Practical Method for the Preparation of Nitrate Esters

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Received 6 September 1993; revised 25 October 1993

A new and cost-effective method was developed for the preparation of nitrate esters in 67–92% yields from the corresponding alkyl toluenesulfonates and sodium nitrate with a catalytic amount of tetrabutylammonium nitrate in benzene and water at 110–135 °C in a sealed tube.

A widely recognized application of nitrate esters is their use as high explosives and as ingredients of rocket propellants;[1] besides, some nitrate esters possess significant biological activities.[2] This type of compounds can be prepared from alcohols,[3–6] alkenes,[7–9] amines,[10,11] organic halides,[12] and sulfonates[13,14] by use of various nitrating agents. These reagents include acetyl nitrate,[3] acridinium nitrate,[11] benzyltrimethylammonium nitrate,[11] bromonium nitrate,[8] dinitrogen tetroxide,[10,15] dinitrogen pentoxide,[15] mercury(I)[12] and mercury(II) chlorides,[9,12] nitric acid,[4,5] *N*-nitrocollidinium tetrafluoroborate,[3] nitronium tetrafluoroborate,[3] *N*-nitropyridinium tetrafluoroborate,[3] silver nitrate,[3,4] tetrabutylammonium nitrate,[13,14] thallium(III) nitrate,[7] thionyl chloride nitrate,[6] and thionyl nitrate.[6] The established methods require acidic conditions, expensive reagents, toxic chemicals, or elaborate safety precautions; and moreover some of them are not suitable for large scale preparations. We report here a new and cost-effective method for the

Table. Conversion of Alkyl Toluenesulfonates **1a–7a** to Nitrate Esters **1b–7b**

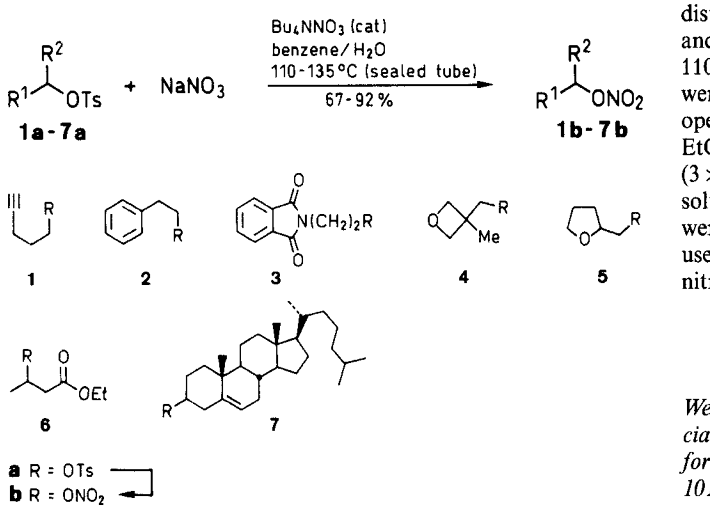
ROTs	Reaction Conditions		Yield (%)	RONO$_2$	mp (°C)	Lit. mp (°C) or bp (°C)/Torr	IR (KBr/film) $\nu_{\mathrm{N-O}}$	^{1}H NMR (CDCl$_3$/TMS) δ, J (Hz)	^{13}C NMR (CDCl$_3$/TMS) δ
	Temp. (°C)	Time (h)							
1a	120	36	81	**1b**[a]	oil		1631	1.96 (t, $J = 6.7$, 2H), 2.01–2.06 (m, 1H, ≡CH), 2.32–2.38 (m, 2H), 4.61 (t, $J = 6.7$, 2H, $\mathrm{CH_2O}$)	14.75 (t), 25.45 (t), 69.62 (s), 71.42 (t), 81.85 (d)
2a	130	20	92	**2b**	oil	49/0.2	1628	3.01 (t, $J = 7.1$, 2H, $\mathrm{CH_2}$), 4.62 (t, $J = 7.1$, 2H, $\mathrm{CH_2O}$), 7.21–7.33 (m, 5H)	32.77 (t), 73.08 (t), 126.69 (d), 128.39 (d), 128.54 (d), 135.99 (s)
3a	130	48	87	**3b**	87–88	–[b]	1609	4.09 (t, $J = 5.4$, 2H, $\mathrm{CH_2}$), 4.71 (t, $J = 5.4$, 2H, $\mathrm{CH_2O}$), 7.76–7.79 (q, $J = 5.5$, $2\mathrm{H_{arom}}$), 7.89–7.91 (q, $J = 5.5$, $2\mathrm{H_{arom}}$)	34.93 (t), 69.58 (t), 123.24 (d), 131.43 (s), 134.07 (d), 167.59 (s)
4a	120	96	71	**4b**	oil	52–54/ 1–2	1634	1.43 (s, 3H, $\mathrm{CH_3}$), 4.45 (d, $J = 6.2$, 2H, $\mathrm{OCH_2}$), 4.53 (d, $J = 6.2$, 2H, $\mathrm{OCH_2}$), 4.63 (s, 2H, $\mathrm{CH_2ON}$)	20.25 (q), 37.93 (s), 76.78 (t), 78.59 (t)
5a	135	96	82	**5b**	oil	–[b]	1633	1.63–1.78 (m, 1H), 1.89–2.01 (m, 2H), 2.03–2.15 (m, 1H), 3.78–3.95 (m, 2H, $\mathrm{OCH_2}$), 4.15–4.24 (m, 1H, OCH), 4.39–4.56 (m, 2H, $\mathrm{CH_2ON}$)	25.39 (t), 27.90 (t), 68.42 (t), 74.44 (t), 74.61 (d)
6a	110	96	67	**6b**	oil	–[b]	1631	1.27 (t, $J = 7.1$, 3H, $\mathrm{CH_3}$), 1.43 (d, $J = 6.4$, 3H, $\mathrm{CH_3}$), 2.58 (dd, $J = 7.2$, 16.0, 1H, CHC=O), 2.74 (dd, $J = 7.2$, 16.0, 1H, CHC=O), 4.17 (q, $J = 7.1$, 2H, $\mathrm{OCH_2}$), 5.46–5.54 (m, 1H, CHON)	13.47 (q), 17.68 (q), 38.27 (t), 60.47 (t), 76.60 (d), 168.75 (s)
7a	120	24	73	**7b**	114–115	115–116[25]	1626	0.68 (s, 3H, $\mathrm{CH_3}$), 0.86 (d, $J = 6.6$, 6H, $2 \times \mathrm{CH_3}$), 0.92 (d, $J = 6.6$, 3H, $\mathrm{CH_3}$), 1.02 (s, 3H, $\mathrm{CH_3}$), 1.06–2.06 (m, 26H), 2.34–2.49 (m, 2H), 4.75–4.87 (m, 1H, OCH), 5.42–5.47 (m, 1H, =CH)	11.75 (q), 18.67 (q), 19.06 (q), 21.03 (t), 22.51 (q), 22.75 (q), 23.92 (t), 24.22 (t), 25.92 (t), 27.93 (d), 28.19 (t), 31.75 (d), 31.86 (t), 35.80 (d), 36.21 (t), 36.51 (s), 36.80 (t), 39.50 (t), 39.68 (t), 42.24 (s), 49.96 (d), 56.21 (d), 56.62 (d), 82.98 (d), 123.74 (d), 138.31 (s)

[a] $\mathrm{C_5H_7NO_3}$ (129.1) calc. C 46.50 H 5.47 N 10.85; found 46.31 5.28 11.13

[b] Not reported.

synthesis of nitrate esters from alkyl toluenesulfonates by use of sodium nitrate in the presence of tetrabutylammonium nitrate as the phase-transfer catalyst.[16]

The *p*-toluenesulfonates **1a**–**7a** were heated at 110–135 °C with sodium nitrate in the presence of catalytic amount of tetrabutylammonium nitrate in benzene and water in a sealed tube[17] to give the desired nitrate esters **1b**–**7b** in 67–92% yield (Scheme, Table). We found that both primary and secondary alkyl *p*-toluenesulfonates can be converted to the corresponding nitrate esters efficiently by the newly developed method. In addition, the reaction conditions were mild so that some functionalities remained intact, including the C–C triple bond in **1a**, the phthalimide moiety in **3a**, the oxetane ring in **4a**, and the tetrahydrofuran ring in **5a**. Furthermore, some potential competing reactions did not occur: nitration of the aromatic ring[3] in **2a** and **3a**; elimination of the *p*-toluenesulfonyl group at the *β*-position in ester **6a** and at the homoallylic position in **7a**.



Scheme

Many nitrate esters are highly explosive; thus appropriate precautions must be taken in their handling.[1] Traces of acidic impurities may sensitize nitrate esters to decompose and cause explosion upon heating, or even on storage at room temperature.[4] We have applied our conditions for preparing nitrate esters **1b**–**7b** more than one hundred times; until now we have not experienced any explosion.

Cainelli et al.[14] used a 1.5 molar excess of tetrabutylammonium nitrate as the nitrating agent for the preparation of nitrate esters from the corresponding toluenesulfonates. In our method, a catalytic amount of tetrabutylammonium nitrate was utilized along with an excess of sodium nitrate, which costs much less than the former (1 : 142).[18] However, this method did not succeed in the preparation of nitrate esters from alkyl chlorides and bromides. The nitrate ester products would react with the halide ions generated in situ; thus most of the starting halides were recovered.[19] We also found that racemization occurred in the preparation of **6b** from **6a**; this was due to displacement of the nitrate ester group in **6b** by the excess nitrate ions.[14]

In conclusion, sodium nitrate was developed as an efficient nitrating agent for the conversion of alkyl *p*-toluenesulfonates to nitrate esters in the presence of tetrabutylammonium nitrate as the phase-transfer catalyst. This new method provided the desired products in good to excellent yields under neutral conditions through a chemoselective nitration process. It is cost-effective and has potential for large scale preparations.

All alcohols, except ethyl 3-hydroxybutanoate,[20] were purchased from E. Merck or Aldrich Chemical Co. and were used without further purification. The tosylates were prepared by reported procedures.[21] IR spectra were measured on a Bomem Michaelson Series MB-100 FT-IR spectrophotometer. Low resolution mass spectral analyses were carried out on a Jeol JMS-SX 102 spectrometer and high resolution on a Jeol JMS-HX110 spectrometer. Spectra of ^1H NMR were obtained on a Gemini 300 (300 MHz) spectrometer; spectra of ^{13}C NMR were recorded at 75 MHz.

Nitrate Esters 1b–7b; General Procedure:

Alkyl *p*-toluenesulfonate **1a**–**7a** (10.0 mmol), $NaNO_3$ (0.100 mol), and Bu_4NNO_3 (0.082 mmol) were charged in a sealable bottle[17] equipped with a stirrer and a Teflon stopper. Benzene (15 mL) and distilled water (14 mL) were added to the bottle, which was sealed and placed in an oil bath. The contents were stirred vigorously at 110–135 °C for 20–96 h. The temperature and pressure of the bottle were then allowed to return to normal, after which it was carefully opened. The contents were poured into H_2O and extracted with EtOAc (2 × 50 mL). The organic phase was washed with water (3 × 50 mL), brine (50 mL), dried ($MgSO_4$) and filtered. After the solvents were removed under reduced pressure, the crude products were purified by flash column chromatography over silica gel by use of a mixture of EtOAc and hexanes (1 : 4) as the eluent. Pure nitrate esters **1b**–**7b** were isolated in 67–92% yields (Table).

We thank Chung-Shan Institute of Science and Technology for financial support and the National Science Council of Republic of China for research grants CS 82-0210-D-007-022 and NSC 83-0208-M007-101.

[+] Recepient of the Federation of Asian Chemical Societies 1992 and 1993 Distinguished Young Chemist Award.

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