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SYNTHESIS OF PYRROLIDINES AND TETRAHYDRO-1H-AZEPINES FROM 4-ARYL-1-BENZOYL(ETHOXY-CARBONYL)METHYL-1-METHYL-1,2,3,6-TETRAHYDROPYRIDINIUM HALIDES

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4-Aryl-1,2,3,6-tetrahydropyridinium quaternary salts which have a benzoylmethyl or ethoxycarbonylmethyl group on atom N-1 generate N-ylides when heated in the presence of NaH and they can rearrange in situ with contraction or expansion of the six-membered heterocycle to give substituted pyrrolidines (as a result of a [2,3]-sigmatropic rearrangement) or 1H-tetrahydroazepine derivatives (via Stevens rearrangement). The presence of an aryl substituent at position C-4 in the tetrahydropyridine ring allows to avoid the formation of elimination products and changes the direction of the reaction towards the preparation of the tetrahydroazepines.

Keywords: 4-aryl-1-benzoyl(ethoxycarbonyl)methyl-1,2,3,6-tetrahydropyridinium halides, N-ylides, pyrollidines, tetrahydro-1H-azepines, 1,2-shift, sigmatropic rearrangement.

In the presence of base, N-methyl-N-phenacyl-1,2,3,6-tetrahydropyridinium halides are converted to N-ylide systems which can rearrange with contraction of the six-membered heterocycle to five-membered forming N-alkyl-2-benzoyl-3-vinylpyrrolidines [1, 2]. Exchange of the N-phenacyl fragment in the starting quaternary tetrahydropyridinium salts for N-(alkoxycarbonyl)methyl also stabilizes the intermediate ylides and leads to derivatives of the natural α-amino acid proline [3-7] which may be important from the viewpoint of biological activity. Key features in the studies [1-7] are as follows: firstly only C-unsubstituted tetrahydropyridines were used as the basic starting materials; secondly a high diastereoselectivity (95%) was found in the substituted pyrrolidines formed; and finally the basic electrophilic [2,3]-sigmatropic rearrangement was accompanied by up to 45% β-elimination with opening of the heterocycle and the formation of dialkylaminopenta-2,4-dienes.

In connection with our systematic investigation of the chemistry of 4-aryl-substituted tetrahydropyridines and related compounds [8, 9] we decided to study the effect of an aryl substituent in the quaternary tetrahydropyridinium salts on the route of their reaction in the presence of base.

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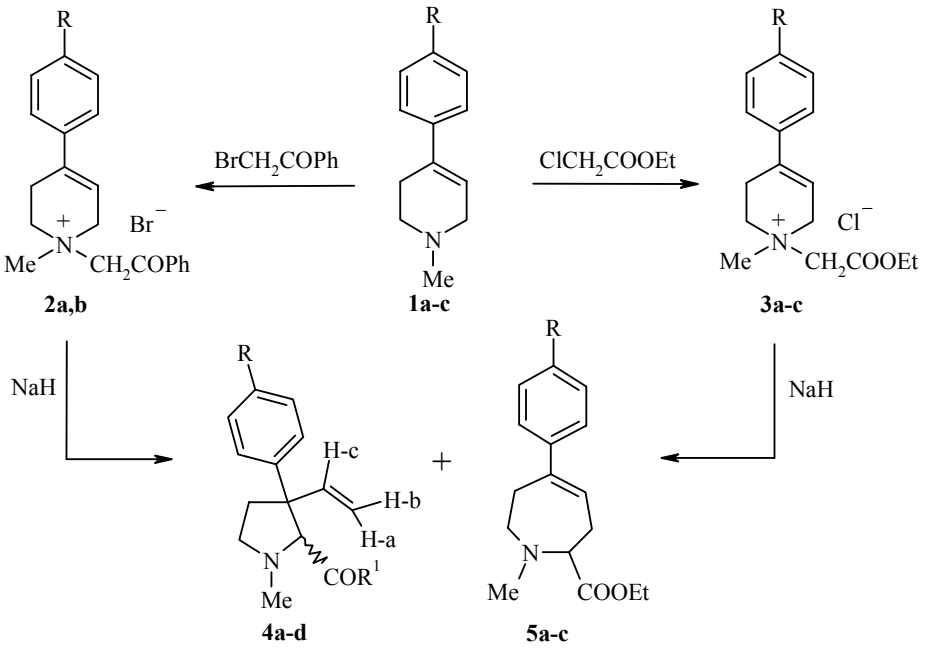


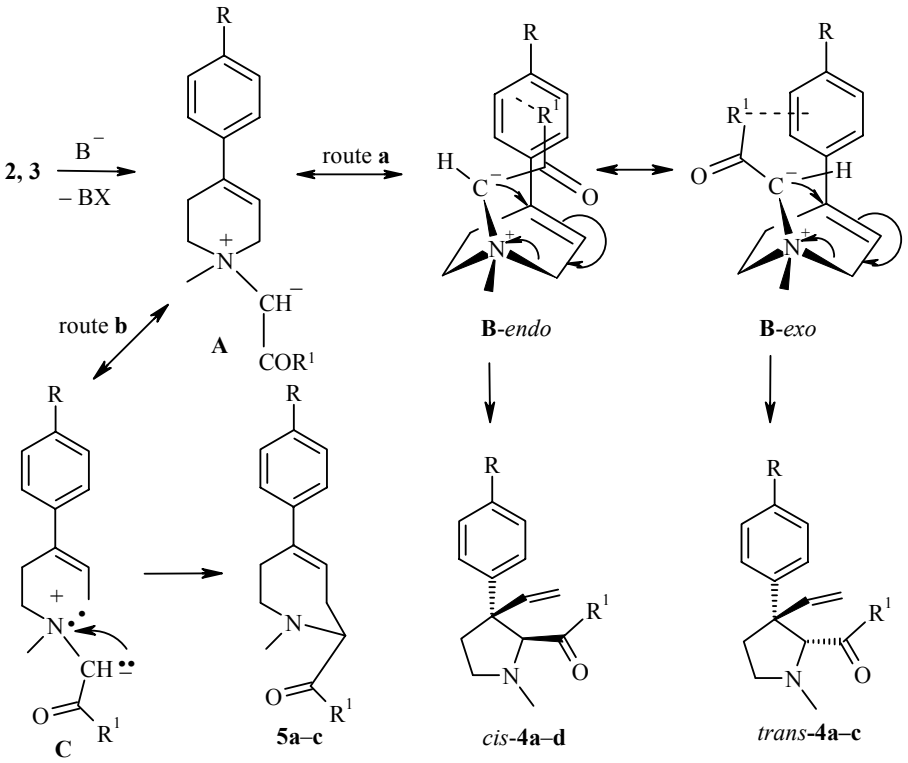
1-3, **5 a** R = H, **b** R = Me, **c** R = Br; **4 a** R = H, R^1 = Ph, **b** R = Br, R^1 = Ph, **c** R = H, R^1 = OEt, **d** R = Me, R^1 = OEt

With this in mind we have used the 4-aryltetrahydropyridines **1a-c** to prepare the quaternary salts **2a,b** and **3a-c** which served as intermediate ylide precursors. The rearrangements were carried out by refluxing the indicated salts in the presence of sodium hydride in dioxane for 2-3 h. In the case of the phenacylbromides **2a,b** column chromatography of the reaction mixture on silica gel led to the separation of only the pyrrolidines **4a,b** in yields of 35 and 15% respectively. According to ^{1}H NMR data these pyrrolidines were obtained as an unresolved mixture of two diastereomers in the ratio 1:1 (for R = H) or 1.5:1 (for R = Br). A comparative analysis of the ^{1}H NMR spectra of the mixture of diastereoisomers **4a,b** and the individual *cis*-(2-H,3-H) diastereomers having a similar structure [3-6] shows that the signals of the all of the aliphatic analogous protons of the *trans*-(2-COPh, 3-CH=CH_2) diastereomers **4a,b** are significantly shifted to low field by up to 0.38 ppm when compared with the signals of the corresponding *cis*-forms.

Hence the introduction of an aryl substituent at position C-4 of the heterocycle in the N-phenacyl salts **2a,b** leads to a marked lowering of the diastereoselectivity of the [2,3]-sigmatropic rearrangement of the tetrahydropyridine nucleus to the pyrrolidine.

In the analogous work up of all quaternary salts **3a-c** the expected pyrrolidines were obtained in 39 (**4c**) and 58% (**4d**) yields respectively. Chromato-mass spectrometric analysis of the mixture of products obtained from the quaternary salt **3c** showed that the corresponding pyrrolidine was obtained in trace amounts. In addition, in all three cases the azepine derivatives **5a-c,** products of expansion of the tetrahydropyridine ring, were obtained (see previous report [10] regarding the formation of compound **5a**). In the case of the phenyl or 4-tolyl substituent (salts **3a,b**) the yield of the tetrahydroazepine **5a,b** was low (25 and 5% respectively). However, upon changing to the quaternary salt **3c** which has a 4-bromophenyl substituent, the yield of the tetrahydroazepine **5c** increased to 60%. The structure of the azepine derivatives **5a-c** was confirmed by their ^{1}H and ^{13}C NMR spectra in which signals of all of the protons and carbon atoms of the C_{quat}–CH_2–CH_2N and C_{quat}=CH–CH_2CH(NMe)COOEt links were observed (see Experimental). The mass spectra showed low intensity molecular ion peaks M^+ as well as fragment ion peaks formed by fission of a methyl or ethyl

group from M^+. The maximum intensity peak is assigned to the fragment arising from fission of the $[CHCOOEt]^+$ fragment and a hydrogen atom from M^+. The IR spectra of the tetrahydroazepine shows strong absorption peaks for the C=O group in the region 1727-1730 cm^{-1}.



It should be noted a similar reaction of N-methyl-N-nitrobenzyl(or N-phenacyl)-6-hydroxy-1,2,3,4-tetrahydroisoquinolinium bromides to tetrahydrobenzazepines has been reported in [11]. However, this work pointed to a dominating effect of the 6-OH group in the benzene ring for expantion of the piperidine ring (only *via* the intermediate quinoid form). Only β-elimination-decyclization processes occurred in the absence of this hydroxyl group!

Hence we have shown in our work that the introduction of a 4-aryl substituent into the tetrahydropyridine ring can lead to a novel route for reaction of the heterocycle, i.e. to a [1,2]-shift with formation of the seven-membered aza ring. For all of the experiments with salts **2** and **3** it should be stressed that, firstly, products of Hofmann [12] decyclization were not identified and, secondly, the expected and unexpected rearrangements of the tetrahydropyridine ring took place only *via* its allylamine fragment.

We finally consider the possible reactions mechanisms for salts **2** and **3**. In the presence of base they firstly form the highly reactive ylides (**A**). The latter in the case of transitions states (**B**-*endo*, **B**-*exo*; route **a**) can be transformed by a [2,3]-sigmatropic rearrangement to *cis*- and/or *trans*-diastereomeric pyrrolidines **4** [13] thanks to the greater (**B**-*endo*) or lesser (**B**-*exo*) degree of secondary orbital control and also due to the electronic and steric interactions between the acyl group and the benzene ring. At the same time, the presence of the arylallylamino fragment and strongly stabilizing N-ylide N-ethoxycarbonyl group permits a second reaction path. In this [1,2]-shift route **b** there occur dissociation-recombination processes transforming the $>N^+(C^-HCOR)CH_2$-6 group of the ylides (**A**) *via* the close biradical states (**C**) [13] to the $>N–CH(COR)CH_2$-3 group in molecule **5**. This anionic [1,2]-shift (Stevens rearrangement) leads in this case to the formation of a stable seven-membered heterosystem.

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were obtained on a Bruker WM-400 instrument (400 and 100 MHz respectively) using DMSO-d_6 (compounds **2a,b** and **3a-c**) or $CDCl_3$ (compounds **4a-d** and **5a-c**) with TMS as internal standard and mass spectra on a Finnigan MAT 95XL chromato-mass spectrometer with ionization energy 70 eV. IR spectra were taken on a Specord IR-75 spectrophotometer using a KBr matrix (quaternary salts **2a,b**, **3a-c**) or paraffin oil (compounds **4a-d**, **5a-c**). Chemapol L 40/100 micron silica gel was used in the preparative column chromatography. Monitoring of the reaction course and the purity of the synthesized compounds was carried out by TLC on Silufol UV-254 plates.

Compounds 1a-c were prepared as reported in [14].

Synthesis of Quaternary Salts 2a,b and 3a-c. ω-Bromoacetophenone (2.39 g, 12 mmol) (synthesis of salts **2a,b**) or ethyl chloroacetate (1.42 g, 12 mmol) (synthesis of salts **3a-c**) were added gradually to a solution of 4-aryl-1-methyl-1,2,3,6-tetrahydropyridine **1a-c** (12 mmol) in absolute benzene (50 ml). The mixture was held for 3 days at 20ºC. The precipitate was separated and purified by recrystallization from acetone to give the reaction product as colorless crystals.

1-Methyl-1-(2-oxo-2-phenylethyl)-4-phenyl-1,2,3,6-tetrahydropyridinium Bromide (2a). Yield 3.21 g (75%); mp 205-208ºC. IR spectrum, ν, cm^{-1}: 1688 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.95 (2H, br. s, 3-CH_2); 3.37 (3H, s, CH_3); 3.92 and 4.06 (each 1H, both m, 2-CH_2); 4.42 and 4.53 (each 1H, both br. d, *J* = 11.8, 6-CH_2); 5.49 and 5.52 (each 1H, both d, *J* = 17.5, NCH_2CO); 6.22 (1H, br. s, 5-CH); 7.38–7.74 (8H, m, H_{arom}); 8.04 (2H, d, *J* = 7.48, OCC_6H_5). Found, %: Br 21.44; N 3.66. $C_{20}H_{22}BrNO$. Calculated, %: Br 21.46; N 3.76.

4-(4-Bromophenyl)-1-methyl-1-(2-oxo-2-phenylethyl)-1,2,3,6-tetrahydropyridinium Bromide (2b). Yield 3.55 g (81%), mp 167-168ºC. IR spectrum, ν, cm^{-1}: 1690 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.93 (2H, br. s, 3-CH_2); 3.36 (3H, s, CH_3); 3.88 and 4.01 (each 1H, both m, 2-CH_2); 4.38 and 4.48 (each 1H, both br. d, *J* = 11.7, 6-CH_2); 5.38 and 5.44 (each 1H, both d, *J* = 17.6, NCH_2CO); 6.24 (1H, br. s, 5-CH); 7.48 and 7.58 (each 2H, AA'BB' spectrum, *J* = 8.35, H_{arom}); 7.61 (2H, m, OCC_6H_5); 7.74 (1H, t, *J* = 7.46 and *J* = 7.31, OCC_6H_5); 8.02 (2H, d, *J* = 7.52, OCC_6H_5). Found, %: Br 35.39; N 3.0. $C_{20}H_{21}Br_2NO$. Calculated, %: Br 35.42; N 3.10.

1-Ethoxycarbonylmethyl-1-methyl-4-phenyl-1,2,3,6-tetrahydropyridinium Chloride (3a). Yield 2.1 g (62%); mp 167-168ºC (dec.). IR spectrum, ν, cm^{-1}: 1740 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.24 (3H, t, *J* = 7.2, C–CH_3); 2.88 (2H, br. s, 3-CH_2); 3.30 (3H, s, N–CH_3); 3.90 (2H, m, 2-CH_2); 4.23 (2H, q, *J* = 7.11, OCH_2); 4.33 and 4.47 (each 1H, both br. d, *J* = 16.45, 6-CH_2); 4.67 and 4.72 (each 1H, both d, *J* = 16.6, NCH_2CO); 6.18 (1H, br. s, 5-CH); 7.26–7.57 (5H, m, C_6H_5). Found, %: Cl 11.63; N 4.91. $C_{16}H_{22}ClNO_2$. Calculated, %: Cl 11.99; N 4.74.

1-Ethoxycarbonylmethyl-1-methyl-4-(4-methylphenyl)-1,2,3,6-tetrahydropyridinium Chloride (3b). Yield 2.51 g (78%); mp 156-158ºC. IR spectrum, ν, cm^{-1}: 1748 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.26 (3H, t, *J* = 7.00, $OCH_2C\underline{H}_3$); 2.30 (3H, s, $ArC\underline{H}_3$); 2.88 (2H, br. s, 3-CH_2); 3.29 (3H, s, N–CH_3); 3.90 (2H, m, 2-CH_2); 4.25 (2H, q, *J* = 7.02, O–CH_2); 4.23 and 4.26 (each 1H, both d, *J* = 16.5, NCH_2CO); 4.30 and 4.41 (each 1H, both br. d, *J* = 16.20, 6-CH_2); 6.12 (1H, br. s, H-5); 7.21 and 7.40 (each 2H, AA'BB' spectrum, *J* = 7.93, H_{arom}). Found, %: Cl 11.40; N 4.5. $C_{17}H_{24}ClNO_2$. Calculated, %: Cl 11.44; N 4.52.

4-(4-Bromophenyl)-1-ethoxycarbonylmethyl-1-methyl-1,2,3,6-tetrahydropyridinium Chloride (3c). Yield 2.36 g (80%); mp 172-174ºC. IR spectrum, ν, cm^{-1}: 1742 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.24 (3H, t, *J* = 7.11, $OCH_2C\underline{H}_3$); 2.87 (2H, br. s, 3-CH_2); 3.31 (3H, s, N–CH_3); 3.92 (2H, m, 2-CH_2); 4.22 (2H, q, *J* = 7.10, O–CH_2); 4.34 and 4.47 (each 1H, both br. d, *J* = 16.31, 6-CH_2); 4.67 and 4.73 (each 1H, both d, *J* = 17.0, NCH_2CO); 6.22 (1H, br. s, 5-CH); 7.47 and 7.57 (each 2H, AA'BB' spectrum, *J* = 8.47, H_{arom}). Found, %: N 3.8. $C_{16}H_{21}BrClNO_2$. Calculated, %: N 3.74.

Transformation of the Quaternary Salts 2a,b and 3a-c to the Pyrollidines 4a-d and Tetrahdro-1H-azepines 5a-c. Sodium hydride (0.14 g, 3.4 mmol as a 60% suspension in absolute toluene) was added to a suspension of the quaternary salt (**2a,b, 3a-c**) (3.4 mmol) in absolute dioxane (30 ml) under a nitrogen atmosphere. After refluxing for 2 h, methanol (1 ml) was added, and the solvent was distilled of *in vacuo*. The residue was treated with water (50 ml) and the organic base was extracted with ether. The extract was washed twice with water, dried over anhydrous $MgSO_4$, and evaporated *in vacuo*. The residue was separated and purified by column chromatography on silica gel using a gradient of hexane–ethyl acetate from 1:0 to 1:10.

2-Benzoyl-3-ethenyl-1-methyl-3-phenylpyrrolidine (4a) was separated as a mixture of two diastereoisomers with a 1:1 ratio of *cis*-(2-COPh, 3-CH=CH_2) to *trans*-(2-COPh, 3-CH=CH_2) isomers from ^{1}H NMR data. Colorless, thick oil. Yield 0.4 g (35%). IR spectrum, ν, cm^{-1}: 1683 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz) (spectrum shows a double set of aliphatic protons signals for the *cis*/*trans* isomers: assignment of the proton signals of the *cis* form was made by analysis of the spectra of analogous pyrrolidines [3-6]; specific vinyl group protons are given in the scheme for the synthesis of compounds **4a-d**): 2.12/2.28 (0.5H/0.5H m/m, 4-CH_2); 2.41/2.47 (1.5H/1.5H, s/s, N–CH_3); 2.66/2.83 (0.5H/0.5H, m/m, 4-CH_2); 2.87/2.97 (0.5H/0.5H, m/m, 5-CH_2); 3.23/3.31 (0.5H/0.5H, dt/dt, *J* = 8.13 and *J* = 1.62, 5-CH_2); 4.68/4.71 (0.5H/0.5H, s/s, 2-CH); 4.91/5.08 (0.5H/0.5H, dd, *J* = 17.26 and *J* = 1.4, H-a); 5.01/5.19 (0.5H/0.5H, dd, *J* = 10.67 and *J* = 1.5, H-b); 5.87/6.22 (0.5H/0.5H, dd, *J* = 17.26 and *J* = 10.67, H-c); 6.95-7.79 (10H, m/m, C_6H_5). Mass spectrum, *m*/*z*: 293 [M^+]. Found, %: C 77.9; H 6.50; N 4.71. $C_{19}H_{19}NO$. Calculated, %: C 77.79; H 6.53; N 4.77.

2-Benzoyl-3-(4-bromophenyl)-3-ethenyl-1-methylpyrrolidine (4b) was separated as a mixture of two diastereomers with a 1.5:1 ratio of *cis*- to *trans*-(2-COPh, 3-CH=CH_2) isomers from ^{1}H NMR data. Colorless, thick oil. Yield 0.18 g (15%). IR spectrum, ν, cm^{-1}: 1701 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz) (spectrum shows a double set of aliphatic protons signals for the *cis*/*trans* isomers): 2.12/2.28 (0.6H/0.4H, m/m, 4-CH_2); 2.37/2.44 (1.8H/1.2H, s/s, N–CH_3); 2.67–3.00 (2H, m, 4-CH_2, 5-CH_2); 3.20/3.28 (0.6H/0.4H, dt/dt, *J* = 6.73 and *J* = 1.8, 5-CH_2); 4.68/4.71 (0.6H/0.4H, s/s, 2-CH); 4.84/5.03 (0.6H/0.4H, dd, *J* = 16.89 and *J* = 1.5, H-a); 4.98/5.16 (0.6H/0.4H, dd, *J* = 10.71 and *J* = 1.5, H-b); 5.82/6.17 (0.6H/0.4H, dd, *J* = 16.71 and *J* = 10.70, H-c); 6.90–7.96 (9H, m, H_{arom}). Mass spectrum, *m*/*z:* 371 [M^+]. Found, %: C 61.37; H 4.9; N 3.72. $C_{19}H_{18}BrNO$. Calculated, %: C 61.30; H 4.87; N 3.76.

3-Ethenyl-2-ethoxycarbonyl-1-methyl-3-phenylpyrrolidine (4c) was separated as a mixture of two diastereomers with a 4:1 ratio of *cis*- and *trans*-(2-COOEt, 3-CH=CH_2) isomers from ^{1}H NMR data. Colorless, thick oil. Yield 0.34 g (39%). IR spectrum, ν, cm^{-1}: 1731 (C=). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.24 (3H, dt, *J* = 7.33, $OCH_2C\underline{H}_3$); 2.28–2.60 (2H, m, 4-CH_2); 2.36/2.40 (2.4H/0.6H, s/s, N–CH_3); 3.14 (0.8H, dd, *J* = 8.0 and *J* = 2.1, 5-CH_2); 3.24–3.46 (12H, m, 5-CH_2); 3.65/3.67 (0.8H/0.2H, s/s, 2-CH), 4.16 (2H, dq, *J* = 7.33, $OC\underline{H}_2Me$); 4.70/5.08 (0.8H/0.2H, dd, *J* = 17.40 and *J* = 1.2, H-a); 5.02/5.27 (0.8H/0.2H, dd, *J* = 10.71 and *J* = 1.2, H-b); 6.03/6.80 (0.8H/0.2H, dd, *J* = 17.4 and *J* = 10.7, H-c); 7.22–7.43 (5H, m, H_{arom}). 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.

3-Ethenyl-2-ethoxycarbonyl-1-methyl-3-(4-methylphenyl)pyrrolidine (4d) was separated as a single *cis*- (2-COOEt, 3-CH=CH_2)-isomer. Colorless, thick oil. Yield 0.45 g (58%). IR spectrum, ν, cm^{-1}: 1742 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.22 (3H, t, *J* = 7.25, $OCH_2C\underline{H}_3$); 2.33 (1H, m, 4-CH_2); 2.29 (3H, s, C–CH_3); 2.36 (3H, s, N–CH_3); 2.42 (1H, m, 4-CH_2); 2.53 (1H, dt, *J* = 8.03 and *J* = 2.2, 5-CH_2); 3.12 (1H, dt, *J* = 8.00 and *J* = 2.1, 5-CH_2); 3.61 (1H, s, 2-CH); 4.13 (2H, q, *J* = 7.28, $OC\underline{H}_2Me$); 4.66 (1H, dd, *J* = 17.41 and *J* = 1.2, H-a); 4.98 (1H, dd, *J* = 10.70 and *J* = 1.2, H-b); 6.00 (1H, dd, *J* = 17.40 and *J* = 10.72, H-c); 7.05 and 7.36 (each 2H, AA'BB' spectrum, *J* = 7.93 and *J* = 1.1, H_{arom}). Mass spectrum, *m*/*z*: 273 [M^+]. Found, %: C 74.72; H 8.44; N 5.10. $C_{17}H_{23}NO_2$. Calculated, %: C 74.69; H 8.48; N 5.12.

2-Ethoxycarbonyl-1-methyl-5-phenyl-2,3,6,7-tetrahydro-1H-azepine (5a). Yield 0.22 g (25%). Colorless, thick oil. IR spectrum, ν, cm^{-1}: 1728 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.24 (3H, t, *J* = 7.2, $OCH_2C\underline{H}_3$); 2.40 (2H, m, 6-CH_2); 2.44 (3H, s, N–CH_3); 2.58–3.00 (4H, m, 3- and 7-CH_2); 3.39 (1H, br. s, H-2);

4.16 (2H, q, J = 7.2, OC<u>H</u>$_2$Me); 5.96 (1H, br. s, H-4); 7.20–7.35 (5H, m, C_6H_5). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 13.8 (C–CH_3); 22.5 (6-CH_2); 35.6 (3-CH_2); 40.0 (N–CH_3); 48.7 (7-CH_2); 57.8 (7-CH); 60.7 (O–CH_2); 119.1 (4-CH); 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.

2-Ethoxycarbonyl-1-methyl-5-(4-methylphenyl)-2,3,6,7-tetrahydro-1H-azepine (5b). Yield 0.05 g (5%). Colorless, thick oil. IR spectrum, ν, cm^{-1}: 1730 (C=O). ^{1}H NMR spectrum, δ, ppm (J, Hz): 1.26 (3H, t, J = 7.10, $OCH_2C\underline{H}_3$); 2.00 (1H, m, 6-CH_2); 2.26 (1H, m, 6-CH_2); 2.32 (3H, s, Ar$C\underline{H}_3$); 2.46 (3H, s, N–CH_3); 2.62 (1H, m, 3-CH_2); 2.72 (1H, m, 7-CH_2); 2.82 (1H, dd, J = 10.88 and J = 4.5, 3-CH_2); 3.04 (1H, m, 7-CH_2); 3.47 (1H, br. s, 2-CH); 4.15 (2H, q, J = 7.05, $OC\underline{H}_2CH_3$); 5.92 (1H, br. s, H-4); 7.09 and 7.24 (each 2H, AA'BB' spectrum, J = 7.83 and J = 1.1, H_{arom}). Mass spectrum, m/z: 273 [M^+]. Found, %: C 74.2; H 8.16; N 5.2. $C_{17}H_{23}NO_2$. Calculated, %: C 74.14; H 8.15; N 5.09.

1-Methyl-5-(4-bromophenyl)-2-ethoxycarbonyl-2,3,6,7-tetrahydro-1H-azepine (5c). Yield 0.68 (60%). Thick, yellowish oil. IR spectrum, ν, cm^{-1}: 1727 (C=O). ^{1}H NMR spectrum, δ, ppm (J, Hz): 1.26 (3H, t, J = 7.04, $OCH_2C\underline{H}_3$); 2.35–2.41 (2H, m, 6-CH_2); 2.43 (3H, s, N–CH_3); 2.53–2.64 (2H, m, 3-CH_2, 7-CH_2); 2.75 (1H, dd, J = 14.51 and J = 4.90, 3-CH_2); 2.98 (1H, m, 7-CH_2); 3.36 (1H, br. s, 2-CH); 4.16 (2H, q, J = 7.06, $OC\underline{H}_2CH_3$); 5.96 (1H, br. s, H-4); 7.19 and 7.47 (each 2H, AA'BB' spectrum, J = 7.67 and J = 1.2, H_{arom}). Mass spectrum, m/z: 337 [M^+]. Found, %: C 56.9; H 5.90; N 4.16. $C_{16}H_{20}BrNO_2$. Calculated, %: C 56.82; H 5.96; N 4.14.

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