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UNEXPECTED COURSE FOR THE REACTION OF 1-DI(ETHOXYCARBONYL)METHYL-1-METHYL-4-PHENYL-1,2,3,6-TETRAHYDROPYRIDINIUM BROMIDE WITH DIMETHYL ACETYLENEDICARBOXYLATE IN THE PRESENCE OF TRIETHYLAMINE

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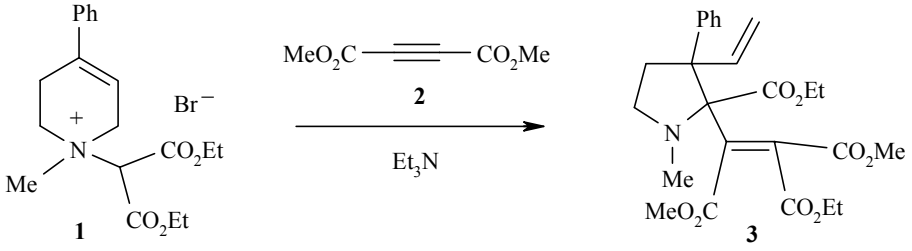
Using acetylenedicarboxylic ester in the presence of base it has been possible to show for the first time that reaction of 2,3-dihydro-1H-indeno[2,1-*c*]pyridinium [1] and 1,2,3,4-tetrahydro-γ-carbolinium [2] quaternary salts to tetrahydroindenoazonines and hexahydroazoninoindoles respectively can occur with expansion of the six membered Δ^3-piperidine ring (with an alkoxycarbonylmethyl substituent on the nitrogen atom) to a nine membered ring [1, 2]. In this work we have studied the reaction of 1-di(ethoxycarbonyl)methyl-1-methyl-4-phenyl-1,2,3,6-tetrahydropyridinium bromide (**1**) with dimethyl acetylenedicarboxylate (**2**) in the presence of triethylamine under analogous conditions (20ºC, 32 h). However, in place of the expected azonine derivative, column chromatography of the reaction mixture unexpectedly gave a 25% yield of the substituted pyrrolidine **3**, the 2-ethenyl group of which contains three alkoxycarbonyl substituents. Its structure was



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unambiguously proved by X-ray crystallographic analysis, from its ^{1}H and IR spectra, and by chromato-mass spectrometry (detailed data from the X-ray structural analysis will be presented in a separate report).

Such a surprising conversion of salt **1** to pyrrolidine **3** involves migration of a ethoxycarbonyl group and this can be rationalized by the following reaction steps. The electrophilic acetylene dicarboxylate ester **2** adds to the initially formed N-ylide and the 1,4-zwitterion formed evidently undergoes a 1→3 acyl shift of one of the ethoxycarbonyl groups to the carbanion center. This shift leads to a new ylide which can undergo a [3,2]-sigmatropic rearrangement with recyclization of the piperidine ring to a pyrrolidine.

The ^{1}H NMR spectra were recorded on a Bruker WP-400 (400 MHz) spectrometer using DMSO-d_6 (compound **1**) or $CDCl_3$ (compound **3**) with the residual deuterated solvent protons as internal standard. IR Spectra were taken on an Infralum FT-801 spectrometer for KBr tablets. An Agilent 1100 liquid chromatograph with DAD, ELSD Sedex 75 detectors combined with an Agilent LC/MSD VL mass spectrometer with electrospray ionization was used to monitor the reaction mixtures and the purity of the separated compound **3**. X-ray structural analysis of compound **3** was carried out by a direct method on a Bruker SMART 1000 CCD diffractometer with MoKα radiation, graphite monochromator, and with θ- and ω-scanning. The starting 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine was prepared as in method [6].

1-Di(ethoxycarbonyl)methyl-1-methyl-4-phenyl-1,2,3,6-tetrahydropyridinium Bromide (1). Bromomalonate ester (2.8 g, 10 mmol) was added to a solution of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (2.1 g, 10 mmol) in absolute THF (20 ml) and the mixture was held with refluxing under a nitrogen atmosphere for 3 h. The cooled reaction mixture was treated with hexane (50 ml) and the precipitate formed was separated and recrystallized from acetone to give compound **1** with mp 78ºC. IR spectrum, ν, cm^{-1}: 1753 and 1741 sh (C=O), 1629 (C=C). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.27 (6H, t, *J* = 7.2, $OCH_2C\underline{H}_3$); 2.92 (2H, m, H-3); 3.35 (3H, s, NCH_3); 3.86 (2H, m, H-2); 4.33 (4H, m, $OC\underline{H}_2CH_3$); 4.41 and 4.53 (each 1H, both br. d, *J* = 16.5, H-6); 6.03 (1H, s, $NC\underline{H}COO$); 6.15 (1H, br. s, H-5); 7.18-7.61 (5H, m, C_6H_5). Found, %: Br 19.52; N 3.42. $C_{19}H_{26}BrNO_4$. Calculated, %: Br 19.42; N 3.39.

2-(2-Ethoxycarbonyl-1-methyl-3-phenyl-3-vinylpyrrolidin-2-yl)-1-ethoxycarbonyl-1,2-di(methoxycarbonyl)ethene (3). Triethylamine (1.8 ml, 14 mmol) was added to a suspension of the quaternary salt **1** (2.0 g, 5 mmol) and acetylenedicarboxylic ester **2** (1.5 g, 10 mmol) in absolute dioxane (30 ml) and stirred at 20ºC under a nitrogen atmosphere for 32 h. Solvent was evaporated *in vacuo* and the residue was column chromatographed on SiO_2 in the system hexane-ethyl acetate using a gradient from 1: 0 to 1: 10 to give compound **3** (0.67 g, 25%) as colorless crystals with mp 112-113ºC. IR spectrum, ν, cm^{-1}: 1731 sh, 1727 (C=O), 1631 (C=C). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.20 (3H, t, *J* = 7.6, $OCH_2C\underline{H}_3$); 1.30 (3H, t, *J* = 7.6, $OCH_2C\underline{H}_3$); 2.24 (3H, s, NCH_3); 2.68 (2H, m, H-4); 2.86 and 3.33 (each 1H, both m, H-5); 3.45 (3H, s, OCH_3); 3.52 (1H, s, OCH_3); 4.08 and 4.22 (each 2H, both q, *J* = 7.6, $OC\underline{H}_2CH_3$); 4.72 (1H, d, *J* = 17.2, CH=CH-cis $\underline{H}$-*trans*); 5.05 (1H, d, *J* = 10.8, CH=C$\underline{H}$-*cis* H *trans*); 6.94 (1H, dd, *J* = 17.2 and 10.8, C$\underline{H}$=CH-*cis* H-*trans*); 7.17-7.58 (5H, m, C_6H_5). Mass spectrum, *m/z*: 474 $[M+H]^+$. Found, %: C 63.12; H 6.71; N 3.02. $C_{25}H_{31}NO_8$. Calculated, %: C 63.42; H 6.55; N 2.96. M 473.

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