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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.[1] Therefore, MCRs have attracted much attention because of their exceptional synthetic efficiency.[2–5] Since all the organic reagents employed are used and moved toward the target compound the purification of products resulting from MCRs is simple.[6,7] 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.[6–13]

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.[14,15] Due to their enormously large and highly reactive surface area, NPs have potential to exhibit superior catalytic activity in comparison to their bulk counterparts.[16,17] In the past, we established a one-pot method for the preparation of organic compounds.[18–24] As part of our ongoing program to develop efficient and robust methods for the synthesis of heteroatom-containing compounds,[25–32] we wish to report the preparation of a new class of 2-(N,N-dialkylamino)-2,4,6-cycloheptatrien-1-one derivatives **5a-h** by a novel 4-component condensation reaction of propionaldehyde **1**, primary amines **2**, isocyanides **3**, and tropolone **4** 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** (1 mmol), primary amine **2** (1 mmol), and tropolone **4** (1 mmol) in CH_3OH (7 mL) was added dropwise a solution of isocyanide **3** (1 mmol) in CH_3OH (2 mL) at 60 °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 **(5a-h)** 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 cm^{-1}. ^{1}H-NMR (400.22 MHz, $CDCl_3$) δ (ppm): 0.79 (t, 3H, J= 7.4 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 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 D_2O addition). ^{13}C-NMR (100.63 MHz, $CDCl_3$) δ (ppm): 11.74 (CH_3), 22.35 (CH_2 of propyl), 24.81, 25.66, 33.11 ($3CH_2$ of cyclohexyl), 47.84 (CH of cyclohexyl), 49.56 ($PhCH_2$), 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 (C_{ip} of Ph), 158.12 (C of tropone), 169.80 (C=O of amide), 184.38 (C=O of tropone). Analysis of $C_{24}H_{30}N_2O_2$ (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]-N^1- (tert-butyl)butanamide (5b)

Yellow oil, (Yield: 90%). IR (neat): v = 3423, 2922, 1742, 1636, 1620, 1461, 1234, 1030 cm^{-1}. ^{1}H-NMR (400.22 MHz, $CDCl_3$) δ (ppm): 0.78 (t, 3H, J =7.4 Hz, CH_3), 1.37 (s, 9H, CMe_3), 1.70-2.10 (m, 2H, CH_2 of propyl), 4.50 (AB, 2H, J = 16.8 Hz, $PhCH_2$), 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 D_2O addition). ^{13}C-NMR (100.63 MHz, $CDCl_3$) δ (ppm): 11.77 (CH_3), 22.20 (CH_2 of propyl), 28.72 ($3CH_3$), 49.43 ($PhCH_2$), 50.67(CMe_3), 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 (C_{ip} of Ph), 158.18 (C of tropone), 170.02 (C=O of amide), 184.46 (C=O of tropone). Analysis of $C_{22}H_{28}N_2O_2$ (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).

N^1-(tert-butyl)-2-[(7-oxo-1,3,5-cycloheptatrienyl)(propyl)amino]butanamide (5c)

Yellow oil, (Yield: 83%). IR (neat): v = 3444, 2922, 1746, 1650, 1608, 1469, 1256, 1084 cm^{-1}. ^{1}H-NMR (400.22 MHz, $CDCl_3$) δ (ppm): 0.70 (t, 3H, J = 7.4 Hz, CH_3 of $(CH_2)_2CH_3$), 0.88 (t, 3H, J = 7.4 Hz, CH_3 of CH_2CH_3), 1.39 (s, 9H, CMe_3), 1.23-2.20 (m, 4H, $2CH_2$), 3.07-3.37 (m, 2H, NCH_2), 4.35 (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 D_2O addition). ^{13}C-NMR (100.63 MHz, $CDCl_3$) δ (ppm): 11.46 and 11.68 (2 CH_3), 19.06 and 21.85 ($2CH_2$), 28.69 ($3CH_3$), 47.01 (CH_2N); 50.51 (CMe_3), 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 $C_{18}H_{28}N_2O_2$ (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).

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

Yellow oil, (Yield: 80%). IR (neat): v = 3445, 2927, 1740, 1654, 1616, 1465, 1260, 1018 cm^{-1}. ^{1}H-NMR (400.22 MHz, $CDCl_3$) δ (ppm): 0.71 (t, 3H, J = 7.4 Hz, CH_3 of $(CH_2)_2CH_3$), 0.85 (t, 3H, J = 7.4 Hz, CH_3 of CH_2CH_3), 0.96-2.39 (m, 14H, 5 CH_2 of cyclohexyl and 2 CH_2 of acyclic), 3.07-3.41 (m, 2H, NCH_2),

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_2O 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), 24.79, 26.65, 32.96 (2 CH_2 of cyclohexyl), 47.03 (CH_2N); 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 $C_{20}H_{30}N_2O_2$ (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): v = 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_2NH), 1.62-2.20 (m, 2H, CH_2 of propyl and s, 2H, CH_2CMe_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_2O addition). ^{13}C-NMR (100.63 MHz, $CDCl_3$) δ (ppm): 11.80 (CH_3), 22.26 (CH_2 of propyl), 29.27 (CMe_2NH), 31.51 (CMe_3), 31.64 (CMe_3), 49.48 ($PhCH_2$), 51.16 (CH_2CMe_3), 54.63 (CMe_2NH), 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 $C_{26}H_{36}N_2O_2$ (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): v = 3424, 2921, 1743, 1652, 1616, 1473, 1220, 1032 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_2O 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_3), 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 of tropone), 170.88 (C=O of amide), 185.61 (C=O of tropone). Analysis of $C_{21}H_{32}N_2O_2$ (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): v = 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_2NH), 1.07-2.30 (m, 10H, 5 CH_2 of cyclohexyl and m, 2H, CH_2 of propyl and s, 2H, CH_2CMe_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_2O addition). ^{13}C-NMR (100.63 MHz, $CDCl_3$) δ (ppm):

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_2CMe_3), 54.54 (CMe_2NH), 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 $C_{25}H_{40}N_2O_2$ (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)

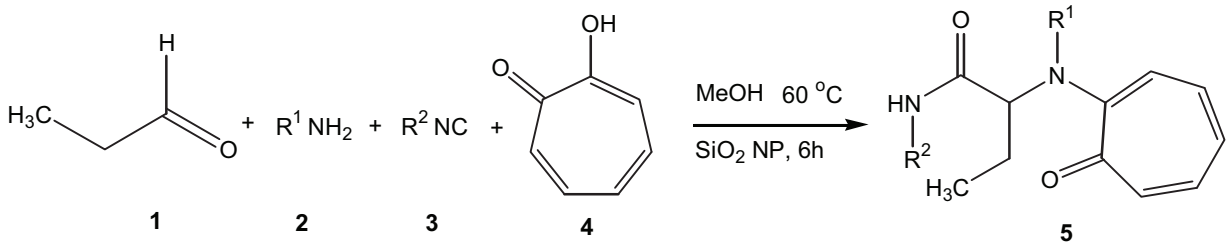
Yellow oil, (Yield: 79%). IR (neat): v = 3340, 2971, 1740, 1653, 1612, 1478, 1222, 1080 cm^{-1}. ^{1}H-NMR (400.22 MHz, $CDCl_3$) δ (ppm): 0.88 (t, 3H, J = 7.4 Hz, CH_3), 0.91-2.20 (m, 20H, 10 CH_2 of 2 cyclohexyl and m, 2H, CH_2 of propyl), 3.20-3.80 (m, 2H, 2 CH of 2 cyclohexyl), 4.01 (t, 1H, J = 7.0 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_2O addition). ^{13}C-NMR (100.63 MHz, $CDCl_3$) δ (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 $C_{23}H_{34}N_2O_2$ (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). We also used silica gel powder (Merck) instead of silica NPs in this reaction, but increasing reaction times and decreasing 2-(N,N-dialkylamino)-2,4,6-cycloheptatrien-1-one yields were observed (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_2O 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



5a: R^1 = Benzyl, R^2 = Cyclohexyl; **5b:** R^1 = Benzyl, R^2 = *tert*-Butyl; **5c:** R^1 = *n*-Propyl, R^2 = *tert*-Butyl; **5d:** R^1 = *n*-Propyl, R^2 = Cyclohexyl; **5e:** R^1 = Benzyl, R^2 = 1,1,3,3-tetramethylbutyl; **5f:** R^1 = Cyclohexyl, R^2 = *tert*-Butyl; **5g:** R^1 = Cyclohexyl, R^2 = 1,1,3,3-tetramethylbutyl; **5h:** R^1 = Cyclohexyl, R^2 = Cyclohexyl.

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].

5	R^1	R^2	Yield (%)[b]
a	Benzyl	Cyclohexyl	92
b	Benzyl	*tert*-Butyl	90
c	*n*-Propyl	*tert*-Butyl	83
d	*n*-Propyl	Cyclohexyl	80
e	Benzyl	1,1,3,3-Tetramethylbutyl	85
f	Cyclohexyl	*tert*-Butyl	75
g	Cyclohexyl	1,1,3,3-Tetramethylbutyl	70
h	Cyclohexyl	Cyclohexyl	79

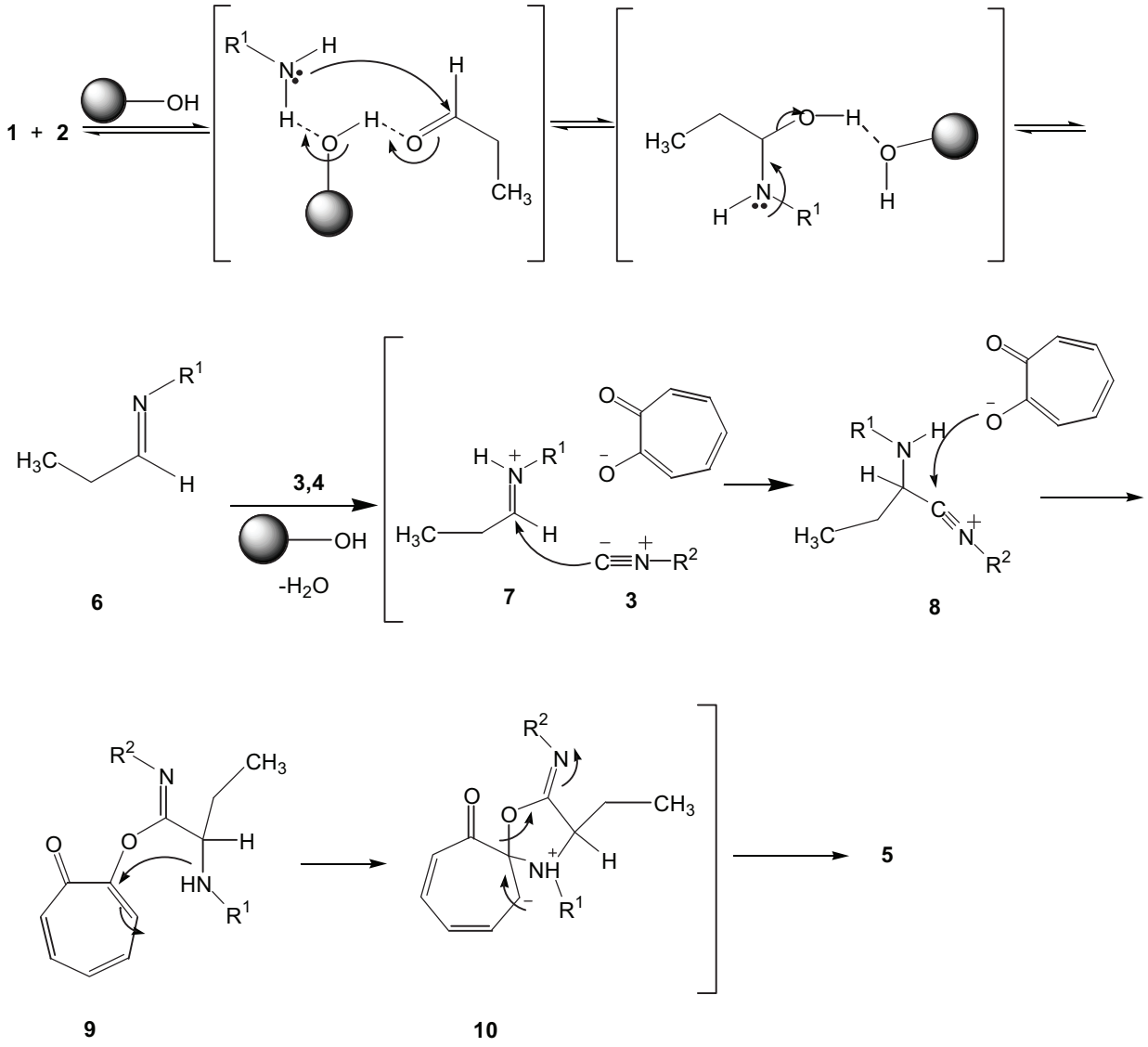
[a] See Scheme 1; 0.2 g SiO_2 NP/mmol reactants were applied. [b] Yield of isolated **5.**

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.

Entry	Catalyst[a] or solvent	Temp (°C)	Time (h)	Yield (%)[b]
1	MeOH	60	24	65
2	H_2O	90	24	57
3	neat	90	24	35
4	MeOH/Silica gel powder (Merck) (0.2 g)	60	24	77
5	MeOH/SiO_2 NP (0.1 g)	60	6	83
6	MeOH/SiO_2 NP (0.2 g)	60	6	92
7	MeOH/SiO_2 NP (0.3 g)	60	6	92

[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-proyl (δ = 0.79 ppm, J = 7.4 Hz), several multiplets for the cyclohexyl and n-propyl (δ =0.86-2.10 ppm) moieties, a multiplet for the NCH (δ = 3.80-4.02 ppm) of cyclohexyl moiety, an AB-quartet for CH_2 of $PhCH_2$ (δ = 4.50 ppm, J = 16.8 Hz), a triplet for the NCH (δ = 4.55 ppm, J = 7.0 Hz) of the acyclic part, a doublet for

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 D_2O (δ = 8.69 ppm, J = 8.0 Hz). The ^{13}C-NMR spectrum of **5a** showed 20 distinct signals. Partial assignment of these signals is given in the experimental section. The ^{1}H- and ^{13}C-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.

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