

# An Efficient Synthesis of Some New Azaspirocycloalkane Derivatives from 1-anilino-cycloalkanecarboxamide

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## Abstract

1-anilino-cyclohexanecarboxamides 2a-c were found to be a versatile precursors for the synthesis of five-, six- and seven-membered ring spiroheterocycles compounds 3-14. A general high yielding protocol for the synthesis of many functionalized spiro heterocyclic systems was presented.

**Keywords:** Azaspiroheterocycles; Cycloalkanones; Anilino-cyclohexane-1-carbonitrile; Spiro heterocyclic

## Introduction

Spiro-compounds form a group of generally less investigated compounds. However, recently growing efforts have been made to synthesize and characterize these compounds. Many spiro compounds possess very promising biological activities as anticancer agents [1,2], antibacterial agents [3,4], anticonvulsant agents [5-7], anti-tuberculosis agents [8], anti-Alzheimer's agents [9], pain-relief agents [10,11], anti-dermatitis agents [12] and antimicrobial agents [13,14]. In addition to their medical uses, some spiro-compounds have found other uses in the agricultural and industrial fields. For example, they are used as antifungal agents [15], pesticides [16], laser dyes [17] and electroluminescent devices [18]. Spiro compounds have also been recently used as antioxidants [19,20]. Furthermore, Nitrogen containing heterocyclic compounds constitute the largest portion of chemical entities, which are part of many natural products, fine chemicals, and biologically active pharmaceuticals vital for enhancing the quality of life [21]. Among a large variety of nitrogen containing heterocyclic compounds, heterocycles containing a spiro system are of interest because they constitute an important class of natural and non-natural products, many of which exhibit useful biological activities and clinical applications [21].

## Methods

All melting points were determined on a Koffler melting point apparatus and are uncorrected. <sup>1</sup>H-NMR spectra were recorded on a Bruker Avance 300 MHz spectrometer using TMS as internal reference (chemical shifts in  $\delta$ , ppm), and IR spectra were obtained on a Nicolet 710 FT-IR spectrometer (KBr,  $\nu_{\max}$  in  $\text{cm}^{-1}$ ).

## Synthesis of 1-anilino-cycloalkanecarboxamide (1-phenyl-aminocycloalkane-1-carboxylic acid amide 2a-c [22])

The nitrile 1 (0.1 mol) was dissolved in conc.  $\text{H}_2\text{SO}_4$  (50 ml) at  $\sim 2^\circ\text{C}$ , in a single necked flask with a  $\text{CaCl}_2$  trap. The reaction mixture was left at room temperature overnight (24 h). Water was added ( $\sim 150$  ml) to the precipitated dihydrogensulphate of amide and then the reaction mixture was neutralized with  $\text{Na}_2\text{CO}_3$ . The precipitated free amide 2a-c was filtered off, washed with water and air dried. Yield: 17 g (83%).

## Synthesis of biazaspiroheterocycles

**General procedure:** A mixture of compound 2 (0.01 mol) and the proper reagent: ethylchloroacetate; bromomalononitrile; chloroacetonitrile; ethylchloroformate; cyclopentanone and/or

cyclohexane (0.01 mol) was dissolved in MeOH (30 ml) then was treated with MeONa (0.01 mol). The reaction mixture was heated under reflux for 8 h, solvent was evaporated *invacuo* and the residual mass was triturated with petroleum ether (60-80). The formed solid was collected by filtration and recrystallized from the proper into the corresponding product 3-8.

## Synthesis of 6-phenyl-6,9-diazaspiro[4.5]decane-8,10-dione 3a-c

The reaction mixture was refluxed for 3 h; solvent was evaporated under reduced pressure, water was added and the formed solid was collected by filtration and recrystallized from aq. EtOH into white needles (Table 1).

## Synthesis of 8-amino-10-oxo-6-phenyl-6,9-diazaspiro[4.5]dec-7-ene-7-carbonitrile 4a-c

The reaction mixture was refluxed for 4 h; solvent was evaporated under reduced pressure, the formed solid was collected and recrystallized from aq. EtOH into pale yellow crystals (Table 1).

## Synthesis of 8-amino-6-phenyl-6,9-diazaspiro[4.5]dec-7-en-10-one 5a-c

The reaction mixture was refluxed for 3 h; solvent was evaporated under reduced pressure, water was added, the formed solid was filtered off and recrystallized from aq. EtOH into white crystals (Table 1).

## Synthesis of 1-phenyl-1,3-diazaspiro[4.4]nonane-2,4-dione 6a-c

The reaction mixture was refluxed for 3 h; solvent was evaporated under reduced pressure, the formed solid was collected and recrystallized from MeOH into brownish crystals (Table 1).

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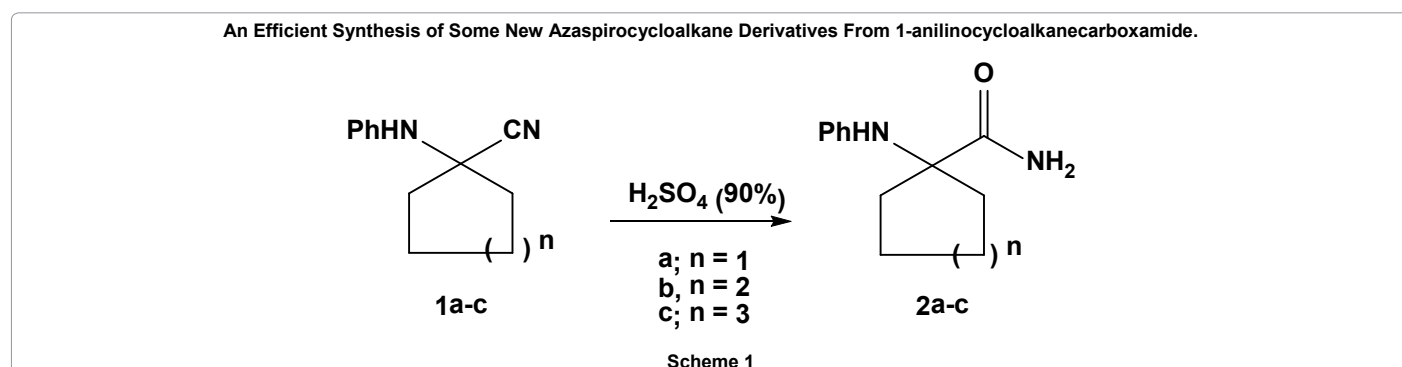
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Comp. No	Mp (°C)*	M. F. (M.W.)	IR (KBr, v, cm <sup>-1</sup> )	<sup>1</sup> H-NMR (DMSO, ppm)
2a	162-163 (161) [22]	C <sub>12</sub> H <sub>16</sub> N <sub>2</sub> O (204.26)	3395, 3308, 3248 (NH <sub>2</sub> , NH), 1674 (CO).	10.21(br, 1H, NH); 7.80-7.44(m, 5H, CH-arom.), 5.35-5.22(br, 2H, NH <sub>2</sub> ), 1.22-0.96(m, 8H, cyclic CH <sub>2</sub> ).
2b	146-150 (148-149) [23]	C <sub>13</sub> H <sub>8</sub> N <sub>2</sub> O (218.27)	3390, 3302 (NH <sub>2</sub> ), 3245 (NH), 16740 (CO).	10.25(br, 1H, NH); 7.77-7.45(m, 5H, CH-arom.), 5.38-5.24(br, 2H, NH <sub>2</sub> ), 1.24-0.96(m, 10H, cyclic CH <sub>2</sub> ).
2c	173-175 (141-142) [24]	C <sub>14</sub> H <sub>20</sub> N <sub>2</sub> O (232.32)	3388, 3310, 3242 (NH <sub>2</sub> , NH), 16748(CO).	10.21(br, 1H, NH); 7.80-7.48(m, 5H, CH-arom.), 5.41-5.30(br, 2H, NH <sub>2</sub> ), 1.28-0.90(m, 12H, cyclic CH <sub>2</sub> ).
3a	172-174	C <sub>14</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub> (244.28)	3280(NH), 1691, 1670(2CO)	10.65(br, 1H, NH); 7.70-7.43(m, 5H, CH-arom.), 3.16(s, 2H, CH <sub>2</sub> ), 1.26-0.95(m, 8H, cyclic CH <sub>2</sub> ).
3b	163-165 (160-163) [25]	C <sub>15</sub> H <sub>18</sub> N <sub>2</sub> O <sub>2</sub> (258.31)	3277(NH), 1685, 1675(2CO)	10.55(br, 1H, NH); 7.75-7.45(m, 5H, CH-arom.), 3.05(s, 2H, CH <sub>2</sub> ), 1.25-0.92(m, 10H, cyclic CH <sub>2</sub> ).
3c	178-180	C <sub>16</sub> H <sub>20</sub> N <sub>2</sub> O <sub>2</sub> (272.34)	3287(NH), 1696, 1678(2CO)	10.52(br, 1H, NH); 7.72-7.45(m, 5H, CH-arom.), 3.12(s, 2H, CH <sub>2</sub> ), 1.30-0.92(m, 12H, cyclic CH <sub>2</sub> ).
4a	212-214	C <sub>15</sub> H <sub>16</sub> N <sub>4</sub> O (268.31)	3395, 3318, 3283(NH <sub>2</sub> , NH); 2202(CN); 1682(CO).	10.82(br, 1H, NH); 7.82-7.53(m, 5H, CH-arom.); 5.82-5.68(br, 2H, NH <sub>2</sub> ); 1.21-0.92(m, 8H, cyclic CH <sub>2</sub> ).
4b	202-204	C <sub>16</sub> H <sub>18</sub> N <sub>4</sub> O (282.28)	3388, 3320, 3290(NH <sub>2</sub> , NH); 2212(CN); 1675(CO).	10.53(br, 1H, NH); 7.75-7.40(m, 5H, CH-arom.); 5.80-5.68(br, 2H, NH <sub>2</sub> ); 1.20-0.90(m, 10H, cyclic CH <sub>2</sub> ).
4c	196-198	C <sub>17</sub> H <sub>20</sub> N <sub>4</sub> O (296.32)	3390, 3302, 3284(NH <sub>2</sub> , NH); 2206(CN); 1681(CO).	10.62(br, 1H, NH); 7.80-7.45(m, 5H, CH-arom.); 5.88-5.72(br, 2H, NH <sub>2</sub> ); 1.35-0.88(m, 12H, cyclic CH <sub>2</sub> ).
5a	192-195	C <sub>14</sub> H <sub>17</sub> N <sub>3</sub> O	3378, 3303, 3268(NH <sub>2</sub> , NH); 1675(CO).	10.21(br, 1H, NH); 7.72-7.40(m, 5H, CH-arom.); 6.60(d, 1H, =CH); 5.65-5.52(br, 2H, NH <sub>2</sub> ); 1.21-0.95(m, 8H, cyclic CH <sub>2</sub> ).
5b	198-200	C <sub>15</sub> H <sub>19</sub> N <sub>3</sub> O	3388, 3319, 3283(NH <sub>2</sub> , NH); 1677(CO).	10.52(br, 1H, NH); 7.75-7.45(m, 5H, CH-arom.); 6.55(d, 1H, =CH); 5.60-5.51(br, 2H, NH <sub>2</sub> ); 1.25-0.93(m, 10H, cyclic CH <sub>2</sub> ).
5c	190-193	C <sub>16</sub> H <sub>21</sub> N <sub>3</sub> O	3383, 3309, 3277(NH <sub>2</sub> , NH); 1678(CO).	10.28(br, 1H, NH); 7.76-7.42(m, 5H, CH-arom.); 6.62(d, 1H, =CH); 5.66-5.55(br, 2H, NH <sub>2</sub> ); 1.28-0.90(m, 12H, cyclic CH <sub>2</sub> ).
6a	202-205	C <sub>13</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub> (230.26)	3284(NH), 1668(CO).	10.48(br, 1H, NH); 7.78-7.45(m, 5H, CH-arom.); 1.22-0.95(m, 8H, cyclic CH <sub>2</sub> ).
6b	211-213	C <sub>14</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub> (244.27)	3274(NH), 1676(CO).	10.43(br, 1H, NH); 7.81-7.47(m, 5H, CH-arom.); 1.25-0.95(m, 10H, cyclic CH <sub>2</sub> ).
6c	212-214	C <sub>15</sub> H <sub>18</sub> N <sub>2</sub> O <sub>2</sub> (258.28)	3278(NH), 1665(CO).	10.40(br, 1H, NH); 7.75-7.45(m, 5H, CH-arom.); 1.28-0.93(m, 12H, cyclic CH <sub>2</sub> ).
7a	241-243	C <sub>17</sub> H <sub>21</sub> NO <sub>2</sub> (271.35)	1732(CO).	7.79-7.45(m, 5H, CH-arom.); 1.45-0.93(m, 16H, cyclic CH <sub>2</sub> ).
7b	246-248	C <sub>18</sub> H <sub>23</sub> NO <sub>2</sub> (285.36)	1740(CO).	7.82-7.47(m, 5H, CH-arom.); 1.50-0.90(m, 18H, cyclic CH <sub>2</sub> ).
7c	250-252	C <sub>19</sub> H <sub>25</sub> NO <sub>2</sub> (299.37)	1738(CO).	7.75-7.43(m, 5H, CH-arom.); 1.55-0.91(m, 18H, cyclic CH <sub>2</sub> ).
8a	305-307	C <sub>20</sub> H <sub>16</sub> N <sub>2</sub> O <sub>3</sub> (334.36)	3289(NH), 1733(CO), 1678(CO).	10.21(br, 1H, NH); 7.95-7.40(m, 9H, CH-arom.); 1.21-0.95(m, 8H, cyclic CH <sub>2</sub> ).
8b	308-310	C <sub>21</sub> H <sub>20</sub> N <sub>2</sub> O <sub>3</sub> (348.37)	3279(NH), 1730(CO), 1668(CO).	10.25(br, 1H, NH); 7.90-7.42(m, 9H, CH-arom.); 1.25-0.93(m, 10H, cyclic CH <sub>2</sub> ).
8c	310-312	C <sub>22</sub> H <sub>22</sub> N <sub>2</sub> O <sub>3</sub> (362.37)	3295(NH), 1741(CO), 1672(CO).	10.18(br, 1H, NH); 7.88-7.41(m, 9H, CH-arom.); 1.28-0.90(m, 12H, cyclic CH <sub>2</sub> ).
9a	182-184	C <sub>15</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub> (254.28)	2203(CN), 1682(CO).	7.77-7.45(m, 5H, CH-arom.); 6.15(s, 1H, CH); 1.22-0.94(m, 8H, cyclic CH <sub>2</sub> ).
9b	180-183	C <sub>16</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub> (268.29)	2210(CN), 1677(CO).	7.75-7.45(m, 5H, CH-arom.); 5.98(s, 1H, CH); 1.25-0.94(m, 10H, cyclic CH <sub>2</sub> ).
9c	188-190	C <sub>17</sub> H <sub>18</sub> N <sub>2</sub> O <sub>2</sub> (282.30)	2205(CN), 1676(CO).	7.80-7.47(m, 5H, CH-arom.); 6.06(s, 1H, CH); 1.30-0.95(m, 12H, cyclic CH <sub>2</sub> ).
10a	220-222	C <sub>15</sub> H <sub>17</sub> N <sub>3</sub> O <sub>2</sub> (271.31)	3380, 3312, 3282(NH <sub>2</sub> , NH); 1675(CO).	9.98(br, 1H, NH), 7.77-7.45(m, 5H, CH-arom.); 6.18-6.12(br, 2H, NH <sub>2</sub> ); 5.56(s, 1H, =CH); 1.20-0.92(m, 8H, cyclic CH <sub>2</sub> ).
10b	225-228	C <sub>16</sub> H <sub>19</sub> N <sub>3</sub> O <sub>2</sub> (285.32)	3395, 3310, 3285(NH <sub>2</sub> , NH); 1677(CO).	9.95(br, 1H, NH), 7.774-7.45(m, 5H, CH-arom.); 6.16-6.12(br, 2H, NH <sub>2</sub> ); 5.41(s, 1H, =CH); 1.25-0.92(m, 10H, cyclic CH <sub>2</sub> ).
10c	228-230	C <sub>17</sub> H <sub>21</sub> N <sub>3</sub> O <sub>2</sub> (299.33)	3383, 3313, 3277(NH <sub>2</sub> , NH); 1667(CO).	10.05(br, 1H, NH), 7.78-7.44(m, 5H, CH-arom.); 6.12-6.08(br, 2H, NH <sub>2</sub> ); 5.45(s, 1H, =CH); 1.32-0.95(m, 12H, cyclic CH <sub>2</sub> ).
11a	233-235	C <sub>21</sub> H <sub>18</sub> N <sub>2</sub> O	2222(CN); 1668(CO)	7.88-7.38(m, 10H, CH-arom.); 1.22-0.96(m, 8H, cyclic CH <sub>2</sub> ).
11b	230-232	C <sub>22</sub> H <sub>20</sub> N <sub>2</sub> O	2220(CN); 1666(CO)	7.82-7.40(m, 10H, CH-arom.); 1.26-0.95(m, 10H, cyclic CH <sub>2</sub> ).
11c	241-243	C <sub>23</sub> H <sub>22</sub> N <sub>2</sub> O	2214(CN); 1671(CO)	7.85-7.42(m, 10H, CH-arom.); 1.32-0.90(m, 12H, cyclic CH <sub>2</sub> ).
12a	251-253	C <sub>23</sub> H <sub>23</sub> N <sub>3</sub> O	3385, 3320, 3265(NH <sub>2</sub> , NH); 2205(CN); 1669(CO).	10.35(br, 1H, NH), 7.83-7.38(m, 10H, CH-arom.); 6.22-6.16(br, 2H, NH <sub>2</sub> ); 4.86(s, 1H, CH); 1.22-0.95(m, 8H, cyclic CH <sub>2</sub> ).
12b	250-253	C <sub>24</sub> H <sub>25</sub> N <sub>3</sub> O	3380, 3315, 3270(NH <sub>2</sub> , NH); 2211(CN); 1675(CO).	10.28(br, 1H, NH), 7.80-7.36(m, 10H, CH-arom.); 6.20-6.16(br, 2H, NH <sub>2</sub> ); 4.75(s, 1H, CH); 1.25-0.95(m, 10H, cyclic CH <sub>2</sub> ).
12c	258-260	C <sub>24</sub> H <sub>27</sub> N <sub>3</sub> O	3387, 3316, 3275(NH <sub>2</sub> , NH); 2218(CN); 1672(CO).	10.40(br, 1H, NH), 7.86-7.36(m, 10H, CH-arom.); 6.24-6.18(br, 2H, NH <sub>2</sub> ); 4.83(s, 1H, CH); 1.35-0.95(m, 12H, cyclic CH <sub>2</sub> ).

13a	244-246	C <sub>27</sub> H <sub>23</sub> NO <sub>2</sub> (393.47)	1778(CO).	8.15-7.30(m, 15H, CH-arom.); 1.20-0.95(m, 8H, cyclic CH <sub>2</sub> ).
13b	248-250	C <sub>28</sub> H <sub>25</sub> NO <sub>2</sub> (407.50)	1776(CO).	8.07-7.33(m, 15H, CH-arom.); 1.25-0.95(m, 10H, cyclic CH <sub>2</sub> ).
13c	255-257	C <sub>27</sub> H <sub>23</sub> NO <sub>2</sub> (421.53)	1773(CO).	8.12-7.32(m, 15H, CH-arom.); 1.32-0.91(m, 12H, cyclic CH <sub>2</sub> ).
14a	302-305	C <sub>27</sub> H <sub>25</sub> N <sub>2</sub> O (394.50)	3250(NH); 1770(CO).	10.25(s, 1H, NH); 8.05-7.38(m, 15H, CH-arom.); 6.42-6.40(s, 1H, =CH); 1.20-0.96(m, 8H, cyclic CH <sub>2</sub> ).
14b	303-305	C <sub>28</sub> H <sub>25</sub> N <sub>2</sub> O (408.53)	3243(NH); 1768(CO).	10.12(s, 1H, NH); 8.01-7.35(m, 15H, CH-arom.); 6.40-6.37(s, 1H, =CH); 1.25-0.95(m, 10H, cyclic CH <sub>2</sub> ).
14c	310-312	C <sub>29</sub> H <sub>30</sub> N <sub>2</sub> O (422.56)	3256(NH); 1775(CO).	10.38(s, 1H, NH); 8.12-7.40(m, 15H, CH-arom.); 6.55-6.52(s, 1H, =CH); 1.35-0.91(m, 12H, cyclic CH <sub>2</sub> ).

Table 1: Analytical and spectral data for the obtained compounds.



### Synthesis of 6-phenyl-6,12-diazadispiro[4.1.4.2]tridecan-13-one 7a-c

The reaction mixture was refluxed for 5 h; solvent was evaporated under reduced pressure, the formed solid was collected and recrystallized from aq. EtOH into white needles (Table 1).

### Synthesis of 6-phenyl-6,13-diazadispiro[4.1.5.2]tetradecan-14-one 8a-c

The reaction mixture was refluxed for 5 h; solvent was evaporated under reduced pressure, the formed solid was collected and recrystallized from aq. EtOH into white powder (Table 1).

### Synthesis of diazaspriroheterocycles 9-14

**General procedure:** A mixture of compound **1** (0.01 mol) and the proper reagent: ethylcyanoacetate; benzylidinemalononitrile and/or chalcone (0.01 mol) was dissolved in dioxane (60 ml) and was treated with solid K<sub>2</sub>CO<sub>3</sub> (~7 g) and TBAB [tetrabutylammonium bromide] (~25 mg). The reaction mixture was stirred at 60°C for 5 h, then cooled and the solid pot. Carbonate was filtered off, washed with dioxane (~10 ml). Dioxane layer was evaporated under reduced pressure and the formed slurry was triturated with petroleum ether (60-80) where compounds **9**, **11** and **13** respectively were formed in low yields (40-45%). Carbonate layer was dissolved in water, acidified with AcOH and left overnight and the formed solids were collected by filtration and were identified as compounds **10**, **12** and **14** respectively (yields: 20-25%).

## Results and Discussion

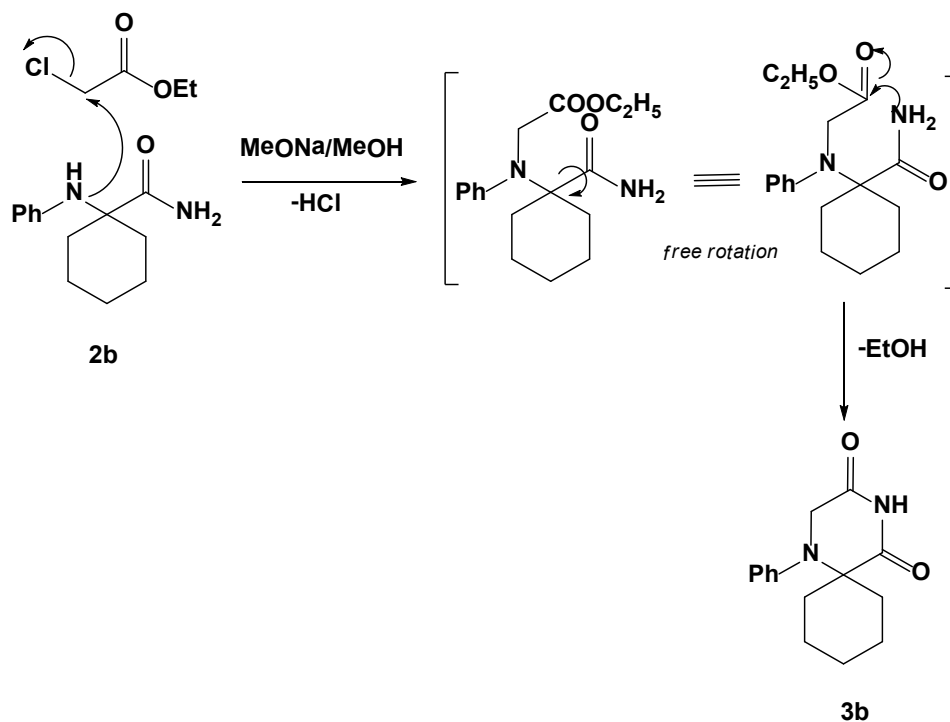
Considering the above reports, we wish to report here a simple, convenient, and high-yielding method for the synthesis of some new spiro nitrogen containing heterocyclic compounds starting with 1-anilinoalkylcarboxamide **2a-c** [22-27] which were obtained from the acid hydrolysis of 1-anilinoalkylcarboxamide **1a-c** (Scheme 1).

We have concentrated most of our work for the preparation of bioactive nitrogen-containing heterocycles, and we have already found that the reaction of 1-anilinoalkylcarboxamide **2b** with ethyl chloroacetate in refluxing MeOH in the presence of a catalytic amount of MeONa afforded 1-phenyl-1,4-diazaspiro[5.5]undecane-3,5-dione **3b** (Scheme 2).

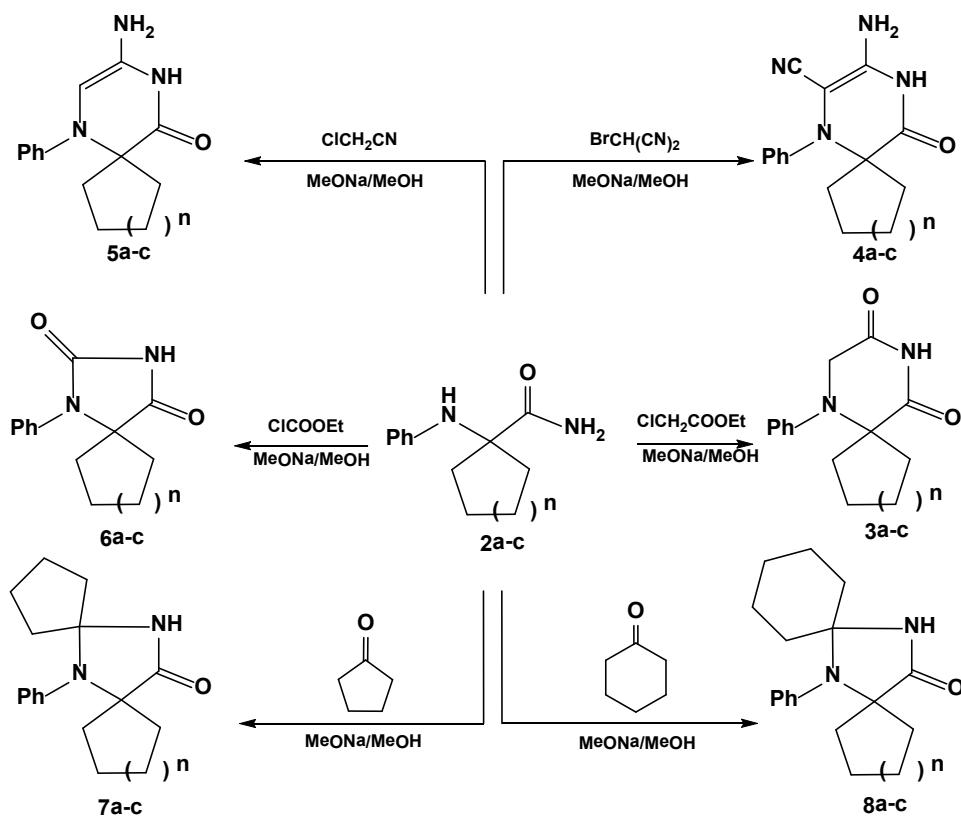
The reaction pathway was assumed to follow a preliminary nucleophilic attack of the secondary amine into the  $\alpha$ -halo ester with subsequent elimination of HCl molecule followed by another nucleophilic attack of the amino group onto the ester carbonyl group with subsequent elimination of EtOH molecule, (Scheme 2). The anticipated structure of compound **3b** was in agreement with the spectral data, where the IR spectra of compound **3b** showed bands at 3277 cm<sup>-1</sup> corresponding to the NH group and two sharp peaks at 1691 and 1670 cm<sup>-1</sup> corresponding to two carbonyl groups, where the <sup>1</sup>H-NMR spectrum of compound **3b** showed a broad band at  $\delta$  10.65 ppm for NH proton, multiplet at 7.70-7.43 ppm for the aromatic protons, singlet at 3.16 ppm for CH<sub>2</sub> group and another multiplet at 1.26-0.95 ppm for cyclic CH<sub>2</sub>.

Encouraged by this success, we extended the reaction of compound **2b** with  $\alpha$ -halo compounds as bromomalononitrile, chloroacetonitrile and ethyl chloroformate under the same experimental conditions (MeONa/MeOH), where the corresponding diazaspriroheterocycles namely 3-amino-5-oxo-1-phenyl-1,4-diazaspiro[5.5]undec-2-ene-2-carbonitrile **4b**, 3-amino-1-phenyl-1,4-diazaspiro[5.5]undec-2-ene-5-one **5b** and 1-phenyl-1,3-diazaspiro[4.5]decane-2,4-dione **6b** were obtained respectively (Scheme 3).

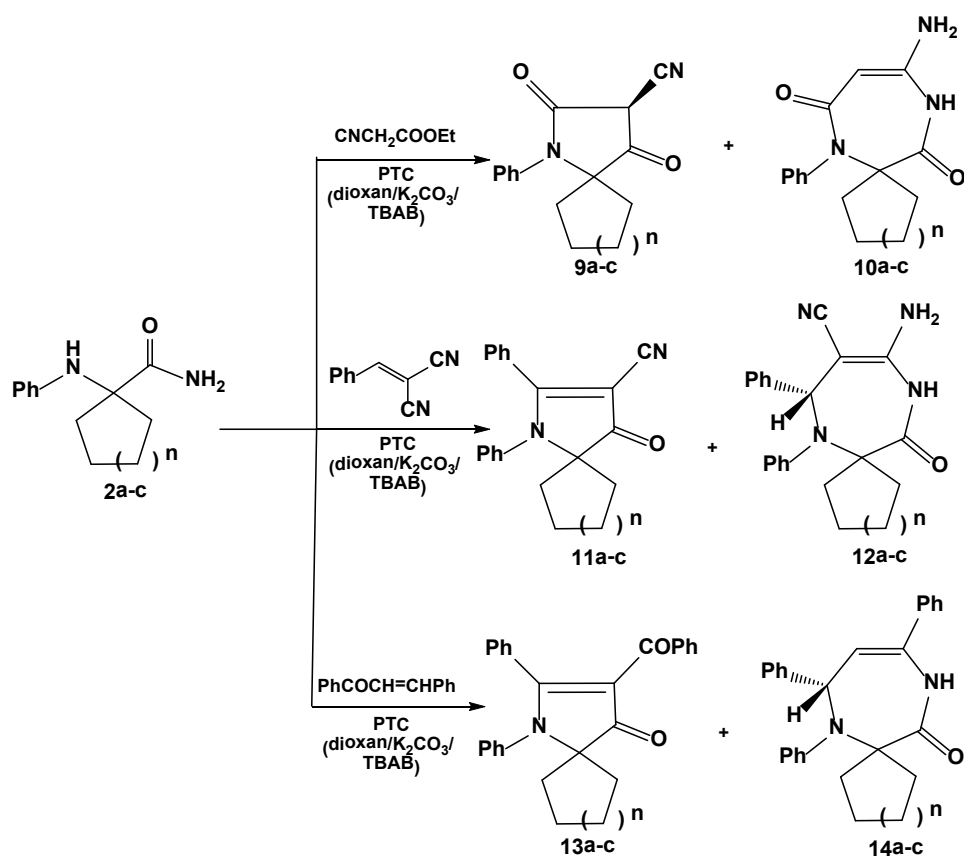
In continuation of our study, compound **2b** was reacted with some cyclic ketones as cyclopentanone and cyclohexanone under the same experimental conditions (MeONa/MeOH) where the corresponding spiroheterocycles 6-phenyl-14-oxa-6-azadispiro[4.1.5.2] tetradecan-



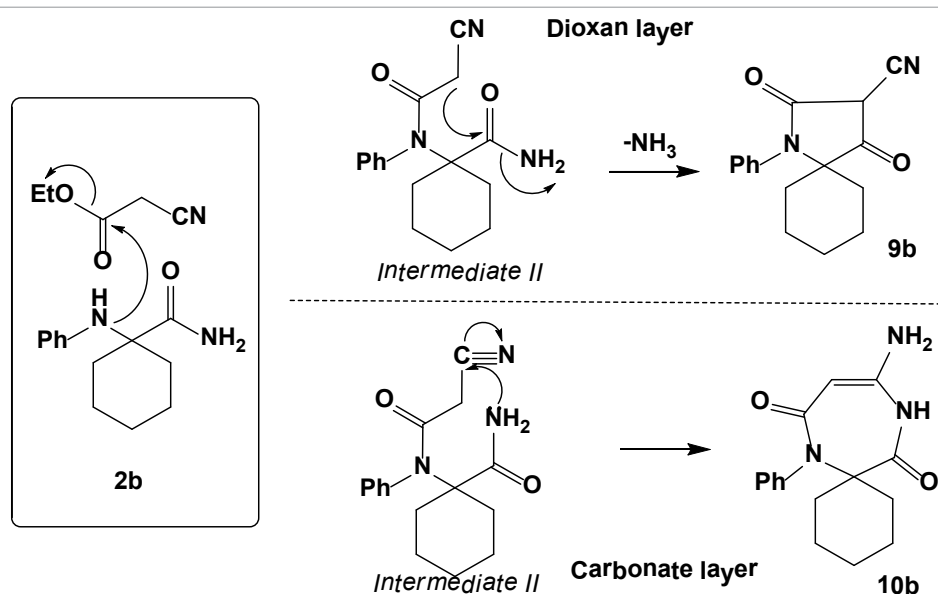
Scheme 2



Scheme 3



Scheme 4



Scheme 5

13-one 7b and 7-phenyl-7,14-diazadispiro[5.1.5.2]-pentadecan-15-one 8b were obtained, respectively (Scheme 3).

On the other hand, the reaction of 1-anilincyclohexancarboxamide 2b with ethyl cyanoacetate under phase transfer conditions

(dioxan/ $K_2CO_3$ /TBAB) afforded a mixture of two compounds one was obtained from dioxan layer and identified as 2,4-dioxo-1-phenyl-1-azaspiro[4.5]decane-3-carbonitrile 9b where the other was isolated from carbonate layer after acidification with AcOH and was identified

as 10-amino-7-phenyl-7,11-diazaspiro[5.6]dodec-9-ene-8,12-dione 10b cf (Scheme 4).

The mechanism of this reaction was assumed to follow a preliminary nucleophilic attack of the secondary amino group onto the ester carbonyl of ethylcyanoacetate and subsequent elimination of EtOH molecule to the nonisolable intermediate II which then undergoes cyclization in two different ways: compound 9b was isolated from dioxan layer and may be formed initially via Michael type addition followed by elimination of NH<sub>3</sub> molecule, where compound 10b was isolated from carbonate layer after acidification with AcOH and was formed via a nucleophilic addition of the amino group into the cyano group (Scheme 5).

Similarly, compound 1b was allowed to react with benzylidenemalononitrile and 1,3-diphenylprop-2-en-1-one (chalcone) where two products were obtained from each reaction one from dioxan and the other from carbonate layer after acidification, Scheme 4. Likewise, the reaction of 1-anilino-cycloheptanecarboxamide 2a and 1-anilino-cycloheptanecarboxamide 2c were subjected to this procedure to produce the corresponding azaspiroheterocycles 3-14 (Table 1).

In conclusion, we have described a direct, simple and highly efficient method for the synthesis of diazaspironheterocycles under traditional basic conditions as well as under phase transfer conditions (PTC).

## Conclusion

The synthesis of five, six and seven-membered ring spiroheterocycles from 1-anilino-cyclohexanecarboxamides 2a-c. A general high yielding protocol for the synthesis of many functionalized spiro heterocyclic systems was presented.

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