A TEREOSELECTIVE SYNTHESIS OF 2-BENZYLIDENEPYRROLIDIN-5-ONES FROM THE AMIDES OF 4-OXO-5-PHENYLPENTANOIC ACID OR THEIR TAUTOMERS, (2-BENZYL-2-HYDROXYPYRROLIDIN-5-ONES)

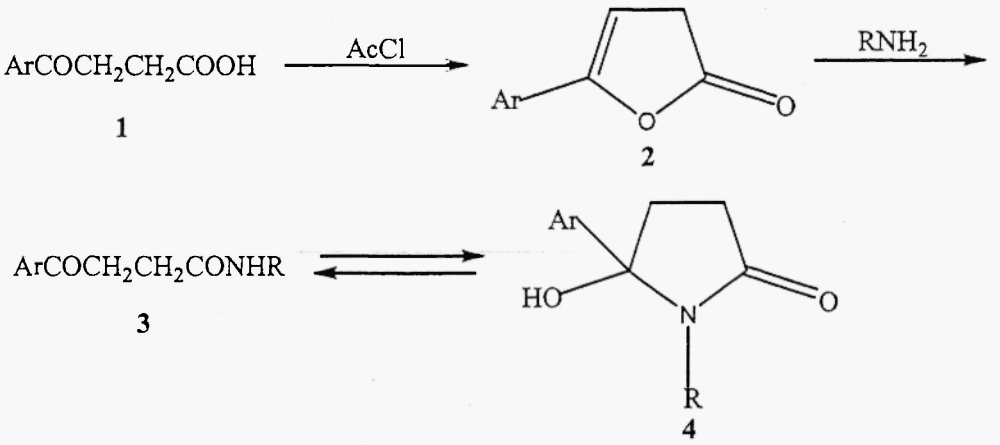
Georgia Tsolomiti and Athanase Tsolomitis
The Laboratory of Organic Chemistry, The School of Chemical Engineering,
The National Technical University of Athens, Athens 157 80, Greece
E-mail: tsolom@chemeng.ntua.gr

Abstract: The reactions of primary amines with the anhydride **6** or the lactone **7** (γ-benzylidene-γ-butyrolactone) of 4-oxo-5-phenylpentanoic acid, gave depending on reaction conditions either: (a) the γ-keto amides **8** or their cyclic tautomers **9** (2-benzyl-2-hydroxypyrrolidin-5-ones), or (b) the 2-benzylidenepyrrolidin-5-ones **10** stereoselectively.

Keywords: 2-Benzylidenepyrrolidin-5-ones, 4-Oxo-5-phenylpentanamides, 2-Benzyl-2-hydroxypyrrolidin-5-ones.

Some 2-alkylidenepyrrolidin-5-ones have been reported[1] useful as central nervous system stimulators, convulsion preventers, analgesics, antipyretics, or for the preparation of artificial plasma or nylon 4. 2-Alkylidene- and 2-arylidenepyrrolidin-5-ones have been prepared[2] as useful synthons for the synthesis of other 2-pyrrolidinone derivatives, while 2-benzylidenepyrrolidin- ium derivatives have been reported[3] to have hypotensive and spasmolytic activities.

In previous works[4,5] we reported a series of γ-keto amides which resulted from the reaction of 5-aryl-2(3H)-furanones **2**, prepared from the corresponding 3-aroylpropionic acids **1**, with different amines, in the course of a program for synthesis of five membered heterocycles. A part of our study in the preparation of these γ-keto amides was the problem of the ring-chain tautomerism, between the open chain (γ-keto amides) **3** and their cyclic tautomers (2-aryl-2-hydroxypyrrolidin-5-ones) **4** (Scheme-1).

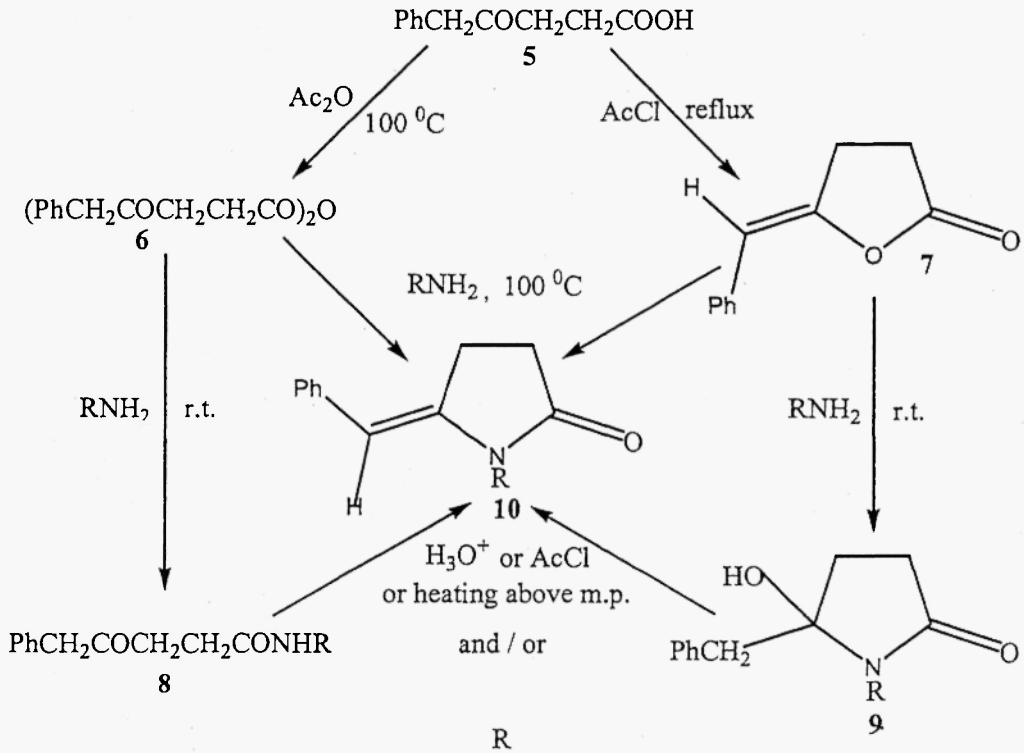


1 2 3 4

Scheme-1

Factors on which the resulting tautomers depend have been investigated [6,7] and were found related to electronic and stereochemical reasons.

In this paper we report the study of some reactions of two activated derivatives of the 4-oxo-5-phenylpentanoic acid **5**, the anhydride **6** and the γ-benzylidene-γ-butyrolactone (**7**) with primary amines. Depending on the nature of the amine and reaction conditions, results are listed in Scheme 2.



R

a: H-
b: CH_3-
c: C_6H_5-
d: 3-$O_2NC_6H_4$-
e: $C_6H_5CH_2$-

Scheme-2

From all the reactions of the amines with the anhydride **6** or the lactone **7** at room temperature conditions, we separated the γ-keto amides **8** or their tautomers 2-hydroxypyrrolidin-5-ones **9** or a mixture of these in the case of 4-oxo-5-phenylpentanamide, **8a** and **9a**, (Scheme-2).

These results were found to be in accordance with observations of other[6,7,8] investigators on other γ-keto amides regarding to the factors favoring either the open chain γ-keto amide tautomer **8** or the cyclic 2-hydroxypyrrolidin-5-one **9**. Two main factors affect the tautomeric equilibrium; the first is the stereochemical factor and especially steric hindrance at the ketonic carbonyl group and amidic nitrogen. The more bulky groups favor the open chain tautomers **8** while the less bulky favor the cyclic tautomers **9**. The second factor affecting this ring-chain tautomerism is relative to the electrophilicity of the ketonic carbonyl on the one side and to the nucleophilicity of the amidic nitrogen on the other. Increase of these two parameters favors the cyclic tautomers **9** vs the open chain tautomers **8**.

In our case one group, the substituent at the ketonic carbonyl, is a benzyl group, therefore only this on the amidic nitrogen differentiates the tautomeric equilibrium. Indeed, our results agree with these observations; the more electron withdrawing is the nitrogen substituent, e.g. 3-nitrophenyl group

(weaker nucleophile the nitrogen and more bulky the substituent), the more the open chain tautomer is favored; in contrary, the more electron donating is the nitrogen substituent, e.g. methyl group (stronger nucleophile the nitrogen and less bulky the substituent), the more the cyclic tautomer is favored.

The use of the anhydride **6** and the lactone **7** was done for comparative reasons, but the experimental results from the two reactions are the same (without any differentiation in tautomeric equilibrium). Of course the total reaction sequence from the acid **5** to the γ-keto amide tautomers **8**, **9**, from a preparative point of view, evidently, is better in the case of the lactone reaction, because in the case of the anhydride half of the initial acid **5** is lost in the form of the acid-amine salt.

The acid anhydride **6** was prepared by the classical method, by heating the corresponding acid **5**[9] with an excess of acetic anhydride on a steam bath, while the lactone **7** was prepared by refluxing a solution of the acid **5** with an excess of acetyl chloride, according to the transformation of a series of 3-aroylpropionic acids to the corresponding γ-lactones, 5-arylfuran-2(3H)-ones.[10] Additionally this transformation appears to be stereoselective, with the Z-2-benzylidene- furan-5-one (**7**) to constitute the main isomer (80-85%) of the reaction's mixture and the E-isomer the minor isomer (15-20%), as ^{1}H NMR spectrum revealed, two triplets at δ 5.38 and 6.18 ppm respectively to Z- and E-isomers, in accordance with the literature.[11] The lactone **7** has been prepared by cyclization of 5-phenyl-4-pentynoic acid, by catalysis with, either mercury(II)oxide[11] or with a Rh(I)complex.[12]

When the reactions of the anhydride **6** and the lactone **7** with amines were carried out at 100 ^{0}C, (steam bath), the corresponding 2-benzylidenepyrrolidin-5-ones **10** were obtained. The same products, (**10**), were obtained from the γ-keto amides **8**, or the hydroxypyrrolidinones **9** or mixture of them (as in the case of **8a** and **9a**) with the following treatments: i. By refluxing with an excess of acetyl chloride, ii. By warming up above their melting points (apparently through a thermal tautomerization of the open-chain tautomers), iii. By treatment at room temperature with 10% aqueous HCl. Especially, the dehydration of hydroxypyrrolidinone **9e** was monitored by ^{1}H NMR spectra of a solution of the compound in $CDCl_3$, which gradually showed the conversion to the pure benzylidenepyrrolidinone **10e**, but this transformation was not detected in CD_3COCD_3 solution, under the same conditions. An analogous dehydration was detected in an attempt to record the electronic spectrum of hydroxypyrrolidinone **9a** in ethanolic solution, where the benzenoid pattern corresponding to **9a** gradually converted into intense absorption band (275-276 nm) of benzylidenepyrrolidinone **10a**. The easiness of dehydration of 2-hydroxypyrrolidinones **9** is characteristic of the stability of the conjugated benzylidene group system, therefore of the exocyclic double bond formation.

All these methods were found to give quantitatively this transformation, and therefore could be used preparatively for the products **10**.

From the reported series of the benzylidenepyrrolidinones **10** the only known substances are **10a**, which have been previously prepared[13] by a Grignard reaction of benzylmagnesium bromide on succinimide followed by treatment with a HCl solution, and **10b** from intermolecular Barbier-type and Reformatsky-type reactions mediated by SmI_2, with N-methylsuccinimide,[14] followed by acid hydrolysis and from the hydroxypyrrolidinone **9b**, (prepared by a Grignard reaction on the N-methylsuccinimide),[15] by warming with potassium hydrogen sulfate. A number of other 2-arylidene- and 2-alkylidenepyrrolidin-5-ones have been prepared,[16] in Z-configuration, by a base-catalyzed intramolecular cyclization of β-alkynylpropanamides. The referred 2-benzylidenepyrrolidin-5-ones **10** must all have the E-configuration which is the more stable thermodynamically.[3,16] In the case of benzylidenepyrrolidinone **10a**, the reaction mixture, from the reactions of anhydride **6** and the lactone **7** with hot ammonia showed before recrystallization a mixture of two products (t.l.c), the ^{1}H NMR spectrum of which revealed two vinylic protons at δ 5.52 (t, J = 1.5 Hz) and 5.90 (t, J = 2 Hz) in proportion 1:2.5. Given[17] that the transoid allylic coupling, in five and six membered rings, is about 0.4 Hz larger than the corresponding cissoid, the signal which corresponds to the main product

suggests an E-configuration, and such is the product effectively separated after recrystallization. It must be pointed out that, from all other reactions, the Z-stereoisomer of **10** was not detected.

In conclusion, the reactions of primary amines with the anhydride **6** or the lactone **7**, of 4-oxo-5-phenylpentanoic acid (**5**), gave their amides in the open-chain form, (γ-keto amides **8**) and / or the cyclic tautomers, (2-hydroxypyrrolidin-5-ones **9**), or their dehydrated derivatives, the 2-benzylidenepyrrolidin-5-ones **10**, stereoselectively. The later are likely to be useful synthons for the preparation of other 2-substituted-pyrrolidin-5-ones. The application of this method on other 4-oxo-5-phenylpentanoic acids substituted on methylene chain is in our immediate plan.

Experimental

General. ^{1}H NMR spectra were recorded at ambient temperature at 60MHz using a Varian EM-360 spectrometer. The data are reported as follows: chemical shift in ppm from internal tetramethylsilane on the δ scale, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants are given in (Hz). Micro analyses were performed by microanalytical laboratory of CNRS (France). Melting points are reported uncorrected. IR spectra were obtained with a Nicolet Magna 560 spectrometer (as nujol mulls). Electonic spectra were obtained with a Perkin Elmer 124 spectrophotometer. Analytical thin layer chromatography, (TLC) was performed on E. Merck precoated silica 60 F_{254} plates.

4-Oxo-5-phenylpentanoic anhydride, (6)

A solution of the acid **5** (3 g, 15.61 mmol) in acetic anhydride (6 ml, 63.53 mmol) was heated on a steam bath for 10 min, the excess of acetic anhydride and the produced acetic acid were evaporated under vacuum. The solid residue was recrystallized from ether to give the anhydride **6,** (1.6 g, 56%), mp 68-69 ^{0}C. Anal. Calcd % for $C_{22}H_{22}O_5$: C, 72.91; H, 6.05. Found: C, 72.75; H, 6.02. UV (EtOH), λ_{max}nm ($\log\varepsilon_{max}$): 248 (2.54), 252 (2.62), 257 (2.69) and 263 (2.63). IR (Nujol mull, cm^{-1}): 1808, 1739, 1701, 1603, 1495 and 1053. ^{1}H NMR (60 MHz, $CDCl_3$): δ 2.63 (m, 8H, A_2B_2, -CH_2CH_2-), 3.66 (s, 4H, -CH_2Ph) and 7.25 (s, 10H, arom).

γ-Benzylidene-γ-butyrolactone, (7)

A solution of the acid **5** (3 g, 15.61 mmol) in acetyl chloride (18 ml, 0.25 mol) was refluxed for 10 min, the solution was concentrated under vacuum, the solid residue recrystallized from ether to give the lactone **7**, (1.63 g, 60%), mp 87-88 ^{0}C, lit.[11] mp 90-91 ^{0}C. Anal. Calcd % for $C_{11}H_{10}O_2$: C, 75.84; H, 5.78. Found: C, 75.87; H, 5.98. UV (EtOH), λ_{max}nm ($\log\varepsilon_{max}$): 255 (4.34), 282 (3.36) and 291 (3.01). IR (Nujol mull, cm^{-1}): 1792 and 1678. ^{1}H NMR (60 MHz, $CDCl_3$): δ 2.30-3.10 (m, 4H, -CH_2CH_2-), 5.40 (t, J = 1.5 Hz, 1H, =CHPh) and 7.00-7.60 (m, 5H, arom.).

General procedure for γ-keto amides 8 and / or hydroxypyrrolidinones 9

A mixture of the anhydride **6** or the lactone **7** (2.75 mmol) and the amine[18] (13.75 mmol) in dry ether (20 ml) was stirred at room temperature for 2 days (7 days for the product **8d**). The new mixture, (solution in the case of methylamine), was concentrated under vacuum, (without heating), to a solid or semisolid residue. The referred yields were taken from the reactions of amines with the lactone **7** and were slightly better, (2-3%), than these of the anhydride **6** with the amines. 4-Oxo-5-phenylpentanamide, (**8a**) and 2-benzyl-2-hydroxypyrrolidin-5-one, (**9a**). The solid residue triturated with ether, the solid filtered and washed with water and then with small quantity of cold ether to give (3.75 g, 66%) of a solid, mp 85-97 ^{0}C. Anal. Calcd % for $C_{11}H_{13}NO_2$: C, 69.08; H, 6.85; N, 7.32. Found: C, 69.13; H, 6.91; N, 7.27. This product appears to be an equimolar mixture of the two above tautomers, as revealed from the ^{1}H NMR spectrum, which contains the proton signals of the two tautomers (see below). This product after fractional crystallization from ether gave the following two products: (i) 4-Oxo-5-phenylpentanamide, (8a) (1.58 g, 30%), mp 110-112 ^{0}C . Anal. Calcd % for $C_{11}H_{13}NO_2$: C, 69.08; H, 6.85; N, 7.32. Found: C, 68.93; H, 6.59; N, 7.18. UV (EtOH), λ_{max}nm

($\log\varepsilon_{max}$): 247.5 (2.39), 252.5 (2.45), 258 (2.48), 264 (2.42), 280 (2.27). IR (Nujol mull, cm^{-1}): 3333, 3145, 1701 and 1639. ^1H NMR (60 MHz, $CDCl_3$): δ 2.26-2.96 (m, 4H, $-CH_2CH_2-$), 3.75 (s, 2H, $-CH_2Ph$), 5.88 (br m, 2H, $-NH_2$), 7.26 (s, 5H, arom.). (ii) 2-Benzyl-2-hydroxypyrrolidin-5-one, (9a), (1.42 g, 27%), mp 94-96 ^0C. Anal. Calcd % for $C_{11}H_{13}NO_2$: C, 69.08; H, 6.85; N, 7.32. Found: C, 68.81; H, 6.60; N, 7.09. UV.[19] IR (Nujol mull, cm^{-1}): 3247, 3077, 1661 and 1605. ^1H NMR (60 MHz, $CDCl_3$): δ 1.77-2.60 (m, 4H, $-CH_2CH_2-$), 3.03 (s, 2H, $-CH_2Ph$), 4.88 (s, 1H, -OH), 7.28 (s, 5H, arom.).

2-Benzyl-2-hydroxy-1-methylpyrrolidin-5-one, (9b): the solid residue after washing with water, recrystallization from ether gave (4.12 g, 73%), of a solid mp 117-119 ^0C. Anal. Calcd % for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.36; N, 6.82. Found: C, 70.13; H, 7.42; N, 6.94. UV (EtOH), λ_{max}nm ($\log\varepsilon_{max}$): 242 (1.92), 247.5 (2.04), 252 (2.17), 257.5 (2.27), 263.5 (2.17), 277 (1.91). IR (Nujol mull, cm^{-1}): 3390, 1661 and 1600. ^1H NMR (60 MHz, $CDCl_3$): δ 1.63-2.50 (m, 4H, $-CH_2CH_2-$), 2.93 (s, 3H, >N-Me), 3.05 (s, 2H, $-CH_2Ph$), 3.66 (br s, 1H, -OH), 7.34 (s, 5H, arom.).

4-Oxo-5-phenylpentan-N-phenylamide, (8c): the semisolid residue after recrystallization from ethanol gave (5.51 g, 75%), of a solid mp 107-108 ^0C. Anal. Calcd % for $C_{17}H_{17}NO_2$: C, 76.45; H, 6.42; N, 5.24. Found: C, 76.43; H, 6.33; N, 5.08. UV (EtOH), λ_{max}nm ($\log\varepsilon_{max}$): 243 (4.13). IR (Nujol mull, cm^{-1}): 3333, 1712, 1672, 1603 and 1538. ^1H NMR (60 MHz, $CDCl_3$): δ 2.43-3.00 (m, 4H, $-CH_2CH_2-$), 3.74 (s, 2H, $-CH_2Ph$), 7.00-7.63 (m, 10H, arom.), 8.60 (br m, 1H, >NH).

4-Oxo-5-phenylpentan-N-(3-nitrophenyl)amide, (8d): the yellow solid after recrystallization from ethanol gave (5.24 g, 61%), of a solid mp 113-115 ^0C. Anal. Calcd % for $C_{17}H_{16}NO_4$: C, 65.37; H, 5.16; N, 8.97. Found: C, 65.23; H, 5.31; N, 9.06. UV (EtOH), λ_{max}nm ($\log\varepsilon_{max}$): 240 (4.01), 329 (2.98), 242 (4.02), 276 (3.47), 324 (2.98). IR (Nujol mull, cm^{-1}): 3279, 1704, 1664, 1526,and 1342. ^1H NMR (60 MHz, $CDCl_3$): δ 2.43-3.13 (m, 4H, $-CH_2CH_2-$), 3.74 (s, 2H, $-CH_2Ph$), 7.16-8.60 (m, 10H, arom. and >NH).

1,2-Dibenzyl-2-hydroxypyrrolidin-5-one, (9e): the semisolid residue after recrystallization from ether gave (4.87 g, 63%), of a solid mp 130-132 ^0C. Anal. Calcd % for $C_{18}H_{19}NO_2$: C, 76.85; H, 6.81; N, 4.97. Found: C,76.65; H, 6.77; N, 5.12. UV (EtOH), λ_{max}nm ($\log\varepsilon_{max}$): 242 (2.13), 247.5 (2.31), 253 (2.45), 258 (2.55), 264 (2.45), 267.5 (2.23), 282 (1.36). IR (Nujol mull, cm^{-1}): 3240, 1640, and 1600. ^1H NMR (60 MHz, $CDCl_3$): δ, 2.83 (m,1H, -OH), 2.90 and 3.16 (q, AB, J = 13.5 Hz, 2H, C-CH_2Ph), 4.70 (d, AB, J = 2 Hz, 2H, >N-CH_2Ph), 7.40-7.70 (m, 10H, arom.).

General procedure for 2-benzylidenepyrrolidin-5-ones 10.

A mixture of the anhydride **6** or the lactone **7** (2.75 mmol) and the amine[20] (5.50 mmol) was heated on a steam bath for 3 h. The solid reaction's mixture was dissolved in $CHCl_3$ and washed with a 10% HCl solution, the organic layer dried and concentrated to a pure solid, (^1H NMR), 2-benzylidenepyrrolidin-5-one **10**. The referred yields are taken from the reactions of amines with the lactone **7** and were slightly better, (2-3%), than these of the anhydride 6 with the amines.

2-Benzylidenepyrrolidin-5-one, (10a): this solid appears, (^1H NMR), to be a mixture of the two stereoisomers (E and Z in ratio 2.5:1 respectively), recrystallization from ethanol gave, (1.62 g, 54%), of a solid, (corresponding to E-isomer), mp 149-152 ^0C. Anal. Calcd % for $C_{11}H_{11}NO$: C, 76.25; H, 6.39; N, 8.08. Found: C, 76.32; H, 6.56; N, 8.29. UV (EtOH), λ_{max}nm ($\log\varepsilon_{max}$): 218 (4.04), 275 (4.38). IR (Nujol mull, cm^{-1}): 3155, 1721, 1661 and 1600. ^1H NMR (60 MHz,$CDCl_3$): δ 2.40-3.23 (m, 4H, $-CH_2CH_2-$), 5.90 (t, J = 2 Hz, 1H, =CH-), 7.25 (s, 5H, arom.), 9.15 (br m, 1H, >NH).

2-Benzylidene-1-methylpyrrolidin-5-one, (10b): the solid after recrystallization, from benzene / hexane, gave (4.48 g, 87%), of a solid mp 98-99 ^0C, lit.[15] m. p. 98 ^0C. Anal. Calcd % for $C_{12}H_{13}NO$: C, 77.00; H, 6.95; N, 7.48. Found: C, 77.12; H, 7.17; N, 7.30. UV (EtOH), λ_{max}nm ($\log\varepsilon_{max}$): 218 (4.00), 276 (4.33). IR (Nujol mull, cm^{-1}): 1704, 1629 and 1590. ^1H NMR (60 MHz, $CDCl_3$): δ 2.20-2.33 (m, 7H, $-CH_2CH_2-$ and >NMe as a s, at 3.08), 5.71 (t, J = 2 Hz, 1H, =CH-), 7.23 (s, 5H, arom.).

2-Benzylidene-1-phenylpyrrolidin-5-one, (10c): the solid after recrystallization from ethanol, gave (4.32 g, 63%), of a solid mp 145-146 ^{0}C. Anal. Calcd % for $C_{17}H_{13}NO$: C, 81.94; H, 6.07; N, 5.62. Found: C, 82.02; H, 5.90; N, 5.87. UV (EtOH), λ_{max}nm (logε_{max}): 220 (4.04), 276 (4.39). IR Nujol mull, cm^{-1}): 1721, 1639 and 1590. ^{1}H NMR (60 MHz, $CDCl_3$): δ 2.60-3.44 (m, 4H, -CH_2CH_2-), 5.60 (t, J = 2Hz, 1H, =CH-), 7.07-7.70 (m, 10H, arom.).

2-Benzylidene-1-(3-nitrophenyl)pyrrolidin-5-one, (10d): the yellow solid after recrystallization from ethanol gave (4.61 g, 57%), of a yellow solid mp 157-158 ^{0}C. Anal. Calcd % for $C_{17}H_{14}N_2O_3$: C, 69.40; H, 4.78; N, 9.51. Found: C, 69.66; H, 4.87; N, 9.38. UV (EtOH), λ_{max}nm (logε_{max}): 270 (4.44). IR (Nujol mull, cm^{-1}): 1724, 1624 and 1592. ^{1}H NMR (60 MHz, $CDCl_3$): δ 2.60-3.43 (m, 4H, -CH_2CH_2-), 5.60 (t, J = 2 Hz, 1H, =CH-), 7.10-8.40 (m, 9H, arom.).

1-Benzyl-2-benzylidenepyrrolidin-5-one, (10e): the solid residue after recrystallization from ethanol gave (5.14 g, 71%), of a solid mp 114-116 ^{0}C. Anal. Calcd % for $C_{18}H_{17}NO$: C, 82.10; H, 6.51; N, 5.31. Found: C, 81.96; H, 6.73; N, 5.16. UV (EtOH), λ_{max}nm (logε_{max}): 204 (4.40), 276 (4.41). IR (Nujol mull, cm^{-1}): 1704, 1634 and 1587. ^{1}H NMR (60 MHz, $CDCl_3$): δ 2.33-3.16 (m, 4H, -CH_2CH_2-), 4.70 (s, 2H, -CH_2Ph), 5.60 (t, J = 2 Hz, 1H, =CH-), 7.07 and 7.21 (two s, 10H, arom.).

References and Notes

1. Yoshio, I.; Fujio, T.; Yoshinori, T. Pat. Appl. JP 19670917. CAN 75:140680.
2. Koseki, Y.; Kusano, S.; Ichi, D.; Yoshida, K.; Nagasaka, T. *Tetrahedron*, **56**, 8855-8865 (2000).
3. Gautier, A. J.; Miocque, M. Pat. Appl. Fr 71-23472 19710628. CAN 79: 53175.
4. Tsolomitis, A.; Sandris, C. *J. Heterocycl. Chem.* **17**, 1645-1646 (1980).
5. Tsolomitis, A.; Sandris. C. *Heterocycles* **25**, 569-575 (1987).
6. Flitsch, W. *Chem. Ber.* **103**, 3205-3213 (1970).
7. (a) Chiron, R.; Graff, Y. *Bull. Soc. Chim. Fr.* 3715-3718 (1967). (b) Laurence, C.; Chiron, R. *C. R. Acad. Sci.*, Ser. C, *268*, 279-282 (1969). (c) Chiron, R.; Graff, Y. *Bull. Soc. Chim. Fr.* 2145-2151 (1971).
8. Keller, O.; Prelog, V. *Helv. Chim. Acta*, 2572-2578 (1971).
9. The 5-phenylpentanoic acid (**5**) prepared by a condensation reaction of benzyl cyanide and diethyl succinate according to the literature.[21]
10. Tsolomitis, A.; Sandris, C. *J. Heterocycl. Chem.* **20**, 1545-1548 (1983).
11. Yamamoto, M. *J. Chem. Soc. Perkin Trans.***1**, 582-588 (**1981**).
12. Chan, D. M. T.; Marder, T. B.; Milstein, D.; Taylor, N. J. *J. Am. Chem Soc.* **109**, 6385-6388 (1987).
13. Lacova, M.; Sraga, J. *Chemicke Zvesti* , **32**, 82-85 (1978).
14. Farcas, S.; Namy, J-L. *Tetrahedron Lett.* **42**, 879-881 (2001).
15. Kolocouris, N. *Bull. Soc. Chim. Fr.* 1057-1060 (1973).
16. Koseki, Y.; Kusano, S.; Nagasaka, T. *Tetrahedron Lett.* **39**, 3517-3520 (**1998**).
17. Jackman, L. M.; Sternhell, S. *"Applications of nuclear magnetic resonance spectroscopy in organic chemistry"*, 2nd ed. Pergamon Press Ltd, Oxford, 1969, p-322.
18. Except of the cases of ammonia and methylamine, where instead of the pure amines, aqueous solutions (25 and 35% respectively) were used.
19. Contrary to its tautomer, the hydroxypyrrolidinone **9a**, in an attempt to record the UV spectrum (in ethanol solution), was observed to give a bathochromic shift of absorption bands to more intense absorptions, with a maximum at 275-276 nm characteristic of electronic spectrum of benzylidenepyrrolidinone **10a**.
20. In the cases of methylamine and ammonia, aqueous solutions were used (35 and 25% respectively) and the reaction mixture after stirring for 2 days at room temperature was heated on a steam bath for 3h and was concentrated under vacuum to a solid residue.
21. Izumi, Y.; Tatsumi, S.; Imaida, M.; Fukuda, Y. *Bull. Chem. Soc. Jpn.* **38**, 1338-1340 (1965).

Received on September 15, 2005