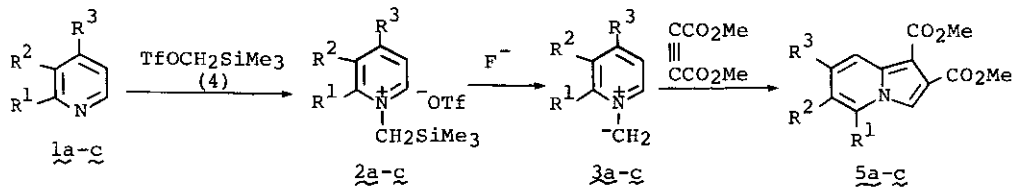
NOVEL SYNTHESIS AND 1,3-DIPOLAR CYCLOADDITION REACTION OF PYRIDINIUM N-METHYLIDE

Yasuyoshi Miki,* Hiroko Hachiken, and Shoji Takemura
Faculty of Pharmaceutical Sciences, Kinki University, 3-4-1
Kowakae, Higashi-Osaka 577, Japan
Masazumi Ikeda
Kyoto College of Pharmacy, Misasagi, Yamashina, Kyoto 607, Japan

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,[1] little work has appeared on the chemistry of pyridinium N-methylide (3a) itself.[2,3] The N-methylide (3a) has been prepared either by deprotonation of N-methylpyridinium salts[2,3] or decarboxylation of pyridinium N-acetate.[3] 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)[4] in 1,2-dimethoxyethane (DME) at room temperature for 2 h gave N-(trimethylsilylmethyl)pyridinium triflate (2a) which, without isolation,[5] 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)[7] 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 (5b)[7] and dimethyl pyrrolo[2,1-a]isoquinoline-1,2-dicarboxylate (5c) in 36.5 and 22.9% yields, respectively.

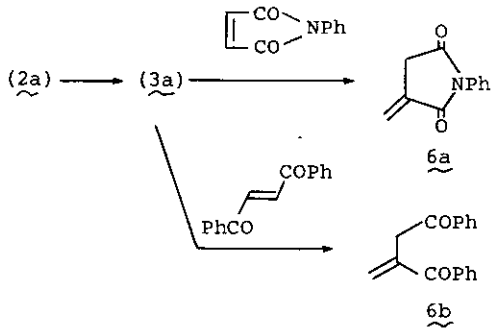


1a-c 2a-c 3a-c 5a-c

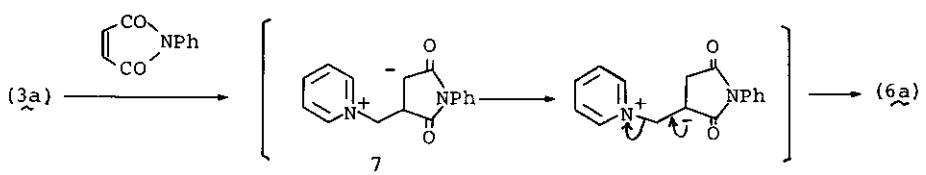
a, $R^1 = R^2 = R^3 = H$; b, $R^1 = R^2 = -(CH)_4-$, $R^3 = H$; c, $R^1 = H$, $R^2 = R^3 = -(CH)_4-$

Tf = CF_3SO_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 tetrahydroindolizine derivative. Similarly the reaction of (2a) with (E)-1,2-dibenzoylethylene 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).



7

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

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5. The triflates (2a-c) could be isolated after reacting (1a-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.

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7. (5a): mp 90-91°C (from methanol); IR (nujol) 1690 and 1735 cm^{-1}; NMR ($CDCl_3$) δ 3.89 and 3.90 (6H, s, $COOCH_3$), 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 ($CDCl_3$) δ 3.93 (6H, s, $COOCH_3$), 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 ($CDCl_3$) δ 3.83 and 4.03 (6H, s, $COOCH_3$), 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 ($CDCl_3$) δ 3.50 (2H, dd, CH_2CO, J =2.5, 2 Hz), 5.74 (1H, d, $H_2C=$, J = 2 Hz), 6.46 (1H, d, $H_2C=$, 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 ($CDCl_3$) δ 4.23 (2H, s, CH_2), 5.81, 5.95 (1H each, s, $H_2C=$), and 7.4-7.6, 7.8-8.1 (10H, m, aromatics).

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