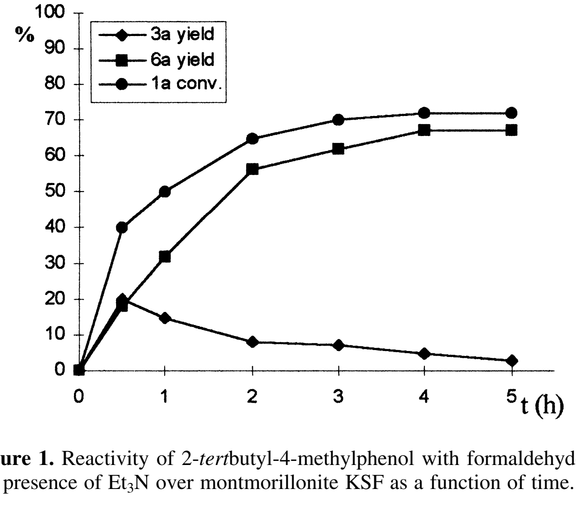


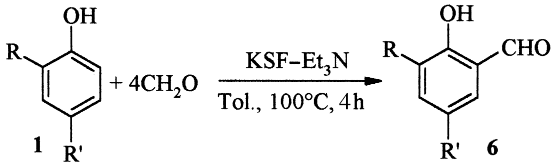
Figure 1. Reactivity of 2-*tert*butyl-4-methylphenol with formaldehyde in the presence of Et_3N over montmorillonite KSF as a function of time.

The activity of the catalyst toward both alkylation (**1a**→**3a**) and redox (**3a**→**6a**) steps as well as the mode of the entire reaction seem to be influenced by the chemical composition of the clay catalyst. In fact, use of montmorillonite K10 with comparable surface acidity but containing less iron than KSF[15] resulted in the production of the intermediate **3a** in 25% yield without any appreciable aldehyde production.

A comparison of results obtained by carrying out the model reaction with different trialkylamines showed that the carbon chain length of the alkyl moiety was significant in determining the activity of the catalyst. In fact, a reduction in phenol **1a** conversion and aldehyde **6a** production was observed with amines bearing increasingly longer carbon atom chains (Et_3N: 72% conversion, 67% yield; Bu_3N: 61% conversion, 56% yield; $Octyl_3N$: 48% conversion, 40% yield).

It is well known that protonatable molecules such as amines can interact with solid acid materials through acid–base reactions. Thus the amine can accept a proton from the acid sites of the clay and the cations formed undergo electrostatic interaction with the negative layer. The consequence of this interaction is the diminishing of both surface acidity and free space on the catalyst surface. The combination of both effects is responsible for the reactivity scale observed with different amines.[16]

Table 1. Synthesis of various salicylic aldehydes



Entry	R	R′	**6** Yield (%)	**1** Rec. (%)	Select.[a] (%)
a	$(CH_3)_3C$	CH_3	67	26	90
b	$(CH_3)_3C$	$(CH_3)_3C$	70	21	89
c	CH_3	H	60	35	92
d	$(CH_3)_3C$	H	63	30	90
e	CH_3	$C_{10}H_{21}$	65	29	91

[a] (**6** Yield/**1** conversion)×100.

The formylation process was then extended to different phenols. Interestingly, with monosubstituted phenols [R=CH_3, $(CH_3)_3C$; R′=H] the formylation exclusively occurred at the *ortho* position (Table 1).

The *ortho*-regioselectivity of the process could be rationalised, assuming the formation of an activated complex resulting from an H-bond between formaldehyde and the OH group of the phenol co-ordinated to the catalyst surface.[17]

Finally, we faced the problem of the catalyst recycle. After filtration and washing with methanol, the montmorillonite KSF was effective only for one cycle, promoting the model reaction in 36% yield.

In conclusion, the discovery and development of this catalytic reaction have led to a new method for the direct formylation of phenols in good yield and high selectivity under environmentally friendly conditions.

Experimental

Melting and boiling points were obtained on an Electrothermal melting point apparatus and are uncorrected. IR spectra were recorded on a Nicolet PC5 spectrophotometer. ^1H NMR spectra were recorded on a Bruker AC300 at 300 MHz. Chemical shifts are expressed in ppm relative to TMS as internal standard. Mass spectra were obtained on a Hewlett–Packard HP-5971 A instrument in EI mode at 70 eV. Microanalyses were carried out by Dipartimento di Chimica Generale ed Inorganica, Chimica Analitica, Chimica Fisica dell'Università di Parma. TLC analyses were performed on Merck 60 PF_{254} silica gel plates using mixtures of hexane–ethyl acetate (5–10%). All the reagents were of commercial quality from freshly opened containers. Montmorillonite KSF (Fluka) was heated at 130°C for 10 h before use.

Synthesis of salicylic aldehydes 6. General procedure

A solution of the selected phenol (10 mmol), paraformaldehyde (40 mmol, 1.2 g), triethylamine (10 mmol, 1.0 g, 1.4 ml) and montmorillonite KSF (1.5 g) in toluene (5 ml), was heated at 100°C in a small autoclave under efficient stirring. After 4 h the reaction mixture was cooled to rt, the catalyst was filtered and washed with boiling methanol (3×50 ml); the solvents were distilled off and the crude was purified by flash chromatography using as eluant mixtures of hexane/ethyl acetate (5–10%). All the known products (**6a–d**) gave spectral data consistent with the reported ones.

3-*tert*Butyl-5-methyl-salicylic aldehyde (6a). Pale yellow oil, bp 110–112°C/7 mm Hg (lit[6] bp 128–130°C/16 mm Hg).

3,5-Di*tert*butyl-salicylic aldehyde (6b). Pale yellow solid, mp 54–56°C (lit[18] mp 54–56°C).

3-Methyl-salicylic aldehyde (6c). Pale yellow oil, bp 210–212°C (lit[13a] bp 211°C).

3-*tert*Butyl-salicylic aldehyde (6d). Pale yellow oil, bp 247–248.5°C (lit[13a] bp 248°C).

3-Methyl-5-decyl-salicylic aldehyde (6e). Pale yellow oil, bp 37–38°C/0.07 mm Hg; ^1H NMR (300 MHz, $CDCl_3$) δ 0.80 (3H, t, J=6.6 Hz, CH_3CH_2), 1.19 (14H, br s, 7 CH_2), 1.5 (2H, m, CH_2CH_2Ar), 2.17 (3H, s, CH_3Ar), 2.47 (2H, t, J=7.7 Hz, CH_2Ar), 7.08 (1H, d, J=2.0 Hz, H-6), 7.13 (1H, br s, H-4), 9.76 (1H, s, CHO), 11.01 (1H, s, OH); IR (NaCl) 3103 (OH), 1654 (C=O) cm^{-1}; MS m/z (M^+) 276 (15%), 149 (100%), 41 (13%). Anal. calcd for $C_{18}H_{28}O_2$: C, 78.2; H, 10.2. Found: C, 78.1; H, 10.3.

Acknowledgements

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11. Conversion and yield were then estimated by GC analysis [SE-30 packed column, 1.5 m, 80°C (2), 10°C/min, 280°C (3)].

12. Solid acid-promoted acetalisation of carbonyl compound with diols is well documented in the literature: Ballini, R.; Bosica, G.; Frullanti, B.; Maggi, R.; Sartori, G.; Schroer, F. *Tetrahedron Lett.* **1998**, *38*, 1615 and references cited therein.

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15. KSF is a commercial (Fluka) montmorillonite with surface area 15±10 m^2/g, acidity 0.70 meq H^+/g (determined in our laboratory by temperature programmed desorption of ammonia gas (NH_3-TPD)) and with the following chemical composition (average value): SiO_2 (54.0%), Al_2O_3 (17.0%), Fe_2O_3 (5.2%), CaO (1.5%), MgO (2.5%), Na_2O (0.4%), K_2O (1.5%); K10 is a commecial (Fluka) montmorillonite with surface area 200±10 m^2/g, acidity 0.65 meq H^+/g and with the following chemical composition (average value): SiO_2 (73.0%), Al_2O_3 (14.0%), Fe_2O_3 (2.7%), CaO (0.2%), MgO (1.1%), Na_2O (0.6%), K_2O (1.9%).

16. Calorimetric measurement of the absorption heat of the three amines (10 mmol) on clay KSF (1.5 g) in dry toluene (90 ml) showed extremely low and quite similar values (~6 cal/g KSF), and ΔpH values of stirred suspension of clay KSF (1.5 g) in dry ethanol (45 ml) after and before addition of the three amines (10 mmol) were 8.63, 8.23 and 8.08 for Et_3N, Bu_3N and $Octyl_3N$, respectively.

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