http://dx.doi.org/10.5012/bkcs.2012.33.1.39

Four-Component Synthesis of 2-(*N*,*N*-Dialkylamino)-2,4,6-Cycloheptatrien-1-One Derivatives from Tropolone, an Isocyanide, a Primary Amine and an Aldehyde *via* Ugi-Smiles Coupling Reaction

Abdolhossain Massoudi,[†] Issa Amini,[†] Ali Ramazani,[‡,*] Fatemeh Zeinali Nasrabadi,[§] and Yavar Ahmadi[§]

[†]*Department of Chemistry, Payame Noor University, P.O. Box 19395-3697, Tehran, Iran*
[‡]*Department of Chemistry, Zanjan Branch, Islamic Azad University, Zanjan 49195-467, Iran. *E-mail: aliramazani@gmail.com*
[§]*Chemistry Department, Zanjan University, Zanjan 45195-313, Iran*
Received September 15, 2011, Accepted October 26, 2011

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 Ugi four-component reaction of isocyanides with tropolone (2-hydroxy-2,4,6-cycloheptatrien-1-one), primary amines and aldehydes proceeds smoothly and cleanly under mild conditions to afford 2-(*N*,*N*-dialkylamino)-2,4,6-cycloheptatrien-1-one derivatives in fairly good yields.

Key Words : Tropolone, Isocyanides, Primary amines, Aldehydes, Ugi-Smiles-type reaction

Introduction

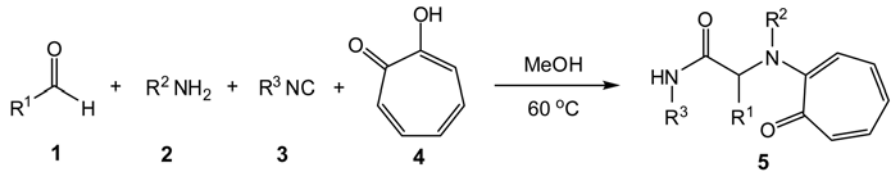
Multicomponent reactions allow more than two facial and flexible building blocks to be combined in practical, time-saving one-pot operations. Due to their valued features such as atom economy, various starting materials and products, inherent simple experimental procedures and their one-pot character, they are perfectly suited for automated synthesis.[1] Therefore, MCRs have attracted much attention because of their exceptional synthetic applications.[2-5] Since all the organic reactants employed are used and moved toward the target compound so purification of products resulting from MCRs is simple.[6,7] Isocyanide-based multicomponent reactions (abbreviated to IMCRs by Ugi and Dömling) have an interesting position. The special features of IMCRs included unique synthetic potential, convergent nature, high atom economy, ease of implementation, and the generation of molecular diversity, are considered as acceptable factors in the relative efficiency of the reactions.[6-13]

In recent years, we have established a one-pot method for the preparation of organic compounds.[14-20] As part of our ongoing program to develop efficient and robust methods for the synthesis of heteroatom-containing compounds,[21-26] we sought to develop a convenient preparation of a new class of 2-(*N*,*N*-dialkylamino)-2,4,6-cycloheptatrien-1-one derivatives **5a-j** by a novel four-component condensation reaction of aldehydes **1**, primary amines **2**, isocyanides **3** and tropolone **4** in fairly good yields (Scheme 1).

Experimental

Starting materials and solvents were obtained from Merck (Germany) and Fluka (Switzerland) and were used without further purification. The methods were used to follow the reactions are TLC and NMR. TLC and NMR indicated that there is no side product. Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. 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-250 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 thin layer chromatography was prepared from Merck silica gel (F_{254}) powder.

General Procedure for Compounds 5a-j. To a magnetically stirred solution of aldehyde (1 mmoL), primary amine (1 mmoL) and tropolone (1 mmoL) in CH_3OH (7 mL), was added dropwise of a solution of isocyanide (1 mmoL) in CH_3OH (2 mL) at 60 °C over 5 min. The reaction mixture was refluxed for 6-24 hrs (See Table 1). The solvent was removed under reduced pressure and the viscous residue was purified by preparative thin layer chromatography (silica gel; petroleum ether-ethyl acetate (4:1) and the products (**5a-j**) were obtained in fairly good yields. The characterization data of the compounds are given below.



Scheme 1. Four-component synthesis of 2-(*N*,*N*-dialkylamino)-2,4,6-cycloheptatrien-1-one derivatives **5** (See Table 1).

Table 1. Synthesis of 2-(*N*,*N*-dialkylamino)-2,4,6-cycloheptatrien-1-one derivatives **5** (See Scheme 1)

5	R^1	R^2	R^3	Time	Yield (%)[a]
a	*n*-Butyl	Benzyl	Cyclohexyl	6 h	96
b	Methyl	Benzyl	*tert*-Butyl	24 h	60
c	Methyl	*n*-Propyl	Cyclohexyl	24 h	66
d	Methyl	*n*-Propyl	*tert*-Butyl	24 h	42
e	*n*-Butyl	Benzyl	*tert*-Butyl	12 h	90
f	Methyl	Benzyl	1,1,3,3-Tetramethylbutyl	24 h	64
g	Methyl	Isobutyl	*tert*-Butyl	24 h	35
h	Methyl	Cyclohexyl	Cyclohexyl	6 h	71
i	Methyl	Cyclohexyl	*tert*-Butyl	24 h	77
j	Methyl	Cyclohexyl	1,1,3,3-Tetramethylbutyl	24 h	75

[a]Isolated yields.

2-[Benzyl(7-oxo-1,3,5-cycloheptatrienyl)amino]-*N*^{1}-cyclohexylhexanamide (5a). Yellow crystals, Yield: 96%, mp 88-89°. IR (KBr): 3268 (NH), 2929, 2846, 1669, 1610, 1078, 1040, 770 cm^{-1}; ^{1}H NMR δ 0.81 (t, $^3J_{HH}$ = 7.2 Hz, 3H, CH_3), 0.86-2.28 (m, 16H, cyclohexyl and 3CH_2 of *n*-butyl), 3.81-3.82 (m, 1H, cyclohexyl, NCH), 4.39 and 4.60 (AB-quartet, $^2J_{HH}$ = 16.6 Hz, 2H, N-CH_2Ph), 4.64 (t, $^3J_{HH}$ = 6.0 Hz, 1H, NCH, acyclic), 6.51 (d, $^3J_{HH}$ = 10.0 Hz, 1H, tropolone), 6.63 (t, $^3J_{HH}$ = 9.0 Hz, 1H, tropolone), 6.84 (t, $^3J_{HH}$ = 10.2 Hz, 1H, tropolone), 7.05-7.30 (m, 7H, 2CH of tropolone, and Ph), 8.64 (d, $^3J_{HH}$ = 8.0 Hz, 1H, NH). ^{13}C NMR δ 184.38 (CO, tropolone) and 169.87 (CO, amide), 157.94 (C, tropolone), 136.01 (C, arom), 136.42, 134.44, 133.71, 128.51, 127.18, 126.98, 126.44, 121.35 (10CH, tropolone and Ph), 61.69 (CH), 49.65 (CH_2 of PhCH_2), 47.86 (CH, cyclohexyl), 33.09, 28.91, 28.62, 25.68, 24.79, 22.46 (8CH_2), 13.88 (CH_3). MS *m/z* (%) 406 (M^+, 5), 315 (16), 280 (100), 210 (61), 188 (22), 176 (31), 132 (14), 105 (8), 91 (92) , 77 (9), 55 (16) and 41 (15). Anal. Calcd for $C_{26}H_{34}N_2O_2$ (406.56): C 76.81, H 8.43, N 6.89. Found: C 76.85, H 8.40, N 6.94.

2-[Benzyl(7-oxo-1,3,5-cycloheptatrienyl)amino]-*N*^{1}-(tert-Butyl)propanamide (5b). Yellow crystals, Yield: 60%, mp 124.0-125.5°. IR (KBr): 3340 (NH), 2971, 2928, 1654, 1648, 1612, 1478, 1080, 766 cm^{-1}; ^{1}H NMR δ 1.29 (d, $^3J_{HH}$ = 7.2 Hz, 3H, CH_3), 1.38 (s, 9H, Me_3C), 4.40 (s, 2H, N-CH_2Ph), 4.63 (q, $^3J_{HH}$ = 6.8 Hz, 1H, NCH), 6.57 (d, $^3J_{HH}$ = 10.4 Hz, 1H, tropolone), 6.68 (t, $^3J_{HH}$ = 9.2 Hz, 1H, tropolone), 6.86 (t, $^3J_{HH}$ = 10.2 Hz, 1H, tropolone), 7.08-7.30 (m, 7H, 2CH of tropolone and Ph), 8.53 (br, s, NH). ^{13}C NMR δ 184.88 (CO, tropolone) and 170.82 (CO, amide), 157.18 (C, tropolone), 136.20 (C, arom), 136.55, 135.22, 133.56, 128.58, 127.46, 127.28, 127.02, 123.10 (10CH, tropolone and Ph), 58.71 (NCH), 50.68 (C), 49.62 (CH_2), 28.71 (3CH_3), 13.01 (CH_3). MS *m/z* (%) 338 (M^+, 9), 266 (9), 247 (24), 238 (100), 210 (28), 146 (23), 105 (9), 91 (92), 77 (15), 65 (10), 57 (15), and 41 (13). Anal. Calcd for $C_{21}H_{26}N_2O_2$ (338.48): C 74.52, H 7.74, N 8.28. Found: C 74.57, H 7.79, N 8.23.

***N*^{1}-Cyclohexyl-2-[7-oxo-1,3,5-cycloheptatrienyl)(propyl)amino]propanamide (5c).** Yellow crystals, Yield: 66%, mp 93.0-94.5°. IR (KBr): 3431 (NH), 2922, 2852, 1628, 1033, 782 cm^{-1}; ^{1}H NMR δ 0.87 (t, $^3J_{HH}$ = 7.2 Hz, 3H, CH_3 of propyl), 0.89-3.35 (m, 10H, 5CH_2 of cyclohexyl, 3H of CH_3 and 4H, 2CH_2 of propyl), 3.78-3.85 (m, 1H, CH, cyclohexyl), 4.50 (q, $^3J_{HH}$ = 6.8 Hz, 1H, NCH, acyclic), 6.71 (d, $^3J_{HH}$ = 10.4 Hz, 1H, tropolone); 6.79 (t, $^3J_{HH}$ = 9.2 Hz, 1H, tropolone); 6.90-7.30 (m, 3H, tropolone), 8.28 (d, $^3J_{HH}$ = 6.8 Hz, 1H, NH). ^{13}C NMR δ 184.73 (CO, tropolone) and 170.83 (CO, amide), 157.73 (C, tropolone), 136.44, 135.27, 133.63, 127.22, 122.22 (5CH, tropolone), 57.91 (CH), 47.94 (CH, cyclohexyl), 47.33, 33.04, 25.65, 24.80, 19.39 (7CH_2), 12.82, 11.51 (2CH_3). MS *m/z* (%) 316 (M^+,17), 223 (11), 190 (100), 148 (49), 132 (18), 126 (11), 120 (17), 105 (25), 92 (15), 86 (43), 77 (46), 69 (17), 55 (43), and 41 (54). Anal. Calcd for $C_{19}H_{28}N_2O_2$ (316.44): C 72.12, H 8.92, N 8.85. Found: C 72.08, H 8.95, N 8.81.

***N*^{1}-(Tert-butyl)-2-[7-oxo-1,3,5-cycloheptatrienyl)(propyl)amino]propanamide (5d).** Yellow oil, Yield: 42%. IR (KBr): 3442 (NH), 2853, 1630, 1498, 1017, 662 cm^{-1}; ^{1}H NMR δ 0.88 (t, $^3J_{HH}$ = 7.4 Hz, 3H, CH_3, propyl), 1.18 (d, $^3J_{HH}$ = 7.2 Hz, 3H, CH_3), 1.41 (s, 9H, Me_3C), 2.92-3.32 (m, 4H, 2CH_2, propyl), 4.45 (q, $^3J_{HH}$ = 7.0 Hz, 1H, NCH, acyclic), 6.70 (d, $^3J_{HH}$ = 10.0 Hz, 1H, tropolone), 6.79 (t, $^3J_{HH}$ = 9.2 Hz, 1H, tropolone), 7.08-7.30 (m, 3H, tropolone), 8.28 (br, s, 1H, NH). ^{13}C NMR δ 184.81 (CO, tropolone) and 171.03 (CO, amide), 157.70 (C, tropolone), 136.43, 135.24, 133.62, 127.20, 122.24 (5CH, tropolone), 58.29 (CH), 50.54 (C, Me_3C), 47.26, 19.39 (2CH_2), 28.70 (3CH_3), 12.57, 11.58 (2CH_3). Anal. Calcd for $C_{17}H_{26}N_2O_2$ (290.40): C 70.31, H 9.02, N 9.65. Found: C 70.26, H 9.06, N 9.67.

2-[Benzyl(7-oxo-1,3,5-cycloheptatrienyl)amino]-*N*^{1}-(tert-butyl)hexanamide (5e). Yellow oil, Yield: 90%. IR (KBr): 3431 (NH), 2922, 2852, 1628, 1033, 782 cm^{-1}; ^{1}H NMR δ 0.80 (t, $^3J_{HH}$ = 7.2 Hz, 3H, CH_3), 0.86-2.34 (m, 15H, 6H of propyl and 9H of Me_3C), 4.37 and 4.59 (AB-quartet, $^2J_{HH}$ = 16.8 Hz, 2H, N-CH_2Ph), 4.59 (t, $^3J_{HH}$ = 7.0 Hz, 1H, NCH, acyclic), 6.50 (d, $^3J_{HH}$ = 10.4 Hz, 1H, tropolone), 6.64 (t, $^3J_{HH}$ = 9.2 Hz, 1H, tropolone), 6.84 (t, $^3J_{HH}$ = 10.2 Hz, 1H, tropolone), 7.07-7.33 (m, 7H, 2CH of tropolone and Ph), 8.65 (br, s, 1H, NH). ^{13}C NMR δ 184.49 (CO, tropolone) and 170.17 (CO, amide), 157.98 (C, tropolone), 135.92 (C, arom), 136.57, 134.29, 133.82, 128.56, 127.23, 126.90, 126.49, 121.29 (10CH, tropolone and Ph), 62.07 (NCH), 50.67 (C, Me_3C), 49.51 (CH_2, PhCH_2), 28.88, 28.70, 28.51, 22.48 (3CH_2 and 3CH_3), 13.90 (CH_3, butyl). Anal. Calcd for $C_{24}H_{32}N_2O_2$ (380.52): C 75.75, H 8.48, N 7.36. Found: C 75.77, H 8.45, N 7.32.

2-[Benzyl(7-oxo-1,3,5-cycloheptatrienyl)amino]-*N*^{1}-(1,1,3,3-tetramethylbutyl)propanamide (5f). Yellow oil, Yield: 64%. IR (KBr): 3440 (NH), 2852, 1650, 1600, 1077, 775 cm^{-1}; ^{1}H NMR δ 1.04 (s, 9H, Me_3C), 1.29 (d, $^3J_{HH}$ = 6.80 Hz, 3H, CH_3), 1.41 (s, 6H, Me_2C), 2.14 (d, $^3J_{HH}$ = 14.4 Hz, 2H, CH_2), 4.42 (s, 2H, N-CH_2Ph), 4.64 (q, $^3J_{HH}$ = 7.0 Hz, 1H, NCH, acyclic), 6.55 (d, $^3J_{HH}$ = 10.0 Hz, 1H, tropolone); 6.68 (t, $^3J_{HH}$ = 8.8 Hz, 1H, tropolone); 6.86 (t, $^3J_{HH}$ = 10.4 Hz, 1H,

tropolone), 7.09-7.38 (m, 7H, 2CH of tropolone and Ph), 8.33 (br, s, 2H, NH). ^{13}C NMR δ 184.62 (CO, tropolone) and 170.48 (CO, amide), 157.11 (C, tropolone), 136.19 (C, arom), 136.32, 135.22, 133.46, 128.54, 127.29, 127.22, 127.00, 122.79 (10CH, tropolone and Ph), 58.20 (CH), 54.67 (C, HNC), 51.23, 49.69 ($2CH_2$), 31.61 (C, Me_3C), 31.48, 29.20, 29.07, 13.14 ($6CH_3$). Anal. Calcd for $C_{25}H_{34}N_2O_2$ (394.55): C 76.10, H 8.69, N 7.10. Found: C 76.06, H 8.71, N 7.07.

***N*^{1}-(Tert-butyl)-2-[isobutyl(7-oxo-1,3,5-cycloheptatrienyl)amino]propanamide (5g).** Yellow oil, Yield: 35%. IR (KBr): 3442 (NH), 2925, 2853, 1540, 1465, 1087, 668 cm^{-1}; ^{1}H NMR δ 0.81-0.91 (2d, 6H, $2CH_3$, isobutyl), 1.17 (d, $^3J_{HH}$ = 7.2 Hz, 3H, CH_3), 1.41 (s, 9H, Me_3C), 1.85 (m, $^3J_{HH}$ = 3.8 Hz, 1H, CH, isobutyl), 2.52-3.28 (m, 2H, CH_2), 4.27 (q, $^3J_{HH}$ = 7.2 Hz, 1H, NCH, acyclic), 6.74 (d, $^3J_{HH}$ = 10.0 Hz, 1H, tropolone), 6.84 (t, $^3J_{HH}$ = 9.2 Hz, 1H, tropolone), 7.07-7.30 (m, 3H, tropolone), 8.44 (br, s , 1H, NH). ^{13}C NMR δ 185.10 (CO, tropolone) and 170.94 (CO, amide), 158.16 (C, tropolone), 136.54, 136.46, 133.39, 128.21, 124.58 (5CH, tropolone), 58.79 (CH), 53.30 (CH_2), 50.54 (C, CMe_3), 28.71 ($3CH_3$, CMe_3), 23.74 (CH, isobutyl), 20.64 ($2CH_3$, isobutyl), 11.99 (CH_3). Anal. Calcd for $C_{18}H_{28}N_2O_2$ (304.43): C 71.02, H 9.27, N 9.20. Found: C 71.05, H 9.31, N 9.15.

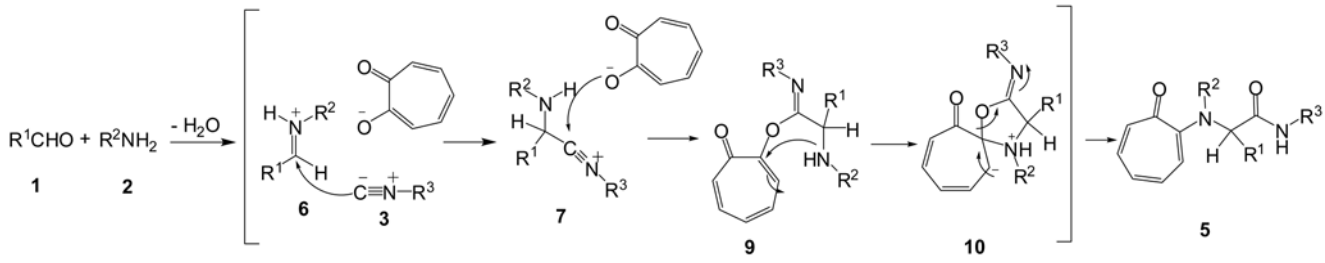
***N*^{1}-Cyclohexyl-2-[cyclohexyl(7-oxo-1,3,5-cycloheptatrienyl)amino]propanamide (5h).** Yellow oil, Yield: 71%. IR (KBr): 3431 (NH), 2922, 2852, 1628, 1033, 782 cm^{-1}; ^{1}H NMR δ 1.06-2.34 (m, 20H, CH_2 of 2cyclohexyl and 3H of CH_3), 3.24-3.76 (m, 2H, 2CH of 2cyclohexyl), 4.06 (q, $^3J_{HH}$ = 7.2 Hz, 1H, NCH, acyclic), 6.76 (t, $^3J_{HH}$ = 9.0 Hz, 1H, tropolone), 6.90-7.30 (m, 4H, tropolone), 8.07 (d, $^3J_{HH}$ = 7.60 Hz, 1H, NH). ^{13}C NMR δ 185.80 (CO, tropolone) and 172.21 (CO, amide), 157.62 (C, tropolone), 135.82, 135.40, 132.76, 128.00, 124.83 (5CH, tropolone), 60.33 (CH), 57.83, 47.86 (2CH, 2cyclohexyl), 32.81, 32.77, 32.48, 31.03, 26.05, 25.99, 25.74, 25.57, 24.74, 24.66 ($10CH_2$, 2cyclohexyl), 15.01 (CH_3). Anal. Calcd for $C_{22}H_{32}N_2O_2$ (356.50): C 74.12, H 9.05, N 7.86. Found: C 74.16, H 9.02, N 7.88.

***N*^{1}-(Tert-butyl)-2-[cyclohexyl(7-oxo-1,3,5-cycloheptatrienyl)amino]propanamide (5i).** Yellow oil, yield: 75%. IR (KBr): 3446 (NH), 3005, 2988, 1458, 1072, 897 cm^{-1}; ^{1}H NMR δ 1.04-2.10 (m, 10H, CH_2 of cyclohexyl, 3H of CH_3 and 9H of CMe_3), 3.31, (m, $^3J_{HH}$ = 11.4 Hz, 1H, cyclohexyl), 4.04 (q, $^3J_{HH}$ = 7.0 Hz, 1H, NCH, acyclic), 6.74 (t, $^3J_{HH}$ = 9.0 Hz, 1H, tropolone), 6.90-7.30 (m, 4H, tropolone), 7.95 (br, s, 1H, NH). ^{13}C NMR δ 185.59 (CO, tropolone) and 172.19 (CO, amide), 157.63 (C, tropolone), 135.80, 134.97, 132.84, 127.57, 123.85 (5CH, tropolone), 60.30, 58.18, (2CH), 50.59 (C, CMe_3), 32.81, 31.03 ($2CH_2$, cyclohexyl), 28.53 ($3CH_3$, *tert*-butyl), 26.13, 26.03, 25.73 ($3CH_2$, cyclohexyl), 14.79 (CH_3). Anal. Calcd for $C_{25}H_{38}N_2O_2$ (398.58): C 72.69, H 9.15, N 8.48. Found: C 72.64, H 9.10, N 8.53.

2-[Cyclohexyl(7-oxo-1,3,5-cycloheptatrienyl)amino]-*N*^{1}-(1,1,3,3-tetramethylbutyl)propanamide (5j). Yellow oil, Yield: 77%. IR (KBr): 3440 (NH), 2925, 2853, 1651, 1557, 1454, 1070, 739 cm^{-1}; ^{1}H NMR δ 0.99 (s, 9H, Me_3C), 1.00-2.20 (m, 10H, $5CH_2$ of cyclohexyl, 3H of CH_3, 6H of Me_2C and 2H of CH_2), 3.35 (m, $^3J_{HH}$ = 11.4 Hz, 1H, cyclohexyl), 4.03 (q, $^3J_{HH}$ = 7.0 Hz, 1H, NCH, acyclic), 6.71 (t, $^3J_{HH}$ = 8.5 Hz, 1H, tropolone), 6.86-7.30 (m, 4H, tropolone), 7.73 (br, s, 1H, NH). ^{13}C NMR δ 185.33 (CO, tropolone) and 171.63 (CO, amide), 157.40 (C, tropolone), 135.55, 134.80, 132.72, 127.26, 123.24 (5CH, tropolone), 60.33, 58.00, (2CH), 54.66 (C, Me_2C), 51.53 (CH_2), 32.86, 31.46, 31.02, 28.95, 28.56, 26.19, 25.73 ($4CH_2$ and CH of cyclohexyl, $2CH_3$ of Me_2C, $3CH_3$ of Me_3C and C of Me_3C), 14.88 (CH_3). Anal. Calcd for $C_{24}H_{32}N_2O_2$ (380.52): C 74.57, H 9.91, N 7.25. Found: C 74.63, H 9.97, N 7.31.

Results and Discussion

The 1:1 imine intermediate generated by the condensation reaction of an aldehyde **1** with a primary amine **2**, is trapped by an isocyanide **3** in the presence of tropolone **4**, to lead 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 and neutral conditions and no side reactions were observed. The structures of the products were deduced from their IR, ^{1}H NMR, ^{13}C NMR spectra and Mass spectrometery. For example the ^{1}H NMR spectrum of **5a** consisted of a triplet for the CH_3 of *n*-butyl (δ 0.81, $^3J_{HH}$ = 7.2 Hz), several multiplets for the cyclohexyl and *n*-butyl (δ 1.1-2.1) moieties, a multiplet for the NCH (δ 3.75-3.90) of cyclohexyl moiety, an AB-quartet for CH_2 of $PhCH_2$ (4.39 and 4.60, $^2J_{HH}$ = 16.6 Hz), a triplet for the NCH (δ 4.64, $^3J_{HH}$ = 6.0 Hz) of acyclic part, a douplet for the tropolone hydrogen (δ 6.51, $^3J_{HH}$ = 10.0 Hz), a triplet for the tropolone hydrogen (δ 6.63, $^3J_{HH}$ = 9.0 Hz), a triplet for the tropolone hydrogen (δ 6.84, $^3J_{HH}$ = 10.2 Hz), a multiplet for a tropolone hydrogen and phenyl group (δ 7.05-7.30) and a douplet for the NH (δ 8.64, $^3J_{HH}$ = 8.0 Hz). The ^{1}H-decoupled ^{13}C NMR spectrum of **5a** showed 22 distinct signals. Partial assignment of these signals is given in the



Scheme 2. Proposed mechanism for the formation of 2-(*N*,*N*-dialkylamino)-2,4,6-cycloheptatrien-1-one derivatives **5a-j**.

experimental section. The ^{1}H and ^{13}C NMR spectra of compounds **5b-j** were similar to those of **5a**, except for the aromatic or aliphatic moieties, which exhibited characteristic signals with appropriate chemical shifts.

A mechanistic pathway for this reaction is provided in Scheme 2. 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 aldehyde **1**, the next step may involve nucleophilic addition of the isocyanide **3** to the imine intermediate **6,** which leads to nitrilium intermediate **7**. 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 a Smiles rearrangements to afford the isolated 2-(*N*,*N*-dialkylamino)-2,4,6-cycloheptatrien-1-one derivatives **5** *via* intermediate **10**.

Conclusion

We believe that 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 aldehydes **1**, primary amines **2**, isocyanides **3** and tropolone **4**. Its ease of work-up, high yields and fairly mild reaction conditions make it a useful addition to modern synthetic methodologies.

References

1. Zhu, J.; Bienayme, H. *Multicomponent Reactions*; Wiley-Weinheim, 2005.
2. Bayat, M.; Imanieh, H.; Zabarjad Shiraz, N.; Shah Qavidel, M. *Monatsh Chem*. **2010**, *141*, 333.
3. Yavari, I.; Mirzaei, A.; Hossaini, Z.; Souri, S. *Mol Divers*. **2010**, *14*, 343.
4. (a) Ramazani, A.; Zeinali Nasrabadi, F.; Karimi, Z.; Rouhani, M. *Bull. Korean Chem. Soc.* **2011**, *32*, 2700. (b) Ramazani, A.; Rezaei, A.; Mahyari, A. T.; Rouhani, M.; Khoobi, M. *Helv. Chim. Acta.* **2010**, *93*, 2033. (c) Ramazani, A.; Mahyari, A. *Helv. Chim. Acta.* **2010**, *93*, 2203. (d) Ramazani, A.; Mahyari, A. T.; Rouhani, M.; Rezaei, A. *Tetrahedron Lett*. **2009**, *50*, 5625.
5. Ramazani, A.; Shajari, N.; Mahyari, A.; Ahmadi, Y. *Mol. Divers*. **2011**, *15*, 521.
6. Ramazani, A.; Nasrabadi, F. Z.; Mashhadi Malekzadeh, A.; Ahmadi, Y. *Monatsh Chem*. **2011**, *142*, 625.
7. Yavari, I.; Sabbaghan, M.; Hossaini, Z. *Mol. Divers*. **2007**, *11*, 1.
8. Yavari, I.; Hossaini, Z.; Sabbaghan, M. *Mol. Divers*. **2006**, *10*, 479.
9. Domling, A. *Chem. Rev.* **2006**, *106*, 17.
10. Ugi, I.; Werner, B.; Dömling, A. *Molecules* **2003**, *8*, 53.
11. Waller, R. W.; Diorazio, L. J.; Taylor, B. A.; Motherwell, W. B.; Sheppard, T. D. *Tetrahedron*. **2010**, *66*, 6496.
12. Ramazani, A.; Ahmadi, Y.; Rouhani, M.; Shajari, N.; Souldozi, A. *Heteroatom. Chem*. **2010**, *21*, 368.
13. (a) Ramazani, A.; Ahmadi, Y.; Tarasi, R. *Heteroatom. Chem*. **2011**, *22*, 79. (b) Souldozi, A.; Ślepokura, K.; Lis, T.; Ramazani, A. *Z. Naturforsch*. **2007**, *62b*, 835. (c) Ramazani, A.; Rezaei, A. *Org. Lett*. **2010**, *12*, 2852. (d) Ramazani, A.; Shajari, N.; Tofangchi Mahyari, A.; Khoobi, M.; Ahmadi, Y.; Souldozi, A. *Phosphorus. Sulfur. Silicon Relat. Elem*. **2010**, *185*, 2496.
14. Stolzenberg, H.; Weinberger, B.; Fehlhammer, W. P.; Pühlhofer, F. G.; Weiss, R. *Eur. J. Inorg. Chem*. **2005**, *21*, 4263.
15. Ramazani, A.; Bodaghi, A. *Tetrahedron. Lett*. **2000**, *41*, 567.
16. Pakravan, P.; Ramazani, A.; Noshiranzadeh, N.; Sedrpoushan, A. *Phosphorus. Sulfur.* **2007**, *182*, 545.
17. Ramazani, A.; Rahimifard, M.; Souldozi, A. *Phosphorus. Sulfur.* **2007**, *182*, 1.
18. Ramazani, A.; Rahimifard, M.; Noshiranzadeh, N.; Souldozi, A. *Phosphorus. Sulfur.* **2007**, *182*, 413.
19. Ramazani, A.; Ahmadi, E.; Kazemizadeh, A. R.; Dolatyari, L.; Noshiranzadeh, N.; Eskandari, I.; Souldozi, A. *Phosphorus. Sulphur.* **2005**, *180*, 2419.
20. Ramazani, A.; Shajari, N.; Gouranlou, F. *Phosphorus. Sulfur.* **2001**, *174*, 223.
21. Ramazani, A.; Amini, I.; Massoudi, A. *Phosphorus. Sulphur.* **2006**, *181*, 2225.
22. Souldozi, A.; Ramazani, A.; Bouslimani, N.; Welter, R. *Tetrahedron. Lett*. **2007**, *48*, 2617.
23. Souldozi, A.; Ramazani, A. *Tetrahedron. Lett*. **2007**, *48*, 1549.
24. Souldozi, A.; Ramazani, A. *Phosphorus. Sulfur.* **2009**, *184*, 3191.
25. Souldozi, A.; Ramazani, A. *Phosphorus. Sulfur.* **2009**, *184*, 2344.
26. Souldozi, A.; Ramazani, A. *Arkivoc.* **2008**, *16*, 235.