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# 1-(N-ALKYLIMINOFORMYL)AZOLE —— A REAGENT OF TRANS-FORMIMIDOYLATION

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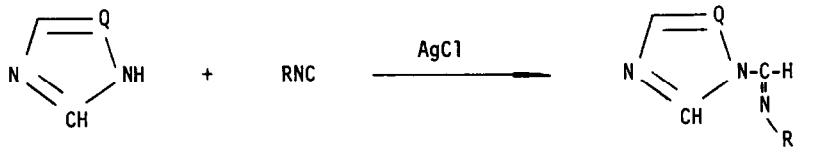
Chemistry of carboxamide of azoles such as imidazole, pyrazole and triazole has been systematically studied in view of the synthetic utilities[1] and biochemical reaction mechanism.[2] The high reactivity of carboxamide of azoles in the nucleophilic substitution is based on that azole is a good leaving group, because of the quasi-aromatic character of azole. Herein, we wish to report a new synthesis of reactive 1-(N-alkyliminoformyl)azoles, 1-(N-alkyliminoformyl)imidazole (Ia) and 1-(N-alkyliminoformyl)triazole (Ib), which are conveniently utilized as a reagent of the transfer reaction of an N-alkyliminoformyl group to active hydrogen compounds including amine, alcohol and the so-called active methylene compound. Ia and Ib were prepared in moderate yields by the insertion[3,4] of isonitrile into N-H linkage of imidazole and triazole, respectively, by means of AgCl catalyst.

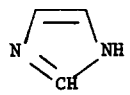
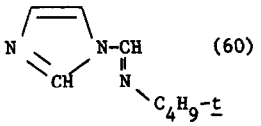
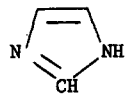
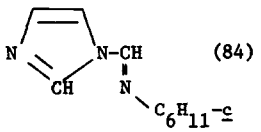
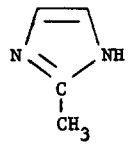
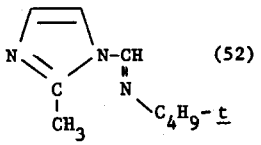
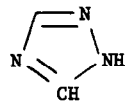
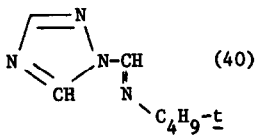



(I) a : Q=CH
b : Q=N

A typical reaction procedure is as follows. A mixture of 6.8 g (0.1 mol) of imidazole, 8.3 g (0.1 mol) of tert-butyl isocyanide, 1.4 g (0.01 mol) of AgCl and 25 ml of dry tetrahydrofuran was stirred at 120° for 6 hr. Distillation of the reaction mixture gave

1-(N-tert-butyliminoformyl)imidazole Ia (bp. 104°/1 mm) slightly contaminated by imidazole. An analytically pure sample of Ia was prepared by preparative glpc. Structure of Ia was supported by nmr [$\tau$ ($CCl_4$) 1.75 (s, 1H), 2.10 (m, 1H, $J_{H_2-H_4}$ = 1.4 cps, $J_{H_2-H_5}$ = 1.2 cps), 2.55 (m, 1H, $J_{H_5-H_4}$ = 0.7 cps, $J_{H_5-H_2}$ = 1.2 cps), 3.05 (m, 1H, $J_{H_4-H_2}$ = 1.4 cps, $J_{H_4-H_5}$ = 0.7 cps), 8.76 (s, 9H)], mass spectrum [151, 84 (P-67)] and ir (neat) [1690 $cm^{-1}$ (C=N)]. Ia was readily hydrolyzed in aq. HCl solution producing N-tert-butyl formamide and imidazole in quantitative yields. Some results are summarized in Table I.

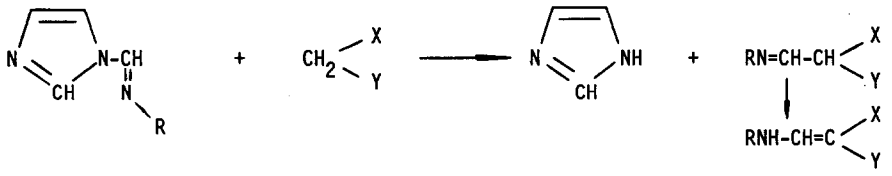
Table I
Synthesis of 1-(N-Alkyliminoformyl)azoles

| Azole | Isocyanide | Reaction Temp(°C) | Reaction Time(hr) | Product (%) |
|---|---|---|---|---|
|  | $t$-$C_4H_9NC$ | 120 | 6 |  (60) |
|  | $c$-$C_6H_{11}NC$ | 120 | 15 |  (84) |
|  | $t$-$C_4H_9NC$ | 120 | 10 |  (52) |
|  | $t$-$C_4H_9NC$ | 120 | 10 |  (40) |

As it was expected, Ia reacted with amine and alcohol to produce N,N'-disubstituted formamidine (IIa) and alkyl N-substituted formimidate (IIb), respectively, according to the following equation.

(II) a : Q=NH b : Q=O

Furthermore, the reaction of Ia with active methylene compounds such as acetylacetone, acetoacetate, malonate and malononitrile gave enamine derivatives (III) in good yields. I is interestingly compared with acylimidazole, which is unable to react with active methylene compounds.

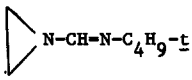


(III)

These "trans-formimidoylation" was successfully carried out simply by heating an equimolar mixture of I and an active hydrogen compound. No catalyst was needed. Some results are summarized in Table II.

Table II

Trans-Imidoylation Reaction of Ia.

| Active hydrogen compounds | Reaction Temp (°C) | Time (hr) | Products (%)[a] | |
|---|---|---|---|---|
|  | 25 | 18 |  | (100) |
| $PhNH_2$ | 100 | 5 | $PhNH-CH=N-C_4H_9-t$ | (94) |
| $n-C_4H_9OH$ | 100 | 14 | $n-C_4H_9O-CH=N-C_4H_9-t$ | (64) |
| $CH_2(COCH_3)_2$ | 50 | 6 | $(CH_3CO)_2C=CHNH-C_4H_9-t$ | (80) |
| $CH_2(CN)_2$ | 50 | 6 | $(NC)_2C=CHNHC_4H_9-t$ | (69) |

[a] All new compounds gave satisfactory elementary analyses and were spectroscopically characterized. Structures of III were established by nmr and ir data. [$(CH_3CO)_2C=CHNH-C_4H_9-t$ : nmr ($CDCl_3$) $\tau$2.15 (d, 1H, $J_{H-H}$ = 15 cps), 7.55 (s, 3H), 7.76 (s, 3H), 8.67 (s, 9H); ir(neat) 3100~3300 $cm^{-1}$ (broad, NH), 1620 ($\nu_{C=C}$)].

An interesting feature in the "trans-formimidoylation" is that the product (III) is formed in the reaction of isonitrile with the active methylene compound in the presence of catalytic amounts of imidazole and AgCl. The reaction of isonitrile with active methylene compounds does not occur in the presence of AgCl alone. The results may reasonably explained as follows, i.e., Ia is first formed in the reaction system, which enters into the "trans-formimidoylation" with the active methylene compound. Thus, imidazole is reproduced and recycled. For instance, in the presence of 10 mol% of imidazole and AgCl, an equimolar mixture of cyclohexyl isocyanide and acetylacetone was heated at 120°, for 13 hr to produce N-cyclohexyl-2,2-diacetylvinylamine in 64% yield. Further studies are currently in progress to evaluate the applicability in synthesis.

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