

F. Foubelo, C. Gómez, A. Gutiérrez and M. Yus*

Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Alicante,
Apdo. 99, 03080 Alicante, Spain
Received April 17, 2000

Dedicated to the memory of Professor Raymond N. Castle

The 4,4'-di-*tert*-butylbiphenyl-catalyzed lithiation of phthalan (**1a**) and isochroman (**1b**) in THF at 0°C affords the corresponding functionalized benzyllithiums **2**, which by reaction with *N*-silylaldimines yield, after acid-base work-up, the expected amino alcohols **3**. Successive treatment of these amino alcohols with thionyl chloride and sodium hydroxide yields the corresponding substituted benzofused six- and seven-membered nitrogen-containing heterocycles **4**.

J. Heterocyclic Chem., **37**, 1061 (2000).

Introduction.

Isoquinoline [1] and benzoazepine [2] derivatives are important molecules due to their presence in many pharmacologically active compounds [3,4]. On the other hand, in the last few years we have been using an arene-catalyzed lithiation reaction [5-7] for the preparation of functionalized organolithium compounds [8,9] by reductive opening of heterocycles [10,11]. In this paper we apply this process to the ring opening of phthalan [12] and isochroman [13] in order to get the corresponding functionalized organolithium compounds for their reaction with *N*-silylimines [14], so making possible the preparation of primary hydroxy amines, adequate starting materials for the generation of nitrogen-containing heterocycles.

Results and Discussion.

The lithiation of phthalan (**1a**) or isochroman (**1b**), with an excess of lithium powder and a catalytic amount of 4,4'-di-*tert*-butylbiphenyl (DTBB, 5 mol %) in THF at 0 °C for 30 minutes, yielded a solution of the corresponding functionalized organolithium compounds **2a,b**. These intermediates were reacted with crude *N*-silylimines (generated by reaction of aldehydes with hexamethyldisilazane and *n*-butyllithium) to give, after hydrolysis with water and acid/base extraction, the expected amino alcohols **3aa-bc** (Scheme I and Table I).

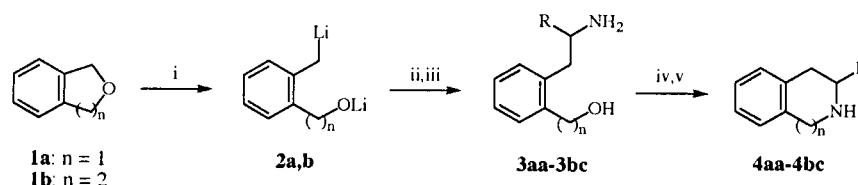
Amino alcohols **3** are adequate precursors of the corresponding nitrogen-containing heterocycles by intramolecular dehydration. Thus, when compounds **3** were successively treated with thionyl chloride in chloroform at 50 °C and then with 5 *M* sodium hydroxide in THF at room temperature, the expected substituted six- or seven-membered nitrogen-containing heterocycles **4** were isolated (Scheme I and Table I). Although crude products **4** were >90% pure (GLC and/or 300 MHz ¹H NMR), they were purified by column chromatography in order to get analytically pure samples. As can be seen in Table I, during the purification some of the compounds decomposed giving rather lower yields.

As a conclusion, we describe here a simple way to generate amino alcohols and benzofused six- or seven-membered nitrogen-containing heterocycles, which are interesting units in many naturally occurring compounds [1-4,15].

EXPERIMENTAL

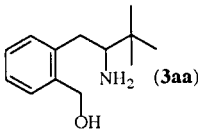
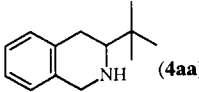
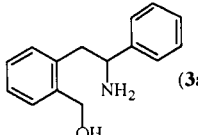
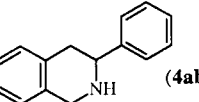
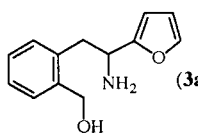
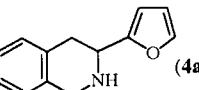
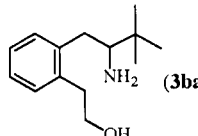
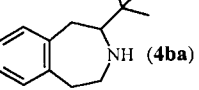
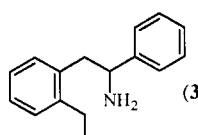
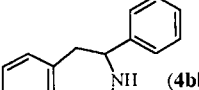
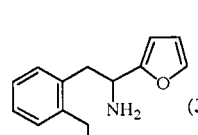
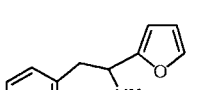
Infrared spectra were obtained on a Nicolet Impact 400D spectrophotometer. Nmr spectra were recorded on a Bruker AC-300 (300 MHz for ¹H and 75 MHz for ¹³C) using CDCl₃ as solvent and TMS as internal standard; chemical shifts are given in δ (ppm) and coupling constants (J) are given in Hz. ¹³C nmr assignments were made on the basis of DEPT experiments. Mass spectra (EI) were obtained at 70 eV on a Shimadzu QP-5000 spec-

Scheme I



Reagents and conditions: i, Li, DTBB cat. (5 mol %), THF, 0°C, then filtration; ii, RCH=NSiMe₃, -45 to 20°C; iii, H₂O-HCl; iv, Cl₂SO, CHCl₃, 50°C; v, NaOH

Table I
Amino Alcohols **3** and Heterocycles **4**

Entry	Starting Material	Intermediate	Product 3 [a]		Product 4 [a]	
			Structure (No.)	Yield (%) [b]	Structure (No.)	Yield (%) [c][d]
1	1a	2a	 (3aa)	45	 (4aa)	38 (>95)
2	1a	2a	 (3ab)	58	 (4ab)	(>95)
3	1a	2a	 (3ac)	60	 (4ac)	42 (69)
4	1b	2b	 (3ba)	58	 (4ba)	44 (93)
5	1b	2b	 (3bb)	65	 (4bb)	42 (91)
6	1b	2b	 (3bc)	46	 (4bc)	36 (90)

[a] All products **3** and **4** were >90 and >95% pure, respectively (GLC and/or 300 MHz ^1H nmr). [b] Isolated yield after acid-base extraction based on the starting material **1**. [c] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the amino alcohols **3**. [d] In parenthesis yield of isolated compounds (>90% pure) before column chromatography.

trometer, fragment ions with relative intensities higher than 10% being given in *m/z*. High resolution mass spectra were performed by the corresponding service at the University of Alicante using a Finnigan MAT 95 S apparatus. The purity of volatile products and the chromatographic analyses (GLC) were determined with a Hewlett Packard HP-5890 instrument equipped with a flame ionization detector and a 12 m capillary column (0.2 mm diameter, 0.33 mm film thickness), using nitrogen (2 ml/minute) as carrier gas, $T_{\text{injector}} = 275\text{ }^\circ\text{C}$, $T_{\text{column}} = 80\text{ }^\circ\text{C}$ (3 minutes) and $80\text{--}270\text{ }^\circ\text{C}$ ($15\text{ }^\circ\text{C}/\text{minute}$). Thin layer chromatography (TLC) was carried out on Schleicher & Schuell F1500/LS 254 plates coated with a 0.2 mm layer of silica gel; R_f values are given under these conditions. Column chromatography was performed using silica gel 60 of 35-70 mesh. All starting materials were commercially available (Acros, Aldrich, Fluka) of the best grade and were used without

further purification. THF was dried over benzophenone ketyl under an argon atmosphere and distilled before use.

General Procedure for the Preparation of *N*-Trimethylsilylimines.

To a solution of hexamethyldisilazane (0.550 ml, 2.5 mmol) in THF (1.0 ml) was added a 1.6 *M* solution of *n*-butyllithium in hexane (1.6 ml, 2.6 mmol) at $0\text{ }^\circ\text{C}$ and the mixture was stirred for 5 minutes at the same temperature, and after that, it was added dropwise to a solution of the corresponding aldehyde (2.2 mmol) in THF (1.0 ml) at $0\text{ }^\circ\text{C}$. Stirring was continued at the same temperature for 0.5 hours. The resulting *N*-trimethylsilylimine solution was used in the synthesis of amino alcohols **3** when reacting with the intermediates **2**, resulting from the reductive opening of phthalan and isochroman.

General Procedure for the Preparation of Aminoalcohols **3** from Phthalan or Isochroman.

To a blue suspension of lithium powder (0.125 g, 18.0 mmol) and a catalytic amount of 4,4'-di-*tert*-butylbiphenyl (0.047 g, 0.18 mmol) in THF (10 ml) at 0 °C was added phthalan (**1a**) (0.220 ml, 2.0 mmol) or isochroman (**1b**) (0.250 ml, 2.0 mmol) under nitrogen, and the mixture was stirred for 0.5 hours at the same temperature. The excess of lithium was filtered off under nitrogen and the resulting mixture was added dropwise to a cooled (-45 °C) THF solution of the corresponding *N*-trimethylsilylimine prepared as indicated above. The reaction mixture was allowed to reach room temperature, hydrolyzed with 3 *M* hydrochloric acid (15 ml) and extracted with ethyl acetate (3 x 20 ml). The aqueous layer was then basified with 2.5 *M* sodium hydroxide (25 ml) and extracted with ethyl acetate (3 x 25 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated (15 Torr). The resulting residue was purified by column chromatography (silica gel; hexane/ethyl acetate) to yield compounds **3**. Yields are included in Table I. Physical and spectroscopic data follow.

2-(2-Amino-3,3-dimethylbutyl)phenylmethanol (**3aa**).

This compound was found as a colorless oil; R_f 0.19 (hexane/ethyl acetate: 1/2); ir: ν NH₂ 3356, 3273, ν ArH 3072 cm⁻¹; ¹H nmr: δ 1.01 (s, 9H, C(CH₃)₃), 2.56 (d, 1H, CHHCH, J = 10.7 Hz), 2.61 (t, 1H, CHNH₂, J = 10.4 Hz), 2.82 (d, 1H, CHHCH, J = 11.0 Hz), 3.31 (br s, 3H, NH₂, OH), 4.32 (d, 1H, CHHOH, J = 11.6 Hz), 4.82 (d, 1H, CHHOH, J = 11.9 Hz), 7.05-7.33 ppm (m, 4H, ArH); ¹³C nmr: δ 26.1 [C(CH₃)₃], 34.5 (CH₂CHNH₂), 34.6 [C(CH₃)₃], 61.9 (CH₂OH), 62.9 (CHNH₂), 126.5, 128.3, 129.9, 130.3, 139.8, 173.7 ppm (ArC); ms: m/z 155, 154, 91, 86, 69, 57, 55, 41. Calcd. for C₁₃H₂₁NO-NH₂: 190.1358. Found: 190.1394.

2-(2-Amino-2-phenylethyl)phenylmethanol (**3ab**).

This compound was found as a colorless oil; R_f 0.16 (hexane/ethyl acetate: 1/2); ir: ν OH 3400-3100, ν NH₂ 3353, 3288, ν ArH 3061 cm⁻¹; ¹H nmr: δ 2.92-3.09 (m, 2H, CH₂CH), 3.09 (br s, 3H, NH₂, OH), 4.14 (dd, 1H, CHNH₂, J = 9.2, 4.6 Hz), 4.43 (d, 1H, CHHOH, J = 11.9 Hz), 4.82 (d, 1H, CHHOH, J = 11.6 Hz), 7.10-7.41 ppm (m, 9H, ArH); ¹³C nmr: δ 42.2 (CH₂CHNH₂), 56.4 (CHNH₂), 63.0 (CH₂OH), 126.0, 126.8, 127.4, 128.2, 128.6, 129.8, 130.2, 137.6, 140.4, 145.0 ppm (ArC); ms: m/z 208, 207, 206, 179, 178, 130, 103, 102, 91, 90, 89, 77, 76, 63, 51. Calcd. for C₁₅H₁₇NO-NH₂: 210.1046. Found: 210.1039.

2-[2-Amino-2-(2-furyl)ethyl]phenylmethanol (**3ac**).

This compound was found as an orange oil; R_f 0.07 (hexane/ethyl acetate: 1/2); ir: ν OH 3500-3100, ν NH₂ 3147, 3119, ν ArH 3066 cm⁻¹; ¹H nmr: δ 3.12-3.50 (m, 2H, CH₂CH), 3.27 (br s, 3H, NH₂, OH), 4.18 (dd, 1H, CHNH₂, J = 8.2, 4.3 Hz), 4.49 (d, 1H, CHHOH, J = 11.9 Hz), 4.75 (d, 1H, CHHOH, J = 11.6 Hz), 6.17 (d, 1H, CCH, J = 3.1 Hz), 6.34 (d, 1H, CHCHO, J = 1.8 Hz), 7.07-7.40 ppm (m, 5H, ArH, CHO); ¹³C nmr: δ 38.5 (CH₂CHNH₂), 50.15 (CHNH₂), 62.9 (CH₂OH), 104.8 (CCH), 110.2 (CCHCH), 127.0, 128.2, 130.2, 130.3, 136.9, 140.5 (ArC), 141.6 (OCH), 157.6 ppm (CCH); ms: m/z 132, 104, 96, 86, 69, 41. Calcd. for C₁₃H₁₅NO-H₂O-NH₂: 182.0732. Found: 182.0728.

2-[2-(2-Amino-3,3-dimethylbutyl)phenyl]ethanol (**3ba**).

This compound was found as a colorless oil; R_f 0.28 (hexane/ethyl acetate: 1/2); ir: ν OH 3400-3100, ν NH₂ 3357,

3296, ν ArH 3060 cm⁻¹; ¹H nmr: δ 1.00 [s, 9H, C(CH₃)₃], 2.53 (dd, 1H, CHHCH, J = 13.4, 10.9 Hz), 2.57 (br s, 3H, NH₂, OH), 2.72-2.88 (m, 3H, CHHCH, CHHCH₂OH), 3.00 (ddd, 1H, CHHCH₂OH, J = 14.0, 8.2, 5.5 Hz), 3.71-3.79 (m, 1H, CHHOH), 3.84-3.91 (m, 1H, CHHOH), 7.05-7.31 ppm (m, 4H, ArH); ¹³C nmr: δ 26.2 [C(CH₃)₃], 33.9 (CH₂CH₂OH), 34.2 (CH₂CHNH₂), 36.15 [C(CH₃)₃], 61.6 (CHNH₂), 63.4 (CH₂OH), 126.3, 126.4, 129.6, 130.2, 138.7, 138.7 ppm (ArC); ms: m/z 222 (M⁺+1), 164, 147, 146, 129, 128, 119, 117, 115, 105, 91, 87, 86, 77, 71, 70, 69, 65, 57, 56, 43, 42, 41. Calcd. for C₁₄H₂₃NO-C₄H₉: 164.1075. Found: 164.1089.

2-[2-(2-Amino-2-phenylethyl)phenyl]ethanol (**3bb**).

This compound was found as a yellow oil; R_f 0.14 (hexane/ethyl acetate: 1/2); ir: ν OH 3400-3100, ν NH₂ 3352, 3288, ν ArH 3061 cm⁻¹; ¹H nmr: δ 3.01 (br s, 3H, NH₂, OH), 3.01-3.12 (m, 4H, CH₂CH, CH₂CH₂OH), 3.77-3.92 (m, 2H, CH₂OH), 4.25 (dd, 1H, CHNH₂, J = 9.2, 5.2 Hz), 7.16-7.42 ppm (m, 9H, ArH); ¹³C nmr: δ 36.3 (CH₂CH₂OH), 41.9 (CH₂CHNH₂), 57.05 (CHNH₂), 63.4 (CH₂OH), 126.3, 126.4, 126.6, 127.2, 128.4, 129.75, 130.2, 137.1, 138.5, 144.9 ppm (ArC); ms: m/z 209, 208, 207, 206, 106, 105, 104, 103, 91, 79, 78, 77, 51, 44, 43, 40. Calcd. for C₁₆H₁₉NO-H₂O-NH₂: 206.1095. Found: 206.1078.

2-[2-[2-Amino-2-(2-furyl)ethyl]phenyl]ethanol (**3bc**).

This compound was found as an orange oil; R_f 0.05 (hexane/ethyl acetate: 1/2); ir: ν OH 3400-3100, ν NH₂ 3356, 3292, ν ArH 3063 cm⁻¹; ¹H nmr: δ 2.37 (br s, 3H, NH₂, OH), 2.81-3.08 (m, 2H, CH₂CH₂OH), 3.05 (dd, 1H, CHHCH, J = 13.7, 8.7 Hz), 3.18 (dd, 1H, CHHCH, J = 13.7, 5.5 Hz), 3.77-3.90 (m, 2H, CH₂OH), 4.24 (dd, 1H, CHNH₂, J = 8.2, 5.3 Hz), 6.13 (d, 1H, CCH, J = 3.1 Hz), 6.31 (dd, 1H, CCHCH, J = 3.4, 1.5 Hz), 7.08-7.34 (m, 4H, ArH), 7.37 ppm (t, 1H, OCH, J = 0.9 Hz); ¹³C nmr: δ 36.1 (CH₂CHOH), 38.7 (CH₂CHNH₂), 50.75 (CHNH₂), 63.4 (CH₂OH), 104.9 (CCH), 110.1 (CHCHO), 126.5, 126.8, 130.0, 130.2, 130.65, 136.65, 138.25 (ArC), 141.4 (OCH), 157.7 ppm (CCH); ms: m/z 97, 96, 69, 41. Calcd. for C₁₄H₁₇NO₂-NH₂: 214.0994. Found: 214.1024.

General Procedure for the Preparation of Tetrahydroisoquinolines and Benzo[*d*]azepines **4**.

To a solution of amino alcohol **3** (1.0 mmol) in chloroform (10 ml) was added dropwise thionyl chloride (0.10 ml, 1.7 mmol) at 0 °C under nitrogen and the reaction mixture was stirred at 50 °C for 4 hours. After that, solvents were evaporated (15 Torr) and the resulting residue was dissolved in THF (5 ml) and a 5 *M* sodium hydroxide solution (10 ml) was added. The resulting mixture was stirred vigorously for 10 hours at 20 °C, and then it was extracted with ethyl acetate (3x25 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated (15 Torr). The resulting residue was purified by column chromatography (silica gel; hexane/ethyl acetate) to yield compounds **4**. Yields are included in Table I. Physical and spectroscopic data follow.

3-(*tert*-Butyl)-1,2,3,4-tetrahydroisoquinoline (**4aa**).

This compound was obtained as a pale yellow oil; R_f 0.43 (hexane/ethyl acetate: 1/2); ir: ν NH 3302, ν ArH 3062 cm⁻¹; ¹H nmr: δ 1.00 [s, 9H, C(CH₃)₃], 1.59 (br s, 1H, NH), 2.55 (dd, 1H, CHHCH, J = 10.7, 4.1 Hz), 2.60-2.69 (m, 1H, CHNH), 2.75 (dd,

1H, CHHCH, $J = 15.6$, 4.0 Hz), 4.03 (d, 1H, CHHNH, $J = 16.5$ Hz), 4.09 (d, 1H, CHHNH, $J = 16.5$ Hz), 7.00-7.25 ppm (m, 4H, ArH); ^{13}C nmr: δ 26.3 [$\text{C}(\text{CH}_3)_3$], 26.7 [$\text{C}(\text{CH}_3)_3$], 29.8 (CH_2CHNH), 49.5 (CH_2NH), 63.1 (CHNH), 125.6, 125.8, 126.0, 129.5, 135.4, 136.1 ppm (ArC); ms: m/z 132, 131, 130, 104, 103, 77, 41. Calcd. for $\text{C}_{13}\text{H}_{19}\text{N}\cdot\text{CH}_3$: 174.1283. Found: 174.1291.

3-Phenyl-1,2,3,4-tetrahydroisoquinoline (4ab).

This compound was obtained as a yellow oil; R_f 0.45 (hexane/ethyl acetate: 1/2); ir: ν NH 3322, ν ArH 3061 cm^{-1} ; ^1H nmr: δ 2.99-3.08 (m, 2H, CH_2CH), 3.91 (br s, 1H, NH), 4.04 (dd, 1H, CH_2CH , $J = 8.9$, 6.1 Hz), 4.17 (d, 1H, CHHNH, $J = 15.7$ Hz), 4.26 (d, 1H, CHHNH, $J = 15.7$ Hz), 7.00-7.46 ppm (m, 9H, ArH); ^{13}C nmr: δ 30.2 (CH_2CH), 41.7 (CH_2NH), 51.35 (CHNH), 119.0, 119.2, 119.3, 119.6, 120.5, 121.6, 122.0, 127.3, 127.5, 136.4 ppm (ArC); ms: m/z 209 (M^+), 208, 132, 105, 104, 103, 78, 77, 51, 40. Calcd. for $\text{C}_{15}\text{H}_{15}\text{N}$: 209.1204. Found: 209.1215.

3-(2-Furyl)-1,2,3,4-tetrahydroisoquinoline (4ac).

This compound was obtained as a dark brown oil; R_f 0.39 (hexane/ethyl acetate: 1/2); ir: ν NH 3302, ν ArH 3062 cm^{-1} ; ^1H nmr: δ 2.27 (br s, 1H, NH), 3.01-3.11 (m, 2H, CH_2CH), 4.04 (d, 1H, CHHNH, $J = 16.2$ Hz), 4.15 (dd, 1H, CHNH, $J = 8.6$, 5.5 Hz), 4.16 (d, 1H, CHHNH, $J = 15.9$ Hz), 6.31 (d, 1H, CCH, $J = 1.8$ Hz), 6.32 (d, 1H, CCHCH, $J = 1.8$ Hz), 7.00-7.35 (m, 4H, ArH), 7.37 ppm (s, 1H, OCH); ^{13}C nmr: δ 33.1 (CH_2CHNH_2), 47.7 (CH_2NH), 51.3 (CHNH), 105.2 (CCH), 110.0 (CCHCH), 125.9, 126.0, 126.1, 129.1, 133.7, 134.9 (ArC), 141.6 (OCH), 156.3 ppm (CCH); ms: m/z 200 (M^++1), 199 (M^+), 198, 182, 105, 104, 103, 78, 51, 40. Calcd. for $\text{C}_{13}\text{H}_{13}\text{NO}$: 199.0997. Found: 199.1001.

2-(*tert*-Butyl)-2,3,4,5-tetrahydro-1H-3-benzazepine (4ba).

This compound was obtained as an orange oil; R_f 0.34 (hexane/ethyl acetate: 1/2); ir: ν NH 3363, ν ArH 3062 cm^{-1} ; ^1H nmr: δ 1.00 [s, 9H, $\text{C}(\text{CH}_3)_3$], 2.24 (dd, 1H, CHNH, $J = 8.6$, 1.2 Hz), 2.39 (br s, 1H, NH), 2.60-2.85 (m, 3H, CHHCH, $\text{CH}_2\text{CH}_2\text{NH}$), 2.89 (dd, 1H, CHHCH, $J = 14.0$, 1.1 Hz), 3.10 (ddd, 1H, CHHNH, $J = 15.0$, 11.0, 2.0 Hz), 3.38 (ddd, 1H, CHHNH, $J = 12.8$, 6.1, 1.8 Hz), 7.05-7.20 ppm (m, 4H, ArH); ^{13}C nmr: δ 26.6 [$\text{C}(\text{CH}_3)_3$], 34.6 (CH_2CH), 38.7 ($\text{CH}_2\text{CH}_2\text{NH}$), 40.1 [$\text{C}(\text{CH}_3)_3$], 49.0 (CH_2NH), 67.8 (CHNH), 126.0, 126.2, 128.9, 129.0, 141.8, 142.0 ppm (ArC); ms: m/z 203 (M^+), 147, 146, 129, 119, 117, 115, 98, 91, 56, 42, 41. Calcd. for $\text{C}_{14}\text{H}_{21}\text{N}$: 203.1674. Found: 203.1674.

2-Phenyl-2,3,4,5-tetrahydro-1H-3-benzazepine (4bb).

This compound was obtained as a yellow oil; R_f 0.36 (hexane/ethyl acetate: 1/2); ir: ν NH 3323, ν ArH 3060 cm^{-1} ; ^1H nmr: δ 2.41 (br s, 1H, NH), 2.75-3.01 (m, 3H, CHNH, $\text{CH}_2\text{CH}_2\text{NH}$), 3.15-3.24 (m, 1H, CHHNH), 3.31-3.43 (m, 1H, CHHNH), 3.37 (d, 1H, CHHCHNH, $J = 9.8$ Hz), 3.72 (d, 1H, CHHCHNH, $J = 9.8$ Hz), 7.05-7.45 ppm (m, 9H, ArH); ^{13}C nmr: δ 38.85 ($\text{CH}_2\text{CH}_2\text{NH}$), 46.9 (CH_2CH), 48.8 (CH_2NH), 63.7 (CHNH), 126.2, 126.4, 126.5, 127.2, 128.6, 129.2, 129.6, 140.8, 142.3, 146.0 ppm (ArC); ms: m/z 223 (M^+), 181, 119, 118, 117, 115, 91. Calcd. for $\text{C}_{16}\text{H}_{17}\text{N}$: 223.1361. Found: 223.1367.

2-(2-Furyl)-2,3,4,5-tetrahydro-1H-3-benzazepine (4bc).

This compound was obtained as a brown oil; R_f 0.22 (hexane/methanol: 1/1); ir: ν NH 3365, ν ArH 3060 cm^{-1} ; ^1H

nmr: δ 2.80-2.98 (m, 2H, CH_2), 3.08 (dd, 1H, CHH, $J = 13.6$, 8.1 Hz), 3.17 (dd, 1H, CHH, $J = 13.7$, 6.1 Hz), 3.54 (br s, 1H, NH), 3.73-3.88 (m, 2H, CH_2), 4.26 (dd, 1H, CHNH, $J = 7.3$, 6.7 Hz), 6.12 (d, 1H, CCH, $J = 3.4$ Hz), 6.28 (dd, 1H, CHCHO, $J = 3.1$, 1.8 Hz), 7.02-7.42 (m, 4H, ArH), 7.17 ppm (d, 1H, OCH, $J = 1.8$ Hz); ^{13}C nmr: δ 36.0 ($\text{CH}_2\text{CH}_2\text{NH}_2$), 38.3 (CH_2CH), 50.6 (CH_2NH), 63.31 (CHNH), 105.5 (CCH), 110.2 (CHCHO), 126.4, 126.9, 130.0, 130.1, 136.3, 138.1 (ArC), 141.6 (OCH), 156.6 ppm (CCH); ms: m/z 214 (M^++1), 96, 69, 41. Calcd. for $\text{C}_{14}\text{H}_{15}\text{NO}$: 213.1154. Found: 213.1170.

Acknowledgement.

The authors are grateful to the Dirección General de Enseñanza Superior (DGES) of the Spanish Ministerio de Educación y Cultura (MEC) for financial support (grant no. PB97-0133).

REFERENCES AND NOTES

- [1] For a review, see: D. J. Le Count, in *Comprehensive Heterocyclic Chemistry*, Vol 9, A. R. Katritzky, C. W. Rees, E. F. V. Scriven and G. R. Newkome, eds, Pergamon Press, Oxford, 1996, pp 1-43.
- [2] For a review, see: C. D. Johnson, in *Comprehensive Heterocyclic Chemistry*, Vol 5, A. R. Katritzky, C. W. Rees, E. F. V. Scriven and A. McKillop, eds, Pergamon Press, Oxford, 1996, pp 1-301.
- [3] Isoquinoline derivatives: P. S. Charifson and S. Charifson, *Drugs Fut.*, **14**, 1179 (1989).
- [4] Benzazepine derivatives: T. Eicher and S. Hauptmann, *The Chemistry of Heterocycles*, G. Thieme Verlag, Stuttgart, 1995, p 469.
- [5] First account of this reaction: D. J. Ramón and M. Yus, *J. Chem. Soc., Chem. Commun.*, 398 (1991).
- [6] For reviews, see: [a] M. Yus, *Chem. Soc. Rev.*, 155 (1996); [b] D. J. Ramón and M. Yus, *Eur. J. Org. Chem.*, 225 (2000) (Microreview).
- [7] For a polymer supported version of this reaction, see: [a] C. Gómez, S. Ruiz and M. Yus, *Tetrahedron Lett.*, **39**, 1397 (1998); [b] C. Gómez, S. Ruiz and M. Yus, *Tetrahedron*, **55**, 7017 (1999).
- [8] For reviews, see: [a] C. Nájera and M. Yus, *Trends Org. Chem.*, **2**, 155 (1991); [b] C. Nájera and M. Yus, *Recent Res. Devel. Org. Chem.*, **1**, 67 (1997).
- [9] Last paper on this topic from our laboratory: E. Lorenzo, F. Alonso and M. Yus, *Tetrahedron Lett.*, **41**, 1661 (2000).
- [10] For a review, see: M. Yus and F. Foubelo, *Rev. Heteroatom Chem.*, **17**, 73 (1997).
- [11] Last paper on this topic from our laboratory: T. Soler, A. Bachki, L. R. Falvello, F. Foubelo and M. Yus, *Tetrahedron: Asymmetry*, **11**, 493 (2000).
- [12] J. Almena, F. Foubelo and M. Yus, *Tetrahedron*, **51**, 3351 (1995).
- [13] J. Almena, F. Foubelo and M. Yus, *Tetrahedron*, **51**, 3365 (1995).
- [14] Leading references: [a] A. Hirao, I. Hattori, K. Yamaguchi and S. Nakahama, *Synthesis*, 461 (1982); [b] D. J. Hart, K. Nakai, D. G. Thomas and T.-K. Yang, *J. Org. Chem.*, **48**, 289 (1983); [c] G. Cainelli and M. Panunzio, *J. Am. Chem. Soc.*, **110**, 6879 (1988); [d] G. Cainelli, D. Giacomini, P. Galletti and A. Gaiba, *Synlett*, 657 (1996); [e] B. Wunsch and S. Nerdiger, *Eur. J. Org. Chem.*, 503 (1999).
- [15] See, for instance: N. Misra, R. Luthra, K.-L. Singh and S. Kumar, in *Comprehensive Natural Products Chemistry*, Vol 4, D. Barton, K. Nakanishi and O. Meth-Cohn, eds, Elsevier, Amsterdam, 1999, pp 25-59.