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A NEW SYNTHESIS OF ALKYLPYRIDINES USING α,β-UNSATURATED ALDIMINE AND NITRILE

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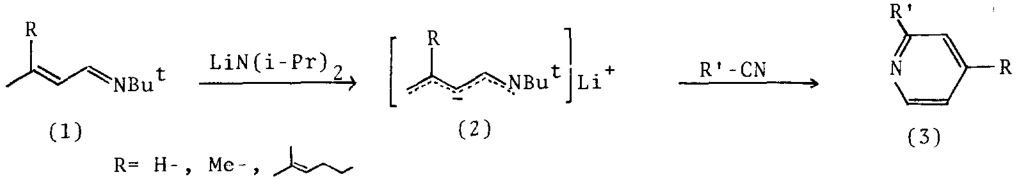
The lithiated imines are very useful intermediates in organic synthesis. Wittig et al. have reported that the lithiated aldimines react with nitrile and α-haloketone to give the primary enamine$^{1)}$ and pyrrole$^{2)}$, respectively. Recently we have shown that α,β-unsaturated aldimine is easily metalated with lithium diisopropylamide and the resulting carbanion reacts with alkyl halide regioselectively$^{3)}$. In this communication we wish to report on a new synthesis of alkylpyridine by the reaction of the lithiated α,β-unsaturated aldimines with nitriles.



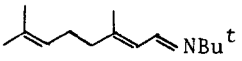
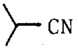
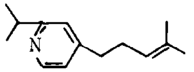
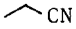
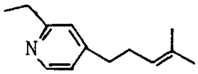
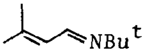
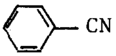
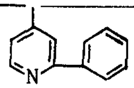
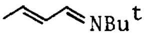
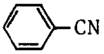
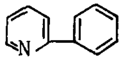
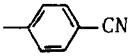
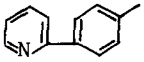
(1) (2) (3)

R= H-, Me-,

Treatment of the aldimine of citral (1a) in anhydrous ether with an equivalent of lithium diisopropylamide at -78°C for 1 hr gave a solution of the carbanion (2a). To this solution was added dropwise an ether solution of an equivalent of freshly distilled iso-butyronitrile at -78°C followed by gradually warming up to room temperature and stirring for 24 hr. The reaction mixture was then treated with water under ice-cooling. After the usual work-up, the distillation of the products afforded 2-isopropyl-4-(4-methyl-3-pentenyl)-pyridine (3a) in a 63% yield as the sole product. [(3a); mass(m/e): M^+ 203, ir (neat, cm^{-1}): 1603 and 825, nmr(CCl_4, δ): 8.27(1H,d,J=5.5Hz), 6.82(1H,s), 6.79 (1H,d,J=5.5Hz), 5.06(1H,t,J=7.0Hz), 2.93(1H,m,J=6.5Hz), 2.62-2.16(4H,m), 1.63 (3H,s), 1.50(3H,s) and 1.25(6H,d,J=6.5Hz)].

Table 1 summarizes the yields of the typical examples investigated.

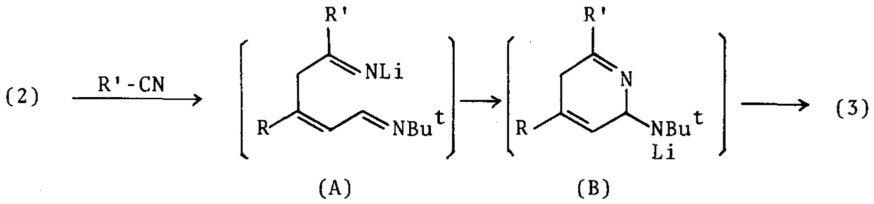
Table 1. Synthesis of Alkylpyridines[a)]

Aldimine	Nitrile	Pyridine	Yields (%)
 (1a)		 (3a)	63 (87)[b)]
			46 (71)[b)]
			38 (54)[b)]
			22
			24

a) The structures of all products were verified by compatible spectral data (ir, nmr and mass spectra).

b) Based on the aldimine consumed.

At present, though the mechanism of this reaction could not be clarify enough, the formation of the pyridine is considered to proceed, after the addition of the lithiated aldimine (2) to nitrile, via intramolecular cyclization of the resulting diimine (A) followed by elimination of t-butylamino group from (B)[4)]. Further development is now in progress.



References and Footnotes

1) G. Wittig, S. Fischer and M. Tanaka, *Ann. Chem.*, 1075 (1973).

2) G. Wittig, R. Roderer and S. Fischer, *Tetrahedron Lett.*, 3517 (1973).

3) K. Takabe, H. Fujiwara, T. Katagiri and J. Tanaka, *Tetrahedron Lett.*, 1237 (1975).

4) This scheme is similar to that of the synthesis of pyrrole from α-bromoketone [P. Duhamel, L. Duhamel and J. Valnot, *Tetrahedron Lett.*, 1339 (1973)].