

# 1,7-Electrocyclisation Reactions of 2-Azaheptatrienyl Lithium Compounds: Synthesis of 1-Acyl-2,3-dihydroazepines

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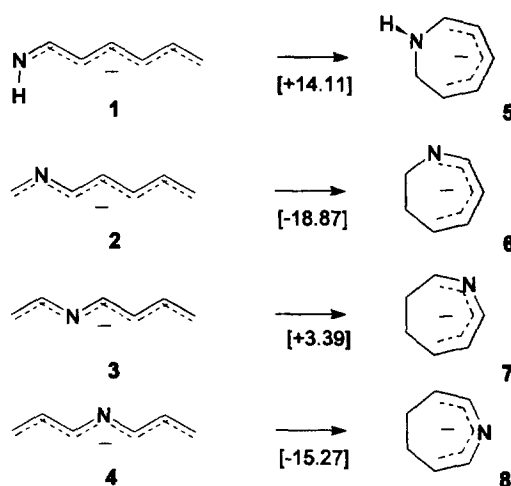
**Abstract:** Deprotonation of the 2-aza-2,4,6-heptatriene **14** at  $-78^{\circ}\text{C}$  using lithium diisopropylamide as base yields the 2-azaheptatrienyl lithium compound **15**. During warming up to  $40^{\circ}\text{C}$  **15** undergoes a 1,7-electrocyclisation to afford the 1-azacycloheptadienyl lithium compound **16**, as predicted by quantum chemical *ab initio* calculations. This cyclisation reaction was monitored in detail by  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopy. Subsequent treatment with various acylating agents provides access to several 1-acyl-2,3-dihydroazepines **17**. A X-ray diffraction structure determination of derivative **17a** shows a *trans* arrangement of the two aromatic substituents in 2- and 3-position, indicating a conrotatory mode of the ring closure reaction. The rotational barrier for the amide rotation in **17b** was determined to 15.4 kcal/mol.

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Electrocyclisation reactions of conjugated acyclic compounds offer a convenient pathway to carbo- and heterocyclic compounds.<sup>3-7</sup> In most cases, neutral precursors are used for the cyclisation reactions. Ring formation starting from a few polyenyl- and heteropolyenyl metal compounds is also reported in the literature.<sup>8-15</sup> In these latter reactions, the relative thermodynamic stability of the cyclic and acyclic compounds seems to direct the mode of the electrocyclic reaction (ring closure versus ring opening) since the influence of kinetic factors is obviously low. Recently, we have demonstrated on the basis of simple perturbation theory arguments, which were supported by quantum chemical *ab initio* calculations, that for cationic and organometallic heteropolyenyl systems the nature and position of the heteroatom within the chain mainly determine the relative energy of such systems.<sup>16</sup> For heteropolyenyl anions (organometallic systems), high relative energy has to be expected, if the electronegative heteroatom is located at an even position within the chain. Such systems should undergo cyclisation reactions to form the heterocyclic analogue. In contrast, systems with the electronegative heteroatom in an odd position have low relative energies and therefore should not cyclize. It may even be expected that the acyclic system may be formed by a ring opening process from the corresponding cyclic isomer. Qualitatively, such systems are low in energy, if the electronegative heteroatom is located in a position with a big HOMO coefficient, and they are high in energy, if the electronegative heteroatom is placed in a nodal position of the HOMO. Examples for such conversions can be found in the literature. For instance, Hunter and Steiner described in 1975<sup>8</sup> the 1,5-electrocyclisation of 2-azapentadienyl

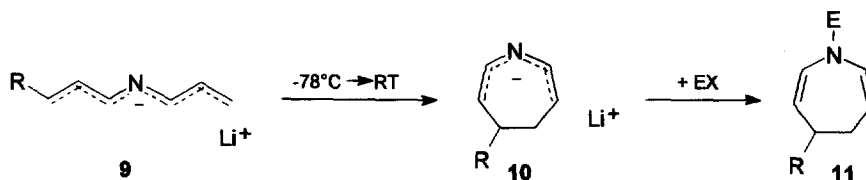
lithium compounds to form dihydropyrroline derivatives. On the other hand, according to studies of Kloosterziel *et al.*<sup>9</sup> 1-oxaheptatrienyl lithium compounds do not cyclize to the corresponding seven-membered ring anion.

These rules have been applied to the isomeric series of azaheptatrienyl anions.<sup>16</sup> According to our *ab initio* calculations,<sup>17</sup> the 1-aza- (1) and the 3-azaheptatrienyl anion (3) have low relative energies, whereas the isomeric 2-aza- (2) and 4-azaheptatrienyl anions (4) are higher in energy and therefore show also enhanced reactivity (Figure 1). In ring closure and ring opening reactions, the relative position of the heteroatom within the conjugated part of the molecule is shifted by one place, either from a "favorable" to a "unfavorable" place or vice versa. In figure 1, the calculated heats of reaction demonstrate these shifts.



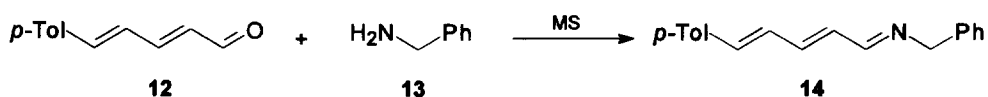
**Figure 1.** Calculated Heats of Reactions for the Electrocyclisation Reaction of Azaheptatrienyl Anions to Azacycloheptadienyl Anions (*ab initio* M2/6-31+G\*//6-31+G\*-results).

Recently, we have reported our experimental results on the ring closure reactions of 4-azaheptatrienyl lithium compounds, which were based on our theoretical predictions.<sup>16</sup>

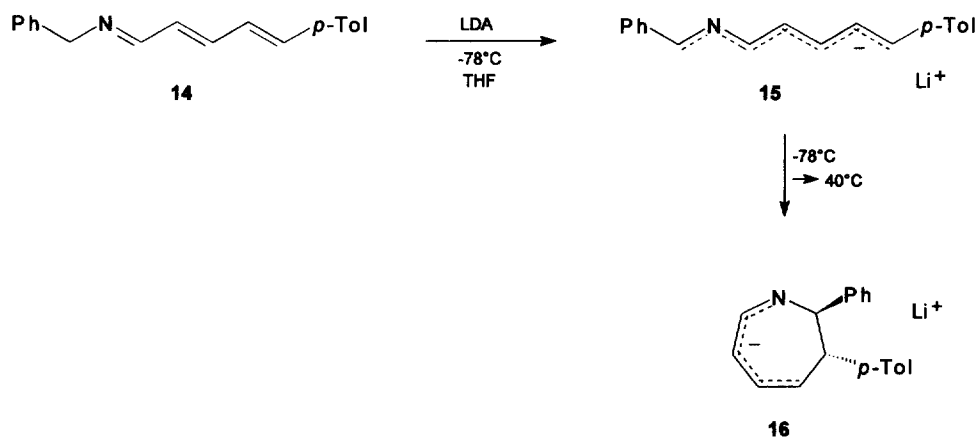


In this paper, we describe the synthesis of a hitherto unknown 2-azaheptatrienyl lithium compound and its cyclisation reaction.

As starting material for the synthesis of a 2-azaheptatrienyl lithium derivative 1-phenyl-7-*p*-tolyl-2-azahepta-2,4,6-triene (**14**) was used, which is readily available by condensation of benzylamine (**13**) with 5-*p*-tolyl-2,4-pentadienal (**12**) in the presence of molecular sieves (4Å).



Deprotonation of the 2-azaheptatriene **14** using lithium diisopropylamide (LDA) in THF at  $-78^{\circ}\text{C}$  yields a deep blue solution. We assign this deep color to the formation of the lithium compound **15** having a widely delocalised  $\pi$ -system. This solution is allowed to warm up to room temperature and is then stirred for about 3h at  $40^{\circ}\text{C}$ . During this time, the color of the solution changes from deep blue to dark green. We interpret this change in color as an indication for the proceeding ring closure reaction, leading to a shorter conjugated  $\pi$ -system.

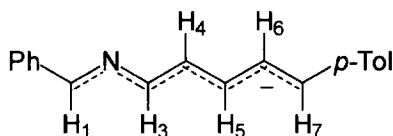


Low-temperature NMR spectroscopy is ideally suited to monitor the progress of the reaction. The  $d_8$ -THF solution of the lithium compound **15** is prepared by use of the syringe technique directly in the NMR tube.

From the  $^1\text{H}$  NMR spectrum, measured at  $-50^{\circ}\text{C}$ , it is easily recognized that the lithium compound **15** is

present in only one of the many possible conformations. From the coupling constants of the olefinic protons (10.4–14.3 Hz) the all-trans conformation is evident<sup>18,19</sup>. The <sup>13</sup>C NMR data give a very good indication of the electron distribution in this hetero system. Thus, the signals of the carbon atoms C-1, C-3, C-5 and C-7 are found at relatively high field, corresponding to big HOMO coefficients. In contrast, the signals of carbon atom C-4 and C-6 appear at low field (nodal positions of these atoms). The influence of the nitrogen atom in 2-position (node) is relatively small; it leads to relative downfield shifts of 15 ppm for the carbon atoms C-1 and C-3, which are directly bound to nitrogen, compared to the shifts of C-5 and C-7, which are further away from the heteroatom. This indicates mainly inductive effects, dominating over mesomeric influence. The alternating electron distribution is also observable in the <sup>1</sup>H NMR spectrum, although less significantly. (Table 1)

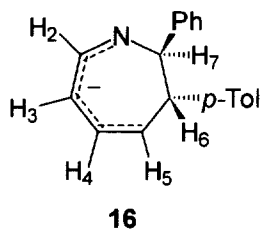
**Table 1:** NMR Chemical Shifts for 1-Phenyl-7-*p*-tolyl-2-aza-hepta-trienyl Lithium (**15**) (d8-THF, -50°C).



**15**

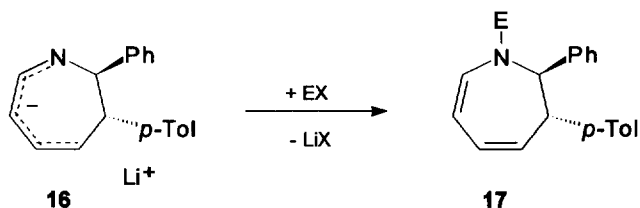
	(1)-CH	(3)-CH	(4)-CH	(5)-CH	(6)-CH	(7)-CH
<sup>1</sup> H	6.85 (s)	6.59 (d) <i>J</i> <sub>34</sub> = 10.4 Hz	6.45 (dd) <i>J</i> <sub>45</sub> = 12.4 Hz	5.28 (dd) <i>J</i> <sub>56</sub> = 12.2 Hz	6.72 (dd) <i>J</i> <sub>67</sub> = 14.3 Hz	5.37 (d)
<sup>13</sup> C	123.47	121.93	138.15	104.55	133.26	107.71

Above -20 °C new signals appear, which are due to the formation of the cyclic lithium compound **16**. At 30°C, the cyclic compound **16** is formed completely without any indication of byproducts. This cyclic system now incorporates the π-system of a 1-azapentadienyl anion. Therefore, the signals of the protons 3-H and 5-H appear at high field, the signals for 2-H and 4-H at low field. The <sup>13</sup>C NMR spectrum again indicates alternating electron distribution for the carbon atoms C-2 to C-5 (Table 2). In this system, the nitrogen atom is able to participate actively in the conjugated system. The chemical shift of carbon atom C-3 (90.40 ppm) is a good indication for its electron polarizing effect.

**Table 2:** NMR Chemical Shifts for 7-Phenyl-6-*p*-tolyl-1-aza-cycloheptadienyl Lithium (**16**) (d8-THF, -50°C).

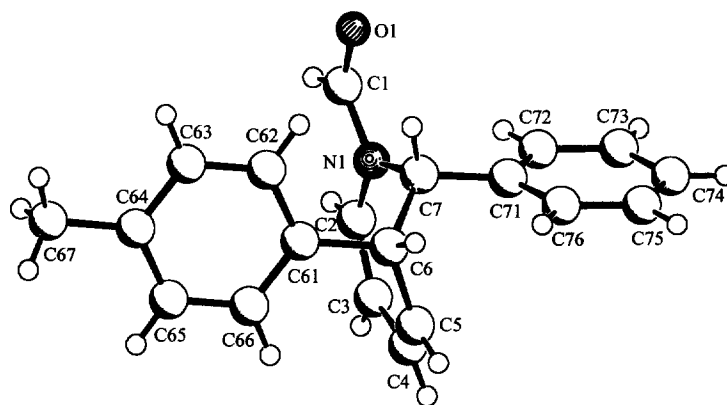
	(2)-CH	(3)-CH	(4)-CH	(5)-CH	(6)-CH	(7)-CH
<sup>1</sup> H	6.80 (d) <i>J</i> <sub>23</sub> = 7.3 Hz	4.13 (dd) <i>J</i> <sub>34</sub> = 7.7 Hz	5.93 (dd) <i>J</i> <sub>45</sub> = 9.7 Hz	4.80-4.86 (m)	3.91-3.92 (m)	4.80-4.86 (m)
<sup>13</sup> C	153.13	90.40	133.02	110.60	60.15	73.97

On a preparative scale, the cyclic lithium compound **16**, obtained by warming up of the solution of the 2-azaheptatrienyl lithium compound **15**, may be trapped by various acylating electrophiles. The reactions occur regioselectively at the nitrogen atom and produce the 1-acyl-2,3-dihydroazepines **17** in moderate to satisfactory yields.

**Table 3.** Substitution Patterns and Yields of the 1-Acyl-2,3-dihydroazepines **17**.

No.	EX	E	Yield (%)
<b>17a</b>	MeOCHO	CHO	54
<b>17b</b>	ClCO <sub>2</sub> Me	CO <sub>2</sub> Me	42
<b>17c</b>	ClCO <sub>2</sub> Et	CO <sub>2</sub> Et	27
<b>17d</b>	PhCOCl	PhCO	29

An interesting stereochemical question concerns the relative position of the two aromatic substituents at C-6 and C-7 (crystallographic numbering) of the seven-membered ring. A X-Ray structure determination of 1-formyl-2-phenyl-3-tolyl-2,3-dihydroazepine (**17a**) clearly shows the *trans* arrangement of these two substituents. This is in good agreement with the predictions of the Woodward-Hoffmann rules, demanding a conrotatory mode for the electrocycloislation. As the *trans* arrangement is the thermodynamically more favorable stereochemistry, the possibility of a thermodynamically controlled bond rotation may not be excluded. Compound **17d**, 1-benzoyl-2-phenyl-3-tolyl-2,3-dihydroazepine, shows the same relative stereochemistry in the crystalline state (X-ray).<sup>20</sup>



SCHAKAL

**Figure 2.** SCHAKAL-Plot<sup>21</sup> of **17a** with crystallographic numbering.

The NMR spectra of the 2,3-dihydroazepines **17b-17d** indicate dynamic behavior of these substances in solution at room temperature, mainly in the amide part of the molecules. At -50 °C two conformers are present in the reaction mixture (for the ratios see Experimental). The 1-formyl-2,3-dihydroazepine **17a** forms even at room temperature an equilibrating mixture of two conformers. For **17b**, the rotational barrier for the amide rotation in this enamide type molecule is estimated to 15.4 kcal/mol ( $T_c \sim 330$  K; 600 MHz <sup>1</sup>H NMR). This value is low compared to amides,<sup>22</sup> due to the extra conjugation in the amine part of the molecule. At lower temperatures indications for dynamic processes involving the seven membered ring system are observed.

On the basis of simple rules, which are supported by quantum chemical *ab initio* calculations, we have

developed a new synthetic route to various 1-acyl-2,3-dihydroazepine derivatives **17** by electrocyclic ring closure reactions. Previously, such systems were only accessible by ring enlargement reactions<sup>23,24</sup> or from addition reactions to 1*H*-azepines.<sup>25,26</sup> A dimeric derivative was obtained by deprotonation of a 3*H*-azepine and subsequent trapping with acetyl chloride.<sup>27</sup> Our low temperature NMR experiments indicate complete deprotonation of the easily obtainable starting materials and their quantitative ring formation under very mild conditions. The final quenching reaction with acylating agents proceeds regioselectively leading to the seven membered ring systems **17**.

## EXPERIMENTAL

IR: Perkin Elmer PE 298 or Nicolet 5DXC FT-IR. - MS: Finnigan MAT C 312. - <sup>1</sup>H NMR: Bruker WM 360 (360 MHz) and Varian (600 MHz), internal reference tetramethylsilane. - <sup>13</sup>C NMR: Bruker WM 360 (90.56 MHz) and Varian Unity 600 (150.84 MHz), internal reference tetramethylsilane. - CHN: Perkin-Elmer CHN-Analysator 240. - Chromatography: Kieselgel 60 (Merck), 0.040-0.063 mm. - Melting points are uncorrected. - Anhydrous conditions requiring reactions are performed in glass ware, which is thoroughly dried by repeated heating under argon and subsequent evacuation. - THF is distilled from sodium-potassium-alloy and benzophenone. Diisopropylamine is distilled from potassium hydroxide and stored over potassium hydroxide.

*l*-Phenyl-7-*p*-tolyl-2-aza-heptatriene (**14**): A solution of 0.95 g (5.5 mmol) 5-*p*-tolyl-2,4-pentadienal<sup>28</sup> **12** in dichloromethane (20 ml) is added to 15 g of molecular sieves (4 Å). While stirring at 0°C 0.60 ml (5.5 mmol) of benzylamine **13** are added dropwise. After stirring the reaction mixture for a period of 0.5 h at 0 °C the molecular sieves are filtered off and washed with dichloromethane. The solvent is removed *in vacuo*. The crude product may be used without further purification. Recrystallisation from n-hexane/dichloromethane yields yellow crystals. Yield (crude): 1.18 g (82 %), yellow solid; m.p.: 89 °C.- <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ = 2.26 (s, 3H, Ph-CH<sub>3</sub>), 4.60 (s, 2H, 1-H), 6.41 (dd, 1H, *J* = 9.1 Hz, *J* = 14.8 Hz), 6.61-6.83 (m, 3H), (4-H, 5-H, 6-H, 7-H), 7.06-7.28 (m, 9H, arom. H), 7.96 (d, 1H, *J* = 9.1 Hz, 3-H).- <sup>13</sup>C NMR (75.47 MHz, CDCl<sub>3</sub>): δ = 21.28 (Ph-CH<sub>3</sub>), 65.28 (CH<sub>2</sub>-N), 126.64, 126.70, 126.84, 127.92, 128.39, 129.33, 131.15 (arom. C, CH, CH), 133.65 (C<sub>ipso</sub>), 136.81 (CH), 138.43, 139.21 (C<sub>ipso</sub>), 142.07 (CH), 163.34 (C=N).- IR (KBr):  $\tilde{\nu}$  = 3080 cm<sup>-1</sup> (vw, CH arom., olef.), 3060 (vw, CH arom., olef.), 3020 (m, CH arom., olef.), 2920 (vw, CH aliph.), 2880 (w, CH aliph.), 2850 (m, CH aliph.), 1625 (s, C=N), 1605 (s, C=C), 1565 (w), 1510 (m), 1490 (m), 1455 (m), 1435 (m), 1375 (w), 1345 (w), 1290 (vw), 1200 (w), 1155 (m), 1000 (vs), 980 (s), 845 (m); 805 (m), 745 (m), 730 (vs), 705 (s), 615 (w).- MS (70 eV); *m/z* (%): 261 (51) [M<sup>+</sup>], 170 (61) [M<sup>+</sup> - C<sub>7</sub>H<sub>7</sub>], 156 (49), 153 (47), 141 (45), 115 (46), 105 (39), 91 (100) [C<sub>7</sub>H<sub>7</sub><sup>+</sup>], 85 (43), 80 (36), 65 (58)

[C<sub>5</sub>H<sub>5</sub><sup>+</sup>], 51 (32).- C<sub>19</sub>H<sub>19</sub>N (261.4): calc. C 87.31 H 7.33 N 5.36 found C 87.40 H 7.33 N 5.66.

*General procedure for the synthesis of 1-acyl-2,3-dihydroazepine derivatives:* A solution of 0.2 g (0.766 mmol) of 1-phenyl-7-tolyl-2-azahepta-2,4,6-triene (**14**) in THF (5 ml) was added dropwise at -78°C over a period of 20 min to a solution of 0.840 mmol of lithium diisopropylamide (prepared in situ from 0.15 ml (1.14 mmol) of diisopropylamine and 0.52 ml (0.84 mmol) of 1.6M *n*-butyl lithium in *n*-hexane) in 20 ml of tetrahydrofuran (THF) with stirring. Stirring at -78°C was continued for 30 min. Then, the reaction mixture was warmed up to 40°C for 3h with stirring. After cooling to -40°C, the electrophile was added dropwise over a period of 20 min. After stirring for 16h at room temperature, the colorless reaction mixture was treated with 400 ml of petrol ether (b.p. 40-60°C). Precipitated lithium salt was removed by filtration over celite. The solvents were removed *in vacuo*. The crude reaction product was purified by column chromatography (SiO<sub>2</sub>) using petrol ether/ethyl acetate = 20:1 as eluent.

*1-Formyl-2-phenyl-3-tolyl-2,3-dihydroazepine (17a):* Following the general procedure, 0.09 g (1.50 mmol) of methyl formate were added to the reaction mixture. After removal of the solvents *in vacuo*, the colorless product (needles) was obtained after recrystallisation from diethyl ether. Yield: 0.12 g (54%); m.p. 108°C. At -50°C, the conformers A and B are found in the ratio A:B=1:0.8 by <sup>1</sup>H NMR integration.

**X-Ray diffraction analysis of 17a:**<sup>29</sup> A yellow block crystal C<sub>20</sub>H<sub>19</sub>NO (from diethyl ether), crystal size 0.4 x 0.3 x 0.3 mm<sup>3</sup>, was measured at -50°C by using an automatic CAD4 Diffractometer (Enraf-Nonius) with Cu-K<sub>α</sub> radiation (λ = 1.54178 Å) and a graphite monochromator. 3369 reflexions were collected in the range 5.58° << 2θ << 148.66° (scan speed variable 5.5 to 16.5°/min). Crystal system: Triclinic, space group *PT*, Z = 2, a = 8.698(1) Å, b = 9.385(1) Å, c = 10.250(1) Å, α = 69.74(1)°, β = 82.46(1)°, γ = 86.35(1)°; V = 778.0(1) Å<sup>3</sup>; Dx = 1.235 g·cm<sup>-3</sup>; μ = 5.9 cm<sup>-1</sup>, empirical absorption correction via ψ-scans. The structure was solved by direct methods (SHELXS-86 program<sup>30</sup>) using 3168 independent reflexions. After the addition of the hydrogen atoms (coupled with respect to position and temperature parameters to the corresponding carbon atoms) anisotropic refinement led to agreement factors R = 0.046 and wR<sup>2</sup> = 0.129 (2699 reflections with I<sub>0</sub> > 2.0σ(I<sub>0</sub>), 201 variable parameters, program SHELXL-93<sup>31</sup>). The molecular shape is presented in Fig. 2.

<sup>1</sup>H NMR (360 MHz, CDCl<sub>3</sub>): δ = 2.22 (s, 3H, Ph-CH<sub>3</sub>)<sup>A</sup>, 2.24 (s, 3H, Ph-CH<sub>3</sub>)<sup>B</sup>, 4.49-4.53 (m, 2H, 3-H)<sup>AB</sup>, 4.90 (d, 1H, J = 3.6 Hz, 2-H)<sup>B</sup>, 5.15-5.21 (m, 1H, 6-H)<sup>A</sup>, 5.32-5.34 (m, 1H, 6-H)<sup>B</sup>, 5.91-6.03 (m, 3H, 4-H<sup>A</sup>, 5-H<sup>B</sup>, 5-H<sup>A</sup>), 6.06-6.12 (m, 1H, 4-H)<sup>B</sup>, 6.22 (d, 1H, J = 4.3 Hz, 2-H)<sup>A</sup>, 6.44 (d, 1H, J = 9.5 Hz, 7-H)<sup>A</sup>, 6.90 (d, 1H, J = 8.1 Hz, 7-H)<sup>B</sup>, 6.97-7.06 (arom. H)<sup>AB</sup>. - <sup>13</sup>C NMR (90,56 MHz, CDCl<sub>3</sub>): δ = 20.95 (Ph-CH<sub>3</sub>), 49.67, 49.90 (C-3)<sup>AB</sup>, 57.87 (C-2)<sup>A</sup>, 64.78 (C-2)<sup>B</sup>, 108.66 (C-6)<sup>A</sup>, 110.60 (C-6)<sup>B</sup>, 125.35, 126.02, 126.17, 126.34, 126.40, 127.06, 127.57, 127.95, 128.13, 128.21, 129.13, 129.25, 129.54, 131.24 (arom. C, C-4<sup>A</sup>, C-5<sup>A</sup>, C-5<sup>B</sup>, C-7<sup>A</sup>, C-7<sup>B</sup>), 131.36 (C-4)<sup>B</sup>; 136.33, 136.44, 137.03, 137.95, 138.84, 139.32 (C<sub>ipso</sub>)<sup>AB</sup>, 162.35, 162.60 (C=O)<sup>AB</sup>. - IR (NaCl):  $\tilde{\nu}$  = 3040 cm<sup>-1</sup> (w,



CH arom., olef.), 3020 (w, CH arom., olef.), 2980 (vw, CH aliph.), 2910 (vw, CH aliph.), 1685 (vs, C=O), 1635 (vs, C=C), 1605 (s), 1505 (m), 1490 (vw), 1440 (m), 1345 (m), 1260 (s), 1230 (m), 1220 (m), 1190 (w), 1180 (m), 1160 (m), 1030 (vw), 1020 (vw), 930 (w), 895 (vw), 850 (m), 810 (m), 755 (m), 735 (vs), 705 (s), 640 (sh), 635 (m).- **MS** (70 eV);  $m/z$  (%) = 289 (86) [ $M^+$ ], 260 (62), 243 (61), 228 (54), 212 (75), 184 (87), 171 (100), 156 (90), 143 (87), 115 (82), 105 (77), 91 (83) [ $Tol^+$ ], 77 (69) [ $Ph^+$ ], 65 (78) [ $C_5H_5^+$ ], 57 (75).- **C<sub>20</sub>H<sub>19</sub>NO** (289.4): calc. C 83.01 H 6.62 N 4.84 found C 83.04 H 6.78 N 4.84

*1-Carbomethoxy-2-phenyl-3-tolyl-2,3-dihydroazepine (17b)*: Following the general procedure, 0.72 g (7.66 mmol) of methyl chloroformate were added to the reaction mixture. After work up and chromatographic purification of the yellow reaction mixture, the colorless product (needles) was obtained after recrystallisation from diethyl ether/n-hexane. Yield: 0.08 g (33%); m.p. 95°C. At -50°C, the conformers A and B are found in the ratio A:B=1:0.6 by  $^1H$  NMR integration.-  **$^1H$  NMR** (300 MHz, 223 K,  $CDCl_3$ ):  $\delta$  = 2.24 (s, 6H,  $Ph-CH_3$ )<sup>AB</sup>, 3.31 (s, 3H,  $OCH_3$ )<sup>B</sup>, 3.56 (s, 3H,  $OCH_3$ )<sup>A</sup>, 4.55-4.61 (m, 2H, 3-H)<sup>AB</sup>, 5.07-5.12 (m, 1H, 6-H)<sup>A</sup>, 5.13-5.18 (m, 1H, 6-H)<sup>B</sup>, 5.84-5.93 (m, 3H, 2-H, 4-H, 5-H)<sup>AB</sup>, 6.01-6.11 (m, 3H, 2-H, 4-H, 5-H)<sup>AB</sup>, 6.72 (d, 1H,  $J$  = 9.9 Hz, 7-H)<sup>A</sup>, 6.86 (d, 1H,  $J$  = 9.9 Hz, 7-H)<sup>B</sup>, 6.96-7.28 (m, 18H, arom. H)<sup>AB</sup>.-  **$^{13}C$  NMR** (90.56 MHz, 223 K,  $CDCl_3$ ):  $\delta$  = 21.04 ( $Ph-CH_3$ )<sup>B</sup>, 21.15 ( $Ph-CH_3$ )<sup>A</sup>, 48.76 (C-3)<sup>A</sup>, 48.95 (C-3)<sup>B</sup>, 53.48 ( $OCH_3$ )<sup>B</sup>, 53.92 ( $OCH_3$ )<sup>A</sup>, 59.50 (C-2)<sup>A</sup>, 60.47 (C-2)<sup>B</sup>, 108.24 (C-6)<sup>A</sup>, 108.72 (C-6)<sup>B</sup>, 125.73, 125.87, 126.14, 126.86, 126.94, 127.65, 127.72, 127.83, 127.98, 128.61, 128.80, 128.88, 130.36, 131.00 (arom. C, C-4, C-5, C-7)<sup>AB</sup>, 136.31, 136.37, 137.20, 137.55, 138.77, ( $C_{ipso}$ )<sup>AB</sup>, 155.01 (C=O)<sup>AB</sup>.- **IR** (NaCl):  $\tilde{\nu}$  = 3040  $cm^{-1}$  (vw, CH arom., olef.), 3010 (m, CH arom., olef.), 2960 (w, CH aliph.), 2940 (m, CH aliph.), 2820 (w, CH aliph.), 1710 (vs, C=O), 1635 (m, C=C), 1600 (s), 1505 (m), 1495 (w), 1430 (vs), 1335 (vs), 1315 (vs), 1295 (s), 1270 (vs), 1255 (sh), 1230 (m), 1170 (m), 1110 (m), 1080 (m), 1060 (m), 970 (w), 930 (m), 905 (vs), 805 (m), 775 (m), 760 (m), 740 (vs), 690 (s), 640 (m), 630 (m).- **MS** (70 eV);  $m/z$  (%) = 319 (80) [ $M^+$ ], 260 (61) [ $M^+ - CO_2CH_3$ ], 244 (63), 214 (65), 201 (100), 167 (71), 157 (74), 128 (69), 115 (74), 105 (72), 91 (76) [ $Tol^+$ ], 77 (64) [ $Ph^+$ ], 65 (47) [ $C_5H_5^+$ ], 59 (55) [ $CO_2CH_3^+$ ].- **C<sub>21</sub>H<sub>21</sub>NO<sub>2</sub>** (319.4): calc. C 78.97 H 6.63 N 4.39 found C 78.95 H 6.61 N 4.53

*1-Carbethoxy-2-phenyl-3-tolyl-2,3-dihydroazepine (17c)*: Following the general procedure, 0.83 g (7.66 mmol) of ethyl chloroformate were added to the reaction mixture. After work up and chromatographic purification of the yellow reaction mixture, the colorless product (needles) was obtained after recrystallisation from diethyl ether/n-hexane. Yield: 0.07 g (27%); m.p. 58°C. At -50°C, the conformers A and B are found in the ratio A:B=1:0.8 by  $^1H$  NMR integration.-  **$^1H$  NMR** (600 MHz, 223 K,  $CDCl_3$ ):  $\delta$  = 0.75 (t, 3H,  $J$  = 7.2 Hz,  $CH_3$ )<sup>A</sup>, 1.04 (t, 3H,  $J$  = 7.2 Hz,  $CH_3$ )<sup>B</sup>, 2.24 (s, 6H,  $Ph-CH_3$ )<sup>AB</sup>, 3.70-3.81 (m, 2H,  $CH_2$ )<sup>B</sup>, 3.92-4.04 (m, 2H,  $CH_2$ )<sup>A</sup>, 4.57-4.63 (m, 2H, 3-H)<sup>AB</sup>, 5.05 (dd, 1H,  $J$  = 9.4 Hz,  $J$  = 7.7 Hz, 6-H)<sup>A</sup>, 5.14 (dd, 1H,  $J$  = 9.4 Hz,  $J$  = 8.3 Hz, 6-H)<sup>B</sup>, 5.84-5.94 (m, 3H, 2-H, 4-

H, 5-H)<sup>AB</sup>, 6.05-6.12 (m, 3H, 2-H, 4-H, 5-H)<sup>AB</sup>, 6.72 (d, 1H, J = 9.4 Hz, 7-H)<sup>A</sup>, 6.83 (d, 1H, J = 9.4 Hz, 7-H)<sup>B</sup>, 6.96-7.29 (m, 18H, arom. H)<sup>AB</sup>. - <sup>13</sup>C NMR (150.93 MHz, 223 K, CDCl<sub>3</sub>): δ = 13.72 (CH<sub>3</sub>)<sup>B</sup>, 14.30 (CH<sub>3</sub>)<sup>A</sup>, 21.01 (Ph-CH<sub>3</sub>)<sup>B</sup>, 21.10 (Ph-CH<sub>3</sub>)<sup>A</sup>, 48.72 (C-3)<sup>B</sup>, 48.75 (C-3)<sup>A</sup>, 59.22 (C-2)<sup>A</sup>, 59.97 (C-2)<sup>B</sup>, 62.30 (CH<sub>2</sub>)<sup>B</sup>, 62.63 (CH<sub>2</sub>)<sup>A</sup>, 108.03 (C-6)<sup>A</sup>, 108.90 (C-6)<sup>B</sup>, 125.81, 125.97, 125.99, 126.16, 126.78, 126.91, 127.67, 127.77, 127.82, 128.00, 128.06, 128.57, 128.76, 128.82, 130.35, 130.83 (arom. C, C-4, C-5, C-7)<sup>AB</sup>, 136.28, 136.35, 137.39, 137.78, 138.76, 138.82 (C<sub>ipso</sub>)<sup>AB</sup>, 154.39, 154.41 (C=O)<sup>AB</sup>. - IR (NaCl):  $\tilde{\nu}$  = 3040 cm<sup>-1</sup> (vw, CH arom., olef.), 3010 (vw, CH arom., olef.), 2960 (m, CH aliph.), 2910 (vw, CH aliph.), 2850 (w, CH aliph.), 1700 (vs, C=O), 1635 (m) (C=C), 1600 (m), 1500 (w), 1435 (m), 1360 (s), 1330 (m), 1310 (m), 1290 (m), 1275 (s), 1255 (s), 1230 (m), 1160 (w), 1110 (s), 1055 (m), 930 (w), 905 (vw), 805 (vw), 760 (m), 690 (m), 605 (m). - MS (70 eV); m/z (%) = 333 (49) [M<sup>+</sup>], 260 (28) [M<sup>+</sup> - CO<sub>2</sub>C<sub>2</sub>H<sub>6</sub>], 256 (25), 228 (30), 215 (100), 184 (26), 168 (31), 143 (41), 115 (28), 105 (29), 91 (38) [Tol<sup>+</sup>], 78 (24) [C<sub>6</sub>H<sub>6</sub><sup>+</sup>], 65 (23) [C<sub>5</sub>H<sub>5</sub><sup>+</sup>]. - C<sub>22</sub>H<sub>23</sub>NO<sub>2</sub> (333.4): calc. C 79.25 H 6.95 N 4.20 found C 79.03 H 7.13 N 4.29

*l*-Benzoyl-2-phenyl-3-tolyl-2,3-dihydroazepine (**17d**): Following the general procedure, 0.39 g (2.80 mmol) of benzoyl chloride were added to the reaction mixture, prepared from 0.37 g (1.42 mmol) of **14**, dissolved in THF (5 ml), and 1.56 mmol of LDA (from 0.25 ml (1.91 mmol) of diisopropylamine and 0.98 ml (1.56 mmol) of 1.6M *n*-butyl lithium in *n*-hexane). After work up and chromatographic purification of the yellow reaction mixture, the colorless product (needles) was obtained after recrystallisation from diethyl ether/*n*-hexane. Yield: 0.15g (29%); m.p. 144°C. At -50°C, the conformers A and B are found in the ratio A:B=1:0.2 by <sup>1</sup>H NMR integration. - <sup>1</sup>H NMR (600 MHz, 223 K, CDCl<sub>3</sub>): δ = 2.23 (s, 3H, Ph-CH<sub>3</sub>)<sup>A</sup>, 2.38 (s, 3H, Ph-CH<sub>3</sub>)<sup>B</sup>, 4.48 (m, 1H, 3-H)<sup>B</sup>, 4.79 (m, 1H, 3-H)<sup>A</sup>, 5.01-5.04 (m, 1H, 6-H)<sup>A</sup>, 5.32 (m, 1H, 2-H)<sup>B</sup>, 5.45-5.48 (m, 1H, 6-H)<sup>B</sup>, 5.92-5.95 (m, 1H, 5-H)<sup>B</sup>, 6.03-6.07 (m, 1H, 5-H)<sup>A</sup>, 6.13-6.16 (m, 1H, 4-H)<sup>B</sup>, 6.22-6.25 (m, 1H, 4-H)<sup>A</sup>, 6.29 (d, 1H, J = 9.5 Hz, 7-H)<sup>A</sup>, 6.62 (m, 1H, 2-H)<sup>A</sup>, 6.81-6.83 (m, 1H, arom. H), 7.10-7.42 (m, 18H, arom. H, 7-H)<sup>AB</sup>. - <sup>13</sup>C NMR (150.93 MHz, 223 K, CDCl<sub>3</sub>): δ = 21.05 (Ph-CH<sub>3</sub>)<sup>A</sup>, 21.16 (Ph-CH<sub>3</sub>)<sup>B</sup>, 48.37 (C-3)<sup>A</sup>, 48.98 (C-3)<sup>B</sup>, 56.88 (C-2)<sup>A</sup>, 63.17 (C-2)<sup>B</sup>, 107.78 (C-6)<sup>A</sup>, 111.61 (C-6)<sup>B</sup>, 125.66 (C-5)<sup>B</sup>, 125.73 (arom. C)<sup>AB</sup>, 126.12 (C-5)<sup>A</sup>, 126.16, 126.81, 127.18, 127.54, 127.72, 128.02, 128.11, 128.62, 128.77, 128.94, 129.14, 129.61 (arom. C, C-7)<sup>AB</sup>, 130.40 (C-7)<sup>A</sup>, 130.95 (C-4)<sup>A</sup>, 131.02 (arom. C)<sup>AB</sup>, 132.12 (C-4)<sup>B</sup>, 134.02<sup>B</sup>, 134.11<sup>A</sup>, 136.54<sup>A</sup>, 136.98<sup>B</sup>, 137.11<sup>A</sup>, 137.18<sup>B</sup>, 138.00<sup>B</sup>, 138.33<sup>A</sup> (C<sub>ipso</sub>), 170.88<sup>A</sup>, 171.76<sup>B</sup> (C=O). - IR (KBr):  $\tilde{\nu}$  = 3040 cm<sup>-1</sup> (w, CH arom., olef.), 3005 (m, CH arom., olef.), 2920 (w, CH aliph.), 2900 (w, CH aliph.), 1650 (vs, C=O), 1620 (vs), 1585 (vs), 1570 (m), 1500 (m), 1485 (m), 1435 (m), 1390 (w), 1335 (vs), 1310 (m), 1295 (m), 1280 (m), 1250 (m), 1225 (w), 1165 (w), 1135 (m), 935 (m), 925 (m), 865 (s), 805 (m), 790 (m), 760 (m), 720 (m), 710 (s), 685 (vs), 670 (m). - MS (70 eV): m/z (%) = 365 (24) [M<sup>+</sup>], 324 (14), 288 (14) [M<sup>+</sup> - Ph], 260 (78) [M<sup>+</sup> - PhCO], 244 (36), 229 (21), 168 (26), 141 (26), 115 (23), 105 (100) [PhCO<sup>+</sup>], 91 (48) [Tol<sup>+</sup>], 77 (86) [Ph<sup>+</sup>], 57 (25). - C<sub>26</sub>H<sub>23</sub>NO (365.47): calc. C 85.45 H 6.34 N 3.83 found: C 85.20 H 6.23 N 3.99

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**REFERENCES AND NOTES**

1. Taken in part from Klötgen, S. Ph.D.Thesis, University of Münster, planned for 1996.
2. X ray Crystal Structure Determination.
3. a) Dauphin, G.; Jamilloux, B.; Kergomard, A.; Planat, D. *Tetrahedron* **1977**, *33*, 1129-1138. b) Dauphin, G.; David, L.; Jamilloux, B.; Kergomard, A.; Veschambre, H. *Tetrahedron* **1972**, *28*, 1055-1073.
4. Molina, P.; Pastor, A.; Vilaplana, M.J. *Tetrahedron* **1993**, *49*, 7769-7778.
5. George, M.V.; Mitra, A.; Sukumaran, K.B. *Angew. Chem.* **1980**, *92*, 1005-1014; *Angew. Chem.Int.Ed.Engl.* **1980**, *19*, 973.
6. Maynard, D.F.; Okamura, W.H. *J. Org. Chem.* **1995**, *60*, 1763-1771.
7. Cullen, K.E.; Sharp, J.T. *J. Chem. Soc. Perkin Trans. 1* **1995**, 2565-2579.
8. Hunter, D.H.; Steiner, R.P. *Can. J. Chem.* **1975**, *53*, 355-365.
9. Kloosterziel, H.; Van Drunen, J.A.A. *Rec. Trav. Chim.* **1970**, *89*, 667-672.
10. Kloosterziel, H.; Van Drunen, J.A.A.; Galama, P. *J. Chem. Soc. Chem. Commun.* **1969**, 885.
11. Bates, R.B.; Deines, W.H.; McCombs, D.A.; Potter, D.E. *J. Am. Chem. Soc.* **1969**, 4608.
12. Bates, R.B., Ogle, C.A. *Carbanion Chemistry*, Springer-Verlag, Berlin, 1983, 72-74.
13. Klärner, F.G.; Yaslak, S.; Drewes, R.; Gesenberg, C.; Peter, M. *Liebigs Ann.* **1995**, 203-210.
14. Steglich, W.; Engel, N. *Angew. Chem.* **1978**, *90*, 719-720; *Angew. Chem.Int.Ed.Engl.* **1978**, *17*, 676.
15. Huisgen, R. *Angew. Chem.* **1980**, *92*, 979-1005; *Angew. Chem.Int.Ed.Engl.* **1980**, *19*, 947.
16. Klötgen, S.; Würthwein, E.-U. *Tetrahedron Letters* **1995**, *36*, 7065-7068.
17. GAUSSIAN 92, Revision B: Frisch, M.J.; Trucks, G.W.; Head-Gordon, M.; Gill, P.M.W.; Wong, M.W.; Foresman, J.B.; Johnson, B.G.; Schlegel, H.B.; Robb, M.A.; Replegle, E.S.; Gomperts, R.; Andres, J.L.; Raghavachari, K.; Binkley, J.S.; Gonzales, C.; Martin, R.L.; Fox, D.J.; DeFrees, D.J.; Baker, J.; Stewart,

- J.J.P.; and Pople, J.A.; Gaussian, Inc., Pittsburgh PA, 1992.
18. Yasuda, H.; Yamauchi, M.; Ohnuma, Y.; Nakamura, A. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1481-1491.
  19. Bates, R.B.; Brenner, S.; Cole, C.M.; Davidson, E.W.; Forsythe, G.D.; McCombs, D.A.; Roth, A.S. *J. Am. Chem. Soc.* **1973**, *95*, 926-927.
  20. Klötgen, S.; Hecht, J.; Fröhlich, R.; Würthwein, E.-U., unpublished.
  21. SCHAKAL-92: Keller, E., University of Freiburg, **1992**.
  22. Oki, M. *Applications of Dynamic NMR Spectroscopy to Organic Chemistry* (Methods in Stereochemical Analysis, Vol. 4, Ed. A. P. Marchand), VCH, Weinheim, 1985.
  23. Eberbach, W.; Carré, J.C. *Chem. Ber.* **1983**, *116*, 563-586.
  24. Klop, W.; Brandsma, L. *J. Chem. Soc. Chem. Commun.* **1983**, 988-989.
  25. Saito, K.; Kozaki, M.; Takahashi, K. *Heterocycles* **1990**, *31*, 1491-1496.
  26. Sasaki, T.; Kanematsu, K.; Yukimoto, Y. *J. Org. Chem.* **1972**, *37*, 890-894.
  27. Satake, K.; Hattori, T.; Kimura, M.; Kashino, S. *Acta Cryst. Sect. C* **1995**, *51*, 2707-2710.
  28. Bellassoued, M.; Salemkour, M. *Tetrahedron Letters* **1993**, *34*, 5281-5284.
  29. Further details of the crystal structure determination may be obtained from the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-76344 Eggenstein-Leopoldshafen 2, Federal Republic of Germany, on quoting the depository number CSD-405593, the names of the authors, and the journal citation.
  30. SHELXS-86: Sheldrick, G. M. *Acta Cryst. Sect. A* **1990**, *46*, 467.
  31. SHELXL-93: Sheldrick, G. M. Univ. Göttingen **1993**.

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