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# REARRANGEMENTS OF N-YLIDE GENERATED FROM 1-ETHOXYCARBONYLMETHYL-1-METHYL-4-PHENYL-1,2,3,6-TETRAHYDROPYRIDINIUM CHLORIDE

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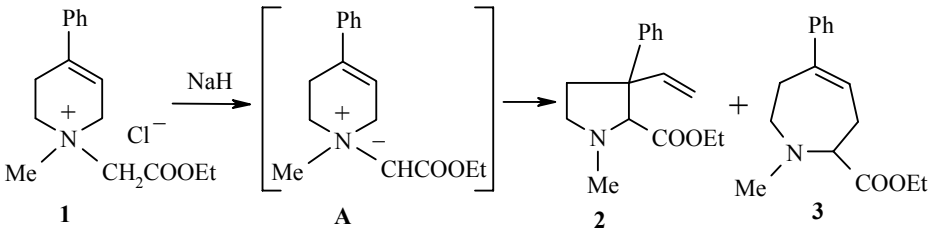
When treated with strong bases, N-ethoxycarbonyl methylides of C-unsubstituted 1,2,3,6-tetrahydropyridines undergo decyclization to form penta-2,4-dienamines [1] or undergo recyclization with contraction of the ring and formation of 2,3-disubstituted pyrrolidines: the products of a [2,3]-sigmatropic rearrangement [2-6]. While continuing our systematic investigations of the chemistry of tetrahydropyridines [7-9], we studied the question of how the ratio of the expected products is affected by the presence of an aryl substituent at C(4) in the anhydro base (the N-ylide **A**) generated from 1-ethoxycarbonylmethyl-1-methyl-4-phenyl-1,2,3,6-tetrahydropyridinium chloride (**1**) when it is heated in the presence of sodium hydride. We found that the presence of a phenyl substituent has a substantial effect on the direction of the reaction: we isolated two compounds from the reaction mixture in 1.5:1 ratio with overall yield 64%, where the first compound had the structure of the expected 4-phenylpyrrolidine **2** while the other compound, to our surprise, proved to be the tetrahydroazepine **3**.




The [1,2]-shift leading to compound **3** is probably due to the electronic effect of the styryl moiety, which stabilizes the allyl cation **C**. Introducing a phenyl substituent conjugated with the *endo* olefin bond was probably the electronic factor which affected the stability of the intermediate zwitterions **B** and **C**.

In the case of zwitterion **B**, a [2,3]-sigmatropic rearrangement occurs, while in the case of the allyl ion **C** there is a Stevens rearrangement (a [1,2]-shift) [6, 10].

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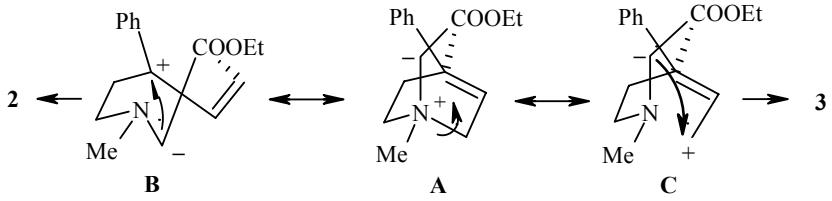


**1-Ethoxycarbonylmethyl-1-methyl-4-phenyl-1,2,3,6-tetrahydropyridinium Chloride (1).** $ClCH_2COOEt$ (1.42 g, 12 mmol) was added to a solution of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (2.0 g, 12 mmol) in absolute benzene (50 ml), and the mixture was held for 3 days at ~20°C. The precipitate was separated and recrystallized from acetone. Compound **1** (2.1 g, 62%) was obtained; mp 167-168°C. $^1$H NMR spectrum (400 MHz, DMSO-$d_6$, δ, ppm (*J*, Hz): 1.24 (3H, t, *J* = 7.2, C–$CH_3$); 2.88 (2H, m, H-3); 3.30 (3H, s, N–$CH_3$); 3.90-4.70 (8H, group of signals, 4$CH_2$); 6.18 (1H, br. s, H-5); 7.26-7.57 (5H, m, $C_6H_5$). Found, %: N 4.91; Cl 11.63. $C_{16}H_{22}ClNO_2$. Calculated, %: N 4.74; Cl 11.99.

**2-Ethoxycarbonyl-1-methyl-3-phenyl-3-vinylpyrrolidine (2) and 2-Ethoxycarbonyl-1-methyl-5-phenyl-2,3,6,7-tetrahydro-1H-azepine (3).** Sodium hydride (0.14 g, 3.4 mmol), as a 60% suspension in absolute toluene, was added with stirring under an $N_2$ atmosphere to a suspension of the quaternary salt **1** (1 g, 3.4 mmol) in absolute dioxane (30 ml). The reaction mixture was refluxed for 2 h. Then methanol (1 ml) was added to the mixture, the solvents were driven off under vacuum, and then the residue was treated with water (50 ml) and extracted with ether. The extract was dried with $MgSO_4$, the solvent was evaporated, and the residue was chromatographed on a column with $SiO_2$ in the hexane–ethyl acetate system with a gradient from 1:0 to 1:10. First 0.22 g (25%) of tetrahydroazepine **3** was isolated, and then 0.34 g (39%) of pyrrolidine **2**, both as a thick oil.

**Compound 3.** $^1$H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.24 (3H, t, *J* = 7.2, $OC_2H_5$); 2.40 (2H, t, $CH_2$-6); 2.44 (3H, s, N–$CH_3$); 2.58-3.00 (4H, m, $CH_2$-3,7); 3.39 (1H, br. s, H-2); 4.16 (2H, q, *J* = 7.2, $OC_2H_5$); 5.96 (1H, br. s, H-4); 7.20-7.35 (5H, m, $C_6H_5$). $^{13}$C NMR spectrum (50 MHz, DMSO), δ, ppm: 13.8 (C–$CH_3$); 22.5 ($CH_2$-6); 35.6 ($CH_2$-3); 40.0 (N–$CH_3$); 48.7 ($CH_2$-7); 57.8 (CH-7); 60.7 (O–$CH_2$); 119.1 (CH-4); 124.8, 128.0, and 128.4 ($C_6H_5$); 134.8 (5-$C_{quat}$); 138.0 ($C_{arom.\ quat.}$); 169.4 (C=O). Mass spectrum, *m/z* ($I_{rel}$, %): 259 $[M]^+$ (5), 244 (8), 230 (3), 186 (2), 172 (100), 157 (3), 141 (6), 128 (10), 115 (10), 91 (9), 77 (5), 42 (27). Found, %: C 74.25; H 8.39; N 5.08. $C_{16}H_{21}NO_2$. Calculated, %: C 74.13; H 8.11; N 5.41.

**Compound 2.** $^1$H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.24 (3H, t, *J* = 7.3, $OC_2H_5$); 2.36 (3H, s, N–$CH_3$); 2.25-2.61 (3H, m, $CH_2$-4,5); 3.14 (1H, dd, *J* = 8.0 and *J* = 2.1, H-5); 3.64 (1H, s, H-2); 4.13 (2H, q, *J* = 7.3, $OC_2H_5$); 4.70 (1H, d, *J* = 17.4, CH=$CH_{cis}\underline{H}_{trans}$); 5.01 (1H, d, *J* = 10.7, CH=C$\underline{H}_{cis}H_{trans}$); 6.03 (1H, dd, *J* = 17.4 and *J* = 10.7, C$\underline{H}$=$CH_{cis}H_{trans}$); 7.22-7.64 (5H, m, $C_6H_5$). Mass spectrum, *m/z* ($I_{rel}$, %): 259 $[M]^+$ (2), 186 (100), 158 (5), 143 (4), 128 (7), 115 (8), 100 (14), 91 (3), 77 (2), 42 (7). Found, %: C 74.09; H 7.92; N 5.33. $C_{16}H_{21}NO_2$. Calculated, %: C 74.13; H 8.11; N 5.41.

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