Synthesis of α-Aminonitriles through Strecker Reaction of *N*-Tosylaldimines Using Molecular Iodine¹

Biswanath Das,* Penagaluri Balasubramanyam, Maddeboina Krishnaiah, Boyapati Veeranjaneyulu, Gandolla Chinna Reddy

Organic Chemistry Division-1, Indian Institute of Chemical Technology, Hyderabad 500007, India Fax +91(40)27160512; E-mail: biswanathdas@yahoo.com *Received 6 May 2009; revised 9 June 2009*

Abstract: The Strecker reaction of *N*-tosylaldimines with trimethylsilyl cyanide in the presence of catalytic amount of iodine at room temperature produces the corresponding protected α -aminonitriles in high yields.

Key words: Strecker reaction, *N*-tosylaldimine, trimethylsilyl cyanide, protected α -aminonitrile, iodine

 α -Aminonitriles are useful intermediates for the preparation of α -amino acids,² various nitrogen containing heterocycles, such as imidazoles and thiadiazoles,³ and pharmaceuticals.^{4,5b} α -Amino acids are highly applicable in chemistry and biology as valuable building blocks.⁵ The Strecker reaction involving nucleophilic addition of a cyanide ion to an imine, is of great importance to modern organic chemistry as it offers one of the most direct feasible methods for the synthesis of α -aminonitriles.⁶ However the experimental procedure of this reaction is tedious. Several modified methods have been subsequently introduced using various cyanide reagents [e.g. diethyl phosphorocyanidate, α -(trimethylsiloxy)nitrile, tributyltin cyanide, trimethylsilyl cyanide, etc.].⁷ Among these cyanide ion equivalents, trimethylsilyl cyanide was found to be more efficient and safer in handling.

The Strecker reaction has been studied extensively by using various Lewis acids,⁸ Lewis bases,⁹ *N*-heterocyclic carbenes,¹⁰ and metal complexes and metal–salen complexes.¹¹ Recently, a number of asymmetric Strecker reactions using effective catalysts have been reported.¹²



Scheme 1 Synthesis of α -aminonitriles by the reaction of *N*-tosylaldimines and trimethylsilyl cyanide

 α -Aminonitriles have also been synthesized by employing Strecker methodology using ionic liquids and water instead of regular organic solvents.^{8a,13}

SYNTHESIS 2009, No. 20, pp 3467–3471 Advanced online publication: 21.08.2009 DOI: 10.1055/s-0029-1216969; Art ID: Z08909SS © Georg Thieme Verlag Stuttgart · New York **Table 1**Evaluation of the Catalytic Activity of Different Catalystsfor the Preparation of α -Aminonitrile $3a^{a}$



^a Conditions: *N*-tosylaldimine **1a** (1.0 mmol), TMSCN **2** (1.3 mmol), catalyst (15 mol%), CH₂Cl₂ (2 mL), r.t.

^b Isolated yield.

There have numerous reports in recent years on the application of *N*-sulfonyl- and *N*-sulfinylimines, which are stable compounds.¹⁴ These sulfonyl and sulfinyl groups are good activators of the C=N bond for nucleophilic addition reactions. Therefore, the addition of trimethylsilyl cyanide to these compounds is expected to be a good method for obtaining α -aminonitriles. There are only a few reports on the Strecker reaction of *N*-sulfonylimines using N-heterocyclic carbenes,^{15a,b} Feng's bifunctional *N*,*N*¹-dioxide,^{15c} Lewis acids and bases,^{8b,9b} and Nap-MgO.^{15d} However, many of these methods suffer from different drawbacks such as requirement for longer reaction times, application of costly reagents, harsh reaction conditions, and unsatisfactory yields.

In continuation of our work on the development of useful synthetic methodologies we have observed that protected α -aminonitriles **3** can efficiently be synthesized by treatment of *N*-sulfonylaldimines **1** with trimethylsilyl cyanide (**2**) in the presence of iodine as a catalyst at room temperature (Scheme 1).

Initially we carried out the reaction of N-tosylbenzaldimine (1a) with trimethylsilyl cyanide (2) in the presence of various catalysts. However, considering the reaction time and yield iodine was found to be most effective Ts

(Table 1). Finally a series of protected α -aminonitriles **3** were prepared (Table 2) from different N-tosylaldimines 2^{14a,c,16} derived from various aromatic, heteroaromatic, and aliphatic aldehydes using trimethylsilyl cyanide (2) in the presence of iodine. The aromatic aldehydes contained both electron-donating as well as electron-withdrawing groups (Table 1, entries 2–12). The aliphatic aldimine derivatives (Table 2, entries 15 and 16) also underwent smooth conversion into α -aminonitriles. The reaction was conducted at room temperature and the conversion was complete within 60–90 minutes and the protected α -aminonitriles 3 were formed in excellent yields (86–94%). The structures of the products 3 were confirmed by their spectral (IR, ¹H and ¹³C NMR, and MS) data. The *N*-tosyl group of the products can easily be deprotected¹⁷ to furnish the corresponding α -aminonitriles which can be used to explore their biological applications.

The catalyst, iodine is inexpensive, easily available, and nontoxic. It efficiently conducts the nucleophilic addition of *N*-sulfonylimines by polarizing the CH=N bond of the compounds.

Table 2 Iodine-Catalyzed Synthesis of α -Aminonitriles **3** by the Reaction of *N*-Tosylaldimines **1** and Trimethylsilyl Cyanide (**2**)^a

R = aryl,	+ TMSCN _ 2 alkyl	I ₂ (15 mol%) CH ₂ Cl ₂ , r.t. 60–90 min	- R 3 86-9	Ts CN 4 %
Entry	R	Time (min	n) Product	Yield ^b (%)
1	Ph	60	3a	94
2	$3-ClC_6H_4$	60	3b	92
3	$4-ClC_6H_4$	60	3c	93
4	4-F-3-ClC ₆ H ₃	70	3d	92
5	2,3,4-F ₃ C ₆ H ₂	80	3e	90
6	$4-O_2NC_6H_4$	80	3f	91
7	4-MeOC ₆ H ₄	90	3g	88
8	$4-BnOC_6H_4$	90	3h	89
9	4-EtOC ₆ H ₄	90	3i	90
10	$4-\text{MeC}_6\text{H}_4$	80	3j	92
11	2,5-Me ₂ C ₆ H ₃	80	3k	90
12	2,4,6-Me ₃ C ₆ H ₂	90	31	88
13	2-furyl	90	3m	86
14	2-thienyl	80	3n	89
15	Et	60	30	91
16	Pr	60	3p	90

^a Reaction conditions: *N*-tosylaldimine **1** (1.0 mmol), TMSCN **2** (1.3 mmol), I_2 (15 mol%), CH_2Cl_2 (2 mL), r.t. ^b Isolated yield.

Synthesis 2009, No. 20, 3467-3471 © Thieme Stuttgart · New York

In conclusion, we have developed a facile method for the synthesis of α -aminonitriles from *N*-tosylaldimines and trimethylsilyl cyanide using iodine as a catalyst. The operational simplicity, mild reaction conditions, application of an easily available catalyst, short reaction times and excellent yields are the notable advantages of the method. The tosyl group of the products can also easily be deprotected to free amines, which can be utilized for the preparation of various desired analogues.

Melting points were measured on a Buchi 510 apparatus and are uncorrected. The IR spectra were recorded with KBr on a Perkin-Elmer RX 1 FT-IR spectrophotometer; the NMR spectra on a Varian Gemini-200 MHz spectrometer using $CDCl_3$ as a solvent and TMS as an internal standard; and the mass spectra on a VG Micromass 7070 H (70 eV) and Thermo Finnegan LCQ ion trap mass spectrometers. Column chromatography was performed over silica gel (BDH, 100–200 mesh) and TLC on silica gel GF 254.

α-Aminonitriles 3; General Procedure

Tosylimine 1 (1 mmol) was taken in CH₂Cl₂ (2 mL) and I₂ (15 mol%) was added. To this mixture TMSCN 2 (1.3 mmol) was added dropwise. The mixture was stirred at r.t. (TLC monitoring). After completion the reaction was quenched with sat. Na₂S₂O₃ soln (10 mL) and the mixture was extracted with CH₂Cl₂ (3 × 10 mL). The combined extracts were dried and concentrated and the residue was subjected to column chromatography (silica gel, hexane–EtOAc) to obtain pure α -aminonitrile 3.

N-[Cyano(phenyl)methyl]-4-methylbenzenesulfonamide (3a) Mp 151–153 °C.

IR: 3264, 2310, 1597, 1448, 1333, 1156 cm⁻¹.

¹H NMR (200 MHz, CDCl₃): δ = 7.82 (d, *J* = 8.0 Hz, 2 H), 7.49–7.36 (m, 7 H), 5.60 (d, *J* = 10.0 Hz, 1 H), 5.47 (d, *J* = 10.0 Hz, 1 H), 2.49 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 144.8, 136.1, 132.2, 130.0, 129.9, 129.4, 127.3, 127.1, 116.5, 48.3, 21.9.

MS (ESI): $m/z = 309 [M + Na]^+$.

Anal. Calcd for $C_{15}H_{14}N_2O_2S$: C, 62.93; H, 4.89; N, 9.79. Found: C, 62.86; H, 4.97; N, 9.84.

N-[3-Chlorophenyl)(cyano)methyl]-4-methylbenzenesulfonamide (3b)

Mp 101–103 °C.

IR: 3278, 2237, 1596, 1437, 1349, 1161 cm⁻¹.

¹H NMR (200 MHz, CDCl₃): δ = 7.78 (d, *J* = 8.0 Hz, 2 H), 7.40–7.31 (m, 6 H), 5.59 (d, *J* = 10.0 Hz, 1 H), 5.39 (d, *J* = 10.0 Hz, 1 H), 2.48 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 145.0, 135.8, 135.3, 133.9, 130.8, 130.1, 130.0, 127.1, 125.2, 116.0, 47.8, 21.9.

MS (ESI): m/z = 343, 345 [M + Na]⁺.

Anal. Calcd for $C_{15}H_{13}ClN_2O_2S$: C, 56.26; H, 4.06; N, 8.74. Found: C, 56.31; H, 4.13; N, 8.62.

N-[(4-Chlorophenyl)(cyano)methyl]-4-methylbenzenesulfonamide (3c)

Mp 133–135 °C.

IR: 3261, 1925, 1594, 1491, 1342, 1159 cm⁻¹.

¹H NMR (200 MHz, CDCl₃): δ = 7.77 (d, *J* = 8.0 Hz, 2 H), 7.43–7.31 (m, 6 H), 5.81 (d, *J* = 10.0 Hz, 1 H), 5.41 (d, *J* = 10.0 Hz, 1 H), 2.48 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 148.9, 136.1, 136.0, 130.9, 130.5, 129.8, 128.2, 127.6, 116.0, 47.7, 21.5.

MS (ESI): m/z = 343, $345 [M + Na]^+$.

Anal. Calcd for $C_{15}H_{13}ClN_2O_2S$: C, 56.25; H, 4.06; N, 8.73. Found: C, 56.22; H, 4.11; N, 8.79.

N-[(3-Chloro-4-fluorophenyl)(cyano)methyl]-4-methylbenzenesulfonamide (3d)

Mp 124–125 °C.

IR: 3279, 1597, 1499, 1443, 1345, 1159 cm⁻¹.

¹H NMR (200 MHz, $CDCl_3$): $\delta = 7.74$ (d, J = 8.0 Hz, 2 H), 7.42 (dd, J = 8.0, 2.0 Hz, 1 H), 7.35 (d, J = 2.0 Hz, 1 H), 7.32 (d, J = 8.0 Hz, 2 H), 7.12 (t, J = 8.0 Hz, 1 H), 5.92 (d, J = 10.0 Hz, 1 H), 5.41 (d, J = 10.0 Hz, 1 H), 2.42 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 157.0, 145.0, 135.9, 130.2, 130.0, 129.6, 127.1, 122.0 (d, *J* = 8.0 Hz), 117.5 (d, *J* = 8.0 Hz), 115.7, 47.1, 21.5.

MS (ESI): m/z = 361, 363 [M + Na]⁺.

Anal. Calcd for $C_{15}H_{12}ClFN_2O_2S$: C, 53.25; H, 3.55; N, 8.28. Found: C, 53.32; H, 3.46; N, 8.21.

N-[Cyano(2,3,4-trifluorophenyl)methyl]-4-methylbenzenesulfonamide (3e)

Mp 96–98 °C.

IR: 3253, 2240, 1600, 1512, 1348, 1153 cm⁻¹.

¹H NMR (200 MHz, CDCl₃): δ = 7.72 (d, *J* = 8.0 Hz, 2 H), 7.38–7.19 (m, 3 H), 7.00 (m, 1 H), 5.92 (d, *J* = 10.0 Hz, 1 H), 5.57 (d, *J* = 10.0 Hz, 1 H), 2.45 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 145.0, 135.9, 130.1, 127.2, 123.0, 122.9, 118.0, 117.9, 116.1, 113.1, 113.0, 42.4, 21.9.

MS (ESI): $m/z = 363 [M + Na]^+$.

Anal. Calcd for $C_{15}H_{11}F_3N_2O_2S$: C, 52.94; H, 3.24; N, 8.24. Found: C, 52.82; H, 3.19; N, 8.17.

N-[Cyano(4-nitrophenyl)methyl]-4-methylbenzenesulfonamide (3f)

Mp 120–122 °C.

IR: 3261, 1920, 1600, 1531, 1459, 1347, 1161 cm⁻¹.

¹H NMR (200 MHz, CDCl₃): δ = 8.26 (d, *J* = 8.0 Hz, 2 H), 7.78 (d, *J* = 8.0 Hz, 2 H), 7.70 (d, *J* = 8.0 Hz, 2 H), 7.38 (d, *J* = 8.0 Hz, 2 H), 5.55 (d, *J* = 10.0 Hz, 1 H), 5.36 (d, *J* = 10.0 Hz, 1 H), 2.7 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 148.7, 145.3, 138.6, 135.5, 130.3, 128.4, 127.3, 124.5, 115.6, 47.5, 21.7.

MS (ESI): $m/z = 354 [M + Na]^+$.

Anal. Calcd for $C_{15}H_{13}N_{3}O_{4}S$: C, 54.39; H, 3.93; N, 12.69. Found: C, 54.30; H, 3.99; N, 12.76.

N-[Cyano(4-methoxyphenyl)methyl]-4-methylbenzenesulfonamide (3g)

Mp 128–130 °C.

IR: 3269, 2320, 1606, 1512, 1437, 1252, 1158 cm⁻¹.

¹H NMR (200 MHz, CDCl₃): δ = 7.70 (d, *J* = 8.0 Hz, 2 H), 7.35 (d, *J* = 8.0 Hz, 2 H), 7.32 (d, *J* = 8.0 Hz, 2 H), 6.88 (d, *J* = 8.0 Hz, 2 H), 5.58 (d, *J* = 10.0 Hz, 1 H), 5.39 (d, *J* = 10.0 Hz, 1 H), 3.79 (s, 3 H), 2.45 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 160.4, 144.5, 136.2, 130.0, 128.4, 127.2, 124.0, 116.8, 114.9, 55.8, 47.9, 21.8.

MS (ESI): $m/z = 339 [M + Na]^+$.

Anal. Calcd for $C_{16}H_{16}N_2O_3S$: C, 60.76; H, 5.06; N, 8.86. Found: C, 60.85; H, 5.13; N, 8.78.

N-{[4-(Benzyloxy)phenyl](cyano)methyl}-4-methylbenzenesulfonamide (3h)

Mp 164–166 °C.

IR: 3258, 2238, 1606, 1513, 1329, 1247 cm⁻¹.

¹H NMR (200 MHz, CDCl₃): δ = 7.81 (d, *J* = 8.0 Hz, 2 H), 7.46– 7.31 (m, 9 H), 6.98 (d, *J* = 8.0 Hz, 2 H), 5.41 (d, *J* = 10.0 Hz, 1 H), 5.17 (d, *J* = 10.0 Hz, 1 H), 5.05 (s, 2 H), 2.46 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 158.8, 145.5, 136.1, 130.1, 128.9, 128.8, 127.3, 124.6, 115.8, 70.1, 48.0, 21.8.

MS (ESI): $m/z = 415 [M + Na]^+$.

Anal. Calcd for $C_{22}H_{20}N_2O_3S;\,C,\,67.35;\,H,\,5.10;\,N,\,7.14.$ Found: C, 67.52; H, 5.04; N, 7.28.

N-[Cyano(4-ethoxyphenyl)methyl]-4-methylbenzenesulfonamide (3i)

Mp 112–114 °C.

IR: 3279, 2250, 1607, 1513, 1337, 1256 cm⁻¹.

¹H NMR (200 MHz, $CDCl_3$): $\delta = 7.79$ (d, J = 8.0 Hz, 2 H), 7.32 (d, J = 8.0 Hz, 2 H), 7.28 (d, J = 8.0 Hz, 2 H), 6.83 (d, J = 8.0 Hz, 2 H), 5.60 (br s, 1 H), 5.36 (d, J = 8.0 Hz, 1 H), 4.00 (q, J = 7.0 Hz, 2 H), 2.43 (s, 3 H), 1.41 (t, J = 7.0 Hz, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 159.9, 144.5, 136.2, 130.0, 128.5, 127.4, 124.0, 116.9, 115.2, 63.9, 47.9, 21.6, 14.6.

MS (ESI): $m/z = 353 [M + Na]^+$.

Anal. Calcd for $C_{17}H_{18}N_2O_3S$: C, 61.82; H, 5.46; N, 8.49. Found: C, 61.94; H, 5.52; N, 8.54.

$N\$ [Cyano(p-tolyl)methyl]-4-methylbenzenesulfonamide (3j) Mp $154\$ -156 °C.

IR: 3269, 2250, 1596, 1437, 1335, 1159 cm⁻¹.

¹H NMR (200 MHz, CDCl₃): δ = 7.82 (d, *J* = 8.0 Hz, 2 H), 7.38 (d, *J* = 8.0 Hz, 2 H), 7.32 (d, *J* = 8.0 Hz, 2 H), 7.19 (d, *J* = 8.0 Hz, 2 H), 5.42 (d, *J* = 10.0 Hz, 1 H), 5.01 (d, *J* = 10.0 Hz, 1 H), 2.50 (s, 3 H), 2.39 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 144.9, 140.2, 136.0, 130.0, 129.1, 127.2, 127.0, 116.5, 48.1, 21.7, 21.1.

MS (ESI): $m/z = 323 [M + Na]^+$.

Anal. Calcd for $C_{16}H_{16}N_2O_2S$: C, 64.00; H, 5.33; N, 9.34. Found: C, 64.08; H, 5.25; N, 9.41.

N-[Cyano(2,5-dimethylphenyl)methyl]-4-methylbenzenesulfonamide (3k)

Mp 137-139 °C.

IR: 3268, 2217, 1596, 1332, 1157 cm⁻¹.

¹H NMR (200 MHz, $CDCl_3$): $\delta = 7.80$ (d, J = 8.0 Hz, 2 H), 7.35 (d, J = 8.0 Hz, 2 H), 7.22 (dd, J = 8.0, 2.0 Hz, 1 H), 7.08 (br s, 2 H), 5.51 (d, J = 10.0 Hz, 1 H), 4.89 (d, J = 10.0 Hz, 1 H), 2.49 (s, 3 H), 2.38 (s, 3 H), 2.31 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 144.5, 136.8, 136.2, 133.1, 131.6, 130.8, 129.9, 128.2, 127.3, 116.8, 46.0, 21.5, 21.0, 18.2.

MS (ESI): $m/z = 337 [M + Na]^+$.

Anal. Calcd for $C_{17}H_{18}N_2O_2S$: C, 64.97; H, 5.73; N, 8.91. Found: C, 64.83; H, 5.82; N, 8.84.

N-[Cyano(mesityl)methyl]-4-methylbenzenesulfonamide (3l) Mp 139–140 °C.

IR: 3277, 1601, 1416, 1334, 1161 cm⁻¹.

¹H NMR (200 MHz, CDCl₃): δ = 7.76 (d, *J* = 8.0 Hz, 2 H), 7.28 (d, *J* = 8.0 Hz, 2 H), 6.81 (s, 2 H), 5.64 (d, *J* = 8.0 Hz, 1 H), 5.52 (br s, 1 H), 2.42 (s, 3 H), 2.31 (s, 6 H), 2.22 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 144.8, 139.8, 136.7, 136.0, 130.2, 130.0, 127.3, 126.1, 116.8, 42.9, 21.2, 20.5, 19.9.

MS (ESI): $m/z = 351 [M + Na]^+$.

Anal. Calcd for $C_{18}H_{20}N_2O_2S{:}$ C, 65.85; H, 6.10; N, 8.54. Found: C, 65.72; H, 6.18; N, 8.63.

$N\$ [Cyano(2-furyl)methyl]-4-methylbenzenesulfonamide (3m) Mp 99–101 °C.

IR: 3113, 1465, 1330, 1241, 1161 cm⁻¹.

¹H NMR (200 MHz, CDCl₃): δ = 7.79 (d, *J* = 8.0 Hz, 2 H), 7.38 (d, *J* = 8.0 Hz, 1 H), 7.32 (d, *J* = 8.0 Hz, 2 H), 6.48 (m, 1 H), 6.32 (m, 1 H), 5.70 (m, 1 H), 5.52 (d, *J* = 8.0 Hz, 1 H), 2.43 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 144.9, 144.5, 144.2, 135.9, 130.1, 127.2, 114.8, 111.1, 110.7, 42.2, 21.7.

MS (ESI): $m/z = 299 [M + Na]^+$.

Anal. Calcd for $C_{13}H_{12}N_2O_3S\colon C,$ 56.52; H, 4.35; N, 10.14. Found: C, 56.61; H, 4.43; N, 10.07.

$N\$ [Cyano(2-thienyl)methyl]-4-methylbenzenesulfonamide (3n) Mp 113–115 °C.

IR: 3238, 2217, 1600, 1333 cm⁻¹.

¹H NMR (200 MHz, CDCl₃): δ = 7.81 (d, *J* = 8.0 Hz, 2 H), 7.40–7.34 (m, 3 H), 7.20 (m, 1 H), 6.98 (m, 1 H), 5.79 (d, *J* = 10.0 Hz, 1 H), 5.65 (d, *J* = 10.0 Hz, 1 H), 2.46 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 145.0, 136.2, 134.9, 130.2, 130.0, 128.2, 128.0, 127.3, 127.2, 126.4, 115.8, 43.9, 21.5.

MS (ESI): $m/z = 315 [M + Na]^+$.

Anal. Calcd for $C_{13}H_{12}N_2O_2S_2$: C, 53.43; H, 4.11; N, 9.59. Found: C, 53.58; H, 4.17; N, 9.48.

$N\mbox{-}(1\mbox{-}\mbox{-}\mbox{cyanopropyl})\mbox{-}4\mbox{-}\mbox{methylbenzenesulfonamide}$ (30) Mp 81–83 °C.

IR: 3269, 2249, 1599, 1441, 1338, 1169 cm⁻¹.

¹H NMR (200 MHz, CDCl3): δ = 7.80 (d, *J* = 8.0 Hz, 2 H), 7.35 (d, *J* = 8.0 Hz, 2 H), 5.80 (br s, 1 H), 4.15 (q, *J* = 7.0 Hz, 1 H), 2.45 (s, 3 H), 1.88–1.76 (m, 2 H), 1.05 (t, *J* = 7.0 Hz, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 144.5, 136.0, 130.1, 127.3, 117.5, 45.6, 27.4, 21.5, 9.8.

MS (ESI): $m/z = 261 [M + Na]^+$.

Anal. Calcd for $C_{11}H_{14}N_2O_2S$: C, 55.46; H, 5.88; N, 11.76. Found: C, 55.38; H, 5.99; N, 11.84.

N-(1-Cyanobutyl)-4-methylbenzenesulfonamide (3p) Mp 84–86 °C.

IR: 3282, 2242, 1597, 1424, 1334, 1160 cm⁻¹.

¹H NMR (200 MHz, CDCl₃): δ = 7.80 (d, *J* = 8.0 Hz, 2 H), 7.35 (d, *J* = 8.0 Hz, 2 H), 5.69 (br s, 1 H), 4.21 (q, *J* = 7.0 Hz, 1 H), 2.45 (s, 3 H), 1.81–1.72 (m, 2 H), 1.52–1.40 (m, 2 H), 0.92 (t, *J* = 7.0 Hz, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 144.5, 136.0, 129.9, 127.0, 117.6, 44.0, 35.8, 21.7, 18.4, 13.0.

MS (ESI): $m/z = 275 [M + Na]^+$.

Anal. Calcd for $C_{12}H_{16}N_2O_2S;\,C,\,57.14;\,H,\,6.35;\,N,\,11.11.$ Found: C, 57.21; H, 6.47; N, 11.04.

Synthesis 2009, No. 20, 3467-3471 © Thieme Stuttgart · New York

Acknowledgment

The author thanks CSIR and UGC, New Delhi for financial assistance.

References

- (1) Part 187 in the series, Studies on Novel Synthetic Methodologies.
- (2) (a) Shafran, Y. M.; Bakulev, V. A.; Mokrushin, V. S. *Russ. Chem. Rev.* **1989**, *58*, 148. (b) March, J. *Advanced Organic Chemistry*, 4th ed.; Wiley: New York, **1999**, 965.
- (3) (a) Weinstock, L. M.; Davis, P.; Handlesman, B.; Tull, R. J. Org. Chem. 1967, 32, 2823. (b) Matier, W. L.; Owens, D. A.; Comer, W. T.; Deitchman, D.; Ferguson, H. C.; Seidehamel, R. J.; Young, J. R. J. Med. Chem. 1973, 16, 901.
- (4) (a) Chemistry and Biochemistry of the Amino Acids; Barrett, G. C., Ed.; Chapman & Hall: London, 1985. (b) Coppala, G. M.; Schuster, H. F. Asymmetric Synthesis Construction of Chiral Molecules Using Amino Acids; Wiley: New York, 1987, and references cited therein.
- (5) (a) Duthaler, R. O. *Tetrahedron* 1994, 50, 1539. (b) Enders, D.; Shilvock, P. *Chem. Soc. Rev.* 2000, 29, 359.
- (6) (a) Strecker, A. Ann. Chem. Pharm. 1850, 75, 27. (b) Yet, L. Angew. Chem. Int. Ed. 2001, 40, 875. (c) Groger, H. Chem. Rev. 2003, 103, 2795.
- (7) (a) Harusawa, S.; Hamada, Y.; Shioiri, T. *Tetrahedron Lett.* **1979**, *20*, 4663. (b) Mai, K.; Patil, G. *Tetrahedron Lett.* **1984**, *25*, 4583. (c) Kobayashi, S.; Ishitani, H. *Chem. Rev.* **1999**, *99*, 1069. (d) Davis, F. A.; Lee, S.; Zhang, H.; Fanelli, D. L. J. Org. Chem. **2000**, *65*, 8704. (e) Mori, Y.; Kimura, M.; Seki, M. *Synthesis* **2003**, 2311. (f) Nakamura, S.; Sato, N.; Sugimoto, M.; Toru, T. *Tetrahedron: Asymmetry* **2004**, *15*, 1513. (g) Herrera, R. P.; Sagarzani, V.; Bernardi, L.; Fini, F.; Pettersen, D.; Ricci, A. J. Org. Chem. **2006**, *71*, 9869.
- (8) (a) Kobayashi, S.; Busujima, T.; Nagayama, S. *Chem. Commun.* **1998**, 981. (b) Bhanu Prasad, B. A.; Bisai, A.; Singh, V. K. *Tetrahedron Lett.* **2004**, *45*, 9565. (c) Royer, L.; De S, K.; Gibbs, R. A. *Tetrahedron Lett.* **2005**, *46*, 4595. (d) Surya Prakash, G. K.; Mathew, T.; Panja, C.; Alconcel, S.; Vaghoo, H.; Do, C.; Olah, G. A. *Proc. Natl. Acad. Sci. U.S.A.* **2007**, *104*, 3703.
- (9) (a) Li, B. F.; Yuan, K.; Zhang, M. J.; Wu, H.; Dai, L. X.; Wang, Q. R.; Hou, X. L. J. Org. Chem. 2003, 68, 6264.
 (b) Takahashi, E.; Fujisawa, H.; Yanai, T.; Mukaiyama, T. Chem. Lett. 2005, 34, 318. (c) Fetterly, B. M.; Jana, N. K.; Verkade, J. G. Tetrahedron 2006, 62, 440.
- (10) (a) Groger, H. *Chem. Eur. J.* 2001, *7*, 5247. (b) Shibasaki, M.; Yoshikawa, N. *Chem. Rev.* 2002, *102*, 2187.
 (c) Tsogoeva, S. B.; Heteley, M. J.; Yalalov, D. A.; Meindl, K.; Weckbecker, C.; Huthmacher, K. *Bioorg. Med. Chem.* 2005, *13*, 5680.
- (11) (a) Krueger, C. A.; Kuntz, K. W.; Dzierba, C. D.; Wirschun, W. G.; Gleason, J. D.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 4284. (b) Banphavichit, V.; Mansawat, W.; Bhanthumnavin, W.; Vilaivan, T. *Tetrahedron* **2004**, *60*, 10559. (c) Blacker, J.; Clutterbuck, L. A.; Crampton, M. R.; Grosjean, C.; North, M. *Tetrahedron: Asymmetry* **2006**, *17*, 1449.
- (12) (a) Iyer, M. S.; Gigstad, K. M.; Namdev, N. D.; Lipton, M. J. Am. Chem. Soc. 1996, 118, 4910. (b) Corey, E. J.; Grogan, M. Org. Lett. 1999, 1, 157. (c) Sigman, M. S.; Vachal, P.; Jacobsen, E. N. Angew. Chem. Int. Ed. 2000, 39, 1279. (d) Liu, B.; Feng, X.; Chen, F.; Zhang, G.; Cui, X.; Jiang, Y. Synlett 2001, 1551.

- (13) (a) Yadav, J. S.; Reddy, B. V. S.; Eshwaraiah, B.; Srinivas, M.; Vishnumurthy, P. *New J. Chem.* 2003, *27*, 462.
 (b) Surendra, K.; Krishnaveni, N. S.; Mahesh, A.; Rao, K. R. *J. Org. Chem.* 2006, *71*, 2532.
- (14) (a) Love, B. E.; Raje, S. P.; Williams, T. C. II Synlett 1994, 493. (b) Liu, G.; Cogan, D. A.; Owens, T. D.; Tang, T. P.; Ellman, J. A. J. Org. Chem. 1999, 64, 1278. (c) Chemla, F.; Hebbe, V.; Normant, J. Synthesis 2000, 75. (d) Tang, T. P.; Volkman, S. K.; Ellman, J. A. J. Org. Chem. 2001, 66, 8772. (e) Ruano, J. G.; Aleman, J.; Cid, M. B.; Parra, A. Org. Lett. 2005, 7, 179.
- (15) (a) Fukuda, Y.; Maeda, Y.; Kondo, K.; Aoyama, T. *Synthesis* 2006, 1937. (b) Fukuda, Y.; Kondo, K.; Aoyama, T. *Synthesis* 2006, 2649. (c) Haung, X.; Haung, J.; Wen, Y.; Feng, X. *Adv. Synth. Catal.* 2006, *348*, 2579. (d) Kantam, M. L.; Mahendar, K.; Sreedhar, B.; Choudary, B. M. *Tetrahedron* 2008, *64*, 3351.
- (16) Jennings, W. B.; Lovely, C. J. Tetrahedron 1991, 47, 5561.
- (17) (a) Nandi, P.; Redko, M. Y.; Petersen, K.; Dye, J. L.; Lefenfeld, M.; Vogt, P. F.; Jackson, J. E. *Org. Lett.* **2008**, *10*, 5441. (b) Bajwa, J. S.; Chen, G.-P.; Prasad, K.; Repic, O.; Blacklock, T. J. *Tetrahedron Lett.* **2006**, *47*, 6425.