Nucleophilic Reactions of α-Aminoalkenenitriles

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Organo-lithium, -magnesium, and -zinc reagents add to α-aminoalkenenitriles in the 1,2-fashion to give α,β-unsaturated ketones, whereas organocuprate, sodium borohydride, sulphide ion, and sulphone-stabilised carbanions react in the 1,4-fashion to furnish α-amino nitriles.

Addition of a nucleophile to α,β-unsaturated compounds is an important synthetic method.[1] The selectivity for 1,2- or 1,4-addition is governed by many factors, such as the solvent, the reaction temperature, the substituents on the α,β-unsaturated compound, and the intrinsic properties of the nucleophile. Generally speaking, reaction in a polar solvent and at an elevated temperature tends to give 1,4-addition products.[2] In an α,β-unsaturated compound, an electron-withdrawing α-substituent, *e.g.* SR (ref. 3) or SiR_3 (ref. 4), can stabilise the intermediate α-carbanion, and thus facilitate 1,4-addition. In contrast, an electron-donating α-substituent (an amino group) may disfavour the Michael-type reaction. In continuation of a study of the captodative properties of α-amino nitriles,[5] we have investigated the nucleophilic reactions of α-aminoalkenenitriles. Such a reaction with the α-aminoalkenenitrile (**1**) might be envisaged as occurring in any of three modes: abstraction of the γ-proton, 1,2-addition to the cyano group, and 1,4-addition at the β-carbon atom. Deprotonation is usually effected by treatment with lithium di-isopropylamide or potassium t-butoxide.[6] Toye and Ghosez have reported 1,2-additions of organolithium to α-dimethylaminoalkenenitriles in ether solution.[7] On the other hand, Ahlbrecht *et al.* have described 1,4-additions of organolithium to α-*N*-methylanilinoalkenenitriles in tetrahydrofuran (THF) solution.[8] We demonstrate here the effect of nucleophiles, including organometallic reagents, with various counterions.

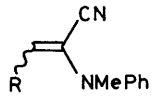
Results and Discussion

A Strecker condensation of crotonaldehyde, *N*-methylaniline, and potassium cyanide, followed by base-catalysed isomerisation, afforded the two geometric isomers (*E*:*Z* 1:6) of 2-*N*-methylanilinopent-2-enenitriles (**1**),[5a] which were separated by chromatography and characterised by spectroscopic methods. Since the various nucleophilic reactions of individual isomers showed the same results, separation of *E*- and *Z*-isomers was not essential. The reaction of the Grignard reagent MeMgI with the alkenenitrile (**1**) produced only the 1,2-addition product (**2**), in modest yield. Compound (**2**) was tentatively assigned the thermodynamically more stable configuration (carbonyl and R^1 *trans*). This assignment was partially supported by the 4-H n.m.r. signal appearing at relatively low field ($\delta > 6.55$), showing the absence of a shielding effect of the amino group. Further conversion of the α-amino-α-alkenone (**2**) into an α-diketone would be expected in acidic conditions by analogy with precedent.[7] Similarly, the nucleophiles BuLi and allylzinc bromide added exclusively to (**1**) in the 1,2-fashion. In the latter reaction, the primary addition product (**4**) was prone to isomerise to the conjugated compound (**5**).[9] On the other hand, 1,4-additions occurred when (**1**) was treated with dibutylcuprate[10] or sodium benzenethiolate. Although the 1,4-addition products (**8**) and (**11**) each comprised two diastereoisomers (1:1), separation seemed unnecessary, since both isomers would be expected to function as the same nucleophilic acyl equivalent.[11] Treatment of (**1**) with $NaBH_4$ yielded the 1,4-reduction product (**9**) (52%) and a 10% yield of *N*-butyl-*N*-methylaniline (**10**). Compound (**10**) may have been derived from reductive decyanation of the α-amino nitrile (**9**).[12]

Overall, the results of the nucleophilic additions of the α-aminopentenenitrile (**1**) (Table) are consistent with the hard and soft acids and bases principle.[13] Accordingly, hard nucleophile (entries 1—3) attacked the hard site (CN), whereas soft

Table. Reactions of 2-*N*-methylanilinopent-2-enenitrile (**1**) with nucleophiles

Entry	Nucleophile	Solvent	1,2-Adduct (% yield)	1,4-Adduct (% yield)
1	MeMgI	Et_2O	(**2**) (60)	
2	BuLi	THF	(**3**) (65)	
3	CH_2=$CHCH_2ZnBr$	THF	(**4**) (5), (**5**) (41)	
4	$PhCH_2MgCl$	Et_2O	(**6**) (36)	(**7**) (19)
5	Bu_2CuLi	Et_2O		(**8**) (52)
6	$NaBH_4$	MeOH		(**9**) (52), (**10**) (10)
7	PhSNa	THF		(**11**) (70)



(**1**) R = Et

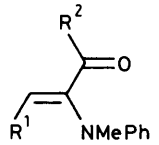
(**13**) R = Bu^t

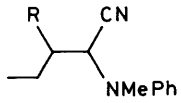
(**16**) R = $Br[CH_2]_3CHPh$

(**17**) R = $HS[CH_2]_3CHPh$

(**19**) R = $Br[CH_2]_4CHMe$

(**20**) R = *p*-$MeC_6H_4SO_2[CH_2]_4CHMe$





(**2**) R^1 = Et, R^2 = Me

(**3**) R^1 = Et, R^2 = Bu

(**4**) R^1 = Et, R^2 = CH_2=$CHCH_2$

(**5**) R^1 = Et, R^2 = CH_3CH=CH

(**6**) R^1 = Et, R^2 = $PhCH_2$

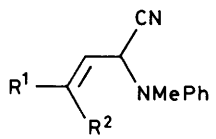
(**14**) R^1 = Bu^t, R^2 = Bu

(**7**) R = $PhCH_2$

(**8**) R = Bu

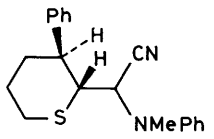
(**9**) R = H

(**11**) R = PhS



(12) $R^1 = R^2 = Me$

(15) $R^1 = Ph$, $R^2 = H$



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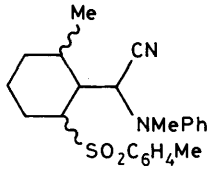

(21)

nucleophile (entries 5—7) attacked at the soft site (C=C). Phenylmagnesium chloride (medium hardness) thus reacted with (**1**) in both 1,2- and 1,4-modes. It is noteworthy that compound (**1**) was reduced by $NaBH_4$ in the 1,4-fashion, whereas the analogous 2-*N*,*N*-dimethylaminobut-2-enenitrile has been reported to give the 1,2-reduction product on treatment with $LiAlH_4$ in refluxing ether. These results indicate that $NaBH_4$, with the more covalent B–H bond, is softer than $LiAlH_4$.[14]

Compound (**13**) with a t-butyl group at the β-position also underwent 1,2-addition readily with BuLi to give an 85% yield of the enone (**14**). Intramolecular 1,4-additions of sulphide ion and sulphone-stabilised carbanion were exemplified with compounds (**17**) and (**20**). The bromo precursors of (**17**) and (**20**) were prepared by regioselective alkylations of allylic anions generated from (**1**) and (**15**), respectively. A methanolic solution of the bromide (**16**) was treated with an excess of Na_2S at room temperature for 4 days to afford an 80% yield of the thiacyclohexyl acetonitrile (**18**). The *trans* configuration was established rigorously by the large coupling constant of 10.4 Hz between the protons at C-1′ and C-6′. Similarly, treatment of the sulphone (**20**) with MeONa in MeOH afforded exclusively the 1,4-addition product (**21**), consisting of two diastereoisomers in 14:1 ratio.

In summary, the nucleophilic reactions of 2-anilinoalkenenitriles follow the hard and soft acids and bases principle as observed in other organometallic reactions. The intramolecular nucleophilic reactions of compounds (**17**) and (**20**) show high regio- and stereo-selectivities. Uses of the resulting enones (from 1,2-additions) and α-amino nitriles (from 1,4-additions) in organic synthesis are well established.[10,11]

Experimental

General information concerning instrumentation and material is given in ref. 15.

2-N-*Methylanilinopent*-2-*enenitrile* (**1**).—To a solution of *N*-methylaniline (1.60 g, 15 mmol), neutralised (pH 6) with 6M HCl (2.7 ml), were added an aqueous solution (3 ml) of KCN (1.05 g, 16 mmol) and a phase-transfer agent [benzyltriethylammonium chloride (0.3 g)]. Crotonaldehyde (1.05 g, 15 mmol) was added dropwise at 0 °C, and the mixture was stirred at room temperature for 4 h, until the yellow oil separated from the aqueous layer. The yellow oil was washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure to give, as a crude oil (2.59 g), 2-*N*-methylanilinopent-3-enenitrile. The oil was dissolved in anhydrous MeOH (30 ml) and MeONa (0.1 g) was added. The mixture was stirred at room temperature for 1 h, quenched with saturated aqueous NH_4Cl (20 ml), and extracted with hexane. The combined extracts were washed with dilute HCl, dried, concentrated, and distilled (110 °C; 0.4 mmHg) to afford, as a pale oil (2.29 g, 82%), 2-*N*-methylanilinopent-2-enenitrile (**1**) (*E*:*Z* 1:6). The two isomers were separated by chromatography (15% EtOAc–hexane); the *E*-isomer is less polar and was eluted earlier. Spectroscopic data have been reported.[5a]

3-N-*Methylanilinohex*-3-*en*-2-*one* (**2**).—Under N_2, an ethereal solution (5 ml) of MeMgI was prepared from magnesium (51 mg, 2.1 mmol) and iodomethane (0.14 ml, 2.2 mmol). The Grignard reagent was added dropwise to an ethereal solution (7 ml) of compound (*E* or *Z*) (372 mg, 2.0 mmol) at 0 °C. The mixture was stirred at room temperature for 24 h, quenched with aqueous NH_4Cl, and extracted with ethyl acetate. The combined extracts were dried, concentrated, and separated by chromatography (2% EtOAc–hexane) to give the *enone* (**2**) (242 mg, 1.2 mmol, 60%); $\nu_{max.}$(neat) 1 679 (C=C–C=O), 1 599, 1 499, 750, and 693 cm^{-1}; *m*/*z* 203 (M^+, 80%), 160 (100), 144 (17), 130 (18), and 82 (20); $\delta_H(CCl_4)$ 1.07 (3 H, t, *J* 7.2 Hz), 1.99 (3 H, s), 2.13 (2 H, dq, *J* 8.0 and 7.2 Hz), 3.08 (3 H, s), 6.55 (4 H, m), and 7.11 (2 H, m); $\delta_C(CDCl_3)$ 12.5 (q), 21.1 (t), 26.4 (q), 38.1 (q), 111.6 (d, 2 C), 116.9 (d), 128.8 (d, 2 C), 142.0 (d, C-4), 143.3 (s, C-2), 147.2 (s), and 197.9 (s, C=O) (Found: C, 76.6; H, 8.5; N, 6.9. $C_{13}H_{17}NO$ requires C, 76.8; H, 8.4; N, 6.9%).

4-N-*Methylanilinonon*-3-*en*-5-*one* (**3**).—To a solution of compound (**1**) (372 mg, 2.0 mmol) in THF (20 ml) was added dropwise a solution of BuLi (1.31 ml; 1.6M in hexane) at room temperature. After 24 h, the mixture was worked up by the foregoing procedure to yield the *enone* (**3**) as an oil (319 mg, 65%); $\nu_{max.}$(neat) 1 695, 1 600, 1 500, 755, and 700 cm^{-1}; *m*/*z* 245 (M^+, 29%), 160 (100), and 77 (30); $\delta_H(CDCl_3)$ 0.74 (3 H, t, *J* 7.3 Hz), 0.93 (3 H, t, *J* 7.3 Hz), 1.14 (2 H, m), 1.42 (2 H, m), 2.04 (2 H, m), 2.31 (2 H, t, *J* 7.3 Hz), 3.00 (3 H, s), 6.48 (2 H, d, *J* 7.7 Hz), 6.60 (2 H, m, 3- and 4′-H), and 7.10 (2 H, m); $\delta_C(CDCl_3)$ 12.6 (q), 13.7 (q), 21.1 (t), 22.2 (t), 25.9 (t), 38.0 (t), 38.4 (q), 111.8 (d, 2 C), 117.1 (d), 129.1 (d, 2 C), 141.5 (d), 143.6 (s), 147.6 (s), and 201.0 (s) (Found: C, 78.15; H, 9.5; N, 5.7. $C_{16}H_{23}NO$ requires C, 78.3; H, 9.45; N, 5.7%).

5-N-*Methylanilino-octa*-1,5-*dien*-4-*one* (**4**) *and* 5-N-*Methylanilino-octa*-2,5-*dien*-4-*one* (**5**).—A solution (5 ml) of allylzinc bromide [from zinc (137 mg, 2.1 mmol) and allyl bromide (0.19 ml, 2.2 mmol)] in THF was added dropwise to a solution (7 ml) of compound (**1**) (372 mg, 2.0 mmol) in THF over 30 min. The mixture was stirred at room temperature for 24 h and quenched with aqueous NH_4Cl; addition of dilute HCl gave a clear solution, which was extracted with $CHCl_3$. The combined extracts were dried, concentrated, and separated by chromatography (2% ethyl acetate–hexane) to give compounds (**4**) (23 mg, 5%) and (**5**) (188 mg, 41%). Compound (**4**) was unstable and prone to isomerise to compound (**5**). Compound (**4**) showed $\delta_H(CCl_4)$ 1.03 (3 H, t, *J* 7.5 Hz), 2.03 (2 H, m), 3.03 (2 H, m), 3.06 (3 H, s), 4.86 (1 H, m), 5.03 (1 H, m), 5.75 (1 H, m), and 6.45—7.17 (6 H, m). The *dienone* (**5**) showed $\nu_{max.}$(neat) 1 670, 1 650, 1 600, 1 500, 750, and 690 cm^{-1}; *m*/*z* 229 (M^+, 70%), 214 (30), and 160 (100); $\delta_H(CCl_4)$ 1.03 (3 H, t, *J* 7.2 Hz), 1.80 (3 H, dd, *J* 6.3 and 1.5 Hz), 2.08 (2 H, m), 3.06 (3 H, s), 6.18 (1 H, dq, *J* 15.0 and 1.5 Hz), and 6.45—7.17 (7 H, m) (Found: C, 78.75; H, 8.4; N, 6.1. $C_{15}H_{19}NO$ requires C, 78.6; H, 8.35; N, 6.1%).

4-N-*Methylanilino*-6-*phenylhex*-3-*en*-5-*one* (**6**) *and* 3-*Benzyl*-2-N-*methylanilinopentanenitrile* (**7**).—An ethereal solution (5 ml) of benzylmagnesium chloride [from magnesium (51 mg,

2.1 mmol) and benzyl chloride (0.25 ml, 2.2 mmol)] was added dropwise to an ethereal solution (7 ml) of compound (**1**) (372 mg, 2.0 mmol) at 0 °C. The mixture was stirred for 24 h, quenched with aqueous NH_4Cl, and extracted with EtOAc. The organic phase was dried, concentrated, and separated by chromatography to give compounds (**6**) (209 mg, 36%) and (**7**) (110 mg, 19%). The two diastereoisomers (1:1) of (**7**) were inseparable but distinguished in the ^{13}C n.m.r. spectrum. The *enone* (**6**) showed $\nu_{max.}$(neat) 1 678, 1 598, 1 498, 750, and 695 cm^{-1}; *m/z* 279 (M^+, 80%), 264 (5), 190 (6), and 160 (100); $\delta_H(CDCl_3)$ 1.00 (3 H, t, *J* 7.5 Hz), 2.10 (2 H, m), 2.92 (3 H, s), 3.66 (2 H, s), 6.56 (2 H, d, *J* 8.3 Hz), 6.73 (2 H, m), 7.03 (2 H, d, *J* 8.3 Hz), and 7.23 (5 H, m); δ_C 12.4 (q), 21.0 (t), 38.1 (q), 45.2 (t), 111.6 (d, 2 C), 117.0 (d), 126.1 (d), 127.8 (d, 2 C), 128.8 (d, 4 C), 133.9 (s), 141.9 (d, C-3), 142.7 (s), 147.0 (s), and 197.7 (s) (Found: C, 82.0; H, 9.4; N, 6.1. $C_{19}H_{21}NO$ requires C, 81.7; H, 9.3; N, 6.1%). The *nitrile* (**7**) showed $\nu_{max.}$(neat) 2 228 (CN), 1 598, 1 494, 751, and 699 cm^{-1}; *m/z* 278 (M^+, 24%), 251 (59), 236 (25), 222 (11), 160 (15), 145 (100), and 107 (24); $\delta_H(CCl_4)$ 1.03 (3 H, t, *J* 6.6 Hz), 1.50 (2 H, m), 2.22 (1 H, m), 2.74 (2 H, m), 2.87 (3 H, s), 4.15 (1 H, d, *J* 7.0 Hz), and 6.70—7.21 (10 H, m); $\delta_C(CDCl_3)$ 9.6/10.1 (q), 20.2/22.3 (t), 34.7 (q), 35.0/35.3 (t), 42.2/42.4 (d), 57.2 (d), 115.9/116.0 (d, 2 C), 117.0/117.4 (s, CN), 120.2/120.3 (d), 126.1/126.2 (d), 128.1/128.3 (d, 2 C), 129.0 (d, 3 C), 138.1/138.6 (s), and 149.0/149.2 (s) (Found: C, 81.9; H, 8.0; N, 10.1. $C_{19}H_{22}N_2$ requires C, 82.0; H, 8.0; N, 10.1%).

3-*Ethyl*-2-N-*methylanilinoheptanenitrile* (**8**).—A solution of BuLi (2.6 ml; 1.6M in hexane) was added dropwise to an ethereal solution (10 ml) of CuI (400 mg, 2.1 mmol) at −40 °C. The resulting cuprate solution was added dropwise to an ethereal solution (7 ml) of compound (**1**) (372 mg, 2.0 mmol) at −20 °C. The mixture was stirred at room temperature for 24 h, quenched with aqueous NH_4Cl, and extracted with EtOAc. The organic phase was dried, concentrated, and purified by chromatography to give the *amino nitrile* (**8**) (254 mg, 52%) as a 1:1 mixture of isomers; $\nu_{max.}$(neat) 2 240, 1 600, 1 490, 760, and 700 cm^{-1}; *m/z* 244 (M^+, 14%), 145 (100), 120 (28), and 77 (30); $\delta_H(CCl_4)$ 0.90 (6 H, m), 1.51 (9 H, m), 2.80 (3 H, s), 4.09 (1 H, d, *J* 9.9 Hz), and 6.75—7.35 (5 H, m); $\delta_C(CDCl_3)$ 9.4/9.8 (q), 13.9 (q), 20.7/22.2 (t), 22.9 (t), 27.2/27.6 (t), 28.0/28.7 (t), 34.3 (q), 39.7 (d), 57.8/58.0 (d), 116.0 (d, 2 C), 117.3 (s), 120.2 (d), 129.0 (d, 2 C), and 149.3 (s) (Found: C, 78.4; H, 10.0; N, 11.6. $C_{16}H_{24}N_2$ requires C, 78.6; H, 9.9; N, 11.5%).

2-N-*Methylanilinopentanenitrile* (**9**) *and* N-*Butyl*-N-*methylaniline* (**10**).—$NaBH_4$ (76 mg, 2 mmol) was added to a solution of compound (**1**) (186 mg, 1 mmol) in anhydrous MeOH (20 ml). The suspension was stirred at room temperature for 48 h, concentrated, and partitioned with water and EtOAc. The organic phase was dried, concentrated, and separated by chromatography to give compounds (**9**) (97 mg, 52%) and (**10**)[16] (16 mg, 10%). The *nitrile* (**9**) showed $\nu_{max.}$(neat) 2 225, 1 600, 1 500, 740, and 680 cm^{-1}; *m/z* 188 (M^+, 14%), 186 (10), 145 (100), and 77 (27); $\delta_H(CCl_4)$ 0.90 (3 H, t, *J* 7.5 Hz), 1.49 (2 H, m), 1.78 (2 H, m), 2.77 (3 H, s), 4.23 (1 H, t, *J* 7.8 Hz), 6.85 (3 H, m), and 7.08 (2 H, m); $\delta_C(CDCl_3)$ 13.2 (q), 18.8 (t), 33.4 (t), 33.9 (q), 53.3 (d), 113.8 (s), 116.0 (d, 2 C), 120.1 (d), 128.8 (d, 2 C), and 148.7 (s) (Found: C, 76.5; H, 8.6; N, 14.9. $C_{12}H_{16}N_2$ requires C, 76.6; H, 8.6; N, 14.9%). The *aniline* (**10**) showed $\nu_{max.}$(neat) 1 600, 1 500, 740, and 680 cm^{-1}; *m/z* 163 (M^+, 24%), 120 (100), and 107 (64); $\delta_H(CCl_4)$ 0.93 (3 H, t, *J* 7 Hz), 1.43 (4 H, m), 2.86 (3 H, s), 3.24 (2 H, t, *J* 7 Hz), 6.53 (3 H, m), and 7.03 (2 H, m).

2-N-*Methylanilino*-3-*phenylthiopentanenitrile* (**11**).—A solution of sodium benzenethiolate and benzenethiol in THF (20 ml) was prepared from sodium (69 mg, 3 mmol) and benzenethiol (0.62 ml, 6 mmol). Compound (**1**) (*E* or *Z*) (558 mg, 3 mmol) in THF (3 ml) was added and the mixture was refluxed for 72 h, cooled, concentrated, and taken up with EtOAc. The organic solution was washed with aqueous 10% Na_2CO_3 and brine. After removal of volatile material, compound (**11a**) (320 mg, 36%) and its diastereoisomer (**11b**) (302 mg, 34%) were isolated by chromatography (3% ethyl acetate–hexane). Compound (**11a**) showed $\nu_{max.}$(neat) 2 250, 1 590, 1 500, 760, and 700 cm^{-1}; *m/z* 296 (M^+, 5%), 186 (29), 171 (37), 151 (32), 145 (100), 120 (35), and 77 (44); $\delta_H(CCl_4)$ 1.20 (3 H, t, *J* 6.9 Hz), 1.75 (2 H, m), 2.60 (3 H, s), 3.25 (1 H, q, *J* 9.0 Hz), 4.35 (1 H, d, *J* 9.0 Hz), and 6.60—7.36 (10 H, m); $\delta_C(CDCl_3)$ 11.2 (q), 24.2 (t), 34.8 (q), 53.3 (d, C-3), 58.9 (d, C-2), 115.4 (d, 2 C), 116.0 (s, CN), 120.0 (d), 127.9 (d), 128.7 (d, 2 C), 129.0 (d, 2 C), 132.8 (s), 134.0 (d, 2 C), and 148.4 (s). *Compound* (**11b**) showed $\nu_{max.}$(neat) 2 240, 1 590, 1 490, 760, and 700 cm^{-1}; *m/z* 296 (M^+, 20%), 151 (100), 146 (40), 145 (30), and 77 (14); $\delta_H(CCl_4)$ 1.13 (3 H, t, *J* 6.0 Hz), 1.86 (2 H, m), 2.83 (3 H, s), 3.07 (1 H, dt, *J* 9.6 and 9.0 Hz), 4.25 (1 H, d, *J* 9.6 Hz), and 6.77—7.55 (10 H, m); $\delta_C(CDCl_3)$ 11.1 (q), 23.5 (t), 34.4 (q), 52.5 (d), 59.5 (d), 115.7 (d, 2 C), 116.8 (s), 120.5 (d), 128.3 (d), 128.9 (d, 2 C), 129.1 (d, 2 C), 131.7 (s), 134.1 (d, 2 C), and 148.5 (s) (Found: C, 73.1; H, 6.8; N, 9.4. $C_{18}H_{20}N_2S$ requires C, 72.9; H, 6.8; N, 9.45%).

General Procedure for Substitution Reactions of Compounds (**1**), (**12**), *and* (**15**).—BuLi (2.2 mmol; 1.6M in hexane) was added dropwise to a solution of di-isopropylamine (0.34 ml, 2.4 mmol) in THF (5 ml). The resulting solution was cooled to −78 °C and hexamethylphosphoric triamide (0.70 ml, 4.0 mmol) and a solution (1 ml) of the aminonitrile (**1**), (**12**), or (**15**) (2 mmol) in THF were added consecutively. After 45 min, the appropriate electrophile (3.0 mmol, MeI, $Br[CH_2]_3Br$, or $Br[CH_2]_4Br$) was added and the mixture was stirred for 0.2—5.0 h. The products [*E*- and *Z*-isomers of (**19**), (**13**), or (**16**)] were extracted with hexane and isolated by chromatography.

2,2-*Dimethyl*-4-N-*methylanilinonon*-3-*en*-5-*one* (**14**).—The enone (**14**) was prepared in 85% yield from addition of BuLi to compound (**13**) by the procedure described for the enone (**3**). This addition reaction was completed in 5 min. The *product* showed $\nu_{max.}$(neat) 1 689, 1 598, 1 498, 748, and 693 cm^{-1}; *m/z* 273 (M^+, 23%), 258 (13), 188 (100), and 132 (27); $\delta_H(CCl_4)$ 0.80 (3 H, t, *J* 7 Hz), 1.10 (9 H, s), 1.25 (4 H, m), 2.20 (2 H, t, *J* 7 Hz), 3.00 (3 H, s), 6.67 (1 H, s), and 6.40—7.15 (5 H, m); $\delta_C(CDCl_3)$ 13.8 (q), 22.2 (t), 26.0 (t), 29.1 (q, 3 C), 33.5 (s), 37.7 (q), 39.9 (t), 111.8 (d, 2 C), 117.0 (d), 129.1 (d, 2 C), 140.8 (s), 148.1 (s), 149.8 (d, C-3), and 201.9 (s) (Found: C, 79.1; H, 10.0; N, 6.4. $C_{18}H_{27}NO$ requires C, 79.1; H, 9.95; N, 6.5%).

2-N-*Methylanilino*-2-(6-*phenyl*-2-*thiacyclohexyl*)*acetonitrile* (**18**).—A mixture of the bromide (**16**) (*Z*-isomer) (369 mg, 1.0 mmol) and sodium sulphide (1.56 g, 20 mmol) in MeOH (30 ml) was stirred at room temperature for 4 days, treated with cold 1M HCl (to pH 6), extracted with EtOAc, and separated by chromatography to give a single *product* (**18**) (258 mg, 80%); $\nu_{max.}$(neat) 2 243, 1 596, 1 499, 751, and 703 cm^{-1}; *m/z* 322 (M^+, 3%), 247 (5), 177 (100), 146 (61), and 91 (60); $\delta_H(CCl_4)$ 1.60—2.11 (4 H, m), 2.71—2.80 (2 H, m), 2.97 (1 H, ddd, *J* 10.4, 10.4, and 3.0 Hz, 6′-H), 3.03 (3 H, s), 3.43 (1 H, dd, *J* 10.4 and 3.8 Hz, 1′-H), 4.65 (1 H, d, *J* 3.8 Hz, 2-H), and 6.10—7.42 (10 H, m); $\delta_C(CDCl_3)$ 26.9 (t), 28.7 (t), 33.9 (t), 36.9 (q), 47.4 (d), 48.6 (d), 56.2 (d), 113.6 (d, 2 C), 115.2 (s), 119.0 (d), 127.3 (d, 2 C), 127.6 (d), 129.0 (d, 2 C), 129.1 (d, 2 C), 142.7 (s), and 147.3 (s) (Found: C, 74.0; H, 6.85; N, 8.7. $C_{20}H_{22}N_2S$ requires C, 74.5; H, 6.9; N, 8.7%).

2-N-*Methylanilino*-2-(2-*methyl*-6-p-*tolylsulphonylcyclohexyl*)*acetonitrile* (**21**).—A mixture of the bromide (**19**) (*Z*-isomer) (642 mg, 2.0 mmol) and sodium toluene-*p*-sulphinate

(712 mg, 4.0 mmol) in MeOH (20 ml) was stirred at room temperature for 6 h. After removal of solvent, the mixture was separated by chromatography to give the sulphone (**20**) (*Z*-isomer) (722 mg, 91%); $\nu_{max.}$(neat) 2 212, 1 597, 1 494, 1 300, 1 144, 817, 756, and 695 cm^{-1}; *m/z* 396 (M^+, 40%), 381 (5), 241 (70), 185 (100), 169 (5), and 91 (20); $\delta_H(CDCl_3)$ 0.95 (3 H, d, *J* 6.5 Hz), 1.10—1.80 (6 H, m), 2.45 (3 H, s), 2.65 (1 H, m), 2.95 (2 H, t, *J* 7 Hz), 3.05 (3 H, s), 6.05 (1 H, d, *J* 10 Hz), and 6.70—7.90 (9 H, m). A mixture of the sulphone (**20**) (396 mg, 1.0 mmol) and MeONa (10.8 mg, 0.2 mmol) in anhydrous MeOH (20 ml) was stirred at room temperature for 24 h, quenched with aqueous NH_4Cl, and extracted with EtOAc. The organic phase was concentrated and purified by chromatography to give compound (**21a**) (278 mg, 70%) and its diastereoisomer (**21b**) (20 mg, 5%). *Compound* (**21a**) showed $\nu_{max.}$(neat) 2 229, 1 596, 1 496, 1 310, 1 147, 789, 760, and 694 cm^{-1}; *m/z* 396 (M^+, 30%), 157 (8), 145 (100), and 91 (12); $\delta_H(CDCl_3)$ 1.43 (3 H, d, *J* 7.4 Hz), 1.20—2.20 (7 H, m), 2.41 (3 H, s), 2.82 (3 H, s), 2.98 (1 H, m, 1′-H), 3.53 (1 H, m, 6′-H), 4.44 (1 H, d, *J* 11.7 Hz, 2-H), and 6.86—7.82 (9 H, m); $\delta_C(CDCl_3)$ 15.6 (t), 20.1 (q), 21.4 (t), 21.6 (q), 27.3 (t), 28.0 (d, C-2′), 34.0 (q), 37.6 (d, C-1′), 57.1 (d), 58.3 (d), 116.6 (s, CN), 117.8 (d, 2 C), 122.1 (d), 128.5 (d, 2 C), 129.6 (d, 2 C), 129.9 (d, 2 C), 136.0 (s), 144.6 (s), and 149.6 (s) (Found: C, 69.9; H, 7.1; N, 7.1; S, 8.05. $C_{23}H_{28}N_2O_2S$ requires C, 69.7; H, 7.1; N, 7.1; S, 8.1%). Compound (**21b**) showed $\nu_{max.}$(neat) 2 220, 1 600, 1 495, 1 310, 1 150, 790, 760, and 695 cm^{-1}; *m/z* 396 (M^+, 25%), 157 (7), 145 (100), and 91 (23); $\delta_H(CDCl_3)$ 1.34 (3 H, d, *J* 6.6 Hz), 1.42—2.20 (7 H, m), 2.43 (3 H, s), 2.86 (3 H, s), 2.93 (1 H, m), 3.37 (1 H, m), 4.55 (1 H, d, *J* 11.2 Hz), and 6.67—7.82 (9 H, m); $\delta_C(CDCl_3)$ 15.7 (t), 19.9 (q), 21.5 (t), 21.6 (q), 24.8 (t), 26.7 (d), 34.5 (q), 38.5 (d), 57.6 (d), 60.2 (d), 116.8 (s), 116.9 (d, 2 C), 121.4 (d), 128.6 (d, 2 C), 129.5 (d, 2 C), 130.0 (d, 2 C), 136.0 (s), 142.5 (s), and 146.0 (s).

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