Carbon–carbon bond cleavage and esterification of phenylacetonitrile and its derivatives affording the corresponding benzoic esters

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Phenylacetonitrile and its derivatives were treated with alcohols in the presence of potassium iodide and iodine affording the corresponding benzoate esters via degradation, oxidation and esterification under mild conditions. The products were characterised by IR, ^{1}H NMR, MS and elemental analysis.

Keywords: carbon–carbon bond cleavage, phenylacetonitrile, benzoate esters, esterification

The classic and well-known esterification methodology involves treating the carboxylic aãd with alcohol, and leads directly to the ester in the presence of sulfuric aãd as a catalyst. Several novel methods for the formation of benzoate esters have been reported recently. Thus, arylamide and aromatic formyl chlorides,[1,2,3] aromatic aldehydes,[4,5] iodobenzene,[6] benzyl type alcohols,[7,8] and aryl methyl ethers[9,10] have been converted into aromatic carboxylic aãd esters. However, to the best of our knowledge, the degradation of phenylacetonitrile derivatives has not been applied to the preparation of the corresponding benzoate esters in one-pot until we found that this conversion could be achieved by using Sm as the catalyst.[11] In continuation of these studies, we used iodine as a catalyst for the conversion. Here, we describe the treatment of phenylacetonitrile and its derivatives, containing electron-withdrawing substituents group in the phenyl ring, with appropriate alcohols in the presence of KI and catalytic amount of I_2 at suitable temperature to afford the corresponding benzoate esters directly, in good yield.

Our investigation of this strategy began with the optimisation of the reaction condition. We used 4-nitrophenylacetonitrile as the substrate, and found that 1.1 mole equivalent KI and 0.1 mole equivalent I_2 are the preferred conditions for this methodology. This conversion can take place in absence of I_2. But when 1.1 equivalent KI was used alone and stirred for 72 h, the yield was merely 63%. This reaction only took 3 h after I_2 was added. When the reaction time was prolonged from 3 h to 72 h, the yield was slightly raised from 78 to 81%. The following reactions were carried out under the optimised conditions, but different reaction times were adopted according to the substrate reactivity.

All reactions were carried out under air atmosphere. No formation of **2a** was observed when **1a** was subjected to this reaction under nitrogen atmosphere while the other conditions were not changed. Therefore, we conclude that oxygen serves as the oxidant during this conversion. As this type of reaction involves in complex factors, the detailed study about its mechanism is presently under investigation.

The majority of reactions were carried out at room temperature in good yields, while higher temperature of 50–60°C is required for the reactions of 3-nitrophenylacetonitrile with isopropyl alcohol, cyclohexyl alcohol and benzyl alcohol (Table 2, **2j–l**).

The degradation, oxidation and esterification of phenylacetonitrile and its derivatives **1a–1h** were carried out under optimal conditions base on the yields listed in Table 1, and the results with different substrates were shown in Table 2. The reaction is outlined in Scheme 1.

From the experimental results shown in Table 2, we see that the reactions of substrates containing an electron-withdrawing group on the phenyl ring were more active than unsubstituted phenylacetonitrile, while the conversion of phenylacetonitrile containing an electron-donating group such as 4-methoxyl on the phenyl ring did not take place. Moreover, the reactivity of 4-nitrophenylacetonitrile is better than 3-nitrophenylacetonitrile and they were all superior to 4-chlorophenylacetonitrile. 4-Chlorophenylacetonitrile did not react with isopropyl alcohol under the established protocol for 48 h based on GC analysis. We also observed that the reactivity of saturated alcohols followed the sequence of primary, secondary and third alcohol. This result may be ascribed to the steric hindrance effect of the alcohols.

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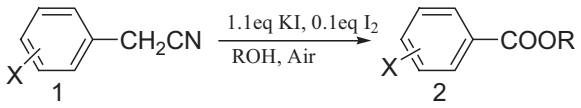
Table 1 The conversion of 4-nitrophenylacetonitrile into 4-nitrobenzoic acid methyl ester[a]

Entry	KI/equi	I_2/equi	Time/h	Yield/%
1	0.5	0	72	56
2	1.0	0	72	62
3	1.1	0	72	63
4	2.0	0	72	63
5	1.1	0.05	3	76
6	1.1	0.1	3	78
7	1.1	0.2	3	75
8	1.1	0.4	3	71
9	1.1	0.1	72	81

[a]4-nitro phenylacetonitrile 1 mmol, methanol 10 ml at room temperature



X=H, 4-chloro, 3-nitro, 4-nitro

R=CH_3, CH_2CH_3, $CH_2CH_2CH_3$, $CH(CH_3)_2$, CH_2Ph, cyclohexyl

Scheme 1

Table 2 The conversion of phenylacetonitrile and its derivatives into the corresponding benzoate esters

Entry	X	R	Temp/°C	Time/h	Yield/%
2a	4-nitro	CH_3	r.t.	3	78
2b	4-nitro	CH_2CH_3	r.t.	3	73
2c	4-nitro	$CH_2CH_2CH_3$	r.t.	4	71
2d	4-nitro	$CH(CH_3)_2$	r.t.	24	67
2e	4-nitro	CH_2Ph	r.t.	40	70
2f	4-nitro	cyclohexyl	r.t.	24	63
2g	3-nitro	CH_3	r.t.	72	71
2h	3-nitro	CH_2CH_3	r.t.	72	74
2i	3-nitro	$CH_2CH_2CH_3$	r.t.	72	74
2j	3-nitro	$CH(CH_3)_2$	60	30	65
2k	3-nitro	CH_2Ph	60	24	72
2l	3-nitro	cyclohexyl	50	21	64
2m	4-chloro	CH_3	r.t.	72	63
2n	H	CH_3	r.t.	96	57

Experimental

Solvents were dried before using. Chemicals were purchased from Acros. Melting points were measured on a YANACO melting points apparatus and were uncorrected. ^{1}H NMR spectra were recorded with Bruker Avance 400 DMX and 500 DMX spectrometers. IR spectra were recorded with Nicolet 230 FT-IR spectrometer. The MS spectrometer was Bruker Esquire 3000 plus. The elemental analysis apparatus was Eager 200.

Typical procedure for the formation of benzoic ether and its derivatives.

Phenylacetonitrile or its derivatives (2 mmol), KI (0.37 g, 2.2 mmol) and I_2(0.05 g, 0.2 mmol) were mixed with the corresponding alcohols (10 ml). The reaction mixture was then well stirred for the proper time at an appropriate temperature (illustrated in Table 2). The alcohols were then removed under vacuum. The mixture was extracted with ethyl ether or toluene. The organic layer was washed with $Na_2S_2O_3$ solution (10 ml) and water (2 × 10 ml) and dried over anhydrous sodium sulfate (Na_2SO_4). The organic solvent was evaporated. The residue was purified by column chromatography on silica gel using ethyl acetate/hexane as eluent.

Methyl 4-nitrobenzoate (**2a**): Pale yellow solid, m.p. 93–95°C (lit.,[12] 93–94°C); δ_H(500 MHz, $CDCl_3$), 8.30(d, J = 8.9 Hz, 2H), 8.22(d, J = 8.9 Hz, 2H), 3.99(S, 3H); υ_{max}(KBr)/cm^{-1}(KBr)3079, 2958, 1719, 822.

Ethyl 4-nitrobenzoate (**2b**): Pale yellow solid, m.p. 54–56°C(lit.,[13] 55–57°C); δ_H(500 MHz, $CDCl_3$), 8.29(d, J = 8.8 Hz, 2H), 8.22 (d, J = 8.8 Hz, 2H), 4.44(q, J = 7.2 Hz, 2H), 1.43(t, J = 7.2 Hz,3H); υ_{max}(KBr)/cm^{-1}(KBr)3119, 2990, 1717, 841.

Propyl 4-nitrobenzoate (**2c**): Pale yellow solid, m.p. 32–33°C(lit.,[14] 34°C); δ_H(500 MHz, $CDCl_3$), 8.28(d, J = 8.8 Hz, 2H), 8.22(d, J = 8.9 Hz, 2H), 4.34(t, J = 6.6 Hz, 2H), 1.81–1.85(m, 2H), 1.05(t, J = 7.5 Hz, 3H); υ_{max}/cm^{-1}(KBr)3109, 2968, 1719, 874.

Isopropyl 4-nitrobenzoate (**2d**): Pale yellow solid, m.p. 104–105°C(lit.,[15] 104–106°C); δ_H(500 MHz, $CDCl_3$), 8.28(d, J = 8.9 Hz, 2H), 8.20(d, J = 8.9 Hz, 2H), 5.28–5.30(m, 1H), 1.40(d, J = 6.3 Hz, 6H); υ_{max}/cm^{-1}(KBr)3116, 2923, 1713, 841.

Phenylmethyl 4-nitrobenzoate (**2e**): Pale yellow solid, m.p. 82–84°C(lit.,[16] 83–84°C); δ_H(500 MHz, $CDCl_3$), 8.28(d, J = 8.9 Hz, 2H), 8.24(d, J = 9.0 Hz, 2H), 7.37–7.46(m, 5H), 5.41(s, 2H); υ_{max}/cm^{-1} (KBr)3114, 2943, 1713, 845.

Cyclohexyl 4-nitrobenzoate (**2f**): Pale yellow solid, m.p. 48–49°C (lit.,[17] 49–51°C); δ_H(500 MHz, $CDCl_3$)8.29(d, J = 8.8 Hz, 2H), 8.22(d, J = 8.8 Hz, 2H), 5.06–5.08(m, 1H), 1.97–1.99(m, 2H), 1.80–1.80(m, 2H), 1.58–1.63(m, 4H), 1.46–1.49(m, 2H); υ_{max}/cm^{-1} (KBr)3114, 2856, 1723, 842.

Methyl 3-nitrobenzote (**2g**): Pale yellow solid, m.p. 76–78°C(lit.,[18] 77–78°C); δ_H(400 MHz, $CDCl_3$), 8.88(s, 1H), 8.37–8.44(m, 2H), 7.66(t, J = 8.0 Hz, 1H), 3.99(s, 3H); υ_{max}/cm^{-1}(KBr)3093, 2960, 1719, 840, 720.

Ethyl 3-nitrobenzote (**2h**): Pale yellow solid, m.p. 44–45°C(lit.,[1] 47°C); δ_H(500 MHz, $CDCl_3$), 8.78(s, 1H), 8.33(m, 2H), 7.62(t, J = 7.2 Hz, 1H), 4.40(q, J = 7.2 Hz, 2H), 1.39(t, J = 7.2 Hz, 3H); υ_{max}/cm^{-1}(KBr)3092, 2976, 1723, 841, 712.

Propyl 3-nitrobenzote (**2i**): Pale yellow oil (lit.[19]), δ_H(400 MHz, $CDCl_3$), 8.80(s, 1H); 8.36(m, 2H), 7.65(t, J = 8.0 Hz, 1H), 4.33(t, J = 7.2 Hz, 2H), 1.83(m, 2H), 1.03(t, J = 7.2 Hz, 3H); υ_{max}/cm^{-1} (NEAT)3092, 2972, 1723, 816, 716.

Isopropyl 3-nitrobenzote (**2j**): Pale yellow oil (lit.[20]), δ_H(400 MHz, $CDCl_3$), 8.79(s, 1H); 8.34(m, 2H), 7.62(t, J = 7.6 Hz, 1H), 5.27(m, 1H), 1.37(d, J = 6.8 Hz, 6H); υ_{max}/cm^{-1}(NEAT)3084, 2984, 1719, 816, 720.

Phenylmethyl 3-nitrobenzote (**2k**): Pale yellow oil (lit.[21]); δ_H(400 MHz, $CDCl_3$), 8.88(s, 1H), 8.42(m, 2H), 7.65(t, J = 7.6 Hz, 1H), 7.43(m, 5H), 5.43(s, 2H); υ_{max}/cm^{-1}(NEAT)3088, 2955, 1723, 820, 716.

Cyclohexyl 3-nitrobenzote (**2l**): Pale yellow oil; δ_H(400 MHz, $CDCl_3$), 8.86(s, 1H), 8.40(m, 2H), 7.66(t, J = 8.0 Hz, 1H), 5.08 (m, 1H), 1.99(m, 2H), 1.82(m, 2H), 1.62(m, 4H), 1.49(m, 2H); υ_{max}/ cm^{-1}(NEAT)3092, 2930, 1727, 774, 712; *m/z* 248.9(100%, M^+); Anal. Calc. for $C_{13}H_{15}NO_4$: C 62.6, H 6.1, N 5.6. Found: C 62.7, H 6.1, N 5.8.

Methyl 4-chlorobenzoate (**2m**): Pale yellow solid, m.p. 38–39°C (lit.,[22] 39°C); δ_H(500 MHz, $CDCl_3$), 7.98(d, J = 8.6 Hz, 2H), 7.42(d, J = 8.6 Hz, 2H), 3.92(s, 3H); υ_{max}/cm^{-1}(NEAT)3059, 2952, 1727, 850.

Methyl benzoate (**2n**): Colourless oil (lit.[1]); δ_H(500 MHz, $CDCl_3$), 8.04(d, J = 8.0 Hz, 2H), 7.55(t, J = 7.6 Hz, 1H), 7.41–7.45(m, 2H), 3.91(s, 3H); υ_{max}/cm^{-1}(NEAT)3034, 2923, 1723.

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