Preparation of 2-((N,N-dialkylamino)-2,4,6-cycloheptatrien-1-one derivatives from an isocyanide, a primary amine, propionaldehyde, and tropolone via Ugi-Smiles coupling reaction in the presence of silica nanoparticles

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The use of Smiles rearrangement in Ugi-type couplings with tropolone allows very straightforward multicomponent formation of 2-((N,N-dialkylamino)-2,4,6-cycloheptatrien-1-one derivatives. The 4-component reaction of isocyanides, tropolone (2-hydroxy-2,4,6-cycloheptatrien-1-one), primary amines, and propionaldehyde in the presence of silica nanoparticles (silica NPs, ca. 42 nm) proceeds easily in methanol to form the title compounds in a new Ugi-Smiles-type reaction.

Key Words: Ugi-type coupling, tropolone, isocyanides, primary amines, silica (NP), Ugi-Smiles-type reaction

Introduction

Multicomponent reactions (MCRs) allow more than 2 simple and flexible building blocks to be combined in practical, timesaving one-pot operations. Due to their valued features such as atom economy, inherent simple

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Experimental procedures, and their one-pot character, they are perfectly suited for automated synthesis. Therefore, MCRs have attracted much attention because of their exceptional synthetic efficiency. Since all the organic reagents employed are used and moved toward the target compound the purification of products resulting from MCRs is simple. Isocyanide-based multicomponent reactions (abbreviated to IMCRs by Ugi and Dömling) have an advantageous position. The special features of IMCRs including unique synthetic potential, high atom economy, convergent nature, ease of implementation, and the molecular diversity generation are considered acceptable factors in the relative advantage of the reactions.

In recent years, nanoparticles (NPs) have attracted tremendous attention in catalysis because of their improved efficiency under mild and environmentally benign conditions in the context of ecological (green) synthesis. Due to their enormously large and highly reactive surface area, NPs have potential to exhibit superior catalytic activity in comparison to their bulk counterparts. In the past, we established a one-pot method for the preparation of organic compounds. As part of our ongoing program to develop efficient and robust methods for the synthesis of heteroatom-containing compounds, we wish to report the preparation of a new class of 2-(N,N-dialkylamino)-2,4,6-cycloheptatrien-1-one derivatives by a novel 4-component condensation reaction of propionaldehyde, primary amines, isocyanides, and tropolone in the presence of silica NPs in excellent yields (Scheme 1).

Experimental

The starting materials and solvents were obtained from Merck (Germany) and Fluka (Switzerland) and were used without further purification. The methods used to follow the reactions were TLC and NMR. TLC and NMR indicated that there were no side products. IR spectra were measured on a Jasco 6300 FTIR spectrometer. \( ^1 \)H- and \( ^13 \)C-NMR spectra (CDCl\(_3\)) were recorded on a BRUKER DRX-400 AVANCE spectrometer at 400.22 and 100.63 MHz, respectively. Elemental analyses were performed using a Heraeus CHN-O-Rapid analyzer. Mass spectra were recorded on a FINNIGAN-MATT 8430 mass spectrometer operating at an ionization potential of 70 eV. Preparative layer chromatography (PLC) plates were prepared from Merck silica gel (F\(_{254}\)) powder.

General procedure for the preparation of compounds 5a-5h

To magnetically stirred silica NPs (0.2 g) and solution of propionaldehyde (1 mmol), primary amine (1 mmol), and tropolone (1 mmol) in CH\(_3\)OH (7 mL) was added dropwise a solution of isocyanide (1 mmol) in CH\(_3\)OH (2 mL) at 60 \( ^\circ\)C over 5 min. The reaction mixture was refluxed for 6 h. The solvent was removed under reduced pressure and the viscous residue was purified by preparative layer chromatography (silica gel (F\(_{254}\)); petroleum ether–ethyl acetate (4:1)). The solvent was removed under reduced pressure and the products were obtained. The characterization data of the compounds are given below.

2-[Benzyl(7-oxo-1,3,5-cycloheptatrienyl)amino]-N\(^1\)-cyclohexylbutanamide (5a)

Yellow oil, (Yield: 92%). IR (neat): \( v = 3440, 2952, 1745, 1651, 1600, 1466, 1227, 1077 \text{ cm}^{-1} \). \(^1\)H-NMR (400.22 MHz, CDCl\(_3\)) \( \delta \) (ppm): 0.79 (t, 3H, \( J = 7.4 \text{ Hz, CH}_3 \)), 0.86-2.1 (m, 10H, 5CH\(_2\) of cyclohexyl and m, 2H, CH\(_2\) of propyl), 3.80-4.02 (m, 1H, CH–N of cyclohexyl), 4.50 (AB, 2H, \( J = 16.8 \text{ Hz, PhCH}_2 \)), 4.55 (t,
1H, J = 7.0 Hz, CH), 6.53 (d, 1H, J = 10.4 Hz, CH of tropone), 6.63 (t, 1H, J = 9.0 Hz, CH of tropone), 6.84 (t, 1H, J = 10.2 Hz, CH of tropone); 7.07-7.35 (m, 7H, CH of tropone and Ph); 8.69 (d, 1H, J = 8.0 Hz, NH exchanged by D₂O addition).¹³C-NMR (100.63 MHz, CDCl₃) δ (ppm): 11.74 (CH₃), 22.35 (CH₂ of propyl), 24.81, 25.66, 33.11 (3CH₃ of cyclohexyl), 47.84 (CH of cyclohexyl), 49.56 (PhCH₂), 63.55 (CH), 121.51, 126.58, 126.98, 127.22, 128.55, 133.83, 134.56, 136.56 (8 CH of tropone and Ph), 135.93 (Cα of Ph), 158.12 (C of tropone), 169.80 (C=O of amide), 184.38 (C=O of tropone). Analysis of C₁₉₂₉₃₁₈₋₂₀₂ (378.23). (% calculation/found): C: 76.16/76.12, H: 7.99/7.96, N: 7.40/7.45. MS, m/z (%): 378 (4), 287 (14), 252 (95), 210 (63), 188 (21), 160 (33), 148 (44), 132 (20), 106 (20), 105 (13), 91 (100), 77 (17), 65 (18), 57 (15), 55 (34), 41 (32).

2-[Benzyl(7-oxo-1,3,5-cycloheptatrienyl)amino]-N¹-(tert-butyl)butanamide (5b)

Yellow oil, (Yield: 90%). IR (neat): ν = 3423, 2922, 1742, 1636, 1620, 1461, 1234, 1030 cm⁻¹. ¹H-NMR (400.22 MHz, CDCl₃) δ (ppm): 0.78 (t, 3H, J =7.4 Hz, CH₃), 1.37 (s, 9H, CMe₃), 1.70-2.10 (m, 2H, CH₂ of propyl), 4.50 (AB, 2H, J = 16.8 Hz, PhCH₂), 4.51 (t, 1H, J = 6.4 Hz, CH), 6.51 (d, 1H, J = 10.4 Hz, CH of tropone), 6.66 (t, 1H, J = 9.0 Hz, CH of tropone), 6.85 (t, 1H, J = 10.2 Hz, CH of tropone), 7.07-7.38 (m, 7H, CH of tropone and Ph), 8.65 (s, 1H, NH exchanged by D₂O addition).¹³C-NMR (100.63 MHz, CDCl₃) δ (ppm): 11.77 (CH₃), 22.20 (CH₂ of propyl), 28.72 (3CH₃), 49.43 (PhCH₂), 50.67(CMe₃), 64.01 (CH), 121.25, 126.47, 126.91, 127.24, 128.57, 133.85, 134.37, 136.57 (8 CH of tropone and Ph), 135.91 (Cα of Ph), 158.18 (C of tropone), 170.02 (C=O of amide), 184.46 (C=O of tropone). Analysis of C₁₉₂₉₃₁₈₋₂₀₂ (352.22). (% calculation/found): C: 74.97/74.94, H: 8.01/8.05, N: 7.95/7.92. MS, m/z (%): 352 (14), 280 (10), 261 (25), 252 (100), 210 (67), 188 (24), 160 (56), 148 (14), 132 (41), 106 (15), 105 (20), 91 (89), 77 (36), 65 (26), 57 (48), 41 (37).

N¹-(tert-butyl)-2-[7-oxo-1,3,5-cycloheptatrienyl]propylamino]butanamide (5c)

Yellow oil, (Yield: 83%). IR (neat): ν = 3444, 2922, 1746, 1650, 1608, 1469, 1256, 1084 cm⁻¹. ¹H-NMR (400.22 MHz, CDCl₃) δ (ppm): 0.70 (t, 3H, J = 7.4 Hz, CH₃ of (CH₂)₂CH₃), 0.88 (t, 3H, J = 7.4 Hz, CH₃ of CH₂CH₃), 1.39 (s, 9H, CMe₃), 1.23-2.20 (m, 4H, 2CH₂), 3.07-3.37 (m, 2H, NCH₂), 3.37 (t, 1H, J = 7.0 Hz, H-C), 6.66 (d, 1H, J = 10.4 Hz, CH of tropone), 6.72 (t, 1H, J = 9.2 Hz, CH of tropone), 7.00-7.30 (m, 3H, CH of tropone), 8.39 (s, 1H, NH exchanged by D₂O addition).¹³C-NMR (100.63 MHz, CDCl₃) δ (ppm): 11.46 and 11.68 (2 CH₃), 19.06 and 21.85 (2CH₂), 28.69 (3CH₃), 47.01 (CH₂N), 50.51 (CMe₃), 64.07 (CH), 119.92, 125.98, 133.93, 134.12, 136.43 (5 CH of tropone), 158.61 (C of tropone), 170.21 (C=O of amide), 184.42 (C=O of tropone). Analysis of C₁₉₂₉₃₁₈₋₂₀₂ (304.22). (% calculation/found): C: 71.02/71.05, H: 9.27/9.25, N: 9.20/9.23. MS, m/z (%): 304 (28), 261 (10), 252 (91), 236 (15), 220 (42), 210 (31), 205 (98), 204 (100), 188 (13), 162 (85), 160 (33), 132 (28), 105 (13), 91 (24), 77 (14), 57 (10), 41 (8).

N¹-cyclohexyl-2-[7-oxo-1,3,5-cycloheptatrienyl]propylamino]butanamide (5d)

Yellow oil, (Yield: 80%). IR (neat): ν = 3445, 2927, 1740, 1654, 1616, 1465, 1260, 1018 cm⁻¹. ¹H-NMR (400.22 MHz, CDCl₃) δ (ppm): 0.71 (t, 3H, J = 7.4 Hz, CH₃ of (CH₂)₂CH₃), 0.85 (t, 3H, J = 7.4 Hz, CH₃ of CH₂CH₃), 0.96-2.39 (m, 14H, 5 CH₂ of cyclohexyl and 2 CH₂ of acyclic), 3.07-3.41 (m, 2H, NCH₂), 7.81
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3.70-3.91 (m, 1H, CH-N of cyclohexyl), 4.40 (t, 1H, J = 7.0 Hz, CH), 6.66 (d, 1H, J = 10.4 Hz, CH of tropone), 6.72 (t, 1H, J = 9.2 Hz, CH of tropone), 7.04-7.30 (m, 3H, CH of tropone), 8.43 (d, 1H, J = 8.0 Hz, NH exchanged by D$_2$O addition). $^{13}$C-NMR (100.63 MHz, CDCl$_3$) δ (ppm): 11.41 and 11.65 (2 CH$_3$), 19.00 and 21.99 (2 CH$_2$ of cyclohexyl), 24.79, 26.65, 32.96 (2 CH$_2$ of cyclohexyl), 47.03 (CH$_2$N); 47.79 (CH of cyclohexyl), 63.60 (CH), 120.02, 126.07, 133.94, 136.44 (5 CH of tropone), 158.57 (C of tropone), 170.03 (C=O of amide), 184.28 (C=O of tropone). Analysis of C$_{20}$H$_{30}$N$_2$O$_2$ (330.23). (% calculation/found): C: 72.69/72.65, H: 9.15/9.18, N: 8.48/8.44.

2-[benzyl (7-oxo-1,3,5-cycloheptatrienyl) amino]-N$_1$-(2,4,4-trimethyl sec. pentyl) butanamide (5e)

Yellow oil, (Yield: 85%). IR (neat): ν = 3429, 2923, 1748, 1651, 1619, 1417, 1221, 1020 cm$^{-1}$. $^1$H-NMR (400.22 MHz, CDCl$_3$) δ (ppm): 0.79 (t, 3H, J = 7.4 Hz, CH$_3$), 1.05 (s, 9H, CMe$_3$), 1.43 (s, 6H, CMe$_2$NH), 1.62-2.20 (m, 2H, CH$_2$ of propyl and s, 2H, CH$_2$CMe$_3$), 4.49 (t, 1H, J = 7.0 Hz, CH), 4.51 (AB, 2H, J = 16.8 Hz, PhCH$_2$), 6.51 (d, 1H, J = 10.4 Hz, CH of tropone), 6.63 (t, 1H, J = 9.0 Hz, CH of tropone), 6.85 (t, 1H, J = 10.4 Hz, CH of tropone), 7.08-7.38 (m, 7H, CH of tropone and Ph), 8.50 (s, 1H, NH exchanged by D$_2$O addition). $^{13}$C-NMR (100.63 MHz, CDCl$_3$) δ (ppm): 11.80 (CH$_3$), 22.26 (CH$_2$ of propyl), 29.27 (CMe$_2$NH), 31.51 (CMe$_3$), 31.64 (CMe$_3$), 49.48 (PhCH$_2$), 51.16 (CH$_2$CMe$_3$), 54.63 (CMe$_2$NH), 64.08 (CH), 121.10, 126.35, 126.91, 127.18, 128.53, 133.75, 134.44, 136.37 (8 CH of tropone and Ph), 135.92 (C$_{ip}$ of Ph), 158.02 (C of tropone), 169.71 (C=O of amide), 184.27 (C=O of tropone). Analysis of C$_{26}$H$_{36}$N$_2$O$_2$ (408.28). (% calculation/found): C: 76.43/76.45, H: 8.88/8.91, N: 6.86/6.82.

N$_1$-(tert-butyl)-2-[cyclohexyl(7-oxo-1,3,5-cycloheptatrienyl)amino]butanamide (5f)

Yellow oil, (Yield: 75%). IR (neat): ν = 3424, 2923, 1743, 1651, 1619, 1417, 1221, 1020 cm$^{-1}$. $^1$H-NMR (400.22 MHz, CDCl$_3$) δ (ppm): 0.88 (t, 3H, J = 7.4 Hz, CH$_3$), 1.33 (s, 9H, CMe$_3$), 0.89-2.20 (m, 10H, CH$_2$ of cyclohexyl and m, 2H, CH$_2$ of propyl), 3.30 (t, 1H, J = 11.4 Hz, CH–N of cyclohexyl), 4.00 (t, 1H, J = 7.0 Hz, H-C), 6.68 (t, 1H, J = 9.0 Hz, CH of tropone), 6.95-7.30 (m, 4H, CH of tropone), 8.23 (s, 1H, NH, exchanged by D$_2$O addition). $^{13}$C-NMR (100.63 MHz, CDCl$_3$) δ (ppm): 12.53 (CH$_3$), 24.00 (CH$_2$ of propyl), 25.73, 26.23, 26.47, 30.62, 33.32 (5 CH$_2$ of cyclohexyl), 28.58 (3CH$_3$), 50.49 (CMe$_2$NH), 60.98 (CH of cyclohexyl), 65.20 (CH), 120.01, 126.44, 133.15, 133.91, 135.92 (5 CH of tropone), 158.42 (C=O of tropone), 170.88 (C=O of amide), 185.61 (C=O of tropone). Analysis of C$_{21}$H$_{32}$N$_2$O$_2$ (344.25). (% calculation/found): C: 73.22/73.18, H: 9.36/9.33, N: 8.13/8.09.

2-[cyclohexyl (7-oxo-1,3,5-cycloheptatrienyl) amino]-N$_1$-(2,4,4-trimethyl sec. pentyl) butanamide (5g)

Yellow oil, (Yield: 70%). IR (neat): ν = 3291, 2933, 1741, 1659, 1608, 1461, 1250, 1071 cm$^{-1}$. $^1$H-NMR (400.22 MHz, CDCl$_3$) δ (ppm): 0.90 (t, 3H, J = 7.4 Hz, CH$_3$), 1.01 (s, 9H, CMe$_3$), 1.42 (s, 6H, CMe$_2$NH), 1.07-2.30 (m, 10H, 5 CH$_2$ of cyclohexyl and m, 2H, CH$_2$ of propyl and s, 2H, CH$_2$CMe$_3$), 3.37 (t, 1H, J = 11.6 Hz, CH–N of cyclohexyl), 3.98 (t, 1H, J = 7.0 Hz, H-C), 6.68 (t, 1H, J = 9.0 Hz, CH of tropone), 6.95-7.30 (m, 4H, CH of tropone), 8.04 (s, 1H, NH, exchanged by D$_2$O addition). $^{13}$C-NMR (100.63 MHz, CDCl$_3$) δ (ppm):
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12.78 (CH$_3$), 24.18 (CH$_2$ of propyl), 25.75, 26.23, 26.49, 30.64, 33.35 (5 CH$_2$ of cyclohexyl), 28.71 (CMe$_2$), 31.48 (CMe$_3$), 31.56 (CMe$_3$), 51.36 (CH$_2$CMe$_3$), 54.54 (CMe$_2$NH), 60.88 (CH of cyclohexyl), 65.11 (CH), 121.57, 126.22, 133.06, 133.87, 135.72 (5 CH of tropone), 158.23 (C of tropone), 170.44 (C=O of amide), 185.33 (C=O of tropone). Analysis of C$_{25}$H$_{40}$N$_2$O$_2$ (400.31). (% calculation/found): C: 74.95/74.99, H: 10.06/10.10, N: 6.99/6.94.

N$^1$-cyclohexyl-2-[cyclohexyl (7-oxo-1,3,5-cycloheptatrienyl)amino] butanamide (5h)

Yellow oil, (Yield: 79%). IR (neat): $\nu$ = 3340, 2971, 1740, 1653, 1612, 1478, 1222, 1080 cm$^{-1}$. $^1$H-NMR (400.22 MHz, CDCl$_3$) $\delta$ (ppm): 0.88 (t, 3H, $J$ = 7.4 Hz, CH$_3$), 0.91-2.20 (m, 20H, 10 CH$_2$ of 2 cyclohexyl and m, 2H, CH$_2$ of propyl), 3.20-3.80 (m, 2H, 2 CH of 2 cyclohexyl), 4.01 (t, 1H, $J$ = 7.0 Hz, H-C), 6.72 (t, 1H, $J$ = 9.0 Hz, CH of tropone), 6.96-7.30 (m, 4H, CH of tropone), 8.31 (d, 1H, $J$ = 8.0 Hz, NH, exchanged by D$_2$O addition). $^{13}$C-NMR (100.63 MHz, CDCl$_3$) $\delta$ (ppm): 12.67 (CH$_3$), 24.09 (CH$_2$ of propyl), 24.72, 24.80, 25.60, 25.74, 26.22, 26.37, 30.74, 32.81, 32.95, 33.03 (10 CH$_2$ of 2 cyclohexyl), 64.77 (CH), 122.94, 126.92, 133.09, 134.39, 135.95 (5 CH of tropone), 158.38 (C of tropone), 170.99 (C=O of amide), 185.83 (C=O of tropone). Analysis of C$_{23}$H$_{34}$N$_2$O$_2$ (370.26). (% calculation/found): C: 74.55/74.59, H: 9.25/9.22, N: 7.56/7.59.

Results and discussion

The 1:1 imine intermediate generated by the addition of primary amine 2 to propionaldehyde 1 is trapped by isocyanide 3 and tropolone 4 in the presence of silica NPs, leading to the formation of 2-([N,N-dialkylamino]-2,4,6-cycloheptatrien-1-one derivatives 5 (Scheme 1 and Table 1). The reaction proceeds smoothly and cleanly under mild conditions, and no side reactions are observed.

Silica NPs were found to catalyze the synthesis of 2-([N,N-dialkylamino]-2,4,6-cycloheptatrien-1-one derivatives from propionaldehyde 1, primary amines 2, isocyanides 3, and tropolone 4 in methanol at 60 °C with high efficiency (Scheme 1 and Table 1). The use of just 0.2 g of silica NPs per mmol of reactants is sufficient to push the reaction forward. Higher amounts of silica NPs (0.3 g) did not improve the result to a great extent (Table 2, entries 4-7). In order to investigate the effects of other reaction media in this reaction, we also carried out the described condensation in MeOH, H$_2$O and solvent-free (neat) systems (Table 2, entries 1-3).

A possible mechanism for the present reaction is shown in Scheme 2, which envisages a tandem sequence. On the basis of the chemistry of isocyanides, it is reasonable to assume that the first step may involve the formation of imine 6 by the condensation reaction of primary amine 2 with propionaldehyde 1; the next step may involve nucleophilic addition of the isocyanide 3 to the imine intermediate 7, leading to nitrilium intermediate 8. This intermediate may be attacked by the conjugate base of the tropolone 4 to form 1:1:1 adduct 9. The intermediate 9 may undergo Smiles rearrangements to afford the isolated 2-([N,N-dialkylamino]-2,4,6-cycloheptatrien-1-one derivatives 5 via intermediate 10. It may be speculated that the polar amphoteric surface (hydroxyl groups of the silica NPs) facilitates the interaction of adsorbed weak acidic and basic components due to stabilization of the corresponding transition states and intermediates by H-bonding. This interaction with
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Scheme 1. Four-component synthesis of 2-(N,N-dialkylamino)-2,4,6-cycloheptatrien-1-one derivatives 5 in the presence of silica NPs (see Table 1).

Table 1. SiO$_2$ NP-promoted synthesis of 2-(N,N-dialkylamino)-2,4,6-cycloheptatrien-1-one derivatives 5$^a$.

<table>
<thead>
<tr>
<th>5</th>
<th>$R^1$</th>
<th>$R^2$</th>
<th>Yield ($%$)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>Benzyl</td>
<td>Cyclohexyl</td>
<td>92</td>
</tr>
<tr>
<td>b</td>
<td>Benzyl</td>
<td>tert-Butyl</td>
<td>90</td>
</tr>
<tr>
<td>c</td>
<td>n-Propyl</td>
<td>tert-Butyl</td>
<td>83</td>
</tr>
<tr>
<td>d</td>
<td>n-Propyl</td>
<td>Cyclohexyl</td>
<td>80</td>
</tr>
<tr>
<td>e</td>
<td>Benzyl</td>
<td>1,1,3,3-Tetramethylbutyl</td>
<td>85</td>
</tr>
<tr>
<td>f</td>
<td>Cyclohexyl</td>
<td>tert-Butyl</td>
<td>75</td>
</tr>
<tr>
<td>g</td>
<td>Cyclohexyl</td>
<td>1,1,3,3-Tetramethylbutyl</td>
<td>70</td>
</tr>
<tr>
<td>h</td>
<td>Cyclohexyl</td>
<td>Cyclohexyl</td>
<td>79</td>
</tr>
</tbody>
</table>

$^a$ See Scheme 1; 0.2 g SiO$_2$ NP/mmol reactants were applied.  
$^b$ Yield of isolated 5.

Table 2. Synthesis of 2-(N,N-dialkylamino)-2,4,6-cycloheptatrien-1-one derivatives 5a from the reaction of propionaldehyde, benzylamine, cyclohexyl isocyanide, and tropolone under various conditions.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst$^a$ or solvent</th>
<th>Temp ($^\circ$C)</th>
<th>Time (h)</th>
<th>Yield ($%$)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MeOH</td>
<td>60</td>
<td>24</td>
<td>65</td>
</tr>
<tr>
<td>2</td>
<td>H$_2$O</td>
<td>90</td>
<td>24</td>
<td>57</td>
</tr>
<tr>
<td>3</td>
<td>neat</td>
<td>90</td>
<td>24</td>
<td>35</td>
</tr>
<tr>
<td>4</td>
<td>MeOH/Silica gel powder (Merck) (0.2 g)</td>
<td>60</td>
<td>24</td>
<td>77</td>
</tr>
<tr>
<td>5</td>
<td>MeOH/SiO$_2$ NP (0.1 g)</td>
<td>60</td>
<td>6</td>
<td>83</td>
</tr>
<tr>
<td>6</td>
<td>MeOH/SiO$_2$ NP (0.2 g)</td>
<td>60</td>
<td>6</td>
<td>92</td>
</tr>
<tr>
<td>7</td>
<td>MeOH/SiO$_2$ NP (0.3 g)</td>
<td>60</td>
<td>6</td>
<td>92</td>
</tr>
</tbody>
</table>

$^a$ Amount of SiO$_2$ catalyst per mmol of reactants.  
$^b$ Yields of isolated 5a.
the neighboring silanol groups is shown in Scheme 2 for the first reaction step. Participation of 2 proximate silanol groups (one as H-bond donor and the other as H-bond acceptor) in the reaction mechanism also seems plausible.

Scheme 2. Proposed mechanism for the formation of 2-(N,N-dialkylamino)-2,4,6-cycloheptatrien-1-one derivatives 5 in the presence of silica NPs.

The structures of the products were deduced from their IR, $^1$H-NMR, and $^{13}$C NMR-spectra and mass spectrometry. For example, the $^1$H-NMR spectrum of 5a consisted of a triplet for the CH$_3$ of n-prolyl ($\delta = 0.79$ ppm, $J = 7.4$ Hz), several multiplets for the cyclohexyl and n-propyl ($\delta = 0.86-2.10$ ppm) moieties, a multiplet for the NCH ($\delta = 3.80-4.02$ ppm) of cyclohexyl moiety, an AB-quartet for CH$_2$ of PhCH$_2$ ($\delta = 4.50$ ppm, $J = 16.8$ Hz), a triplet for the NCH ($\delta = 4.55$ ppm, $J = 7.0$ Hz) of the acyclic part, a doublet for
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the tropolone hydrogen (δ = 6.53 ppm, J = 10.4 Hz), a triplet for the tropolone hydrogen (δ = 6.63 ppm, J = 9.0 Hz), a triplet for the tropolone hydrogen (δ = 6.84 ppm, J = 10.2 Hz), a multiplet for a tropolone hydrogen and phenyl group (δ = 7.07-7.35 ppm), and a doublet for the NH that was exchangeable with D₂O (δ = 8.69 ppm, J = 8.0 Hz). The ¹³C-NMR spectrum of 5a showed 20 distinct signals. Partial assignment of these signals is given in the experimental section. The ¹H- and ¹³C-NMR spectra of compounds 5b–h were similar to those of 5a, except for the aromatic or aliphatic moieties, which exhibited characteristic signals with appropriate chemical shifts.

Conclusions

In summary, the reported method offers a mild, simple, and efficient route for the preparation of 2-(N,N-dialkylamino)-2,4,6-cycloheptatrien-1-one derivatives 5 from propionaldehyde 1, primary amine 2, isocyanide 3, and tropolone 4 in the presence of silica NPs. Its ease of work-up, high yields, and fairly mild reaction conditions make it a useful addition to modern synthetic methodologies.

References

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