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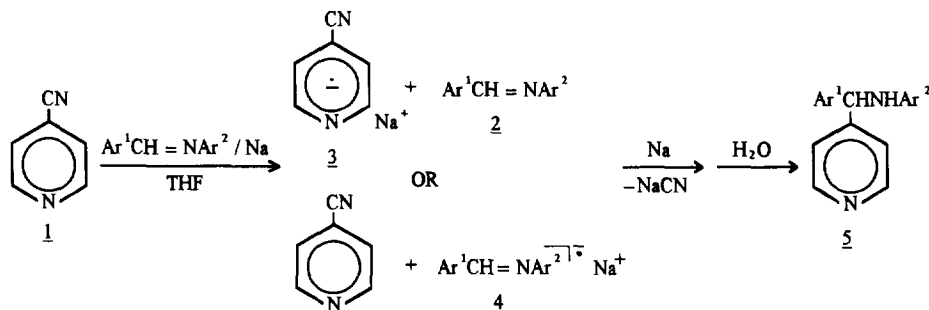
A Novel Aminoalkyl-decyanation of 4-Pyridinecarbonitrile with Imines: A Facile Selective Synthesis of 4-Pyridinemethanamines

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Abstract: Reactions of 4-pyridinecarbonitrile with sodium and aromatic imines provide a convenient and useful method for synthesising a new kind of substituted 4-pyridinemethanamines in good yields. Copyright © 1996 Elsevier Science Ltd

Backman and Karickhoff¹, and Scheinkman et al.² reported that pyridine can undergo condensation with imines in the presence of magnesium or aluminium amalgams and/or sodium alone to give 2-pyridinemethanamines. However, no 4-pyridine analogues were isolated from the reactions. Furthermore, no report dealing with α ,N-diaryl-4-pyridinemethanamines and its synthetic methodologies has appeared in the literature so far. We recently reported the hydroxyalkyl-decyanation of 4-pyridinecarbonitrile alkali metal complex with ketones or aldehydes to produce 4-pyridinemethanols³. We wish now to communicate the extension of this kind of reaction to a novel radical Ipso substitution⁴ of aminoalkyl-decyanation of 4-pyridinecarbonitrile radical anion sodium complex with aromatic imines, and the development of a new one-step synthesis of α ,N-diaryl-4-pyridinemethanamines, as shown in Scheme 1:



Scheme 1

The representative results of reaction are shown in Table 1. All compounds are new and characterized by microanalyses and IR, NMR and/or mass spectroscopy. It will be noted that it is ready to form intermediate **3** and **4** under the reaction conditions^{2,3}, and generally, a small amount of dipyridyl and dimer of imine as by product is found in the reaction mixture. It seems that the reaction may proceed via either pathway as shown in Scheme 1. As can be seen in Table 1, a strong electron-donating group (e.g. MeO or EtO) which substitutes in the aromatic nuclei of imine, makes the yields somewhat lower, and a considerable amount of

unreacted imine is found after the reaction. It is probable that the strong electron-donating substituent lowers electron affinity of imine making it reluctant to accept electron from sodium and form a stable imine radical anion **4**. On the contrary, a strong electron-withdrawing substituent (e.g. CF_3) facilitates the reaction. Further studies on the reaction mechanism and scope are in progress. In summary, the reaction is applicable to a wide range of aromatic imines and the yields are fairly good. It makes available a series of new compounds of potential interest as intermediates in the preparation of drug and agricultural chemicals.

Table 1 Aminoalkyl-decyanation of 4-CN-C₅H₄N with Ar¹CH=NAr²

| Entry | Ar ¹ CH=NAr ² | | Compound mp °C | Yield ^a (%) |
|-------|---------------------------------------|---|-------------------|---------------------------|
| | Ar ¹ | Ar ² | | |
| 1 | 2a Ph | Ph | 5a 99.5~100.5 | 85 |
| 2 | 2b Ph | 2-MeC ₆ H ₄ | 5b 108.0~109.0 | 87 |
| 3 | 2c Ph | 2-EtC ₆ H ₄ | 5c 61.0~62.5 | 61 |
| 4 | 2d Ph | 3-EtC ₆ H ₄ | 5d 107.5~108.5 | 72 |
| 5 | 2e Ph | 4-EtC ₆ H ₄ | 5e 115.0~115.5 | 65 |
| 6 | 2f Ph | 3-ClC ₆ H ₄ | 5f 97.0~97.5 | 54 |
| 7 | 2g Ph | 3-CF ₃ C ₆ H ₄ | 5g 124.0~125.0 | 80 |
| 8 | 2h Ph | 4-EtOC ₆ H ₄ | 5h 134.0~135.0 | 57 |
| 9 | 2i 4-MeOC ₆ H ₄ | Ph | 5i 148.0~148.7 | 55 |
| 10 | 2j 4-MeOC ₆ H ₄ | 3-CF ₃ C ₆ H ₄ | 5j 147.0~148.0 | 72 |

a) Isolated yield based on starting 4-pyridinecarbonitrile or imines.

A typical procedure is described for the synthesis of α -phenyl-N-(2-methylphenyl)-4-pyridine-methanamine(**5b**): To a stirred absolute THF (20ml) was added freshly cut sodium (0.50g, 22mmol) in small pieces and 4-pyridinecarbonitrile (1.04g, 10mmol) at -5°C under nitrogen. After stirring for 2-3 min. N-benzylidene-2-methylaniline⁵ (1.95g, 10mmol) was added, the mixture allowed to warm to room temperature and the stirring continued for 5h. Then another part of sodium pieces (2.0g, 9 mmol) was added and the mixture allowed to stand over night after stirring for 1h. The brown black mixture was hydrolysed with water (20ml) and extracted with ether (15ml x 3), dried over Na₂CO₃ and concentrated. The residue was chromatographed on silica gel with a mixture of light petroleum ether, ether and acetone as eluent, yielding 2.4g (87%) of **5b**⁶, mp 108.0~109.0°C (petroleum ether-ether).

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References and Notes

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- Selected spectral data: ν_{max} 3340, 3032, 2973, 2932, 2858, 1606, 1590, 1486, 1454, 796, 748, 701 cm⁻¹. ¹HMR (CCl₄): δ 8.34 (2H, d), 6.07-7.13 (11H, m), 5.35 (1H, d), 3.82 (1H, br s), 2.10 (3H, s). MS: m/z 274 (M⁺, 50%), 196 (16), 168 (100), 91 (3). Anal: Calcd for C₁₉H₁₈N₂: C, 83.18; H, 6.61; N, 10.21. Found: C, 82.99; H, 6.65; N, 10.16.

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