Gem-Disubstituted 4-Oxocyclohexanes: Source for Spiro Heterocycles

Venkatapuram Padmavathi*, Shaik Mahaboob Basha, Dandu Rangayapalle Chinna Venkata Subbaiah, Tippireddy Venkata Ramana Reddy and Adivireddy Padmaja

Department of Chemistry, Sri Venkateswara University, Tirupati 517 502, India
Received October 28, 2004

Novel spiro heterocycles, substituted spiro-pyrimidine, pyrazole and isoxazole compounds are prepared by the cyclocondensation of 4-oxocyclohexane *gem*-dicarboxylates and cyano esters with nucleophiles.

J. Heterocyclic Chem., **42**, 797 (2005).

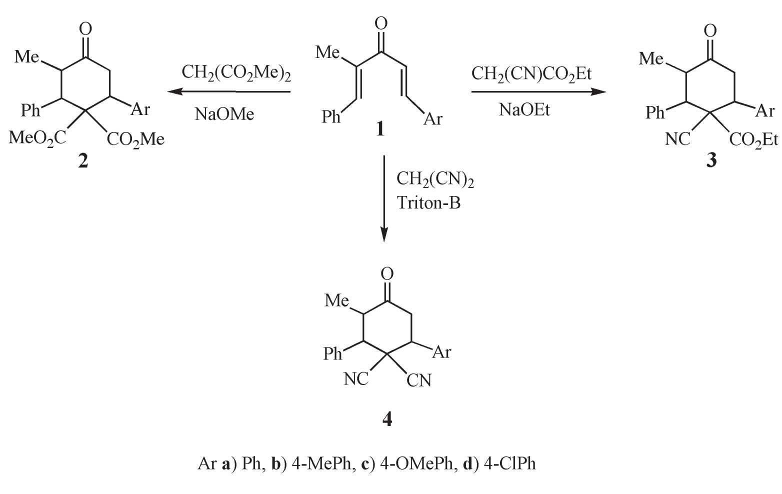
Introduction.

In the recent past, we have been actively engaged in the double Michael addition of active methylene compounds to activated bis olefins [1]. The cyclic adducts obtained have been used to prepare a variety of spiro heterocycles [2]. In continuation of our ongoing programme to develop some more interesting heterocycles, we thought of exploiting the double Michael adducts to build spiro-heterocycles; pyrimidine, pyrazole and isoxazole derivatives spiro to cyclohexanone system.

The synthetic scheme involves passing of dry gaseous hydrogen chloride into the mixture of unsymmetrical ketone and benzaldehyde to get 3-methyl-4-phenyl-3-buten-2-one [3]. The Claisen-Schmidt like reaction of the latter with araldehyde gave 1,5-diaryl-2-methyl-1,4-pentadien-3-one [4] (**1**). The latter is subjected to double Michael addition reaction with active methylene compounds *viz.*, dimethyl malonate, ethyl cyanoacetate and malononitrile in alcohol with 10% sodium alkoxide as a catalyst. The products after analysis were found to be 1,1-dimethoxycarbonyl-3-methyl-2-phenyl-6-aryl-4-oxocyclohexane (**2**), 1-cyano-1-ethoxycarbonyl-3-methyl-2-phenyl-6-aryl-4-oxocyclohexane (**3**) and 1,1-dicyano-3-methyl-2-phenyl-6-aryl-4-oxocyclohexane (**4**) [5] (Scheme 1).

It is well documented that pyrimidine, thioxopyrimidine, pyrazole and isoxazole derivatives were prepared by treating *gem*-dicarboxylates or *gem*-cyanoesters with urea, thiourea, hydrazine hydrate and hydroxylamine hydrochloride [6]. The cyclocondensation of **2** with the above nucleophiles afforded 7,11-diaryl-8-methyl-2,4-diazaspiro[5.5]undecane-1,3,5,9-tetraone (**5**), 7,11-diaryl-8-methyl-3-thioxo-2,4-diazaspiro[5.5]undecane-1,5,9-trione (**6**), 6,10-diaryl-7-methyl-2,3-diaza-spiro[4.5]decane-1,4,8-trione (**7**) and 6,10-diaryl-7-methyl-2-oxa-3-aza-spiro[4.5]decane-1,4,8-trione (**8**) (Scheme 2 and Table 1). Similar cyclocondensation of **3** with urea, thiourea, hydrazine hydrate and hydroxylamine hydrochloride produced 5-amino-3-hydroxy-8-methyl-7,11-diaryl-2,4-diazaspiro[5.5]undeca-2,4-diene-1,9-dione (**9**), 5-amino-3-mercapto-8-methyl-7,11-diaryl-2,4-diazaspiro[5.5]undeca-2,4-diene-1,9-dione (**10**), 4-amino-7-methyl-6,10-diaryl-2,3-diaza-spiro[4.5]dec-3-ene-1,8-dione (**11**) and 4-amino-7-methyl-6,10-diaryl-2-oxa-3-azaspiro[4.5]dec-3-ene-1,8-dione (**12**) (Scheme 3 and Table 1). The IR spectra of **5**-**12** exhibited absorption bands in the region 1495-1515 (C=S), 1645-1720 (*CO*NH), 1735-1775 (CO-O), 3300-3335 (OH), 3100-3300 (CONH and NH_2). The absorption for the SH group generally appears as a weak band around 2550-2600 [6],

Scheme 1



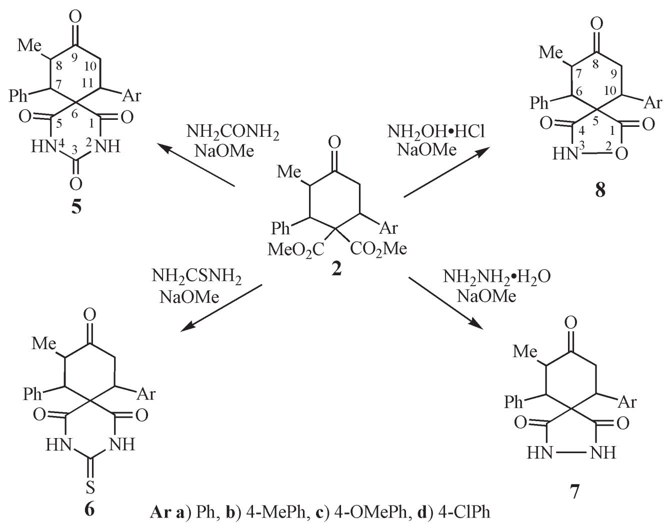
Ar **a**) Ph, **b**) 4-MePh, **c**) 4-OMePh, **d**) 4-ClPh

Table 1

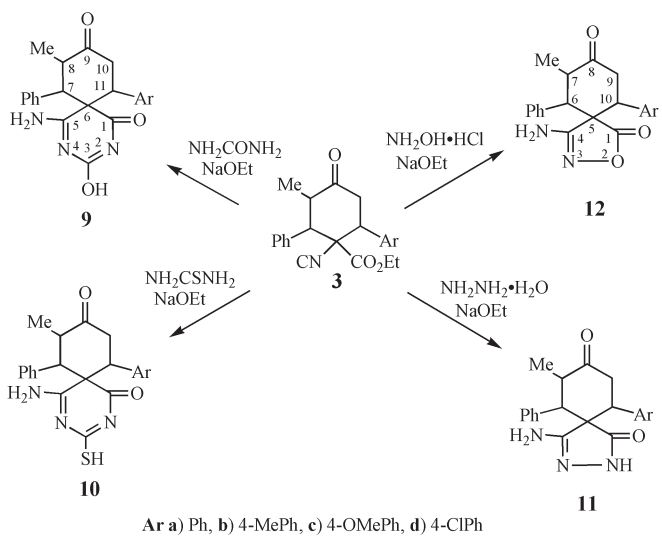
Physical Properties for Compounds **5-12**

Comp.	M.P (°C)	Yield (%)	Molecular formula (Molecular weight)	Calcd. (Found) % C	H	N
5a	296-298	56	$C_{22}H_{20}N_2O_4$ 376.41	70.20 (70.32)	5.36 (5.32)	7.44 (7.59)
5b	208-210	58	$C_{23}H_{22}N_2O_4$ 390.43	70.76 (70.85)	5.68 (5.63)	7.18 (7.08)
5c	228-230	55	$C_{23}H_{22}N_2O_5$ 406.43	68.00 (67.89)	5.45 (5.48)	6.89 (6.96)
5d	298-300	60	$C_{22}H_{19}ClN_2O_4$ 410.85	64.32 (64.22)	4.66 (4.70)	6.82 (6.76)
6a	294-296	59	$C_{22}H_{20}N_2O_3S$ 392.48	67.33 (67.26)	5.14 (5.12)	7.14 (7.20)
6b	212-214	61	$C_{23}H_{22}N_2O_3S$ 406.50	67.96 (67.86)	5.45 (5.40)	6.89 (6.98)
6c	225-227	57	$C_{23}H_{22}N_2O_4S$ 422.50	65.38 (65.52)	5.25 (5.21)	6.63 (6.79)
6d	290-292	55	$C_{22}H_{19}ClN_2O_3S$ 394.85	66.92 (66.81)	4.85 (4.90)	7.09 (7.02)
7a	182-184	65	$C_{21}H_{20}N_2O_3$ 348.40	72.39 (72.30)	5.79 (5.86)	8.04 (8.14)
7b	200-202	68	$C_{22}H_{22}N_2O_3$ 350.41	71.98 (72.10)	6.33 (6.28)	7.99 (8.07)
7c	222-224	62	$C_{22}H_{22}N_2O_4$ 366.41	68.84 (68.94)	6.05 (6.11)	7.64 (7.60)
7d	226-228	64	$C_{21}H_{19}ClN_2O_3$ 382.84	65.88 (65.80)	5.00 (4.92)	7.32 (7.40)
8a	176-178	67	$C_{21}H_{19}NO_4$ 349.39	72.19 (72.32)	5.48 (5.53)	4.00 (4.10)
8b	218-220	70	$C_{22}H_{21}NO_4$ 363.42	72.71 (72.82)	5.83 (5.80)	3.85 (3.80)
8c	224-226	64	$C_{22}H_{21}NO_5$ 379.42	69.64 (69.51)	5.53 (5.58)	3.69 (3.70)
8d	230-232	66	$C_{21}H_{18}ClNO_4$ 383.83	65.71 (65.68)	4.73 (4.70)	3.65 (3.60)
9a	292-294	57	$C_{22}H_{21}N_3O_3$ 375.43	70.38 (70.41)	5.64 (5.67)	11.19 (11.29)
9b	218-220	59	$C_{23}H_{23}N_3O_3$ 389.45	70.93 (71.00)	5.95 (5.90)	10.79 (10.88)
9c	238-240	56	$C_{23}H_{23}N_3O_4$ 405.45	68.13 (68.25)	5.72 (5.75)	10.36 (10.30)
9d	289-291	61	$C_{22}H_{20}ClN_3O_3$ 409.87	64.47 (64.40)	4.92 (4.90)	10.25 (10.18)
10a	280-282	62	$C_{22}H_{21}N_3O_2S$ 391.50	67.49 (67.42)	5.41 (5.35)	10.73 (10.82)
10b	222-224	59	$C_{23}H_{23}N_3O_2S$ 405.52	68.12 (68.24)	5.72 (5.76)	10.36 (10.47)
10c	236-238	68	$C_{23}H_{23}N_3O_3S$ 421.52	65.54 (65.62)	5.49 (5.45)	9.97 (9.92)
10d	282-284	65	$C_{22}H_{20}ClN_3O_2S$ 425.94	62.04 (62.10)	4.73 (4.75)	9.87 (9.93)
11a	215-217	67	$C_{21}H_{21}N_3O_2$ 347.42	72.60 (72.70)	6.09 (6.05)	12.09 (12.18)
11b	234-236	70	$C_{22}H_{23}N_3O_2$ 361.44	73.11 (73.00)	6.41 (6.37)	11.63 (11.73)
11c	240-242	72	$C_{22}H_{23}N_3O_3$ 377.44	70.00 (70.09)	6.14 (6.10)	11.13 (11.06)
11d	244-246	65	$C_{21}H_{20}ClN_3O_2$ 381.86	66.05 (66.00)	5.28 (5.24)	11.00 (11.12)
12a	185-187	70	$C_{21}H_{20}N_2O_3$ 348.40	72.39 (72.49)	5.79 (5.72)	8.04 (8.11)
12b	180-182	68	$C_{22}H_{22}N_2O_3$ 362.42	72.91 (72.97)	6.12 (6.15)	7.73 (7.69)
12c	190-192	59	$C_{22}H_{22}N_2O_4$ 378.42	69.76 (69.69)	5.86 (5.90)	7.40 (7.48)
12d	198-200	72	$C_{21}H_{19}ClN_2O_3$ 382.84	65.88 (65.80)	5.00 (4.97)	7.32 (7.40)

Scheme 2



Scheme 3



however, this is not observed for these compounds. The ^{1}H NMR spectra of **5-12** can be rationalized by presuming that the two aryl groups at C-7 and C-11 in **5**, **6**, **9** and **10** and at C-6 and C-10 in **7**, **8**, **11** and **12** are in true *cis*-1,3-arrangement in the preferred rigid chair conformation of cyclohexanone moiety whereas the pyrimidine, pyrazole and isoxazole rings which are nearly planar would be perpendicular to the average plane of the cyclohexanone ring [7] (Figure 1).

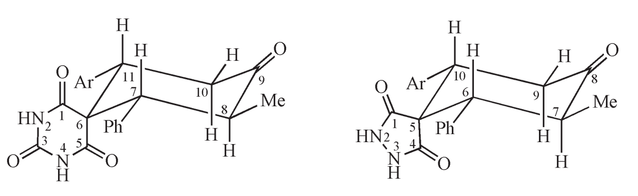


Figure 1

The C_7-H showed a doublet at 3.85 (**5a**), 3.88 (**6a**), 3.79 (**9a**) and 3.76 (**10a**), C_8-H a quintet at 4.26 (**5a**), 4.25 (**6a**), 4.19 (**9a**) and 4.17 (**10a**), C_{10}-H_{ax} a triplet at 3.08 (**5a**), 3.07 (**6a**), 3.04 (**9a**) and 3.02 (**10a**), C_{10}-H_{eq} a double doublet at 2.64 (**5a**), 2.63 (**6a**), 2.59 (**9a**) and 2.61 (**10a**), and C_{11}-H a double doublet at 4.39 (**5a**), 4.38 (**6a**), 4.27 (**9a**) and 4.29 (**10a**) in their ^{1}H NMR. However in the compounds **7a**, **8a**, **11a** and **12a** the C_6-H displayed a doublet at 3.96, 3.89, 3.84 and 3.87, C_7-H a quintet at 4.33, 4.35, 4.19 and 4.21, C_9-H a multiplet at 2.93, 2.93, 2.86 and 2.89 and C_{10}-H a double doublet at 4.44, 4.41, 4.32 and 4.35. All the compounds displayed signals due to NH and/or NH_2 protons, which disappeared on deuteration (Table 2). The structures of the compounds **5-12** were further confirmed by ^{13}C NMR spectral data (Table 2).

EXPERIMENTAL

Melting points were determined in open capillaries on a Mel-Temp apparatus and are uncorrected. The purity of the compounds was checked by TLC (silica gel H, BDH, ethyl acetate/hexane, 1:3). The IR spectra were recorded on a Perkin-Elmer 1600-series FT-IR spectrophotometer using KBr pellets and wave numbers are given in cm^{-1}. ^{1}H NMR spectra were recorded in $CDCl_3$ on a Varian EM-360 spectrophotometer 300 MHz. ^{13}C NMR spectra were recorded in $CDCl_3$ on a Varian VXR spectrometer at 75.5 MHz. All chemical shifts were reported in ppm from TMS as an internal standard. The elemental analyses were performed at Regional Sophisticated Instrumentation center, Punjab University, Chandigarh, India.

1,1-Dimethoxycarbonyl-3-methyl-2-phenyl-6-aryl-4-oxocyclohexane (**2**).

To a solution of 5 mmoles of **1** in 50 ml of methanol, 7 mmoles of dimethyl malonate was added. Then, freshly prepared 10 ml of 10% NaOMe solution (10 ml) was added dropwise and the contents were stirred for 8-10 hours at room temperature. The solution was concentrated and cooled in an ice bath. The separated solid was collected by filtration, washed with aqueous methanol, dried and recrystallized from methanol. **2a**: yield, 70%, mp, 178-180 °C; **2b**: yield, 65%, mp, 176-177 °C; **2c**: yield, 62%, mp, 190-191 °C; **2d**: yield, 72%, mp, 180-181 °C.

1-Cyano-1-ethoxycarbonyl-3-methyl-2-phenyl-6-aryl-4-oxocyclohexane (**3**).

A mixture of 5 mmoles of **1**, 7 mmoles of ethyl cyanoacetate and 40 ml of absolute ethanol were taken. To this, 10 ml of 10% NaOEt solution was added and the reaction mixture was refluxed for 3-4 hours. The contents were concentrated and kept in refrigerator overnight. The separated solid was collected by filtration, washed with cold alcohol, dried and recrystallized from ethanol. **3a**: yield, 72%, mp, 129-130 °C; **3b**: yield, 70%,

Table 2

Spectroscopic Data of Compounds **5-12**

Compd.	^{1}H NMR (CDCl$_3$), ppm	^{13}C NMR (CDCl$_3$), ppm
5a	0.96 (d, 3H, CH$_3$), 2.64 (dd, 1H, C$_{10}$-Heq, *J*=14.5, 4.6 Hz), 3.08 (t, 1H, C$_{10}$-Hax), 3.85 (d, 1H, C$_7$-H, *J*= 6.5 Hz), 4.26 (q, 1H, C$_8$-H), 4.39 (dd, 1H, C$_{11}$-H, *J*=13.8 Hz), 7.08-7.34 (m, 10H, Ar-H), 10.82 (bs, 2H, NH)	12.4 (CH$_3$), 179.6 (C$_1$ & C$_5$), 164.5 (C$_3$), 60.7 (C$_6$), 44.6 (C$_7$), 47.3 (C$_8$), 205.4 (C$_9$), 45.5 (C$_{10}$), 42.8 (C$_{11}$), 126.9, 128.7, 139.8 (Ar-C)
5b	0.98 (d, 3H, CH$_3$), 2.32 (s, 3H, Ar-CH$_3$), 2.65 (dd, 1H, C$_{10}$-Heq, *J*=14.4, 4.6 Hz), 3.11 (t, 1H, C$_{10}$-Hax), 3.83 (d, 1H, C$_7$-H, *J*= 6.3 Hz), 4.24 (q, 1H, C$_8$-H), 4.32 (dd, 1H, C$_{11}$-H, *J*=13.5 Hz), 6.98-7.36 (m, 9H, Ar-H), 10.76 (bs, 2H, NH)	12.2 (CH$_3$), 21.4 (Ar-CH$_3$), 178.5 (C$_1$ & C$_5$), 166.3 (C$_3$), 59.5 (C$_6$), 43.9 (C$_7$), 47.7 (C$_8$), 204.2 (C$_9$), 44.9 (C$_{10}$), 43.2 (C$_{11}$), 126.2, 128.1, 128.8, 129.6, 135.4, 136.7, 140.2 (Ar-C)
5c	0.89 (d, 3H, CH$_3$), 2.65 (dd, 1H, C$_{10}$-Heq, *J*=14.5, 4.5 Hz), 3.13 (t, 1H, C$_{10}$-Hax), 3.75 (s, 3H, Ar-OCH$_3$), 3.91 (d, 1H, C$_7$-H, *J*= 6.2 Hz), 4.28 (q, 1H, C$_8$-H), 4.38 (dd, 1H, C$_{11}$-H, *J*=13.6 Hz), 6.65-7.32 (m, 9H, Ar-H), 10.79 (bs, 2H, NH)	12.2 (CH$_3$), 51.8 (Ar-OCH$_3$), 179.2 (C$_1$ & C$_5$), 164.2 (C$_3$), 60.2 (C$_6$), 43.8 (C$_7$), 47.5 (C$_8$), 202.6 (C$_9$), 45.2 (C$_{10}$), 42.9 (C$_{11}$), 114.3, 126.4, 129.3, 130.5, 132.2, 140.2, 160.1 (Ar-C)
5d	1.04 (d, 3H, CH$_3$), 2.66 (dd, 1H, C$_{10}$-Heq, *J*=14.3, 4.5 Hz), 3.11 (t, 1H, C$_{10}$-Hax), 3.89 (d, 1H, C$_7$-H, *J*= 6.4 Hz), 4.25 (q, 1H, C$_8$-H), 4.38 (dd, 1H, C$_{11}$-H, *J*=13.5 Hz), 7.14-7.35 (m, 9H, Ar-H), 10.87 (bs, 2H, NH)	12.6 (CH$_3$), 176.5 (C$_1$ & C$_5$), 165.3 (C$_3$), 60.6 (C$_6$), 43.7 (C$_7$), 48.2 (C$_8$), 202.5 (C$_9$), 45.6 (C$_{10}$), 41.8 (C$_{11}$), 126.5, 128.2, 128.8, 130.2, 132.0, 138.4, 140.2 (Ar-C)
6a	0.89 (d, 3H, CH$_3$), 2.63 (dd, 1H, C$_{10}$-Heq, *J*=14.3, 4.5 Hz), 3.07 (t, 1H, C$_{10}$-Hax), 3.88 (d, 1H, C$_7$-H, *J*= 6.4 Hz), 4.25 (q, 1H, C$_8$-H), 4.38 (dd, 1H, C$_{11}$-H, *J*=13.6 Hz), 7.04-7.42 (m, 10H, Ar-H), 9.87 (bs, 2H, NH)	12.3 (CH$_3$), 174.8 (C$_1$ & C$_5$), 159.6 (C$_3$), 59.8 (C$_6$), 43.5 (C$_7$), 46.9 (C$_8$), 203.7 (C$_9$), 42.7 (C$_{10}$), 40.5 (C$_{11}$), 126.5, 128.9, 140.2 (Ar-C)
6b	0.87 (d, 3H, CH$_3$), 2.24 (s, 3H, Ar-CH$_3$), 2.61 (dd, 1H, C$_{10}$-Heq, *J*=14.4, 4.7 Hz), 3.11 (t, 1H, C$_{10}$-Hax), 3.85 (d, 1H, C$_7$-H, *J*= 6.5 Hz), 4.27 (q, 1H, C$_8$-H), 4.41 (dd, 1H, C$_{11}$-H, *J*=13.8 Hz), 6.94-7.40 (m, 9H, Ar-H), 9.85 (bs, 2H, NH)	12.1 (CH$_3$), 21.5 (Ar-CH$_3$), 175.2 (C$_1$ & C$_5$), 159.3 (C$_3$), 58.7 (C$_6$), 43.9 (C$_7$), 47.1 (C$_8$), 202.6 (C$_9$), 42.3 (C$_{10}$), 41.6 (C$_{11}$), 126.4, 128.5, 128.9, 129.8, 135.6, 137.1, 140.5 (Ar-C)
6c	0.93 (d, 3H, CH$_3$), 2.60 (dd, 1H, C$_{10}$-Heq, *J*=14.2, 4.5 Hz), 3.09 (t, 1H, C$_{10}$-Hax), 3.76 (s, 3H, Ar-OCH$_3$), 3.85 (d, 1H, C$_7$-H, *J*= 6.5 Hz), 4.26 (q, 1H, C$_8$-H), 4.37 (dd, 1H, C$_{11}$-H, *J*=13.5 Hz), 6.96-7.39 (m, 9H, Ar-H), 9.91 (bs, 2H, NH)	12.2 (CH$_3$), 51.5 (Ar-OCH$_3$), 177.3 (C$_1$ & C$_5$), 158.4 (C$_3$), 60.1 (C$_6$), 42.8 (C$_7$), 46.5 (C$_8$), 203.3 (C$_9$), 42.9 (C$_{10}$), 41.2 (C$_{11}$), 114.2, 126.3, 129.5, 130.0, 131.1, 132.1, 140.4, 160.3 (Ar-C)
6d	0.95 (d, 3H, CH$_3$), 2.66 (dd, 1H, C$_{10}$-Heq, *J*=14.3, 4.4 Hz), 3.09 (t, 1H, C$_{10}$-Hax), 3.89 (d, 1H, C$_7$-H, *J*= 6.5 Hz), 4.23 (q, 1H, C$_8$-H), 4.42 (dd, 1H, C$_{11}$-H, *J*=13.5 Hz), 7.15-7.48 (m, 9H, Ar-H), 9.94 (bs, 2H, NH)	12.0 (CH$_3$), 177.5 (C$_1$ & C$_5$), 158.1 (C$_3$), 59.6 (C$_6$), 43.7 (C$_7$), 47.1 (C$_8$), 202.7 (C$_9$), 41.9 (C$_{10}$), 40.3 (C$_{11}$), 126.4, 128.5, 129.3, 130.4, 132.1, 138.6, 141.3 (Ar-C)
7a	1.02 (d, 3H, CH$_3$), 2.93 (m, 2H, C$_9$-H), 3.96 (d, 1H, C$_6$-H, *J*= 6.7 Hz), 4.33 (q, 1H, C$_7$-H), 4.44 (dd, 1H, C$_{10}$-H, *J*=13.5 Hz), 7.04-7.43 (m, 10H, Ar-H), 10.94 (bs, 2H, NH)	11.9 (CH$_3$), 170.6 (C$_1$ & C$_4$), 60.5 (C$_5$), 44.7 (C$_6$), 46.8 (C$_7$), 202.3 (C$_8$), 45.7 (C$_9$), 43.6 (C$_{10}$), 126.3, 129.6, 140.8 (Ar-C)
7b	0.99 (d, 3H, CH$_3$), 2.24 (s, 3H, Ar-CH$_3$), 2.90 (m, 2H, C$_9$-H), 3.97 (d, 1H, C$_6$-H, *J*= 6.5 Hz), 4.29 (q, 1H, C$_7$-H), 4.45 (dd, 1H, C$_{10}$-H, *J*=13.3 Hz), 6.95-7.41 (m, 9H, Ar-H), 10.89 (bs, 2H, NH)	11.6 (CH$_3$), 21.4 (Ar-CH$_3$), 171.2 (C$_1$ & C$_4$), 60.9 (C$_5$), 43.9 (C$_6$), 46.6 (C$_7$), 202.5 (C$_8$), 45.8 (C$_9$), 43.4 (C$_{10}$), 126.5, 128.7, 129.2 (Ar-C)
7c	1.01 (d, 3H, CH$_3$), 2.95 (m, 2H, C$_9$-H), 3.78 (s, 3H, Ar-OCH$_3$), 3.94 (d, 1H, C$_6$-H, *J*= 6.5 Hz), 4.34 (q, 1H, C$_7$-H), 4.42 (dd, 1H, C$_{10}$-H, *J*=13.2 Hz), 6.97-7.44 (m, 9H, Ar-H), 10.90 (bs, 2H, NH)	12.0 (CH$_3$), 51.8 (Ar-OCH$_3$), 170.7 (C$_1$ & C$_4$), 60.8 (C$_5$), 43.8 (C$_6$), 46.1 (C$_7$), 202.2 (C$_8$), 45.9 (C$_9$), 42.9 (C$_{10}$), 114.6, 126.4, 128.6, 129.9, 130.5, 132.6, 140.4, 160.6 (Ar-C)
7d	1.05 (d, 3H, CH$_3$), 2.96 (m, 2H, C$_9$-H), 3.95 (d, 1H, C$_6$-H, *J*= 6.6 Hz), 4.35 (q, 1H, C$_7$-H), 4.47 (dd, 1H, C$_{10}$-H, *J*=13.3 Hz), 7.12-7.47 (m, 9H, Ar-H), 10.98 (bs, 2H, NH)	11.9 (CH$_3$), 171.2 (C$_1$ & C$_4$), 60.8 (C$_5$), 45.1 (C$_6$), 46.3 (C$_7$), 202.7 (C$_8$), 45.5 (C$_9$), 43.7 (C$_{10}$), 126.3, 128.8, 129.2, 131.4, 132.2, 138.6, 141.2 (Ar-C)
8a	1.04 (d, 3H, CH$_3$), 2.93 (m, 2H, C$_9$-H), 3.89 (d, 1H, C$_6$-H, *J*= 6.7 Hz), 4.35 (q, 1H, C$_7$-H), 4.41 (dd, 1H, C$_{10}$-H, *J*=13.4 Hz), 7.10-7.45 (m, 10H, Ar-H), 10.87 (bs, 1H, NH)	11.3 (CH$_3$), 169.4 (C$_1$), 171.6 (C$_4$), 60.4 (C$_5$), 44.9 (C$_6$), 45.8 (C$_7$), 203.3 (C$_8$), 45.7 (C$_9$), 43.5 (C$_{10}$), 125.9, 129.7, 140.3 (Ar-C)
8b	1.02 (d, 3H, CH$_3$), 2.23 (s, 3H, Ar-CH$_3$), 2.91 (m, 2H, C$_9$-H), 3.90 (d, 1H, C$_6$-H, *J*= 6.6 Hz), 4.34 (q, 1H, C$_7$-H), 4.43 (dd, 1H, C$_{10}$-H, *J*=13.5 Hz), 6.97-7.43 (m, 9H, Ar-H), 10.92 (bs, 1H, NH)	11.5 (CH$_3$), 21.6 (Ar-CH$_3$), 168.2 (C$_1$), 170.6 (C$_4$), 60.6 (C$_5$), 44.8 (C$_6$), 46.1 (C$_7$), 202.6 (C$_8$), 45.3 (C$_9$), 43.6 (C$_{10}$), 126.2, 128.1, 128.8, 129.7, 135.2, 137.4, 140.7 (Ar-C)
8c	1.04 (d, 3H, CH$_3$), 2.94 (m, 2H, C$_9$-H), 3.76 (s, 3H, Ar-OCH$_3$), 3.87 (d, 1H, C$_6$-H, *J*= 6.6 Hz), 4.33 (q, 1H, C$_7$-H), 4.42 (dd, 1H, C$_{10}$-H, *J*=13.3 Hz), 6.95-7.43 (m, 9H, Ar-H), 10.93 (bs, 1H, NH)	11.8 (CH$_3$), 51.3 (Ar-OCH$_3$), 169.5 (C$_1$), 171.6 (C$_4$), 60.5 (C$_5$), 45.2 (C$_6$), 45.8 (C$_7$), 201.8 (C$_8$), 45.6 (C$_9$), 43.3 (C$_{10}$), 115.1, 126.8, 129.9, 131.2, 132.4, 140.3, 160.5 (Ar-C)
8d	1.06 (d, 3H, CH$_3$), 2.95 (m, 2H, C$_9$-H), 3.88 (d, 1H, C$_6$-H, *J*= 6.6 Hz), 4.36 (q, 1H, C$_7$-H), 4.45 (dd, 1H, C$_{10}$-H, *J*=13.6 Hz), 7.14-7.46 (m, 9H, Ar-H), 10.92 (bs, 1H, NH)	12.2 (CH$_3$), 169.9 (C$_1$), 172.3 (C$_4$), 61.2 (C$_5$), 44.9 (C$_6$), 46.3 (C$_7$), 201.9 (C$_8$), 45.9 (C$_9$), 44.1 (C$_{10}$), 126.2, 129.2, 129.8, 130.7, 132.5, 138.7, 141.2 (Ar-C)
9a	0.87 (d, 3H, CH$_3$), 2.59 (dd, 1H, C$_{10}$-Heq, *J*=14.3, 4.5 Hz), 3.04 (t, 1H, C$_{10}$-Hax), 3.79 (d, 1H, C$_7$-H, *J*= 6.6 Hz), 4.19 (q, 1H, C$_8$-H), 4.27 (dd, 1H, C$_{11}$-H, *J*=13.6 Hz), 6.69 (bs, 3H, NH$_2$ & OH), 7.02-7.44 (m, 10H, Ar-H)	12.2 (CH$_3$), 177.4 (C$_1$), 162.6 (C$_3$), 187.3 (C$_5$), 61.2 (C$_6$), 45.4 (C$_7$), 48.3 (C$_8$), 202.9 (C$_9$), 45.8 (C$_{10}$), 43.7 (C$_{11}$), 126.4, 129.7, 141.6 (Ar-C)
9b	0.89 (d, 3H, CH$_3$), 2.24 (s, 3H, Ar-CH$_3$), 2.58 (dd, 1H, C$_{10}$-Heq, *J*=14.2, 4.4 Hz), 3.06 (t, 1H, C$_{10}$-Hax), 3.77 (d, 1H, C$_7$-H, *J*= 6.5 Hz), 4.18 (q, 1H, C$_8$-H), 4.24 (dd, 1H, C$_{11}$-H, *J*=13.3 Hz), 6.67 (bs, 3H, NH$_2$ & OH), 6.93-7.46 (m, 9H, Ar-H)	12.1 (CH$_3$), 21.2 (Ar-CH$_3$), 176.7 (C$_1$), 161.5 (C$_3$), 188.2 (C$_5$), 60.9 (C$_6$), 45.2 (C$_7$), 47.6 (C$_8$), 202.8 (C$_9$), 45.5 (C$_{10}$), 43.2 (C$_{11}$), 126.6, 128.8, 129.2, 129.8, 135.6, 137.2, 146.2 (Ar-C)

Table 2 (continued)

Compd.	^{1}H NMR (CDCl$_3$), ppm	^{13}C NMR (CDCl$_3$), ppm
9c	0.86 (d, 3H, CH$_3$), 2.63 (dd, 1H, C$_{10}$-Heq, J=14.4, 4.6 Hz), 3.07 (t, 1H, C$_{10}$-Hax), 3.74 (s, 3H, Ar-OCH$_3$), 3.78 (d, 1H, C$_7$-H, J= 6.5 Hz), 4.21 (q, 1H, C$_8$-H), 4.26 (dd, 1H, C$_{11}$-H, J=13.5 Hz), 6.71 (bs, 3H, NH$_2$ & OH), 6.96-7.48 (m, 9H, Ar-H)	12.2 (CH$_3$), 51.2 (Ar-OCH$_3$), 175.7 (C$_1$), 161.6 (C$_3$), 189.2 (C$_5$), 60.5 (C$_6$), 45.3 (C$_7$), 47.2 (C$_8$), 202.2 (C$_9$), 45.5 (C$_{10}$), 43.6 (C$_{11}$), 115.4, 127.2, 130.1, 131.5, 132.8, 141.6, 160.7 (Ar-C)
9d	0.91 (d, 3H, CH$_3$), 2.62 (dd, 1H, C$_{10}$-Heq, J=14.4, 4.5 Hz), 3.07 (t, 1H, C$_{10}$-Hax), 3.78 (d, 1H, C$_7$-H, J= 6.5 Hz), 4.21 (q, 1H, C$_8$-H), 4.32 (dd, 1H, C$_{11}$-H, J=13.5 Hz), 6.71 (bs, 3H, NH$_2$ & OH), 7.14-7.48 (m, 9H, Ar-H)	12.0 (CH$_3$), 176.9 (C$_1$), 162.7 (C$_3$), 189.4 (C$_5$), 60.8 (C$_6$), 45.6 (C$_7$), 48.0 (C$_8$), 202.3 (C$_9$), 45.6 (C$_{10}$), 43.3 (C$_{11}$), 126.3, 129.2, 130.2, 131.2, 132.5, 138.8, 141.5 (Ar-C)
10a	0.91 (d, 3H, CH$_3$), 2.61 (dd, 1H, C$_{10}$-Heq, J=14.4, 4.7 Hz), 3.02 (t, 1H, C$_{10}$-Hax), 3.76 (d, 1H, C$_7$-H, J= 6.4 Hz), 4.17 (q, 1H, C$_8$-H), 4.29 (dd, 1H, C$_{11}$-H, J=13.4 Hz), 6.58 (bs, 3H, NH$_2$ & SH), 7.00-7.48 (m, 10H, Ar-H)	12.0 (CH$_3$), 176.7 (C$_1$), 162.9 (C$_3$), 179.9 (C$_5$), 60.2 (C$_6$), 46.1 (C$_7$), 47.9 (C$_8$), 201.4 (C$_9$), 44.6 (C$_{10}$), 42.8 (C$_{11}$), 126.4, 129.6, 141.6 (Ar-C)
10b	0.87 (d, 3H, CH$_3$), 2.23 (s, 3H, Ar-CH$_3$), 2.62 (dd, 1H, C$_{10}$-Heq, J=14.3, 4.5 Hz), 3.04 (t, 1H, C$_{10}$-Hax), 3.79 (d, 1H, C$_7$-H, J= 6.5 Hz), 4.14 (q, 1H, C$_8$-H), 4.32 (dd, 1H, C$_{11}$-H, J=13.2 Hz), 6.62 (bs, 3H, NH$_2$ & SH), 6.92-7.45 (m, 9H, Ar-H)	12.1 (CH$_3$), 21.8 (Ar-CH$_3$), 176.6 (C$_1$), 162.9 (C$_3$), 178.7 (C$_5$), 60.3 (C$_6$), 45.9 (C$_7$), 47.6 (C$_8$), 202.2 (C$_9$), 43.6 (C$_{10}$), 43.3 (C$_{11}$), 126.7, 128.6, 129.3, 130.2, 135.4, 136.3, 141.5 (Ar-C)
10c	0.88 (d, 3H, CH$_3$), 2.64 (dd, 1H, C$_{10}$-Heq, J=14.5, 4.8 Hz), 3.02 (t, 1H, C$_{10}$-Hax), 3.74 (d, 1H, C$_7$-H, J= 6.3 Hz), 3.79 (s, 3H, Ar-OCH$_3$), 4.18 (q, 1H, C$_8$-H), 4.28 (dd, 1H, C$_{11}$-H, J=13.5 Hz), 6.61 (bs, 3H, NH$_2$ & SH), 6.91-7.47 (m, 9H, Ar-H)	12.8 (CH$_3$), 51.5 (Ar-OCH$_3$), 175.8 (C$_1$), 161.3 (C$_3$), 179.2 (C$_5$), 60.5 (C$_6$), 46.0 (C$_7$), 47.8 (C$_8$), 202.6 (C$_9$), 44.5 (C$_{10}$), 42.6 (C$_{11}$), 115.2, 126.8, 129.5, 130.7, 132.4, 140.5, 160.3 (Ar-C)
10d	0.92 (d, 3H, CH$_3$), 2.68 (dd, 1H, C$_{10}$-Heq, J=14.3, 4.8 Hz), 3.05 (t, 1H, C$_{10}$-Hax), 3.79 (d, 1H, C$_7$-H, J= 6.5 Hz), 4.19 (q, 1H, C$_8$-H), 4.32 (dd, 1H, C$_{11}$-H, J=13.5 Hz), 6.56 (bs, 3H, NH$_2$ & SH), 7.12-7.50 (m, 9H, Ar-H)	12.5 (CH$_3$), 177.2 (C$_1$), 161.4 (C$_3$), 179.0 (C$_5$), 60.2 (C$_6$), 45.8 (C$_7$), 47.3 (C$_8$), 201.6 (C$_9$), 43.7 (C$_{10}$), 41.6 (C$_{11}$), 126.9, 128.7, 129.2, 130.5, 132.2, 138.6, 141.4 (Ar-C)
11a	1.01 (d, 3H, CH$_3$), 2.86 (m, 2H, C$_9$-H), 3.84 (d, 1H, C$_6$-H, J= 6.5 Hz), 4.19 (q, 1H, C$_7$-H), 4.32 (dd, 1H, C$_{10}$-H, J=13.3 Hz), 6.61 (bs, 3H, NH2 & NH), 6.99-7.39 (m, 10H, Ar-H)	11.9 (CH$_3$), 173.2 (C$_1$), 165.5 (C$_4$), 60.8 (C$_5$), 45.3 (C$_6$), 47.7 (C$_7$), 200.8 (C$_8$), 44.9 (C$_9$), 43.7 (C$_{10}$), 126.3, 128.9, 140.9 (Ar-C)
11b	1.03 (d, 3H, CH$_3$), 2.20 (s, 3H, Ar-CH$_3$), 2.84 (m, 2H, C$_9$-H), 3.85 (d, 1H, C$_6$-H, J= 6.4 Hz), 4.21 (q, 1H, C$_7$-H), 4.29 (dd, 1H, C$_{10}$-H, J=13.5 Hz), 6.58 (bs, 3H, NH$_2$ & NH), 6.87-7.36 (m, 9H, Ar-H)	11.7 (CH$_3$), 21.5 (Ar-CH$_3$), 173.6 (C$_1$), 166.7 (C$_4$), 60.7 (C$_5$), 44.9 (C$_6$), 47.5 (C$_7$), 201.2 (C$_8$), 44.6 (C$_9$), 42.9 (C$_{10}$), 126.9, 128.7, 129.5, 130.4, 135.6, 136.7, 141.2 (Ar-C)
11c	0.99 (d, 3H, CH$_3$), 2.88 (m, 2H, C$_9$-H), 3.75 (s, 3H, Ar-OCH$_3$), 3.88 (d, 1H, C$_6$-H, J= 6.2 Hz), 4.16 (q, 1H, C$_7$-H), 4.35 (dd, 1H, C$_{10}$-H, J=13.2 Hz), 6.59 (bs, 3H, NH$_2$ & NH), 6.94-7.38 (m, 9H, Ar-H)	11.3 (CH$_3$), 51.6 (Ar-OCH$_3$), 172.9 (C$_1$), 165.6 (C$_4$), 60.8 (C$_5$), 45.2 (C$_6$), 47.4 (C$_7$), 201.5 (C$_8$), 44.8 (C$_9$), 43.5 (C$_{10}$), 114.8, 126.5, 129.7, 130.3, 132.6, 140.4, 160.5 (Ar-C)
11d	1.02 (d, 3H, CH$_3$), 2.86 (m, 2H, C$_9$-H), 3.87 (d, 1H, C$_6$-H, J= 6.6 Hz), 4.18 (q, 1H, C$_7$-H), 4.36 (dd, 1H, C$_{10}$-H, J=13.3 Hz), 6.65 (bs, 3H, NH2 & NH), 7.12-7.48 (m, 9H, Ar-H)	11.5 (CH$_3$), 171.8 (C$_1$), 166.9 (C$_4$), 60.9 (C$_5$), 45.4 (C$_6$), 47.8 (C$_7$), 200.3 (C$_8$), 44.9 (C$_9$), 43.9 (C$_{10}$), 126.7, 128.5, 129.6, 130.4, 132.6, 138.8, 141.3 (Ar-C)
12a	1.06 (d, 3H, CH$_3$), 2.89 (m, 2H, C$_9$-H), 3.87 (d, 1H, C$_6$-H, J= 6.6 Hz), 4.21 (q, 1H, C$_7$-H), 4.35 (dd, 1H, C$_{10}$-H, J=13.2 Hz), 6.59 (bs, 2H, NH$_2$), 6.95-7.42 (m, 10H, Ar-H)	12.2 (CH$_3$), 170.4 (C$_1$), 164.1 (C$_4$), 60.7 (C$_5$), 45.5 (C$_6$), 47.9 (C$_7$), 201.6 (C$_8$), 45.1 (C$_9$), 43.8 (C$_{10}$), 126.9, 129.8, 141.3 (Ar-C)
12b	1.03 (d, 3H, CH$_3$), 2.21 (s, 3H, Ar-CH$_3$), 2.87 (m, 2H, C$_9$-H), 3.84 (d, 1H, C$_6$-H, J= 6.5 Hz), 4.22 (q, 1H, C$_7$-H), 4.38 (dd, 1H, C$_{10}$-H, J=13.3 Hz), 6.57 (bs, 2H, NH$_2$), 6.88-7.43 (m, 9H, Ar-H)	12.1 (CH$_3$), 21.2 (Ar-CH$_3$), 170.8 (C$_1$), 165.2 (C$_4$), 61.2 (C$_5$), 44.8 (C$_6$), 48.2 (C$_7$), 201.7 (C$_8$), 44.3 (C$_9$), 43.6 (C$_{10}$), 126.7, 128.5, 129.4, 130.3, 135.2, 136.6, 140.9 (Ar-C)
12c	1.04 (d, 3H, CH$_3$), 2.90 (m, 2H, C$_9$-H), 3.78 (s, 3H, Ar-OCH$_3$), 3.90 (d, 1H, C$_6$-H, J= 6.5 Hz), 4.23 (q, 1H, C$_7$-H), 4.38 (dd, 1H, C$_{10}$-H, J=13.3 Hz), 6.62 (bs, 2H, NH$_2$), 6.88-7.45 (m, 9H, Ar-H)	11.9 (CH$_3$), 51.7 (Ar-OCH$_3$), 171.9 (C$_1$), 164.9 (C$_4$), 61.3 (C$_5$), 44.9 (C$_6$), 48.3 (C$_7$), 200.9 (C$_8$), 43.9 (C$_9$), 42.8 (C$_{10}$), 115.3, 126.7, 129.4, 130.3, 132.8, 140.6, 160.5 (Ar-C)
12d	1.06 (d, 3H, CH$_3$), 2.92 (m, 2H, C$_9$-H), 3.92 (d, 1H, C$_6$-H, J= 6.5 Hz), 4.24 (q, 1H, C$_7$-H), 4.36 (dd, 1H, C$_{10}$-H, J=13.3 Hz), 6.64 (bs, 2H, NH2), 7.15-7.48 (m, 9H, Ar-H)	12.4 (CH$_3$), 171.3 (C$_1$), 163.8 (C$_4$), 61.8 (C$_5$), 45.7 (C$_6$), 48.5 (C$_7$), 202.6 (C$_8$), 44.7 (C$_9$), 43.6 (C$_{10}$), 126.8, 128.6, 129.5, 130.3, 132.5, 138.7, 141.1 (Ar-C)

mp, 131-132 °C; **3c**: yield, 75%, mp, 125-126 °C; **3d**: yield, 68%, mp, 148-149 °C.

1,1-Dicyano-3-methyl-2-phenyl-6-aryl-4-oxocyclohexane (**4**).

A solution of 5 mmoles of **1** and 7 mmoles of malononitrile in 50 ml methanol was stirred for 30 minutes and then Triton-B (8 ml) was added. The stirring was continued for 5-6 hours at room temperature. The separated solid was collected by filtration, washed with cold aqueous methanol, dried and recrystallized from alcohol. **4a**: yield, 74%, mp, 154-155 °C; **4b**: yield, 68%, mp, 136-138 °C; **4c**: yield, 70%, mp, 144-146 °C; **4d**: yield, 65%, mp, 138-140 °C.

7,11-Diaryl-8-methyl-2,4-diaza-spiro[5.5]undecane-1,3,5,9-tetraone (**5**) 7,11-Diaryl-8-methyl-3-thioxo-2,4-diaza-spiro[5.5]-undecane-1,5,9-trione (**6**) 6,10-Diaryl-7-methyl-2,3-diaza-spiro-[4.5]decane-1,4,8-trione (**7**) and 6,10-Diaryl-7-methyl-2-oxa-3-azaspiro[4.5]decane-1,4,8-trione (**8**).

A mixture of 5 mmoles of **2** and urea or thiourea (5 mmoles) or 80% hydrazine hydrate (8 mmoles) or hydroxylamine hydrochloride (5 mmoles) in 15 ml of ethanol and 5 ml of 10% NaOMe was refluxed for 8-10 hours. Then, it was cooled and poured onto crushed ice containing concentrated HCl. The product obtained was collected by filtration, dried and purified by recrystallization from methanol.

5-Amino-3-hydroxy-8-methyl-7,11-diaryl-2,4-diaza-spiro-[5.5]undeca-2,4-diene-1,9-dione (**9**) 5-Amino-3-mercapto-8-methyl-7,11-diaryl-2,4-diaza-spiro[5.5]undeca-2,4-diene-1,9-dione (**10**) 4-Amino-7-methyl-6,10-diaryl-2,3-diaza-spiro[4.5]-dec-3-ene-1,8-dione (**11**) and 4-Amino-7-methyl-6,10-diaryl-2-oxa-3-aza-spiro[4.5]dec-3-ene-1,8-dione (**12**).

To a solution of 5 mmoles of **3** in 15 ml of ethanol, urea or thiourea (5 mmoles) or 80% hydrazine hydrate (8 mmoles) or hydroxylamine hydrochloride (5 mmoles) and 5 ml of 10% NaOEt was added and refluxed for 8-12 hours. The contents were cooled and poured onto crushed ice containing concentrated HCl. The product that separated was collected by filtration and dried. Recrystallization of the crude compound from ethanol resulted pure sample.

Acknowledgements.

We thank Prof. D. Bhaskar Reddy, Emeritus Professor of UGC for his helpful discussion and suggestion. The authors are grateful to CSIR, New Delhi for financial assistance under major research project.

REFERENCES AND NOTES

* To whom correspondence should be addressed: Email: vkpuram2001@yahoo.com

[1a] D. Bhaskar Reddy, V. Padmavathi and S. Reddy, *Sulfur Lett*., **13**, 123 (1991); [b] D. Bhaskar Reddy, V. Padmavathi and M. Muralidhar Reddy, *Indian J. Chem*., **31B**, 407 (1992); [c] V. Padmavathi, T. V. Ramana Reddy, K. Venugopal Reddy, K. Audisesha Reddy and D. Bhaskar Reddy, *Indian J. Chem*., **40B**, 667 (2001); [d] D. Bhaskar Reddy, N. Chandrasekhar Babu and V.Padmavathi, *J. Heterocyclic Chem*., **38**, 769 (2001).

[2a] D. Bhaskar Reddy, V. Padmavathi, B. Seenaiah and M. V. Ramana Reddy, *Org. Prep. Proced. Int*., **24**, 21 (1992); [b] D. Bhaskar Reddy, V. Padmavathi and P. V. Ramana Reddy, *Indian J. Chem*., **31B**, 774 (1992); [c] D. Bhaskar Reddy, V. Padmavathi, B. Seenaiah and A. Padmaja, *Heteroatom Chem*., **4**, 55 (1993); [d] D. Bhaskar Reddy, M. V. Ramana Reddy and V. Padmavathi, *Indian J. Chem*., **37B**, 167 (1998); [e] D. Bhaskar Reddy, M. V. Ramana Reddy and V. Padmavathi, *Heteroatom Chem*., **10**, 17 (1999); [f] D. Bhaskar Reddy, N. Chandrasekhar Babu and V. Padmavathi, *Heteroatom Chem*., **12**, 131 (2001).

[3] M. T. Bogert and D. Davidson, *J. Am. Chem. Soc*., **54**, 334 (1932).

[4] K. Ramalingam, K. D. Berlin, R. A. Loghry, D. H. Helm and N. Satya Murthy, *J. Org. Chem*., **44**, 477 (1979).

[5] V. Padmavathi, T. V. Ramana Reddy, K. Venugopal Reddy, K. Audisesha Reddy and D. Bhaskar Reddy, *Indian J. Chem.*, **40B**, 667 (2001).

[6a] V. G. Voronin, O. Yu. Polevaya, V. G. Makhanova, M. A. Landau, V. M. Kolbanov, T. P. Privol'neva, V. V. Chugunov and E. F. Laverlskaya, *Khim-Farm Zh*., **10**, 43 (1976); [b] M. I. Al-Asmawi, K. M. Ghoneim and M. Khalifa, *Pharmazie*, **35**, 591 (1980); [c] C. Abdehmajid and F. Houda, *Ann Furin Fr*., **38**, 429 (1980); [d] D. Bhaskar Reddy, N. Chandrasekhar Babu and V. Padmavathi, *J. Heterocyclic Chem*., **38**, 769 (2001); [e] V. Padmavathi, A. Balaiah, K. Venugopal Reddy, A. Padmaja and D. Bhaskar Reddy, *Indian J. Chem.*, **41B**, 1670 (2002); [f] V. Padmavathi, A. Balaiah, A. Padmaja and D. Bhaskar Reddy, *Phosphorous, Sulfur & Silicon*, **177**, 2791 (2002); [g] V. Padmavathi, A. Balaiah and D. Bhaskar Reddy, *J. Heterocyclic Chem.*, **39**, 649 (2002); [h] V. Padmavathi, A. Balaiah, T. V. Ramana Reddy, B. Jagan Mohan Reddy and D. Bhaskar Reddy, *Heteroatom Chem.*, **14**, 513 (2003); [i] V. Padmavathi, D. R. C. Venkata Subbaiah, M. Rajagopala Sarma and A. Balaiah, *Heteroatom Chem.*, **15**, 477 (2003).

[7] R. M. Silverstein, G. C. Bassler and T. C. Morrill, Spectrometric Identification of Organic Compounds fifth edition, John Wiley & Sons, New York.

[8] H. A. P. De Jongh and H. Blynberg, *Tetrahedron*, **21**, 515 (1965).