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1-(3-CHLOROPROPYL)-3-PHENYLBENZOTHIENO-[2,3-*c*]PYRIDINE: AN INTERMEDIATE IN SYNTHESIS OF 5-PHENYLBENZOTHIENO[2,3-*e*]INDOLIZINIUM SALTS

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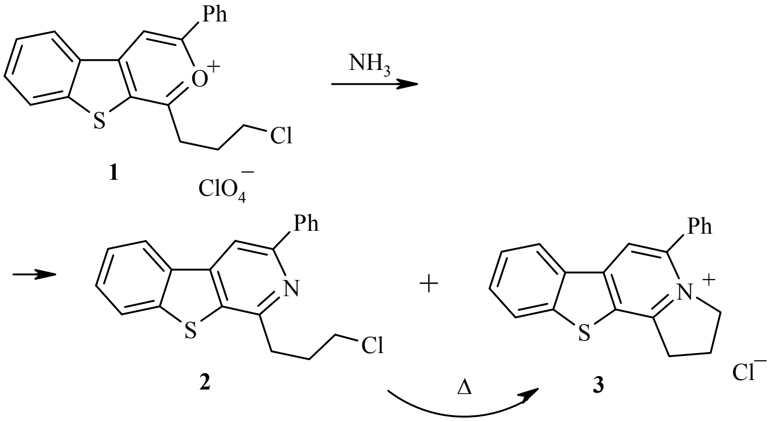
When 1-(3-chloropropyl)benzo[*c*]pyrylium perchlorate is reacted with nitrogen-containing nucleophiles such as ammonia, hydrazine, or hydroxylamine, several sequential reactions occur that result in formation of benzo[*f*]indolizinium, pyridazino[3,2-*a*]isoquinolinium, or oxazino[3,2-*a*]isoquinolinium derivatives [1]. The sequence of the processes occurring has not been established.

Based on the ANRORC mechanism for the reaction of condensed pyrylium salts with nucleophiles, we may hypothesize intermediate formation of 1-(3-chloropropyl)isoquinoline. The same paper discussed the hypothesis that the latter was impossible to isolate because of its fast cyclization rate.



When studying recyclization of 1-(3-chloropropyl)-3-phenylbenzothieno[2,3-*c*]pyrylium perchlorate (**1**) with ammonia at room temperature, we isolated two products: 1-(3-chloropropyl)-3-phenylbenzothieno[2,3-*c*]-pyridine (**2**) and 5-phenyl-2,3-dihydro-1H-benzothieno[2,3-*e*]indolizinium chloride (**3**). When the reaction time and temperature are increased, the yield of salt **3** increases, reaching as much as 85% (boiling the reaction mixture for 2 h). Product **2** is readily converted to the indolizinium derivative **3** when heated.

Thus we have shown that 1-(3-chloropropyl) derivatives are intermediates in cyclizations of this type [2].

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The ^{1}H NMR spectra were taken on a Varian Gemini-200 and a Bruker Avance-400, internal standard TMS.

1-(3-Chloropropyl)-3-phenylbenzothieno[2,3-*c*]pyrylium Perchlorate (1) was obtained from 2-benzo[*b*]thiophen-3-yl-1-phenylethanone in 60% yield as finely dispersed orange crystals, mp 212-213°C, by a procedure similar to that described for 3,4-dimethyloxyphenylacetone in [1]. ^{1}H NMR spectrum (CDCl$_3$, 200 MHz), δ, ppm (*J*, Hz): 2.71 (2H, m, J = 6.0, $CH_2\underline{CH_2}CH_2Cl$); 3.81 (4H, t, J = 6.0, $–\underline{CH_2}CH_2\underline{CH_2}Cl$); 7.63-7.81 (3H, m, H-3,4,5 Ph); 7.86 (1H, t, J = 8.0, H-6); 8.06 (1H, t, J = 8.0, H-7); 8.14-8.30 (3H, m, H-5, H-2,6 Ph); 8.70 (1H, d, J = 8.0, H-8); 8.94 (1H, s, H-4). Found, %: C 54.77; H 3.59; Cl 16.03; S 7.42. $C_{20}H_{16}Cl_2O_5S$. Calculated, %: C 54.68; H 3.67; Cl 16.14; S 7.30.

1-(3-Chloropropyl)-3-phenylbenzothieno[2,3-*c*]pyridine (2). A 40 mass % solution of ammonia in *i*-PrOH (5 ml) was added to a suspension of compound **1** (0.7 g, 1.6 mmol) in methanol (5 ml) and stirred for 0.5 h at room temperature. The solution was filtered and the filtrate was evaporated under vacuum without heating. The residue was diluted with water and extracted with benzene, which then was removed under vacuum. The dry residue was crystallized from a 1:1 benzene–petroleum ether mixture. Yield 0.21 g (40%) as light-green crystals with an indistinct mp ~253-254°C (due to partial cyclization in compound **3** during heating). ^{1}H NMR spectrum (C$_6$D$_6$, 400 MHz), δ, ppm (*J*, Hz): 2.30 (2H, m, $–CH_2\underline{CH_2}CH_2Cl$); 3.07 (2H, t, J = 7.2, $–CH_2CH_2\underline{CH_2}Cl$); 3.34 (2H, t, J = 6.5, $–\underline{CH_2}CH_2CH_2Cl$); 7.12-7.21 (2H, m, H-2,6 Ph); 7.22-7.30 (1H, m, H-4 Ph); 7.35-7.41 (2H, m, H-3,5 Ph); 7.45-7.50 (1H, m, H-6); 7.77-7.81 (1H, m, H-7); 8.03 (1H, s, H-4); 8.23-8.28 (2H, m, H-5,8). Found, %: C 71.22; H 4.86; Cl 10.33; N 4.05; S 9.56. $C_{20}H_{16}ClNS$. Calculated, %: C 71.10; H 4.77; Cl 10.49; N 4.15; S 9.49.

5-Phenyl-2,3-dihydro-1H-benzothieno[2,3-*e*]indolizinium Chloride (3). A. A 40 mass % solution of ammonia in *i*-PrOH (5 ml) was added to a suspension of compound **1** (0.7 g, 1.6 mmol) in methanol (5 ml), and the mixture was boiled for 2 h. The precipitate formed was filtered out and washed with acetone and then ether. Yield 0.54 g (85%) as white crystals with mp 283-284°C.

B. A solution of compound **2** (0.1 g) in methanol was boiled for 2 h; the precipitate formed was filtered out and washed with acetone and then ether. Yield 0.08 g (80%). ^{1}H NMR spectrum (DMSO-d$_6$, 400 MHz), δ, ppm (*J*, Hz): 2.47-2.58 (2H, m, $ArCH_2\underline{CH_2}CH_2N$); 3.81 (2H, t, J = 7.6, $Ar\underline{CH_2}CH_2CH_2N$); 4.75 (2H, t, J = 7.6, $ArCH_2CH_2\underline{CH_2}N$); 7.69-7.74 (3H, m, H-3,4,5 Ph); 7.75-7.83 (3H, m, H-2,6 Ph, H-8); 7.91 (1H, m, H-9); 8.42 (1H, d, J = 8.4, H-7); 8.31 (1H, d, J = 8.4, H-9); 8.98 (1H, s, H-6). Found, %: C 71.18; H 4.69; Cl 10.39; N 4.23; S 9.53. $C_{20}H_{16}ClNS$. Calculated, %: C 71.10; H 4.77; Cl 10.49; N 4.15; S 9.49.

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