Selective Monoalkylation of Tosylacetonitrile

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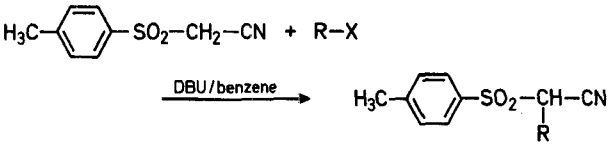
Alkylation of tosylacetonitrile with alkyl halides was attempted to prepare a series of α-monoalkyl derivatives. The literature reports that alkylation of tosylacetonitrile with alkyl halides and sodium ethoxide in ethanol yields dialkyl derivatives[1]. In general, the selective monoalkylation of relatively stable carbanions involves difficulties[2]. We now report a simple method for the selective monoalkylation of tosylacetonitrile using 1,8-diazabicyclo[5.4.0]-7-undecene (DBU) in benzene as base.

The procedure is quite simple; for example, a solution of tosylacetonitrile, DBU, and ethyl iodide in benzene is stirred for one hour at room temperature. Simple work-up affords pure 2-tosylbutanenitrile in 92% yield. The corresponding dialkylated product cannot be detected by T.L.C. Monoalkyl derivatives of tosylacetonitrile were thus obtained in high yields using *prim*-alkyl halides (Table 1). Introduction of secondary alkyl groups is also possible by this method, although the yields are somewhat lower. Analytical and spectral data (I.R. and N.M.R.) of the compounds prepared are consistent with the assigned structures.



Triethylamine failed to induce alkylation under similar conditions.

Alkylation of tosylacetonitrile with ethyl iodide by the conventional method (sodium hydride in dimethylformamide, or phase-transfer conditions[3]) resulted in the formation of considerable amounts of the dialkylated product (Table 2). As can be seen from Tables 1 and 2, the present method for alkylation of tosylacetonitrile is much simpler and more selective than the conventional method.

Table 2. The Effect of Base and Solvent on the Alkylation of Tosylacetonitrile with Ethyl Iodide (room temperature, 1 h, ratio substrate : base : $C_2H_5J = 1 : 1 : 2$)

DBU	Solvent	Monoalkylation (%)[a]	Dialkylation (%)[a]
DBU	Benzene	99.5	0.5
NaH	DMF	52.0	48.0
50% NaOH/TEBA	Benzene[b]	86.5	13.5

[a] Determined by G.L.C.

[b] Phase-transfer condition: TEBA (triethylbenzylammonium chloride) was used; see Ref.[3].

Tosylacetonitrile:

To a stirred suspension of sodium *p*-toluenesulfinate tetrahydrate (37.5 g, 0.15 mol) in dimethylformamide (150 ml) is added a solution of chloroacetonitrile (7.55 g, 0.10 mol) in dimethylformamide (30 ml) and the mixture is stirred for 24 h at room temperature. Then, ice water (500 ml) is added and the mixture is extracted

Table 1. 2-Tosylalkanenitriles obtained from Tosylacetonitrile and Alkyl Halides (R—X) in the Presence of DBU

R—X	Reaction time at room temperature [h]	Yield[a] [%]	m.p.	Molecular formula[b]	I.R. (Nujol) ν_{max} [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]
CH_3J	0.5	88	66°	(Ref.[4], m.p. 66°)		
C_2H_5—J	1.0	92	42–43°	$C_{11}H_{13}NO_2S$ (223.3)	1155 1335	1.12 (t, 3H); 2.00 (m, 2H); 2.46 (s, 3H); 3.94 (m, 2H); 7.40 (d, 2H); 7.80 (d, 2H)
C_2H_5—Br	15	93				
n-C_3H_7—Br	15	95	36–37°	$C_{12}H_{15}NO_2S$ (237.5)	1150 1330	1.01 (t, 3H); 1.60 (m, 2H); 1.80 (m, 3H); 2.45 (s, 3H); 3.92 (m, 1H); 7.40 (d, 2H); 7.80 (d, 2H)
i-C_3H_7—J	10	41	55–56°	$C_{12}H_{15}NO_2S$ (237.5)	1150 1330	1.20 (d, 6H); 2.46 (s, 3H); 2.70 (m, 1H); 3.92 (d, 1H); 7.40 (d, 2H); 7.80 (d, 2H)
n-C_4H_9—Br	15	96	38–39°	$C_{13}H_{17}NO_2S$ (261.3)	1155 1330	0.92 (t, 3H); 1.40 (m, 4H); 1.90 (m, 2H); 2.45 (s, 3H); 3.94 (m, 1H); 7.40 (d, 2H); 7.80 (d, 2H)
n-C_8H_{17}—Br	24	95	47–48°	$C_{17}H_{25}NO_2S$ (307.4)	1140 1310	0.92 (t, 3H); 1.22 (m, 12H); 1.85 (m, 2H); 2.45 (s, 3H); 4.00 (m, 1H); 7.40 (d, 2H); 7.80 (d, 2H)

[a] Yield of isolated product.

[b] The microanalyses of all new products were in satisfactory agreement with the calculated values: C, ±0.15; H, ±0.12; N, ±0.19.

with benzene. The extract is washed with water, dried with magnesium sulfate, and evaporated in vacuo. The residue is recrystallized from ethanol; yield: 17.0 g (87%); m.p. 153–154° (Ref.[5], m.p. 146°).

This method gives better yields than that of Ref.[5].

2-Tosylbutanenitrile; Typical Alkylation Procedure:

To a stirred solution of tosylacetonitrile (1.95 g, 0.01 mol) and DBU (1.67 g, 0.011 mol) in benzene (50 ml) is added at once ethyl iodide (3.12 g, 0.02 mol) and the solution is stirred for 1 h at room temperature. The precipitated DBU-HJ salt is removed by filtration. The filtrate is washed with dilute hydrochloric acid, then with water, and dried with magnesium sulfate. Benzene is evaporated in vacuo. The residue is recrystallized from ethanol; yield: 2.04 (92%); m.p. 42–43°.

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