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Triazolopyridines. 16[1]. Lithiation of 3-Cyano[1,2,3]triazolo[1,5-a]-pyridine

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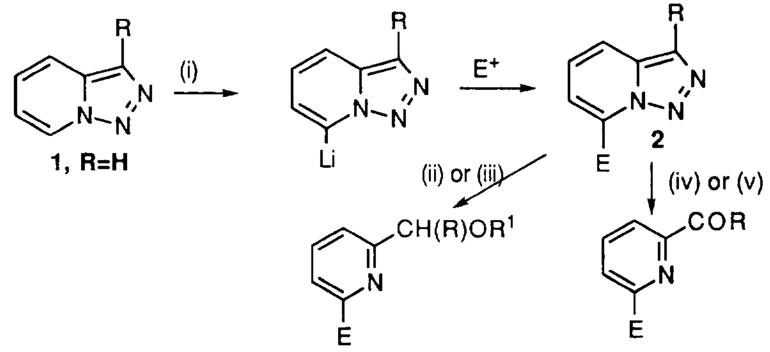
Abstract; Various methods for the synthesis of 3-cyanotriazolopyridine **8** by diazo transfer to 2-pyridylacetonitrile are described. Lithiation of the triazolopyridine **8** using LDA or TMPA followed by quenching with TMS chloride, gave the 4-mono-, the 7-mono- , and the 4,7- di TMS derivatives **14, 18,** and **15,** and the amidines **16** and **17,** in contrast to the previously reported regiospecific attack at position 7. A Grignard reaction on compound **8** gave 3-propionyl triazolo-pyridine, **13.**

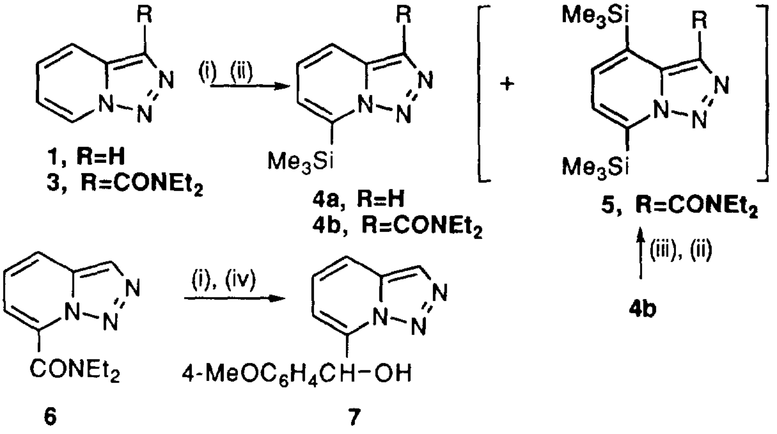
We have reported that [1,2,3]triazolo[1,5-a]pyridine, **1**, and some of its derivatives can be regiospecifically substituted at position 7 by lithiation, followed by treatment with an electrophile.[2-4] Furthermore, such substituted triazolopyridines **2** can be converted in high yield to 2,6-disubstituted pyridines, so that the whole sequence provides a route from pyridine-2-carbaldehydes or ketones to 2,6-disubstituted pyridines, as illustrated in Scheme 1. We have examined various possible routes to give triazolopyridines which are regioselectively substituted in positions other than 7, in the hope of widening the scope of the synthesis, and we describe here our most successful efforts.



(i) LDA or n-BuLi (ii) H_2SO_4 (R^1=H) (iii) AcOH (R^1=Ac) (iv) Br_2, then AgOH (v)SeO_2

Scheme 1

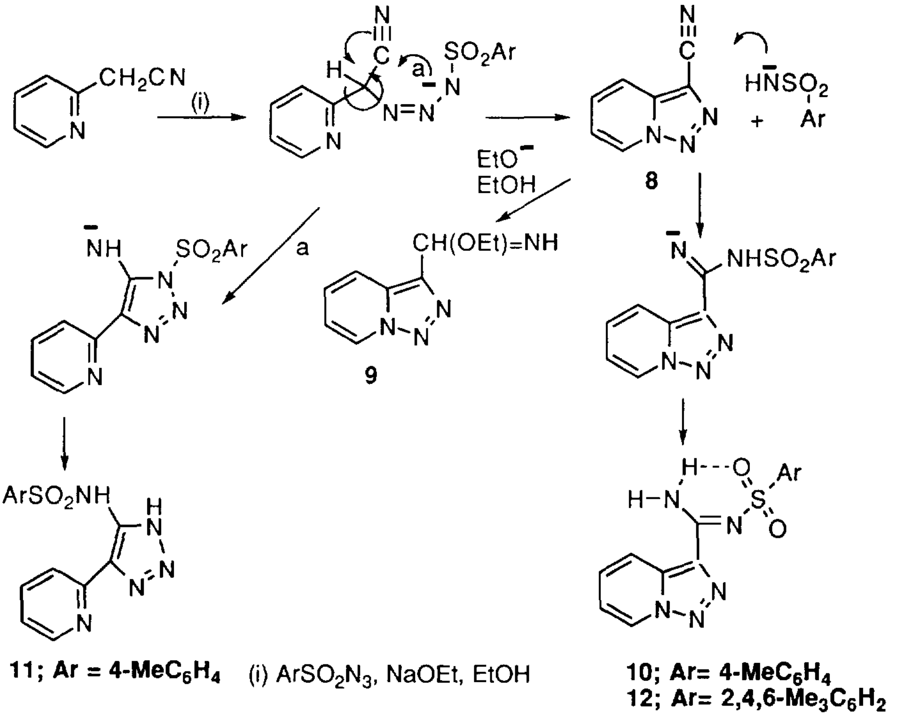
Regiospecific substitution at sites other than position 7 could, in principle, be achieved by two methods. The first, and least desirable, since it introduces an extra step into the synthesis, would be to introduce a blocking group into position 7, *via* our usual lithiation, and subsequently to repeat the lithiation sequence. We have prepared 7-methyltriazolopyridine , but, as expected from analogy with pyridine, lithiation occurred on the methyl substituent.[2] The most commonly used blocking group in lithiation experiments is TMS, and we have studied the preparation of two 7-trimethylsilyltriazolopyridines **4a** and **4b** and have also studied the lithiation of compound **4b**. The monosubstituted derivative **4a** was used to check the feasibility of removal of the blocking group after further substitution, and this was indeed removed by CsF in DMF/H_2O (10 h. boiling). The disubstituted compound **4b** was then subjected to various lithiation conditions with TMS chloride as quenching agent, in the hope of inducing regiospecific substitution at position 4. No lithiation was achieved with LDA (-40°C), with *n*- or *sec*-butyllithium and TMEDA (both at -40°C), but *n*-butyllithium with TMP (2,2,6,6-tetramethylpiperidine) gave a 5% yield of the 4,7-diTMS triazolopyridine **5**. It is interesting to note that direct lithiation of the amide **3** using two equivalents of LDA gave, after quenching with TMS, a 10% yield of compound **5** as well as 30% of compound **4b**. In these experiments we have combined the use of a blocking group with the second main approach to diversification of our pyridine synthesis, in which the group is capable of regioselective direction of the incoming lithiating species , and we should mention briefly other attempts of this type. From the 7-lithio-derivative of triazolopyridine and N,N-diethylcarbamoyl chloride we obtained 7-(N,N-diethylcarbamoyl)triazolopyridine **6** . The well documented capacity of such tertiary amides to direct lithiation into an adjacent *ortho* position should give access to 6-substituted triazolopyridines, and hence, eventually, to 2,5-disubstituted pyridines, but lithiation of amide **6** and subsequent treatment with anisaldehyde gave the 7-substituted triazolopyridine **7**, the lithiation having caused displacement of the amide residue. The use of a methoxyl group in the 5 position as a group directing into positions 4 or 6 was also unsuccessful[3] and we have returned to the possibility of direction by a substituent in position 3 as a route to 4-substituted triazolopyridines.



1, R=H
3, R=CONEt$_2$
4a, R=H
4b, R=CONEt$_2$
5, R=CONEt$_2$
6
7

(i) LDA, -40°C, Et_2O (ii) TMSCl (iii)*n*-ButylLi, TMP, -40°C, Et_2O (iv) Anisaldehyde

Since the experiments using a 3-carbamoyltriazolopyridine showed lithiation predominantly at position 7, although with some indication of substitution at position 4, we reasoned that reduced steric hindrance might improve the amount of 4-substitution, and thus we have prepared 3-cyanotriazolopyridine **8** and studied its lithiation. The cyano derivative could be obtained by a diazo transfer reaction from 2-pyridylacetonitrile and 2-azido-1-ethylpyridinium tetrafluoroborate[5] in 73% yield, or in 76% yield by preparing the diazo compound *in situ*, as reported by Monteiro[6] for other active methylene compounds . We have found the Regitz method of diazo transfer, using tosyl azide in basic medium,[7] to be particularly useful for large scale synthesis, so we applied the method to 2-pyridylacetonitrile, with some unexpected results. A yield of compound **8** of only 30% was achieved using DMF as solvent and sodium hydride as base, but under the more normal conditions (sodium ethoxide in ethanol), a number of other products were obtained. The most easily identified was the imidate **9**, obtained in up to 46% yield. We were able to show that this product derives from the nitrile **8**, 2-pyridylacetonitrile being stable to attack by ethoxide under these conditions. A second product, the yield of which could be raised to 76% if the reaction temperature was kept below -10°C was a solid, with a molecular weight of 315 and a molecular formula of $C_{14}H_{13}N_5O_2S$. The ^1H nmr spectrum was that of a 3-substituted triazolopyridine, although the signals in the aromatic region were shifted downfield (for example the H7 doublet was at ∂9.25). In addition there were two NH signals and a pair of doublets, each 2H, characteristic of the *p*-toluenesulphonamido residue. The structure was settled as **10** by X-Ray diffraction (Figure 1) ; it is presumably formed by the action of the sulphonamide anion on the nitrile **8** . At 90°C the two non-equivalent NH signals coalesce, when the hydrogen bonds between NH_2 and sulphonamide SO are broken.



Scheme 2

A third product was isolated when the amount of base was increased, and shown to be an isomer of compound **10**, but with the ^1H nmr spectrum of an α-substituted pyridine. Of the possible structures we prefer the 2-pyridyltriazole **11**, the best of a number of tautomers. These compounds, and their probable modes of formation, are summarized in Scheme 2. These results confirm that in the triazolopyridine series the

Regitz procedure gives consistently high yields only when activation is provided by a ketonic carbonyl group. The use of mesitylsulphonyl azide in the diazo transfer gave the imidate **9** and the triazolopyridine **12**.

With substantial amounts of 3-cyanotriazolopyridine **8** available, we examined briefly its use for the preparation of other 3-substituted triazolopyridines. Reaction with ethylmagnesium bromide gave, in 96% yield , the 3-propionyl derivative **13**. The successful conversion of the cyanide to the imidate **9** suggests that the cyanide could be a source of the 3-carboxylic acid, but basic hydrolysis of compound **9** proved extremely difficult.

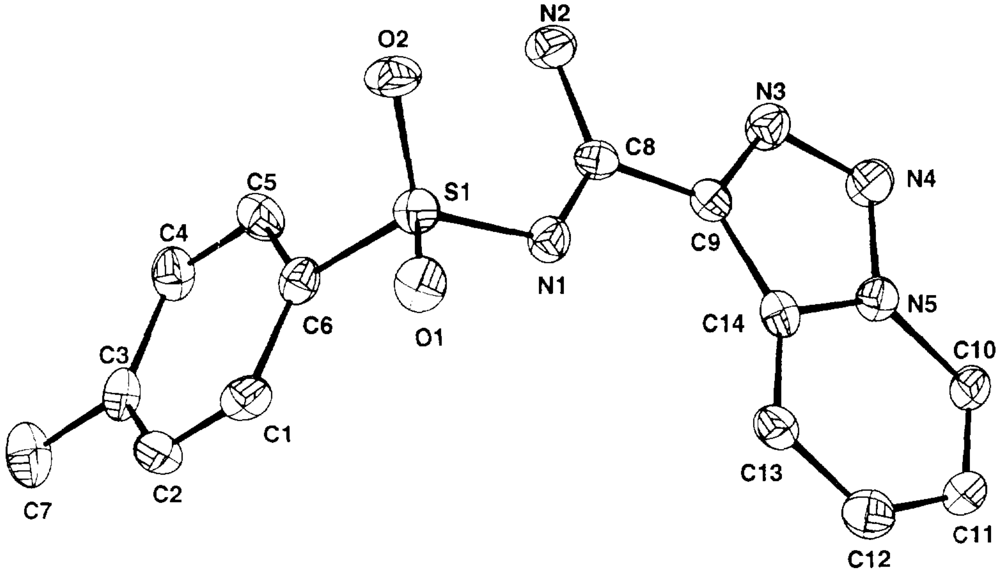
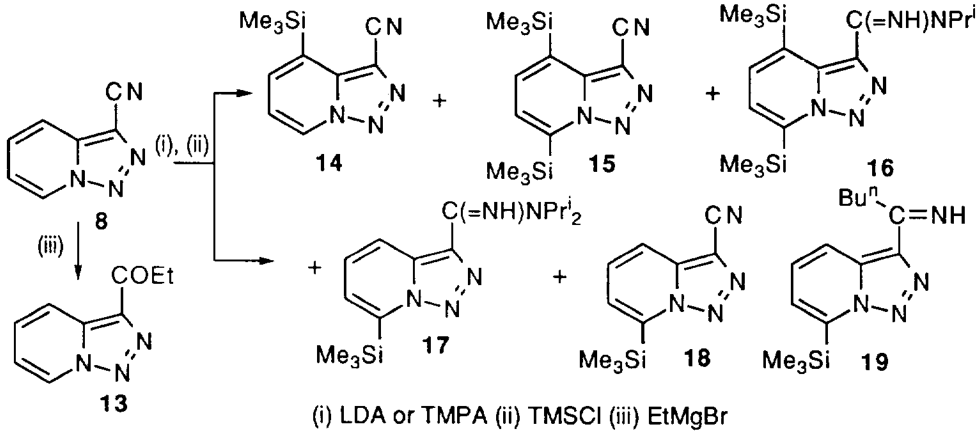


Figure 1. X-Ray diffraction diagram of compound (**10**) (crystallographic numbering)

Lithiation of compound **8** was first carried out under our standard conditions using LDA in THF at -40°C. The characteristic deep red colour of the anion quickly developed, and the reaction was quenched after 1 hr. with TMS chloride. Four products were isolated, two containing an intact cyano group (^{13}C nmr signal at δ138 and ν_{max} at 2229cm^{-1}). The molecular weights showed one of these to be a mono-TMS and the other a di-TMS derivative. The mono substituted compound had a very simple ^{1}H nmr spectrum, with a large singlet at δ0.51 and three signals in the aromatic region, at δ8.83 (d, J=6.85Hz), 7.67 (d, J=6.65Hz), and 7.17(dd, J=6.65 and 6.85 Hz), indicating three adjacent hydrogens. Most significantly, the missing signal, compared with the starting material, was a downfield doublet due to H4, and hence this product is the 4-trimethylsilyl derivative **14**. The second cyanide , with two TMS substituents, showed only two doublets

(J=6.6 Hz), at δ7.63 and 7.23, and is hence the 4,7-disubstituted compound **15**. The second pair of compounds, without a cyano group, differed from compounds **14** and **15** in molecular weight by 101 mu, or one molecule of diisopropylamine, confirmed by signals in the ^{1}H nmr spectra at δ3.73 or 3.86(m) and at 1.42 or 1.49(d) in a ratio of 1:6. These compounds are amidines, the compound with two TMS substituents **16** being derived from nitrile **15** with diisopropylamine. However, the ^{1}H nmr spectrum of the substance with only one TMS group had signals at δ7.85(dd, J=7 and 1 Hz), 7.26(t, J=7Hz), and 7.04(dd, J=7 and 1 Hz), and is the 7-substituted derivative **17**. Unfortunately, the yields from the lithiation were very variable, with a 20% maximum for compound **14**. Doubling the amount of LDA gave increased yields of amidine **17** (up to 34%), while the use of the hindered base lithium 2,2,6,6-tetramethylpiperidide (TMPA) suppressed formation of amidines but gave some unchanged 3-cyanotriazolopyridine **8**, and a new product in up to 50% yield. The new product had one TMS substituent, and retained the cyano group. From the aromatic region of the ^{1}H nmr spectrum, with signals at δ7.90(dd, J=8.9 and 1.22Hz), 7.54(dd, J=8.9 and 6.59Hz), and 7.26(dd, J=6.59 and 1.22Hz) the new substituent is in the 7 position, and the compound has structure **18**. In a few cases when excess of *n*-butyllithium was used, a compound **19** was obtained, clearly derived from compound **18**.The full range of bases used and the various conditions are given in the Table in the experimental section.



(i) LDA or TMPA (ii) TMSCl (iii) EtMgBr

Our observations from these lithiation experiments lead us to conclude that useful substitution at position 4 of triazolopyridines remains impractical. The less hindered base LDA , while allowing 4-substitution (albeit with poor and variable yields) also leads to substantial amounts of amidines by attack on the cyano group. The more hindered base TMPA forces the lithiation back to the more normal 7-position. It might be possible to perform selective functionalisation of the 4,7-disubstituted derivative, **15**, but the increased number of steps would make this an impractical route to 2,3-disubstituted pyridines by an adaptation of Scheme 1.

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EXPERIMENTAL

M. p.s were determined on a heated stage and are uncorrected. Chromatography was performed on a Chromatotron, using 2 or 4 mm plates of silica 60Pf$_{254}$, or for larger amounts by flash chromatography. Elution was with mixtures of petroleum ether, b. p. 60-80°C, and ethyl acetate. Nmr spectra were recorded on an Hitachi-Perkin Elmer R-24B instrument (60 MHz), a Jeol EX270 instrument (270 MHz), and a Varian VXR400 instrument (400 MHz). For ^{13}C spectra, the off-resonance multiplicity is recorded thus(s). Infrared spectra were recorded for solutions or as KBr discs.

7-Trimethylsilyl[1,2,3]triazolo[1,5-a]pyridine, (4a).- Triazolopyridine **1** was lithiated as previously described[2], using 1g of triazolopyridine. To the solution was added TMS chloride (4.56g), discharging the colour, and the mixture stirred (1 hr). After hydrolysis and evaporation of the organic extracts, a brown oil was obtained (2g), purified by column chromatography, to give, after crystallization from petroleum (b. p. 40-60°C), pure TMS derivative **4a**, m. p. 58-60°C (Found: C,56.50; H, 6.96; N,22.10. $C_9H_{13}N_3Si$ requires C,56.54; H,6.80; N,21.98%). δ_H(60MHz, $CDCl_3$)1.12(9H, m, $(CH_3)_3Si$), 6.4-6.7(2H, m, H5 and H6), 7.15(1H, dd, H4), 7.54(1H, s, H3). m/z 191(M^+, 100%).

3-(N,N-diethylcarbamoyl)-7-trimethylsilyl[1,2,3]triazolo[1,5-a]pyridine, 4b and 3-(N,N-diethylcarbamoyl)-4,7-di(trimethylsilyl)[1,2,3]triazolo[1,5-a]pyridine, 5.- a)Using the standard lithiation procedure[2] on the amide **3** (5g) with two equivalents of LDA and three equivalents of TMS chloride; the brown oil (7.4g) isolated after work-up was chromatographed on alumina (activity IV) ; elution with petroleum ether/ethyl acetate (95:5) gave the solid derivative **4b**, crystallized from petroleum (60-80°C), m. p. 68-70°C (2.14g, 33%)(Found: C, 57.90; H,7.71; N,19.17. $C_{14}H_{22}N_4OSi$ requires C,57.93; H,7.58; N,19.31%). δ_H(60MHz, $CDCl_3$)0.78(9H, s, $(CH_3)_3Si$), 1.57(6H, m, 2xCH_3CH_2), 3.7-3.9(2H, q, CH_3CH_2N), 4.2-4.4(2H, q, CH_3CH_2N), 7.3-7.5(2H, m, H5 and H6), 8.68(1H, dd, H4). ν_{max} 1 640cm^{-1}. m/z 290(M^+, 100%). Further elution with increasing proportions of ethyl acetate gave the di-TMS derivative, **5**, m. p. 91-93°C (0.4g, 5%)(Found: C, 56.31; H,8.40; N,15.46. $C_{17}H_{30}N_4OSi_2$ requires C,56.35; H,8.29; N,15.46%). δ_H (60MHz,$CDCl_3$)0.5(18H, s, 2x$(CH_3)_3Si$), 1.35(6H, t, 2xCH_3CH_2), 3.64(4H, br q, 2xCH_3CH_2N), 7.0-7.5, m, H5 and H6). m/z 390(M^+, 30%). ν_{max} 1 660cm^{-1}.

b) To a solution of *n*-butyllithium (1.5cm^3, 1.2M), and TMP (0.3) in ether (50cm^3) at -40°C, was slowly added the carboxamide **4b** (0.53g). The solution was stirred at -40°C (8h), then TMS chloride (0.23cm^3) was added. The solution was allowed to come to room temperature , then left for a further 2h before hydrolysis with ammonium chloride in ammonia (s.g.0.880). Work up by extraction with dichloromethane, followed by evaporation and purification on a Chromatotron, gave starting material (0.3g) and compound **5** (0.03g, 5%).

3-Cyano[1,2,3]triazolo[1,5-a]pyridine, (8).-a) Prepared as described by Balli and coworkers[5] ; over a period of days, crystalline cyano compound formed, and was filtered off to give a yield of 73%.

b) 2-Azido-1-ethylpyridinium tetrafluoroborate was prepared *in situ* by the addition of sodium azide (0.78g., 0.011 mol) to a stirred solution of 2-chloro-1-ethylpyridinium tetrafluoroborate (2.78g., 0.011 mol) in absolute ethanol (30cm^3), externally cooled in ice. After 10min. 2-pyridylacetonitrile (1.18g., 0.01 mol) and anhydrous sodium acetate (0.98g., 0.011 mol) were added, producing a cloudy suspension. After 3h. stirring at room temperature, the mixture was left overnight and filtered; dilution of the ethanolic solution followed by ether extraction gave a yield of nitrile **8** of 1.1g (76%).

c) To a stirred suspension of sodium hydride (8.32g., 0.233 mol, 60% dispersion in paraffin) in DMF (250cm^3, anhydrous) in an ice bath, was slowly added 2-pyridylacetonitrile (25g., 0.212 mol). Freshly prepared tosyl azide (50.08g., 0.254 mol) was added dropwise to the resulting bright yellow suspension. The mixture was allowed to reach room temperature and left (1h.) then the solvent was evaporated *in vacuo*. Flash chromatography of the dark residue and recrystallisation from petroleum ether (b. p. 60-80°C) gave nitrile **8**, m. p. 146°C(lit. [5] m. p. 146°C) (9.21g., 30%). (Found: C, 58.09; H, 2.65; N, 38.52. Calc. for $C_7H_4N_4$, C,58.33; H,2.80; N,38.87%). δ_H (270MHz, $CDCl_3$) 7.31(1H, t, H6, $J_{5,6}=J_{6,7}=6.84Hz$), 7.69(1H, dd, H5, $J_{4,5}=8.79Hz$, $J_{5,6}=6.84Hz$), 7.98(1H, d, H4, $J_{4,5}=8.79Hz$), and 8.93(1H, d, H7, $J_{6,7}=6.84Hz$). δ_C(68MHz, $CDCl_3$) 111.67(s, C3a), 111.98(s, C3), 116.89(d, C6), 117.17(d, C4), 126.58(d, C7), 130.20(d, C5), 136.63(s, CN). ν_{max}(KBr) 2 238cm^{-1}.

Base catalysed Diazo Transfer to 2-Pyridylacetonitrile- Isolation of Compounds (8), (9), (10), and (11).- A procedure is described which produced substantial quantities of compounds **(9)** - **(11)** when tosyl azide was used. Substitution of mesitylsulphonyl azide gave compound **(12)**.

a) A solution of 2-pyridylacetonitrile(2g, 0.017mol) in anhydrous ethanol (10cm^3) was added dropwise to a solution of sodium (0.585g, 1.5meq) in anhydrous ethanol (25cm^3), at 15-20°C under nitrogen. Tosyl azide (3.67g, 1.1 mol) was added dropwise, with external cooling, and the reaction mixture stirred forlh. before water was added. Acidification using 1M HCl and extraction with dichloromethane gave a mixture, separated by flash chromatography. Basification of the aqueous layer followed by extraction (CH_2Cl_2) gave, after recrystallisation from cyclohexane, **ethyl [1,2,3]triazolo[1,5-a]pyridine-3-carboximidate(9)**, m. p. 111-113°C(1.48g, 46%). (Found: C,56.66; H,5.17; N,29.32. $C_9H_{10}N_4$ requires C,56.83; H,5.30; N,29.46%). δ_H (270MHz, $CDCl_3$) 1.50(3H, t, $C\mathit{H_3}CH_2$), 4.51(2H, q, $CH_3C\mathit{H_2}$) , 7.07(1H, dd, H6, J=8.06 and 7.05Hz), 7.37(1H, dd, H5, J=8.06 and 8.86Hz), 8.10(1H, d, H4, J=8.86Hz), 8.52(1H, br s, NH), and 8.75(1H, d, H7, J=7.05Hz). δ_C (68MHz, $CDCl_3$) 14.37(q, CH3), 61.60(t, CH2), 115.91(d, C6), 119.84(d, C4), 125.50(d, C7), 127.58(d, C5), 130.74(s, C3), 131.46(s, C3a), 162.10(s, C=NH). m/z 190(M$^+$, 8.9%), 175(M$^+$-Me, 5.9), 105(100). From the acid extract was isolated **(N-tosyl)[1,2,3]triazolo[1,5-a]-pyridine-3-carboxamidine (10)**, m. p. 209-210°C(aq. EtOH), (0.7g, 13%). (Found: C,53.08; H, 4.11; N,22.32. $C_{14}H_{13}N_5O_2S$ requires C,53.32; H, 4.15; N,22.21%). δ_H(200MHz, d_6-DMSO) 2.38(3H, s, CH3), 7.20(3H, m), 7.75(1H, dd, H5, J=9 and 6Hz), 7.91(2H, d, H2',H6', J=8Hz), 8.12(1H, brs NH),8.25(1H, d, H4, J=9Hz), 9.19(1H, brs, NH), and 9.25(1H, d, H7, J=7Hz). δ_C(100MHz, TFA) 22.02(q, CH_3), 119.81(d, C6), !21.03(d, C7), 127.40(s, C3), 129.04(d, C4), 129.13(d, C2',C6'), 132.42(d, C3',C5'), 135.28(d, C5), 135.82(s, C1'), 136.42(s, C3a), 150.29(s, C4'), and 157.50(s, C=N). m/z 315(M$^+$, 15.5%), 148(20.5), 105(100), 91(20.1), 78(58.8). The second product from this extract was **4-(2-pyridyl)-5-(tosylamido)-**

[1,2,3]triazole(11), m. p. 165-167°C(absolute EtOH), (2.19g, 41%). (Found: C,53.50; H,4.16; N,22.20. $C_{14}H_{13}N_5O_2S$ requires C,53.32; H, 4.15; N,22.21%). δ_H(200MHz, d_6-DMSO) 2.34(3H, s, CH_3), 7.32(2H, d, H3',H5'), 7.36-7..44(2H, m, H3 and H5), 7.64(2H, d, H2',H6'), 7.91(2H, m, H4 and NH), 8.65(1H, d, H6, J=5Hz). δ_C(100MHz, TFA), 22.03(q, CH_3), 128.41(d, C5), 129.27(d, C3), 129.57(d, C2',C6'), 132.51(d, C3',C5'), 134.42(s, C1'), 136.45(s, triazole), 141.98(s, triazole), 143.69(d, C4), 143.98(s, C4'), 150.15(s, C2) and 150.52(d, C6). m/z 315(M^+, 19%), 132(34), 105(100), 91(47), 78(67).

On using mesityl sulphonyl azide, the products were the imidate **9** and **N-(mesitylsulphonyl)[1,2,3]triazolo[1,5-a]pyridine-3-carboxamidine (12)** m. p. 247-251°C(from MeCN), (42%). (Found: C,55.80; H,5.05; N, 20.36. $C_{16}H_{17}N_5O_2S$ requires C, 55.96; H, 4.99; N.20.39%). δ_H(270MHz, d_6-DMSO), 2.26(3H, s, CH_3), 2.65(6H, s, 2xCH_3), 7.02(2H, s, H3',H5'), 7.37(1H, dd, H6, J=6.84 and 6.85Hz), 7.72(1H, dd, H5, J=8.87 and 6.84Hz), 7.85(1H, brs, NH), 8.09(1H, d, H4, J=8.87Hz), 8.95(1H, brs, NH), 9.23(1H, d, H7, J=6.85). δ_C (68MHz, d_6-DMSO) 20.32(q), 22.27(q), 117.30(d, C6), 118.54(d, C7), 129.87(s, C3), 130.54(d, C4), 131.37(d, C5), 131.47(d, C3',C5'), 132.94(s, C1'), 136.97(s, C3a), 137.58(s, C2', C6'), 141.10(s, C4'), 155.08(s, C=N). m/z 343(M^+, 2.4%), 175(34.9), 105(100), 78(49.6).

Lithiation of 3-cyanotriazolopyridine (8).- General procedure; a solution of n-butyllithium in hexane was added to diisopropylamine or TMP, with external cooling. A solution of compound **8** in anhydrous THF was added dropwise with stirring, and stirring continued while the lithiation was monitored by quenching samples with D_2O followed by examination of the ^1H nmr spectrum. In all cases a deep red colour developed. When the lithiation was complete, a solution of TMS chloride in THF was added and the reaction mixture allowed to come to room temperature overnight. Treatment with ammonia (s. g. 0.880) saturated with ammonium chloride, was followed by extraction with CH_2Cl_2, $CHCl_3$, and ethyl acetate. The dried solvent was evaporated, and the residue separated by chromatography (Chromatotron for 0.5g. samples, flash for larger samples). From the nine experiments performed, listed in the Table, conditions are given for two, from which all products could be obtained.

a) At -40°C, with 1.1 meq of LDA. The products isolated were;

3-Cyano-4-trimethylsilyl[1,2,3]triazolopyridine (14) (20%), m. p. 107-110°C. δ_H nmr details given in discussion. δ_C (68MHz, $CDCl_3$) -0.51(q, CH_3Si) , 112.65(s, C3), 113.96(s, C3a), 116.37(d, C6), 126.69(d, C7), 131.47(s, C4), 136.24(d, C5), 138.51(s, CN). ν_{max} 2229cm^{-1}. m/z 216(M^+,11.8%), 215(38.9), 188(M^+-N_2, 34.4%), 187(M^+-N_2H, 48.3), 172(98), 146(100) 73(Me_3Si^+).

3-Cyano-4,7-di(trimethylsilyl)[1,2,3]triazolo[1,5-a]pyridine (15),- m. p. 182-183°C(sublimed) (20%). (Found: C,54.27; H,6.92; N,19.63. $C_{13}H_{20}N_4Si_2$ requires C,54.12; H,6.99; N, 19.42%). δ_H (270MHz, $CDCl_3$) 0.52(18H, s, 2x $(CH_3)_3Si$) , 7.23(1H, d, H6, J=6.6Hz), 7.63(1H, d, H5, J=6.6Hz). δ_C (68MHz, $CDCl_3$) -2.28(q, CH_3Si), 0.56(q, CH_3Si), 111.97(s, C3), 114.44(s, C3a), 126.16(d, C6), 130.95(s, C4), 135.35(d, C5), 138.03(s, CN), 143.10(s, C7). m/z 288(M^+, 16.3%), 245(41.8), 73(Me_3Si^+, 100).

N,N- Diisopropyl-4,7-di(trimethylsilyl)[1,2,3]triazolo[1,5-a]pyridine-3-carboxamidine (16).- m. p. 111-112°C (5%). δ_H(270MHz, $CDCl_3$) 0.40(9H, s, $(CH_3)_3Si$) , 0.46(9H, s, $(CH_3)_3Si$) , 1.41(12H, d, $(CH_3)_2CH$), 3.73(2H, m, $CH(CH_3)_2$), 6.99(1H, d, H6, J=6.45Hz), 7.38(1H, d, H5, J=6.45Hz). δ_C (68MHz, $CDCl_3$) -2.26(q), 0.95(q), 20.50(q), 121.85(d,2xCH), 131.76(s, C4), 133.08(d, C5 and C6), 133.30(s, C3), 137.50(s, C3a), 141.31(s, C7), 156.11(s, C=NH). m/z 389(M^+, 16.0%), 388(24.4), 346(29,9), 345(100), 317(33.6), 100(30.2), 73(83.1), 43(49.9).

N,N-Diisopropyl-7-trimethylsilyl[1,2,3]triazolo[1,5-a]pyridine-3-carboxamidine (17).- m. p. 105-107°C (5%). δ_H (60MHz, $CDCl_3$) 0.51(9H, s, $(C\mathit{H}_3)_3Si$), 1.51(12H, d, $(C\mathit{H}_3)_2CH$), 3.86(2H, m, $C\mathit{H}(CH_3)_2$), 5.92(1H, brs, NH), 7.04(1H, dd,H6, J=7 and 1Hz), 7.26(1H, t, H5, J=7Hz), 7.85(1H, dd, H4, J=7 and 1Hz). m/z 317(M+, 18.9%), 302(21.2), 275(22.1), 274(84.7), 246(29.4), 177(50.2), 161(39.4), 100(31.2), 86(26.3), 73(100), 44(23.6), 43(24.8).

b) Using TMP and *n*- butyllithium (1.1mol) at -70°C, 24% of unchanged cyano compound (**8**), 9% of compound (**15**), and 50% of compound (**18**) were obtained. **3-Cyano-7-trimethylsilyl[1,2,3]triazolo[1,5-a]pyridine (18)** had m. p.151-153°C(from cyclohexane). (Found: C,55.10; H, 5.51; N, 25.97. $C_{10}H_{12}N_4Si$ requires C, 55.12; H, 5.59; N, 25.90%). ^1H nmr details as given in discussion + 0.53(9H, Me_3Si). δ_C (68MHz, $CDCl_3$) -2.25(q, (CH_3Si), 111.26(s, C3), 112.37(s, C3a), 116.92(d, C6), 123.63(d, C4), 128.97(d, C5), 136.26(s, CN), 143.39(s, C7). ν_{max}(KBr) 2 233cm^{-1}. m/z 216(M^+, 8.9%), 195(35.8), 73(100).

3-(1-Iminopentyl)-7-trimethylsilyl-[1,2,3]triazolo[1,5-a]pyridine (19).- Isolated when an excess of *n*-butyllithium was used, compound **19** had m.p.108-109°C (from cyclohexane)(Found: C, 61.20; H, 7.85; N, 20.82. $C_{14}H_{22}N_4Si$ requires C, 61.27; H, 8.08; N, 20.41%). δ_H(270MHz, $CDCl_3$) 0.33(9H, s), 0.89(3H, t), 1.40(2H, m), 1.74(2H, m), 3.26(2H, t), 7.41(1H, dd, H6), 7.63(1H, dd,H5), 7.99(1H, dd, H4), 13.92(1H, brs, NH). m/z 274(M^+, 26%).δ_C (68MHz, $CDCl_3$) -1.75(q, CH_3Si), 13.91 (q, CH_3), 22.64 (t, CH_2) 25.28 (t, CH_2), 31.23 (t, CH_2), 120.23 (d, C6), 127.14 (d, C4), 134.54 (d, C5), 142.56 (s, C3), 142.99 (s, C3a), 151.23 (s, C7), 167.74 (s, C=NH).

3-Propionyl[1,2,3]triazolo[1,5-a]pyridine (13).- The Grignard reagent from ethyl bromide (7.28mmol) in anhydrous ether (20cm^3) was added dropwise to a solution of compound (**8**) (3.47 mmol), in ether (50cm^3) under argon, to give a cream coloured suspension. After 1hr. ice-cold 2M HCl (50cm^3) was added, the ethereal layer separated, and extracted with more 2M HCl (30cm^3). The combined acid layers were poured on to ice, and neutralized with ammonia (s.g. 0.880). Extraction with CH_2Cl_2, drying ($MgSO_4$) and evaporation of the solvent gave a solid, recrystallized from petroleum ether (b. p. 60-80°C), to give the ketone (**13**) , m. p. 114-117°C, (0.56g, 92%). (Found: C, 61.51; H, 4.97; N, 24.08. $C_9H_9N_3O$ requires C, 61.70; H, 5.18; N, 23.99%). δ_H (270MHz, $CDCl_3$) 1.31(3H, t, $C\mathit{H}_3CH_2$), 3.31(2H, q, $CH_3C\mathit{H}_2$), 7.19(1H, t , H6, J=6.8Hz), 7.58(1H, dd, H5, J=8.8 and 6.8Hz), 8.43(1H, d, H4, J=8.8Hz), 8.85(1H, d, H7, J=6.8Hz). ν_{max} (KBr) 1 667cm^{-1}. m/z 175(M^+, 43.9%), 174(74.8), 173(93.7), 132(100), 118(41.5), 106(36.4), 104(42.1), 79(47.7), 78(73.8), 39(33.0). δ_C (68 MHz, $CDCl_3$) 8.18 (q, CH_3), 32.66 (t, CH_2), 116.73 (d, C6), 120.15 (d, C4), 125.73 (d, C7), 129.84 (d, C5), 133.90 (s, C3), 136.91 (s, C3a), 196.41 (s, C=O).

Table: Lithiation experiments on Nitrile (8)

Base(meq)	Nitrile(mol)	Temp.°C	Solvent(cm^3)	Time(h)	TMS(meq)	Products and(Yields)
LDA(1.1)	$3.47x10^{-3}$	-40	H(20) T(40)	1	1.1	**14**(20);**15**(20); **16**(5); **17**(5)
LDA(1.1)	$3.47x10^{-3}$	-40	H(10 T(40)	1	1.1	**17**(5);**18**(27);**8**(20)
LDA(1.1)	$3.47x10^{-3}$	-40	H(20) T(40)	0.5	1.1	**17**(34);**18**(15)
LDA(2.2)	$3.47x10^{-3}$	-40	H(10) T(40)	1	2.2	**16**(4);**17**(29)
LDA(2.2)	$3.47x10^{-3}$	-10	H(10) T(40)	1	2.2	**17**(33)

TMPA(1.1)	$3.47x10^{-3}$	-70	H(10)T(50)	8	1.1	**18**(5);**19**(15);**8**(55)
TMPA(1.1)	$3.47x10^{-3}$	-70	H(10)T(50)	0.5	1,1	**15**(9);**18**(50);**8**(24)

LDA = lithium diisopropylamide; TMPA = *n*-butyllithium + TMP; H = hexane ;T = THF

X-Ray Crystallography.- X-ray measurements were made using an Enraf-Nonius FAST TV area detector diffractometer and graphite monochromated Mo-Ka radiation following previously described procedures[8]. The structure was solved by direct methods and refined by full-matrix least squares. All non-hydrogen atoms were refined anisotropically and hydrogens isotropically. The final R1 values for 2021/5041 data and 251 parameters was 0.059 (I>2sigma(I)) and 0.1153 (all data). Full details of the structure determination have been submitted as supplementary material. Fractional atomic coordinates have been deposited at the Cambridge Crystallographic Data Centre.

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