NOVEL SYNTHESIS AND 1,3-DIPOLAR CYCLOADDITION REACTION OF PYRIDINIUM N-METHYLIDE

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Abstract — Pyridinium N-methylide, generated in situ by treating N-(trimethylsilylmethyl)pyridinium triflate with fluoride ion, was found to react with dimethyl acetylenedicarboxylate to give dimethyl indolizine-1,2-dicarboxylate. Similarly, the N-methylides derived from quinoline and isoquinoline gave the corresponding indolizine derivatives. With N-phenylmaleimide and (E)-1,2-dibenzoylethylene, however, pyridinium N-methylide afforded N-phenylitaconimide and 2,3-dibenzoylpropene, respectively.

Although there are a number of reports on the syntheses and reactions of pyridinium N-acylmethylides, little work has appeared on the chemistry of pyridinium N-methylide (3a) itself. The N-methylide (3a) has been prepared either by deprotonation of N-methylpyridinium salts or decarboxylation of pyridinium N-acetate. The most direct and versatile route to (3a), however, appears to be via desilylation of N-(trimethylsilylmethyl)pyridinium salt. In this communication we wish to report a new synthesis and 1,3-dipolar reactivity of (3a) and its benzologs.

Reaction of pyridine (1a) with an equimolar quantity of trimethylsilylmethyl triflate (4) in 1,2-dimethoxyethane (DME) at room temperature for 2 h gave N-(trimethylsilylmethyl)pyridinium triflate (2a) which, without isolation, was treated with dimethyl acetylenedicarboxylate (DMAD) in the presence of cesium fluoride at 0°C for 3 h to give dimethyl indolizine-1,2-dicarboxylate (5a) in 31.2% yield. Alternatively, the solution of (2a) in DME was treated with a 1M solution of tetra-n-butylammonium fluoride (TBAF) in tetrahydrofuran (THF) at -70°C for 1.5 h to give the same indolizine (5a) in 37.7% yield.
Similar reaction of quinoline (1b) and isoquinoline (1c) with (4) in DME followed by treatment of the resulting (2b,c)\(^5\) with DMAD in the presence of TBAF at 0°C for 3-4 h afforded dimethyl pyrrolo[1,2-a]quinoline-2,3-dicarboxylate (3b)\(^7\) and dimethyl pyrrolo[2,1-a]isoquinoline-1,2-dicarboxylate (3c)\(^6\) in 36.5 and 22.9% yields, respectively.

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\begin{align*}
(1a-c) & \quad \text{R}^1 = R^2 = R^3 = H; \\
(2a-c) & \quad R^1 = R^2 = -(CH)_n, R^3 = H; \\
(3a-c) & \quad R^1 = H, R^2 = R^3 = -(CH)_n.
\end{align*}
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Tf = CF\(_3\)SO\(_2\)

In contrast to the reaction of (2a) with DMAD, reaction of (2a) with N-phenylmaleimide in DME in the presence of TBAF at 0°C for 2 h gave N-phenylitaconimide (6a)\(^6,7\) in 11.7% yield instead of the expected tetrahydropyrrolizidine derivative. Similarly, the reaction of (2a) with (E)-1,2-dibenzylethylene gave 2,3-dibenzoylpropene (6b)\(^7\) in 23.9% yield.

A possible mechanism for the formation of (6) would involve an initial Michael addition of (3a) to the olefin (e.g., N-phenylmaleimide) to form an intermediate (7) which undergoes 1,2-proton migration followed by elimination of pyridine leading to (6).

Further studies on the chemistry of these ylides are in progress.
REFERENCES AND NOTES


5. The triflates (2a-c) could be isolated after reacting (la-c) with (4) in dichloromethane at room temperature for 2 h: (2a) (91.9%), mp 108-109°C (from ethyl acetate); (2b) (99.1%), mp 95-96°C (from ethyl acetate); (2c) (92.2%), mp 84-85°C.


7. (5a): mp 90-91°C (from methanol); IR (nujol) 1690 and 1735 cm⁻¹; NMR (CDCl₃) δ 3.89 and 3.90 (6H, s, COOCH₃), 6.73 (1H, dt, H-6, J = 7, 1.5 Hz), 7.04 (1H, ddd, H-7, J = 9.5, 7, 1 Hz), 7.61 (1H, s, H-3), 7.92 (1H, dt, H-5, J = 7, 1 Hz), and 8.10 (1H, brd, H-8, J = 9 Hz).

(5b): mp 132-134°C (from methanol); IR (nujol) 1690 and 1725 cm⁻¹; NMR (CDCl₃) δ 3.93 (6H, s, COOCH₃), 7.33 (1H, d, H-5, J = 10 Hz), 7.44 (1H, dt, H-7, J = 7.5, 1 Hz), 7.60 (1H, ddd, H-8, J = 8, 7.5, 1.5 Hz), 7.71 (1H, dd, H-6, J = 7.5, 1.5 Hz), 7.91 (1H, br d, H-9, J = 8 Hz), 7.99 (1H, d, H-4, J = 10 Hz), and 8.24 (1H, s, H-1).

(5c): mp 134-135°C (from methanol); IR (nujol) 1710 and 1730 cm⁻¹; NMR (CDCl₃) δ 3.83 and 4.03 (6H, s, COOCH₃), 6.86 (1H, d, H-5, J = 7.5 Hz), 7.4-7.6 (3H, m, H-6, H-7, and H-8), 7.64 (1H, d, H-4, J = 7.5 Hz), 7.69 (1H, s, H-3), and 8.24 (1H, br d, H-9, J = 7 Hz).

(6a): mp 116-117°C (lit.6 mp 108-110.5°C) (from n-hexane-benzene); IR (nujol) 1705 and 1770 cm⁻¹; NMR (CDCl₃) δ 3.50 (2H, dd, CH₂CO, J = 2.5, 2 Hz), 5.74 (1H, d, H₂C=, J = 2 Hz), 6.46 (1H, d, H₂C=, J = 2.5 Hz), and 7.2-7.6 (5H, m, aromatics).

(6b): mp 59-60°C (from n-hexane); IR (nujol) 1660 and 1680 cm⁻¹; NMR (CDCl₃) δ 4.23 (2H, s, CH₂), 5.81, 5.95 (1H each, s, H₂C=), and 7.4-7.6, 7.8-8.1 (10H, m, aromatics).

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