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Short Note

1-(6-Ethoxy-6-oxohexyl)-4-methylquinolinium Iodide

Angela Winstead * and Stanley Oyaghire

Morgan State University, 1700 E. Cold Spring Lane, Baltimore, MD 21251, USA

* Author to whom correspondence should be addressed; E-Mail: angela.winstead@morgan.edu.

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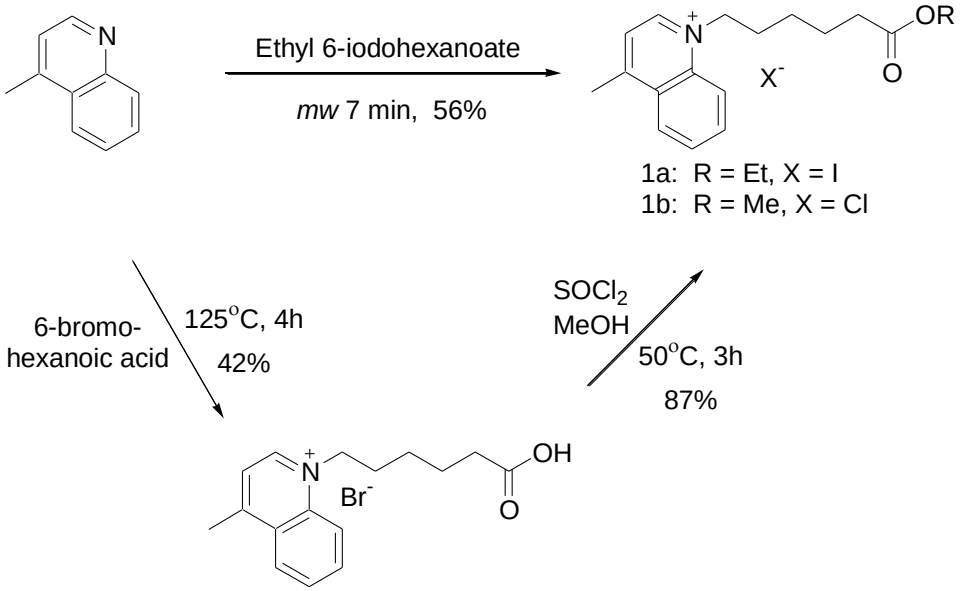
Abstract: The *N*-ethoxycarbonylhexyl quaternary salt of lepidine has been synthesized in one step in 56% yield. ^{1}H and ^{13}C NMR data are reported.

Keywords: quaternary ammonium salts; heterocyclic

Introduction

N-alkyl quaternary ammonium salts are used extensively as precursors of photochromic spiropyrans [1], RNA antagonists [2], and various cyanine dyes [3]. They are usually prepared from the reaction between a heterocyclic base and an alkyl halide refluxing in solvent for 6–48 h [4]. One example requires refluxing in acetonitrile for 24 h, treatment with diethyl ether followed by filtration [3]. This process was repeated 1-3 times on the concentrated filtrates to achieve the published yields. An interesting RNA antagonist precursor, 1-(6-ethoxy-6-oxohexyl)-4-methylquinolinium iodide quaternary ammonium salt (**1a**), has been synthesized, but the experimental details and characterization of the compound was not reported [2]. However, 1-(6-methoxy-6-oxohexyl)-4-methylquinolinium chloride quaternary salt **1b** has been synthesized in two steps in 37% overall yield (Scheme 1) [5]. We report the rapid solvent-free synthesis of the *N*-ethoxycarbonylhexyl quaternary salt (**1a**) from commercially available lepidine in one step in 56% yield with minimal purification.

Scheme 1. Synthesis of quaternary salt.



Experimental Section

General

^{1}H and ^{13}C NMR spectra were obtained using a Varian Gemini 400 NMR and were recorded at 400 MHz and 100 MHz respectively. High resolution ESI-MS was acquired with a Bruker Apex-Qe instrument. All reagents and chemicals were obtained from Aldrich Chemical Company (USA) and were used as received. Microwave reactions conducted in a Biotage Initiaor ESP.

Synthesis of 1-(6-ethoxy-6-oxohexyl)-4-methylquinolinium iodide

Lepidine (0.250 g, 1.754 mmol) and ethyl 6-iodohexanoate (0.522 g, 1.929 mmol) were combined in a 5 mL Biotage microwave vial equipped with a stir bar. The vial was placed in the Biotage microwave with a ramp time of 4 min and held at 120 ℃ for 5 min. The vial with reaction mixture was allowed to sit for 5 min. and irradiated again with a ramp time of 4 min and held at 120 ^{o}C for 2 min. The resulting dark brown solid was dissolved in a mixture of ethyl acetate (5 mL) and methanol (0.5 mL). The dark brown mixture was purified by eluting on a coarse frit packed with silica gel. Ethyl acetate (400 mL) was used to wash the product and a mixture of dichloromethane and methanol (90:10) was used for subsequent washes. The dichloromethane and methanol washes were concentrated and dried to obtain a brown oil (56%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 9.45 (d, J = 6.05 Hz, 2H), 8.56 (m, 2H), 8.27 (m, 1H), 8.08 (m, 2H), 5.02 (t, J = 7.47 Hz, 2H), 4.02 (q, J = 7.11, Hz, 2H), 3.00 (s, 3H), 1.95 (m, 2H), 1.60 (m, 2H), 1.55 (m, 2H), 1.38 (m, 2H), 1.15 (t, J = 7.47 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-d_6): 172.7 (C), 158.5 (C), 148.4 (CH), 136.6 (CH), 135.0 (CH), 129.5 (CH), 128.9 (CH), 127.1 (CH), 122.6 (CH), 119.3 (CH), 59.7 (CH_2), 56.6 (CH_2), 33.1 (CH_2), 29.0 (CH_2), 25.1, (CH_2), 23.8 (CH_2), 19.7 (CH_3), 14.1 (CH_3).

HR ESI-MS for $C_{18}H_{24}NO_2$: m/z = 286.1805; calculated: 286.1807.

Acknowledgements

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