Chem Sci Trans., 2012, **1(2),** 329-334
DOI:10.7598/cst2012.213

Chemical Science Transactions
ISSN/E-ISSN: 2278-3458/2278-3318

RESEARCH ARTICLE

2,4,4,6-Tetrabromocyclohex-2,5-dien-1-one: An Excellent Reagent for Dibromination of Methyl at C-6 in Biginelli Compounds

SUDHIR C PAL*, GOPAL C PATRA, SANKAR C BHUNIA and MONOJ K ROY

Chemistry Department, Midnapore College, Midnapore, W.B., India
sudhirpal08@gmail.com

Received 28 May 2012 / Accepted 15 June 2012

Abstract: Biginelli compounds (ethyl 4-substituted-2-oxo-1,2,3,4-tetrahydropyrimidine-6-carboxylates) prepared from cyclodehydration of ethyl acetoacetate, urea and aromatic (or aliphatic) aldehydes have been subjected to bromination using (i) $Br_2/CHCl_3$ (ii) Br_2/AcOH and (iii) 2,4,4,6-tetrabromocyclohex-2-en-1-one (TBCO) separately. The last one *viz*., TBCO is found to be the best reagent in preparing the 6-dibromethyl derivative in terms of yield and green context.

Keywords: 2,4,4,6-Tetrabromocyclohex-2-en-1-one, Biginelli compounds, Dibromination, Bromine

Introduction

Multicomponent reactions are assuming importance day by day because these involve lesser number of steps and have several other distinct advantages over linear type syntheses.[1] Biginelli condensation is one such reaction that yields products having dihydropyrimidine core. These compounds are being evaluated for various pharmacological activities.[2] The substituents at various positions are important in controlling bioactivity. As such elaboration / modification of different functionalitities and groups of Biginelli compounds (DHPMs) are being carried to prepare newer derivatives that would be / are being tested for medicinal and other biological activities.

Reactive methyl group at C-6 offer one scope for modification and introduction of interesting moieties. Conversion into $–CH_2Br$ and $–CHBr_2$ is one easy route for this purpose. This would reverse the polarity and provide access to nucleophilic group to be introduced at this position. Indeed one multidirectional cyclisation[3] leading to furo[3,4-*d*]pyrimidine, pyrrolo[3,4-*d*]pyrimidine and pyrimido[4,5-*d*]pyridazines was reported using $–CH_2Cl$ at C-6 in a solid phase synthesis. However –Cl was present in the starting active methylene compound in this case. In another citation the same group of workers[4] used click chemistry to prepare triazole derivatives of DHPMs *via* formation of $–CH_2Br$ under flow reaction condition. They followed the reported bromination of only a few DHPMs with bromine/chloroform by Zigeuner and associates[5]. The same bromination route was followed in order to prepare some condensed heterocycles[6] from Biginelli compounds. In another

communication C-6 sulfonylmethyl derivatives were prepared in which the DHPMs were monobrominated at C-6 methyl employing dioxane dibromide[7] as brominating agent. Kheder and co-workers[8] prepared some C-6 derivatives of DHPMs *via* monobromination of the C-6 methyl group. They used Br_2 in acetic acid as brominating agent. A C-6 $–CHBr_2$ was reported to be converted into –CN group by Kappe[9] in which the same Zigeuner method[5] was followed to prepare $–CHBr_2$ derivative from only one DHPM.

Experimental

The chemicals were purchased from Spectrochem and Hi-Media and were used as such. The solvents were purified and dried by standard procedure. 2,4,4,6-Tetrabromocyclohex-2,5-dien-1-one (TBCO) was prepared from 4-bromophenol. The ^{1}H NMR spectra were recorded with Bruker instruments. The ^{13}C NMR spectra of two samples (8 & 10) were recorded on Bruker 150 MHz spectrometer.

*General procedure for the preparation of dibromides (**1-10**) using Br_2/ acetic acid*

Substrate (2 mmol) was dissolved in ~ 10 mL glacial acetic acid and stirred magnetically in cold (15 – 20^{o}C). A solution of bromine (6 mmol) in acetic acid was added slowly. The mixture was allowed to attain room temperature and the stirring was continued until no further improvement in conversion was noticed (TLC). Almost an hour was needed to attain equilibrium. The mixture was then diluted with water, neutralized with $NaHCO_3$, and then extracted with DCM. The dried extract was chromatographed over silica gel (60 – 120 mesh). The melting points and yield of products are given in Table 2.

*General procedure for the preparation of dibromides (**1-10**) using 2,4,4,6-tetrabromocyclohex-2,5-dien-1-one (TBCO)*

Substrate (2 mmol) was dissolved in ~ 10 mL dry DCM and stirred magnetically. A solution of TBCO (6 mmol) in ~10 mL dry DCM was added slowly. The stirring was continued for 30 – 35 minutes during which almost complete conversion occurred. A little more solvent was added and the mixture was washed free from tribromophenol by repeated washing with aqueous K_2CO_3 solution. The dried extract was slowly evaporated to give crystals. In most cases (II – V, VII – XI) these products were once more recrystalised from chloroform to give pure products. Only in case of (VI) and (X) products were purified by column chromatography (silica gel; 60 – 120 mesh). All the products were white solids. The melting points and yield of products are given in Table 2.

Spectral and analytical data of the dibromides (1-10)

*Ethyl 6-dibromomethyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-6-carboxylate (**1**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.036 (s, 1H, -C<u>H</u>Br_2), 7.390 – 7.260 (m, 5H, -C_6<u>H</u>$_5$), 7.161 (s, 1H, -N<u>H</u>-), 5.607 (s, 1H, -N<u>H</u>-), 5.384 (d, *J* = 2.7 Hz, 1H, <u>H</u>-4), 4.129 (q, *J* = 7.2 Hz, 2H, -OC<u>H</u>$_2$-), 1.196 (t, *J* = 7.2 Hz, 3H, -C<u>H</u>$_3$).

*Ethyl 4-[4-chlorophenyl]-6-dibromomethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-6-carbo-xylate (**2**)*

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.012 (s, 1H, -C<u>H</u>Br_2), 7.316 (d, *J* = 8.4 Hz, 2H, <u>H</u>-3′ and <u>H</u>-5′), 7.228 (d, *J* = 8.4 Hz, 2H, <u>H</u>-2′ and <u>H</u>-6′), 7.170 (s, 1H, -N<u>H</u>-), 5.801 (s, 1H, -N<u>H</u>-), 5.371 (d, *J* = 2.8 Hz, 1H, <u>H</u>-4), 4.144 (q, *J* = 7 Hz, 2H, -OC<u>H</u>$_2$-), 1.194 (t, *J* = 7 Hz, 3H, -C<u>H</u>$_3$). LCMS: *m/z* 451.0 (M^+ +1), 452.1, 455.0. Anal. Calcd. for $C_{13}H_{13}Br_2ClN_2O_3$: C 35.45, H 2.97, N 6.36%. Found: C 35.51, H 3.01 and N 6.33%.

*Ethyl 4-[4-bromophenyl]-6-dibromomethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-6-carboxylate (**3**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.007 (s, 1H, -C<u>H</u>Br_2), 7.466 (d, *J* = 8.4 Hz, 2H, <u>H</u>-3′ and <u>H</u>-5′), 7.183 (s, 1H, -N<u>H</u>-), 7.170 (d, *J* = 8.4 Hz, 2H, <u>H</u>-2′ and <u>H</u>-6′), 5.720 (s, 1H, -N<u>H</u>-), 5.356 (d, *J* = 3 Hz, 1H, <u>H</u>-4), 4.145 (q, *J* = 7.2 Hz, 2H, -OC<u>H_2</u>-), 1.197 (t, *J* = 7.2 Hz, 3H, -C<u>H_3</u>). **HRMS**: *m/z* 516.8366 (M^++23), 518.8353, 520.8337, 522.8289 in the intensity ratio of 1:3:3:1 (Cald. for $C_{14}H_{13}N_2O_3Br_3Na$: 516.8374, 518.8354, 520.8334, 522.8317).

*Ethyl 6-dibromomethyl-4-[3-nitrophenyl]-2-oxo-1,2,3,4-tetrahydropyrimidine-6-carboxylate (**4**)*

^{1}H NMR (200 MHz, $CDCl_3$): δ 8.200 – 8.165 (m, 2H, <u>H</u>-2′ and 4′), 8.061 (s, 1H, -C<u>H</u>Br_2), 7.685 – 7.510 (m, 2H, <u>H</u>-5′ and 6′), 7.379 (s, 1H, -N<u>H</u>-), 6.129 (s, 1H, -N<u>H</u>-), 5.530 (d, *J* = 3 Hz, 1H, <u>H</u>-4), 4.140 (q, *J* = 7 Hz, 2H, -OC<u>H_2</u>-), 1.31 (t, *J* = 7 Hz, 3H, -C<u>H_3</u>). **MS**: *m/z* 483.94 (M^++23), 485.93 and 487.94 in the intensity ratio 1:2:1. Anal. Calcd. for $C_{13}H_{13}Br_2N_3O_5$: C 34.62, H 2.90, N 9.32%. Found: C 34.51, H 2.88 and N 9.40%.

*Ethyl 6-dibromomethyl-4-[4-nitrophenyl]-2-oxo-1,2,3,4-tetrahydropyrimidine-6-carboxylate (**5**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.120 (d, *J* = 8.4 Hz, 2H, <u>H</u>-3′ and <u>H</u>-5′), 7.907, (s, 1H, , -C<u>H</u>Br_2), 7.392 (d, *J* = 8.4 Hz, 2H, <u>H</u>-2′ and <u>H</u>-6′), 7.260 (s, 1H, -N<u>H</u>-), 6.033 (s, 1H, -N<u>H</u>-), 5.424 (d, *J* = 2.1 Hz, 1H, <u>H</u>-4), 4.066 (q, *J* = 7 Hz, 2H, -OC<u>H_2</u>-), 1.107 (t, *J* = 7 Hz, 3H, -C<u>H_3</u>). Anal. Calcd. for $C_{13}H_{13}Br_2N_3O_5$: C 34.62, H 2.90, N 9.32%. Found: C 34.67, H 2.85 and N 9.36%.

*Ethyl 4-[4-coumarin-6-yl]-6-dibromomethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-6-carboxylate (**6**)*

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.998, (s, 1H, -C<u>H</u>Br_2), 7.663 (d, *J* = 10 Hz, 1H, <u>H</u>-4 of coumaryl group), 7.470 (dd, *J* = 8.5 and 2 Hz, 1H, <u>H</u>-7 of coumaryl group), 7.411 (d, *J* = 2 Hz, 1H, <u>H</u>-5 of coumaryl group), 7.320 (d, *J* = 8.5 Hz, 1H, <u>H</u>-8 of coumaryl group), 7.084, (s, 1H, -N<u>H</u>-), 6.453 (d, *J* = 10 Hz, 1H, <u>H</u>-3 of coumaryl group), 5.466, (s, 1H, -N<u>H</u>-), 5.297 (s, 1H, <u>H</u>-4), 4.168 (q, *J* = 7 Hz, 2H, -OC<u>H_2</u>-), 1.080 (t, *J* = 7 Hz, 3H, -C<u>H_3</u>). **HRMS**: *m/z* 506.9170 (M^+ + 23), 508.9147, 510.9145 in the intensity ratio of 1:2:1 (calculated for $C_{17}H_{14}N_2O_5Br_2Na$: 506.9167, 508.9148, 510.9131).

*Ethyl 6-dibromomethyl-4-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-6-carboxylate (**7**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.942 (s, 1H, -C<u>H</u>Br_2), 7.058, (br. s, 1H, -N<u>H</u>-), 5.436 (br. s, 1H, -N<u>H</u>-), 4.490 – 4.50 (m, 1H, <u>H</u>-4), 4.340 – 4.190 (m, 2H, -OC<u>H_2</u>-), 1.350 - 1.300 (m, 6H, 2 -C<u>H_3</u>). **MS**: *m/z* 376.97 (M^+ +23), 378.97 and 380.97 in the intensity ratio 1:2:1.

*Ethyl 6-dibromomethyl-4-[4-methylphenyl]-2-oxo-1,2,3,4-tetrahydropyrimidine-6-carboxylate (**8**)*

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.020 (s, 1H, , -C<u>H</u>Br_2), 7.157 (ABq, 4H, -C_6<u>H_4</u>-), 6.991 (s, 1H, -N<u>H</u>-), 5.344 (d, *J* = 2.5 Hz, 1H, <u>H</u>-4), 5.297 (s, 1H, -N<u>H</u>-), 4.127 (q, *J* = 7 Hz, 2H, -OC<u>H_2</u>-), 2.328, (s, 3H, benzylic -C<u>H_3</u>), 1.190 (t, *J* = 7 Hz, 3H, -C<u>H_3</u>). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 163.88 (-<u>C</u>$O_2$$CH_3$), 152.39 (-HN<u>C</u>ONH-), 144.12 (><u>C</u>=), 139.25 (><u>C</u>=), 138.30 (><u>C</u>=), 129.61 (2 X –CH=), 126.55 (2 X –CH=), 100.49 (><u>C</u>=), 61.25 (-O<u>C</u>H_2), 55.10 (4-<u>C</u>H<), 31.95 (-<u>C</u>HBr_2), 21.10 (-$C_6$$H_4$<u>C</u>$H_3$), 13.89 (-$CH_2$<u>C</u>$H_3$). **LCMS**: *m/z* 452.99 (M^+ +23), 455 and 456.99 in the intensity ratio 1:2:1. Anal. calcd. for $C_{14}H_{16}Br_2N_2O_3$: C 40.03, H 3.84, N 6.67%. Found: C 39.81, H 3.88 and N 6.73%.

*Ethyl 6-dibromomethyl-4-[4-methoxyphenyl]-2-oxo-1,2,3,4-tetrahydropyrimidine-6-carboxylate (**9**)*

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.015 (s, 1H, -CHBr$_2$), 7.210 (d, *J* = 7.8 Hz, 2H, H-3′ and H-5′), 7.081, (s, 1H, -NH-), 6.855 (d, *J* = 7.8 Hz, 2H, H-2′ and H-5′) 5.465 (s, 1H, -NH-), 5.334 (d, *J* = 2.7 Hz, 1H, H-4), 4.131 (q, *J* = 7 Hz, 2H, -OCH$_2$-), 3.819, (s, 3H, -OCH$_3$), 1.191 (t, *J* = 7 Hz, 3H, -CH$_3$). Anal. Calcd. for $C_{14}H_{16}Br_2N_2O_4$: C 38.56, H 3.70, N 6.42%. Found: C 38.50, H 3.64 and N 6.49%.

*Ethyl 6-dibromomethyl-4-[3-bromo-4-hydroxy-5-methoxyphenyl]-2-oxo-1,2,3,4-tetrahydropyrimidine-6-carboxylate (**10**)*

IR: λ_{max} 3510, 1710 and 1695 cm^{-1}. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.045 (s, 1H, -CHBr$_2$), 7.027, (s, 1H, disappeared D_2O shaking, -NH-), 7.010 (d, *J* = 2 Hz, 1H, H-2′ / H-6′), 6.752 (d, *J* = 2 Hz, 1H, H-6′ / H-2′), 5.955 (s, 1H, disappeared on D_2O shaking, -OH), 5.377, (s, 1H, disappeared on D_2O shaking, -NH-), 5.283 (d, *J* = 2.7 Hz, 1H, H-4), 4.146 (q, *J* = 7.2 Hz, 2H, -OCH$_2$-), 3.833, (s, 3H, -OCH$_3$), 0.905 (t, *J* = 7.2 Hz, 3H, -CH$_3$). **^{13}C NMR** (150 MHz, $CDCl_3$): δ 163.52 (-CO$_2$CH$_3$), 151.16 (-HNCONH-), 147.71 (=C<), 144.16 (=C<), 143.43 (=C<), 134.73 (=C<), 123.32 (-CH<), 108.06 (=C<), 107.68 (-CH=), 100.49 (>C<), 61.53 (-OCH$_2$), 56.33 (-OCH$_3$), 55.18 (4-CH<), 31.99 (-CHBr$_2$), and 13.96 (-CH$_3$). **MS**: *m/z* 562.87 (M^+ +23), 564.85, 566.85 and 568.87 in the intensity ratio 1:3:3:1. Anal. calcd. for $C_{14}H_{15}Br_3N_2O_5$: C 31.67, H 2.85, N 5.28%. Found: C 31.77, H 2.90 and N 5.22%.

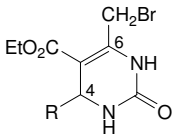
Conversion of (3) into ethyl 4-[4-bromophenyl]-6-formyl-2-oxo-1,2,3,4-tetra-hydropyrimidine-6-carboxylate (A):

The substrate (0.5 mmol) was dissolved in methanol. To this a cold aqueous methanolic solution of silver acetate (0.5 mmol) was added and stirred magnetically for 20 minutes. Then methanol was removed, the mixture was diluted with 20 ml water and then extracted with ethyl acetate. The product, after chromatographic separation, recrystallised out as colouless solid, m. p. 202 °C ($CHCl_3$-MeOH) in good yield (55%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 10.484 (s, 1H, -CHO), 7.495 (d, *J* = 8.1 Hz, 2H, H-3′ and H-5′), 7.434 (s, 1H, -NH-), 7.226 (d, *J* = 8.1 Hz, 2H, H-2′ and H-6′), 5.939 (s, 1H, -NH-), 5.530 (d, *J* = 2.7 Hz, 1H, H-4), 4.212 (q, *J* = 7.0 Hz, 2H, -OCH$_2$-), 1.253 (t, *J* = 7.2 Hz, 3H, -CH$_3$).

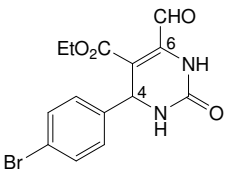
Results and Discussion

We are looking for an efficient method to prepare C_6 –$CHBr_2$ derivatives from a large number of Biginelli compounds appearing in the literature. A –$CHBr_2$ group could be equivalent to a –CHO. In fact we are able to convert one dibromide derivative **3** (Figure 2) into the corresponding aldehyde **A** (Figure 1) in good yield. This is important since oxidation of C-6 methyl to –CHO is not successful.[10]

We used molecular bromine in $CHCl_3$ and in acetic acid for the preparation of the dibromides. The results were not satisfactory. The methods gave incomplete conversion and resulted in a mixture of mono- and dibromo-products along with some unreacted substrates even after a considerable period of time and using excess of the reagents. We used 2,4,4,6-tetrabromocyclohex-2,5-dienone (TBCO)[11] for the purpose. This gave much higher yield of dibromo derivatives. A comparison of yield and mono-/dibromo- products ratio for three substrates (structures given in Figure 1 and 2) is presented in Table 1.

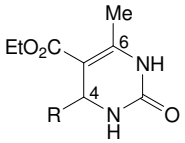


(1a) : R = C_6H_5
(8a) : R = 4-$CH_3C_6H_4$

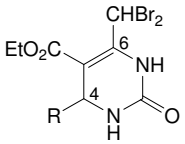


(A)

Figure 1. Structure of monobromide derivative



(I) : R = C_6H_5
(II) : R = 4-ClC_6H_4
(III) : R = 4-BrC_6H_4
(IV) : R = 3-$O_2NC_6H_4$
(V) : R = 4-$O_2NC_6H_4$
(VI) : R = Coumarin-6-yl
(VII) : R = CH_3
(VIII) : R = 4-$CH_3C_6H_4$
(IX) : R = 4-$CH_3OC_6H_4$
(X) : R = 4-HO-3-MeO-C_6H_3



(1) : R = C_6H_5
(2) : R = 4-ClC_6H_4
(3) : R = 4-BrC_6H_4
(4) : R = 3-$O_2NC_6H_4$
(5) : R = 4-$O_2NC_6H_4$
(6) : R = Coumarin-6-yl
(7) : R = CH_3
(8) : R = 4-$CH_3C_6H_4$
(9) : R = 4-$CH_3OC_6H_4$
(10) : R = 3-Br-4-HO-5-MeO-C_6H_3

Figure 2. Structure of dibromide derivative

Table 1. Comparative bromination of DHPMs with different reagents[a]

Substrate	Ratio of products	$Br_2/CHCl_3$ (% Yield)[b]	Br_2/AcOH (%Yield)[b]	TBCO (%Yield)[b]
(I)	(1a) : (1)	1:2.5 (72%)	1:3 (80%)	1:8 (91%)
(II)	(2a) : (2)	1:4 (74%)	1:7 (80%)	1:10 (93%)
(VIII)	(8a) : (8)	1:4 (80%)	1:7 (83%)	1:9.5 (94%)

[a]*Sufficient time was given to attain equilibrium (i.e., until no further improvement in conversion was noted (TLC)).* [b]*Total yield.*

Thereafter we carried bromination on a number of substrates using Br_2 /AcOH and TBCO. The yield of dibromides is much better with TBCO (Table 2), and in some cases pure products were obtained simply by recrystallisation. The method with TBCO is at the same time non-hazardous, too. The reactions with TBCO were carried under mild conditions at room temperature in anhydrous dichloromethane. The reactions required some 30 - 45 minutes for completion using two mmol of the substrate. Less time (~ 15 minutes) was needed if reactions are carried under reflux. The product from vanillin contained one more Br at the phenolic aryl group. This could not be avoided even by limiting the amount of reagent. TBCO was found to be selective in bromination of C-6 methyl without affecting the double bond of the lactone ring in coumarin (VI). Bromine in acetic acid gave a complex mixture of products in this case; probably this double bond was also affected[12] under this condition. Structures of all the substrates and products are given in Figure 2.

All the dibromo-compounds have been characterized by spectral analyses (Mass, ^{1}H NMR). A typical sharp singlet at ~δ 8.0 in all the ^{1}H NMR spectra is due to proton of –$CHBr_2$ group. The purity of the new products was checked by either by HRMS (compounds 3 and 6) data or elemental analyses (samples 2, 4, 5, 8, 9 and 10).

Table 2. Yield and melting points of dibromoderivatives (**1** – **10**)

Substrate	Product	M.P. (^oC)	Yield (%)[a]	
			Br_2/AcOH[b]	TBCO[c]
I	1	186^o (lit.181^o)[5]	60	80
II	2	104 – 05^o	78	85
III	3	176 – 77^o	82	92
IV	4	140 – 42^o	58	90
V	5	159^o	60	87
VI	6	209 - 10^o	-[d]	87
VII	7	160 – 62^o (lit.161^o)[5]	50	84
VIII	8	170^o	80	85
IX	9	176^o	83	93
X	10[e]	179^o	65	88

[a]Isolated yield. [b]Time: 1 hour for 2 mmol of a substrate. [c]Time: 30 – 35 minutes for 2 mmol of substrate. [d]The product was a mixture that could not be separated. [b]The product contains one Br at the aromatic ring (2 equiv. of reagent was used).

Conclusion

In conclusion it can be said that 2,4,4,6-tetrabromocyclohex-2,5-dienone is a very effective and green reagent for dibromination of C-6 methyl of dihydropyrimidones (Biginelli compounds).

Acknowledgements

The authors acknowledge the financial assistance of the UGC in the form of minor research project.

References

1. (a) Armstrong R W, Combs A P, Tempest P A, Brown S D and Keating T A, *Acc Chem Res.,* 1966, **29**, 123-131; (b) Domling A, Ugi I, *Angew Chem., Int. Ed.* 2000, **39**, 3168-3210.
2. (a) Kappe C O, *Eur J Med Chem.,* 2000, **35***,* 1043-1052 *and the references cited therein;* (b) Tawfik H A, Bassyouni F, Gamal-Eldin A M, Abo-Zeid M A and El-Hamouly W S, *Pharmacological Reports,* 2009, **61***,* 1153-1162.
3. Perez R, Beryozkina T, Zbruyev I, Haas W and Kappe O C, *J Comb Chem.,* 2002, **4**, 501-510.
4. Khanetskyy B, Dallinger D and Kappe C O, *J Comb Chem.,* 2004, **6**, 884-892.
5. (a) Zigeuner G, Hamberger H, Blascke H and Sterk H, *Monatsh Chem*., 1966, **97**, 1408-1421; (b) Zigeuner G and Knopp C. *Monatsh. Chem*., **1970**, 101, 1541-1546.
6. George T, Tahilramani R and Mehta D V, *Synthesis,* 1975, 405-7.
7. Quan Z J, Wei Q B, Ma D D, Da Y X, Wang X C and Shen M S, *Synthetic Commun.,* 2009, **39**, 2230-2239.
8. Kheder N A, Mabkhot Y N and Farag A M, *Heterocycl.,* 2008, **75**, 887-897.
9. Kappe C O, *Liebigs Ann Chem.,* 1990, 505-507.
10. Khanna E L and Dubur*s* G, *Khimya Geterotsiklicheskikh Soedinenii,* 1982, **(4),** 535-538.
11. Matveeva E D, Feshin D B and Zefirov N S, *Russian J Org Chem,*. 2001, **17***,* 52-55.
12. Fuson R C, Kneisley J W, Kaiser E W, *Org Synth., Coll,* 1955, **3**, 209.