Regioselective Aryl Radical Cyclization: Access to Pyrimidine-Annelated *Spiro* Heterocycles Through *5-exo* Ring Closure

K. C. Majumdar,* P. P. Mukhopadhyay

Department of Chemistry, University of Kalyani, Kalyani 741 235, West Bengal, India
Fax +91(33)25828282; E-mail: kcm@klyuniv.ernet.in

Received 20 February 2004; revised 26 April 2004

Abstract: Aryl radical cyclization of a range of 6-(2′-bromophenoxymethyl)-1,3-dimethyluracils **4a**–**g** was carried out with tributyltin chloride and sodium cyanoborohydride in the presence of AIBN for four hours to give exclusively the '5-*exo*' cyclization products, 1,3-dimethylspiro[pyrimidine-6,3′-2′,3′-tetrahydrobenzofuran]-2,4-diones **5a**–**g** in 92–95% yield. The starting materials were in turn prepared in 90–92% yield by refluxing 6-chloro methyl-1,3-dimethyl uracil with various 2-bromophenols or 2-bromonaphthol in acetone in the presence of anhydrous potassium carbonate for eight hours.

Key words: heterocyclic compounds, spiro heterocycles, organotin reagent, 6-chloromethyl-1,3-dimethyl uracil, radical cyclization, 5-exo-trig

Introduction

Intramolecular radical cyclizations to an unsaturated double bond are extremely useful for the construction of five- and six-membered carbo- and heterocyclic rings.[1] In particular, the intramolecular addition of aryl radicals to double bonds is well documented in the literature[2] for the synthesis of spiro heterocycles.[3] In contrast, for the addition to carbocycles there are relatively few reports dealing with the intramolecular addition of aryl radicals to heterocyclic rings.[4–7] It was observed that the parent 5-hexenyl radical cyclized preferentially to the cyclopentyl methyl radical via '5-*exo*' cyclization and not to the more stable cyclohexyl radical via '6-*endo*' cyclization.[8] This is generally predicted by using the Beckwith[9] transition state model. Beckwith[10] rationalized this regiochemical preference by postulating that the bond formation between a radical and a π-system stereoelectronically required an approach angle of about 110° between the free radical centre and the olefinic plane. This transition state geometry is less constrained in '5-*exo*' ring closure, a fact later elaborated by Baldwin.[11] Recent theoretical calculations have also supported the Beckwith transition state model.[12b,c] The regiochemical outcome of a radical cyclization may be changed by the presence of radical stabilizing groups to the acceptor double bond.[12] It was also suggested that this effect may be partly due to a change in the required approach trajectory for radical additions to the substituted acceptor double bond. The direction of approach of a radical to an unfunctionalized double bond may be from above and directly behind the *p*-orbitals,[9b,c] causing more angle strain for the '5-*exo*' transition state. The presence of a carbonyl group may change this required trajectory in accordance with Baldwin's approach vector analysis,[13] so that the radical now approaches the double bond more easily at the above stated direction. Many examples have been reported of a useful '6-*endo*' cyclization where the carbonyl substituent[12a,c] or the nitrogen substituent[14] is regarded as strongly activating towards '6-*endo*' cyclization. Our present investigation on the regioselective radical cyclization is solely controlled by the FMO interactions.

Recently we reported[15] the '6-*endo*' cyclization of 5-(2′-bromobenzyloxy)pyrimidine-2,4-dione with tri-*n*-butyltin chloride and sodium cyanoborohydride in the presence of azobisisobutyronitrile (AIBN). As part of our ongoing work, we became interested in the synthesis of pyrimidine derivatives due to their proven biological activity and medicinal utility. Recently, a 6-substituted uracil derivative, 1-(2-hydroxyethoxymethyl)-6-phenylthio thymine (HEPT)[16–18] has attained considerable significance as a specific inhibitor for HIV-1,[19] a causative agent of AIDS. Functionalization of uracils at C-5 and C-6 leads to biologically interesting molecules but it is not a simple task, requiring rather sophisticated and tedious reaction conditions.[20,21] We have recently reported the synthesis of a number of pyrimidine-annelated heterocycles fused at the C-5 and C-6 positions of uracil.[15,22] Herein we report the regioselective formation of spiro pyrimidine heterocycles.

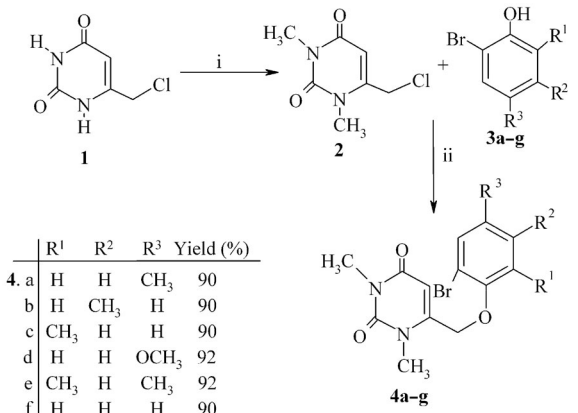
Results and Discussion

We started our investigation by examining the cyclization of several 6-(2′-bromophenoxymethyl)-1,3-dimethyluracils (**4a**–**g**) which were readily prepared in 90–92% yields from various *o*-bromophenols or 2-bromonaphthol **3a**–**g** and 6-chloromethyl-1,3-dimethylpyrimidine-2,4-dione (**2**) in eight hours in the presence of anhydrous K_2CO_3 (Scheme 1).

The ethers were treated with *n*-Bu_3SnH–AIBN to induce radical cyclization. Compound **4a**, when heated with *n*-Bu_3SnCl in the presence of $Na(CN)BH_3$ and small amounts of AIBN in refluxing degassed benzene under nitrogen for four hours afforded exclusively **5a** in excellent yield (95%) (Scheme 2).

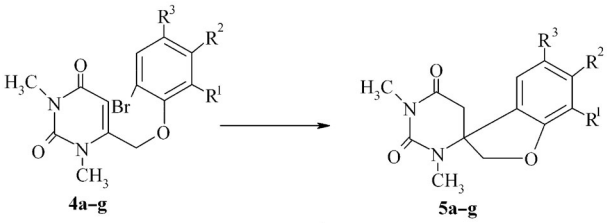
SYNTHESIS 2004, No. 11, pp 1864–1868
Advanced online publication: 05.07.2004
DOI: 10.1055/s-2004-829133; Art ID: Z04304SS
© Georg Thieme Verlag Stuttgart · New York

Downloaded by: University of Liverpool. Copyrighted material.



	R^1	R^2	R^3	Yield (%)
4. a	H	H	CH_3	90
b	H	CH_3	H	90
c	CH_3	H	H	90
d	H	H	OCH_3	92
e	CH_3	H	CH_3	92
f	H	H	H	90
g	5,6-phenylene		H	90

Scheme 1 *Reagents and conditions:* i) $(CH_3)_2SO_4$, aq NaOH, reflux, 1.5 h; ii) Acetone, K_2CO_3, reflux, 8 h.

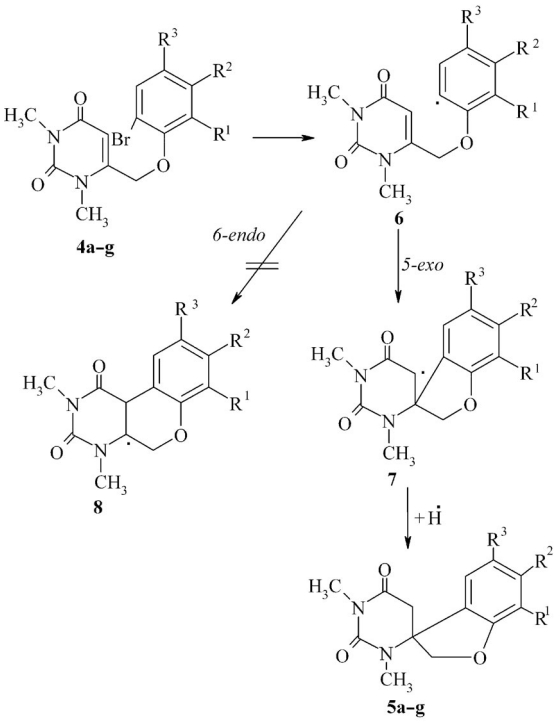


	R^1	R^2	R^3	Yield (%)
5. a	H	H	CH_3	95
b	H	CH_3	H	92
c	CH_3	H	H	92
d	H	H	OCH_3	94
e	CH_3	H	CH_3	92
f	H	H	H	94
g	5,6-phenylene		H	95

Scheme 2 *Reagents and conditions:* AIBN, *n*-Bu_3SnCl, $Na(CN)BH_3$, benzene, reflux under N_2 atmosphere for 4 h.

The ^1H NMR spectrum of the product **5a** revealed one proton doublet at δ = 2.93 (*J* = 16.5 Hz) and another one proton doublet at δ = 3.07 (*J* = 16.5 Hz) due to $COCH_2$ and another OCH_2 protons appear as two one proton doublet each at δ = 4.34 and 4.45 (*J* = 10 Hz). Final confirmation for structure **5a** came from its COSY, HETCOR and ^{13}C NMR spectrum. COSY spectrum of compound **5a** shows that $COCH_2$ protons at δ = 2.93 and 3.07 correlate with each other and OCH_2 protons at δ = 4.34 and 4.45 correlate with each other. The ^{13}C NMR chemical shifts of the compound **5a** are assigned by DEPT and HETCOR experiments. DEPT shows eight protonated carbons, three CH_3, three >CH, and two $>CH_2$ groups. Protonated carbon resonances are established by direct correlation with proton resonance by HETCOR experiment (normal one bond C-H coupling). Methyl protons ($ArCH_3$) resonance at δ = 2.32 is related with protonated carbon resonance at δ = 21.06 whereas another methyl protons at δ = 2.80 and 3.26 (NCH_3) are related with protonated carbon resonance at δ = 28.19 and 31.08, respectively. Methylene protons resonance at δ = 2.93 (CH_2CO) and 4.34 (OCH_2) are related with carbon resonance at δ = 42.77 and 78.90, respectively. Methine protons (ArH) resonance at δ = 6.77, 6.94 and 7.09 are related with protonated carbon resonance at δ = 110.96, 123.98 and 132, respectively. Encouraged by this result, other substrates **4b**–**g** were similarly treated to give spiro heterocycles **5b**–**g** in 92–95% yield. Our attempt to extend this reaction to 6-(2′-bromoanilinomethyl)-1,3-dimethyl uracil and 6-(2′-bromo-*N*-methylanilinomethyl)-1,3-dimethyl uracil afforded a complex mixture of products, which could not be separated.

The regioselective formation of 5-membered heterocyclic ring can be explained by the application of the FMO theory. Aryl radicals are high-energy species and hence are nucleophilic in character. The presence of highly electron-withdrawing carbonyl group confers considerable electrophilic character to the C-6 position of the uracil moiety. Thus in the case of nucleophilic radical **6**, FMO theory suggests that the mode of ring closure is largely determined by the interaction between the radical SOMO (≡ HOMO) and the alkene LUMO of the acceptor (electron deficient centre) and accordingly more favorable bond formation occurs between the radical centre (nucleophilic) and C_6 of the uracil ring for '5-*exo*' product **5a**–**g** (Scheme 3). The same explanation may be extended to our earlier results[15,22a] for the formation of '6-*endo*' products from uracil substrates.



Scheme 3

Previously we reported[15] the synthesis of 1*H*,3*H*,6*H*-[2]benzopyrano[4,3-*d*]pyrimidine-2,4-diones where regioselective '6-*endo*' cyclization had occurred whereas in our present investigation we find that the regioselective '5-*exo*' cyclization has taken place. As this reaction is ir-

Downloaded by: University of Liverpool. Copyrighted material.

reversible and hence kinetically controlled, the outcome of these radical cyclization cannot be explained by the stability of the intermediate product radical **7**. The result can only be explained by FMO interactions. This is a simple and facile method for the synthesis of spiroheterocycles.

Melting points were determined in an open capillary and are uncorrected. IR spectra were recorded on a Perkin-Elmer L 120-000A spectrometer (ν_{max} in cm^{-1}) on KBr disks. UV absorption spectra were recorded in EtOH on a Shimadzu UV-2401PC spectrophotometer (λ_{max} in nm). ^1H NMR (300 MHz, 500 MHz) and ^{13}C NMR (75.5 MHz, 125.7 MHz) spectra were recorded on a Bruker DPX-300 and Bruker DPX-500 spectrometer in $CDCl_3$ (chemical shift in δ) with TMS as internal standard. Elemental analyses and mass spectra were recorded on a JEOL JMS-600 instrument. ^1H NMR and ^{13}C NMR spectra were recorded at the Indian Institute of Chemical Biology, Kolkata and Bose Institute, Kolkata. Silica gel (60–120 mesh, Spectrochem, India) was used for chromatographic separation. Silica gel G (E-Merck, India] was used for TLC. Petroleum ether refers to the fraction boiling between 60 °C and 80 °C.

Preparation of 6-(2′-Bromophenoxymethyl)pyrimidine-2,4-diones (4a–g), General Procedure

A mixture of 6-chloromethyl-1,3-dimethyl uracil (**2**, 5 mmol), and either 2-bromophenols **3a–f** or 2-bromonaphthol (**3g**, 5 mmol) and anhyd K_2CO_3 (5 g) was heated at reflux in anhyd acetone (125 mL) in a water bath for 8 h. The reaction mixture was then cooled, filtered and the solvent was removed. The residual mass was extracted with CH_2Cl_2 (3 × 50 mL). The CH_2Cl_2 extract was washed with 10% Na_2CO_3 solution (2 × 25 mL) to remove unreacted 6-chloromethyl-1,3-dimethyl uracil and then with brine (3 × 50 mL) and dried (Na_2SO_4). The residual mass after removal of the solvent (CH_2Cl_2) was subjected to column chromatography over silica gel using petroleum ether–EtOAc (4:1) as eluant to give compounds **4a–g** which were then recrystallized from $CHCl_3$–petroleum ether.

6-(2′-Bromo-5′-methylphenoxymethyl)-1,3-dimethyl-1*H*-pyrimidine-2,4-dione (4a)

Yield: 90%; white solid; mp 178–180 °C.

IR (KBr): 1444, 1655, 1698, 2922 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.29 (s, 3 H, $ArCH_3$), 3.36 (s, 3 H, NCH_3), 3.53 (s, 3 H, NCH_3), 4.83 (s, 2 H, OCH_2), 5.97 (s, 1 H, =CH), 6.80 (d, *J* = 8 Hz, 1 H, ArH), 7.06 (d, *J* = 8 Hz, 1 H, ArH), 7.40 (s, 1 H, ArH).

MS: *m*/*z* = 338, 340 [M^+].

UV (EtOH): λ_{max} = 230, 266 nm.

Anal. Calcd for $C_{14}H_{15}N_2O_3Br$: C, 49.57; H, 4.45; N, 8.25. Found: C, 49.31; H, 4.69; N, 8.43.

6-(2′-Bromo-4′-methylphenoxymethyl)-1,3-dimethyl-1*H*-pyrimidine-2,4-dione (4b)

Yield: 90%; white solid; mp 198–200 °C.

IR (KBr): 1440, 1661, 1709, 2923 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.57 (s, 3 H, $ArCH_3$), 3.38 (s, 3 H, NCH_3), 3.61 (s, 3 H, NCH_3), 4.78 (s, 2 H, OCH_2), 5.96 (s, 1 H, =CH), 6.94 (d, *J* = 8 Hz, 1 H, ArH), 7.42 (d, *J* = 8 Hz, 1 H, ArH), 7.78 (s, 1 H, ArH).

MS: *m*/*z* = 338, 340 [M^+].

UV (EtOH): λ_{max} = 229, 268 nm.

Anal. Calcd for $C_{14}H_{15}N_2O_3Br$: C, 49.57; H, 4.45; N, 8.25. Found: C, 49.78; H, 4.26; N, 8.40.

6-(2′-Bromo-2′-methylphenoxymethyl)-1,3-dimethyl-1*H*-pyrimidine-2,4-dione (4c)

Yield: 90%; white solid; mp 160–162 °C.

IR (KBr): 1452, 1660, 1709, 2920 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.28 (s, 3 H, $ArCH_3$), 3.39 (s, 3 H, NCH_3), 3.56 (s, 3 H, NCH_3), 4.70 (s, 2 H, OCH_2), 5.94 (s, 1 H, =CH), 6.95 (m, 1 H, ArH), 7.40 (m, 2 H, ArH).

MS: *m*/*z* = 338, 340 [M^+].

UV (EtOH): λ_{max} = 231, 267 nm.

Anal. Calcd for $C_{14}H_{15}N_2O_3Br$: C, 49.57; H, 4.45; N, 8.25. Found: C, 49.38; H, 4.67; N, 8.33.

6-(2′-Bromo-5′-methoxyphenoxymethyl)-1,3-dimethyl-1*H*-pyrimidine-2,4-dione(4d)

Yield: 92%; white solid; mp 180–182 °C.

IR (KBr): 1442, 1657, 1696, 2928 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 3.37 (s, 3 H, NCH_3), 3.54 (s, 3 H, NCH_3), 3.78 (s, 3 H, OCH_3), 4.79 (s, 2 H, OCH_2), 5.93 (s, 1 H, =CH), 6.82 (d, *J* = 8 Hz, 1 H, ArH), 6.87 (d, *J* = 8 Hz, 1 H, ArH), 7.13 (s, 1 H, ArH).

MS: *m*/*z* = 354, 356 [M^+].

UV (EtOH): λ_{max} = 230, 267 nm.

Anal. Calcd for $C_{14}H_{15}N_2O_4Br$: C, 47.34; H, 4.25; N, 7.88. Found: C, 47.48; H, 3.98; N, 8.05.

6-(2′-Bromo-3′,5′-dimethylphenoxymethyl)-1,3-dimethyl-1*H*-pyrimidine-2,4-dione (4e)

Yield: 92%; white solid; mp 170–172 °C.

IR (KBr): 1452, 1660, 1709, 2923 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.38 (s, 3 H, $ArCH_3$), 2.39 (s, 3 H, $ArCH_3$), 3.39 (s, 3 H, NCH_3), 3.56 (s, 3 H, NCH_3), 4.68 (s, 2 H, OCH_2), 5.96 (s, 1 H, =CH), 7.28 (s, 1 H, ArH), 7.35 (s, 1 H, ArH).

MS: *m*/*z* = 352, 354 [M^+].

UV (EtOH): λ_{max} = 230, 266 nm.

Anal. Calcd for $C_{15}H_{17}N_2O_3Br$: C, 51.00; H, 4.85; N, 7.93. Found: C, 51.13; H, 4.98; N, 8.15.

6-(2′-Bromophenoxymethyl)-1,3-dimethyl-1*H*-pyrimidine-2,4-dione (4f)

Yield: 90%; white solid; mp 165–167 °C.

IR (KBr): 1442, 1662, 1697, 2925 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.37 (s, 3 H, NCH_3), 3.53 (s, 3 H, NCH_3), 4.87 (s, 2 H, OCH_2), 5.99 (s, 1 H, =CH), 6.97 (m, 2 H, ArH), 7.57 (m, 2 H, ArH).

MS: *m*/*z* = 324, 326 [M^+].

UV (EtOH): λ_{max} = 230, 265 nm.

Anal. Calcd for $C_{13}H_{13}N_2O_3Br$: C, 48.02; H, 4.02; N, 8.62. Found: C, 47.76; H, 4.18; N, 8.90.

6-(2′-Bromopheneoxymethyl)-1,3-dimethyl-1*H*-pyrimidine-2,4-dione (4g)

Yield: 90%; white solid; mp 160–162 °C.

IR (KBr): 1449, 1663, 1709, 2955 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 3.41 (s, 3 H, NCH_3), 3.64 (s, 3 H, NCH_3), 4.91 (s, 2 H, OCH_2), 6.06 (s, 1 H, =CH), 7.55 (m, 4 H, ArH), 7.86 (m, 1 H, ArH), 7.96 (m, 1 H, ArH).

MS: *m*/*z* = 374, 376 [M^+].

UV (EtOH): λ_{max} = 233, 273 nm.

Downloaded by: University of Liverpool. Copyrighted material.

Anal. Calcd for $C_{17}H_{15}N_2O_3Br$: C, 54.41; H, 4.02; N, 7.46. Found: C, 54.58; H, 3.88; N, 7.25.

Preparation of 1,3-Dimethylspiro[pyrimidine-6,3′-2′,3′-tetrahydrobenzofuran]-2,4-dione 5a–g; General Procedure

The compounds **4a**–**g** (0.5 mmol), *n*-Bu_3SnCl (0.08 mL, 0.296 mmol), $Na(CN)BH_3$ (250 mg, 3.98 mmol) and AIBN (15 mg) were dissolved in degassed anhyd benzene (8 mL) and the mixture was heated at reflux for 4 h under N_2 atmosphere. Solvent was evaporated under reduced pressure and the residue was taken up in water (10 mL) and was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extract was washed with 1% aq NH_4OH (2 × 10 mL) and brine, and dried (Na_2SO_4). Evaporation of the solvent furnished the residual mass, which was then stirred with sat. solution of KF for 24 h. It was then extracted with CH_2Cl_2 (3 × 10 mL) and was washed several times with water and dried (Na_2SO_4). The residual mass after removal of the solvent (CH_2Cl_2), was subjected to column chromatography using petroleum ether–EtOAc (19:1) as eluant to give cyclized products **5a**–**g** which were then recrystallized from $CHCl_3$–petroleum ether.

Compound 5a

Yield: 95%; white solid; mp 120–122 °C.

IR (KBr): 1494, 1672, 1713, 2918 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.32 (s, 3 H, $ArCH_3$), 2.80 (s, 3 H, NCH_3), 2.93 (d, *J* = 16.5 Hz, COCH, 1 H), 3.07 (d, *J* = 16.5 Hz, 1 H, COCH), 3.27 (s, 3 H, NCH_3), 4.34 (d, *J* = 10 Hz, 1 H, OCH), 4.45 (d, *J* = 10 Hz, 1 H, OCH**)**, 6.77 (d, *J* = 8 Hz, 1 H, ArH), 6.95 (s, 1 H, ArH), 7.09 (d, *J* = 8 Hz, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 21.06 (CH_3), 28.19 (NCH_3), 31.08 (NCH_3), 42.77 ($COCH_2$), 64.56 (NC), 78.90 (OCH_2), 110.97, 123.98, 125.87, 131.67, 132.00, 153.84 (ArC), 157.90, 167.32 (NCO).

MS: *m*/*z* = 260 [M^+].

UV (EtOH): λ_{max} = 230, 289 nm.

Anal. Calcd for $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.19; N, 10.76. Found: C, 64.81; H, 5.95; N, 10.59.

Compound 5b

Yield: 92%; white solid; mp 138–140 °C.

IR (KBr): 1464, 1660, 1710, 2952 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.42 (s, 3 H, $ArCH_3$), 2.81 (s, 3 H, NCH_3), 2.96 (d, *J* = 16.5 Hz, 1 H, COCH), 3.07 (d, *J* = 16.5 Hz, 1 H, COCH), 3.26 (s, 3 H, *N*CH_3), 4.48 (d, *J* = 10 Hz, 1 H, OCH), 4.57 (d, *J* = 10 Hz, 1 H, OCH**)**, 6.90 (d, *J* = 8 Hz, 1 H, ArH), 6.99 (d, *J* = 8 Hz, 1 H, ArH), 7.38 (s, 1 H, ArH).

MS: *m*/*z* = 260 [M^+].

UV (EtOH): λ_{max} = 230, 288 nm.

Anal. Calcd for $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.19; N, 10.76. Found: C, 64.38; H, 6.37; N, 10.56.

Compound 5c

Yield: 92%; white solid; mp 96–98 °C.

IR (KBr): 1471, 1668, 1717, 2954 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.21 (s, 3 H, $ArCH_3$), 2.82 (s, 3 H, NCH_3), 2.94 (d, *J* = 16.5 Hz, 1 H, COCH), 3.05 (d, *J* = 16.5 Hz, 1 H, COCH), 3.25 (s, 3 H, NCH_3), 4.39 (d, *J* = 10 Hz, 1 H, OCH), 4.48 (d, *J* = 10 Hz, 1 H, OCH**)**, 6.91 (m, 3 H, ArH).

MS: *m*/*z* = 260 [M^+].

UV (EtOH): λ_{max} = 231, 289 nm.

Anal. Calcd for $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.19; N, 10.76. Found: C, 64.86; H, 5.98; N, 10.53.

Compound 5d

Yield: 94%; white solid; mp 120–122 °C.

IR (KBr): 1493, 1670, 1709, 2944 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.83 (s, 3 H, NCH_3), 2.96 (d, *J* = 16.5 Hz, 1 H, COCH), 3.08 (d, *J* = 16.5 Hz, 1 H, COCH), 3.25 (s, 3 H, NCH_3), 3.78 (s, 3 H, OCH_3), 4.36 (d, *J* = 10 Hz, 1 H, OCH), 4.45 (d, *J* = 10 Hz, 1 H, OCH**)**, 6.69 (s, 1 H, ArH), 6.81 (d, *J* = 8 Hz, 1 H, ArH), 6.86 (d, *J* = 8 Hz, 1 H, ArH).

MS: *m*/*z* = 276 [M^+].

UV (EtOH): λ_{max} = 232, 305 nm.

Anal. Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.83; N, 10.13. Found; C, 61.01; H, 5.95; N, 10.30.

Compound 5e

Yield: 92%; white solid; mp 162–164 °C.

IR (KBr): 1473, 1668, 1718, 2928 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.29 (s, 3 H, $ArCH_3$), 2.38 (s, 3 H, $ArCH_3$), 2.81 (s, 3 H, NCH_3), 2.92 (d, *J* = 16.5 Hz, 1 H, COCH), 3.04 (d, *J* = 16.5 Hz, 1 H, COCH), 3.26 (s, 3 H, NCH_3), 4.36 (d, *J* = 10 Hz, 1 H, OCH), 4.46 (d, *J* = 10 Hz, 1 H, OCH**)**, 6.87 (s, 1 H, ArH), 7.36 (s, 1 H, ArH).

MS: *m*/*z* = 274 [M^+].

UV (EtOH): λ_{max} = 231, 297 nm.

Anal. Calcd for $C_{15}H_{18}N_2O_3$: C, 65.67; H, 6.61; N, 10.21. Found: C, 65.81; H, 6.35; N, 10.39.

Compound 5f

Yield: 94%; white solid; mp 110–112 °C.

IR (KBr): 1480, 1671, 1723, 2956 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.79 (s, 3 H, NCH_3), 2.97 (d, *J* = 16.5 Hz, 1 H, COCH), 3.08 (d, *J* = 16.5 Hz, 1 H, COCH), 3.26 (s, 3 H, NCH_3), 4.37 (d, *J* = 10 Hz, 1 H, OCH), 4.47 (d, *J* = 10 Hz, 1 H, OCH**)**, 6.88 (m, 2 H, ArH), 6.16 (m, 2 H, ArH).

MS: *m*/*z* = 246 [M^+].

UV (EtOH): λ_{max} = 231, 281 nm.

Anal. Calcd for $C_{13}H_{14}N_2O_3$: C, 63.40; H, 5.73; N, 11.37. Found: C, 63.56; H, 5.45; N, 11.50.

Compound 5g

Yield: 95%; white solid; mp 168–170 °C.

IR (KBr): 1444, 1662, 1718, 2957 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.81 (s, 3 H, NCH_3), 3.00 (d, *J* = 16.5 Hz, 1 H, COCH), 3.20 (d, *J* = 16.5 Hz, 1 H, COCH), 3.29 (s, 3 H, NCH_3), 4.59 (d, *J* = 10 Hz, 1 H, OCH), 4.68 (d, *J* = 10 Hz, 1 H, OCH**)**, 7.22 (m, 4 H, ArH), 7.85 (m, 2 H, ArH).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 28.47 (NCH_3), 31.40 (NCH_3), 43.33 ($COCH_2$), 65.91 (NC), 79.91 (OCH_2), 118.91, 120.29, 121.28, 122.19, 122.71, 126.79, 127.90, 128.49, 135.75, 154.13 (ArC), 156.47, 167.58 (NCO).

MS: *m*/*z* = 296 [M^+)].

UV (EtOH): λ_{max} = 241, 300 nm.

Anal. Calcd for $C_{17}H_{16}N_2O_3$: C, 68.90; H, 5.44; N, 9.45. Found: C, 68.81; H, 5.65; N, 9.59.

Downloaded by: University of Liverpool. Copyrighted material.

Acknowledgment

We thank the CSIR (New Delhi) for financial assistance. P. P. Mukhopadhyay is grateful to CSIR (New Delhi) for a Senior Research Fellowship. We also thank the DST (New Delhi) for providing the UV-VIS spectrophotometer and FT-IR spectrometer under DST-FIST.

References

(1) (a) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*; Pergamon: New York, **1986**. (b) Curran, D. P. *Synthesis* **1988**, 417. (c) Curran, D. P. *Synthesis* **1988**, 489. (d) Jasperse, C. P.; Curran, D. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237. (e) *Radicals in Organic Synthesis*, Vol. 1; Renaud, P.; Sibi, M., Eds.; Wiley-VCH: Weinheim, **2001**. (f) *Radicals in Organic Synthesis*, Vol. 2; Renaud, P.; Sibi, M., Eds.; Wiley-VCH: Weinheim, **2001**. (g) Majumdar, K. C.; Basu, P. K. *Heterocycles* **2002**, *57*, 2413. (h) Bowman, W. R.; Fletcher, A. J.; Potts, G. B. S. *J. Chem. Soc., Perkin Trans. 1* **2002**, 2747.

(2) (a) Togo, H.; Kikuchi, O. *Tetrahedron Lett.* **1988**, *29*, 4133. (b) Hart, D. J.; Wu, K. *Tetrahedron Lett.* **1991**, *32*, 4099. (c) Clark, A. J.; Jones, K. *Tetrahedron* **1992**, *48*, 6875. (d) Glover, S. A.; Warkentin, J. *J. Org. Chem.* **1993**, *58*, 2115. (e) Jones, K.; Brunton, S. A.; Gosain, R. *Tetrahedron Lett.* **1999**, *40*, 8935. (f) Majumdar, K. C.; Mukhopadhyay, P. P. *Synthesis* **2003**, 99.

(3) (a) Flanagan, S. R.; Harrowven, D. C.; Bradley, M. *Tetrahedron Lett.* **2003**, *44*, 1795. (b) Escolano, C.; Jones, K. *Tetrahedron* **2002**, *58*, 1453. (c) Zhang, W.; Pugh, G. *Tetrahedron* **2003**, *59*, 3009. (d) Zhang, W.; Pugh, G. *Tetrahedron* **2003**, *59*, 4237.

(4) (a) Da Mata, M. L. E. N.; Motherwell, W. B.; Ujjainwalla, F. *Tetrahedron Lett.* **1997**, *38*, 141. (b) Harrowven, D. C.; Hon, B. J. S.; Coulton, S. *Tetrahedron Lett.* **2001**, *42*, 9061. (c) Bonfand, E.; Forslund, L.; Motherwell, W. B.; Vazquez, S. *Synlett* **2000**, 475.

(5) (a) Shankaran, K.; Solan, C. P.; Snieckus, V. *Tetrahedron Lett.* **1985**, *26*, 6001. (b) Solan, C. P.; Cuevas, J. C.; Quesnelle, C.; Snieckus, V. *Tetrahedron Lett.* **1988**, *29*, 4685. (c) Zhang, W.; Pugh, G. *Tetrahedron Lett.* **1999**, *40*, 7591.

(6) (a) Du, W.; Curran, D. P. *Org. Lett.* **2003**, *5*, 1765. (b) Harrowven, D. C.; Browne, R. *Tetrahedron Lett.* **1994**, *35*, 5301. (c) Harrowven, D. C.; Sutton, B. J.; Coulton, S. *Tetrahedron* **2002**, *58*, 3387. (d) Harrowven, D. C.; Nunn, M. I. T.; Blumire, N. J.; Fenwick, D. R. *Tetrahedron* **2001**, *57*, 4447.

(7) (a) Tsuge, O.; Hatta, T.; Tsuchiyama, H. *Chem. Lett.* **1998**, 155. (b) Fiumana, A.; Jones, K. *Tetrahedron Lett.* **2000**, *41*, 4209. (c) Sundberg, R. J.; Cherney, R. J. *J. Org. Chem.* **1990**, *55*, 6028.

(8) (a) Beckwith, A. L. J.; Ingold, K. U. In *Rearrangement in Ground and Excited States*, Vol. 1; de Mayo, P., Ed.; Academic Press: New York, **1980**, 161. (b) Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073.

(9) (a) Beckwith, A. L. J.; Easton, C. J.; Lawrence, T.; Serelis, A. K. *Aust. J. Chem.* **1983**, *36*, 545. (b) Beckwith, A. L. J.; Schiesser, C. H. *Tetrahedron Lett.* **1985**, *26*, 373. (c) Beckwith, A. L. J.; Schiesser, C. H. *Tetrahedron* **1985**, *41*, 3925. (d) Spellmeyer, D. C.; Houk, K. N. *J. Org. Chem.* **1987**, *52*, 959.

(10) Struble, D. A.; Beckwith, A. L. J.; Gream, G. A. *Tetrahedron Lett.* **1968**, *9*, 3701.

(11) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734.

(12) (a) Ahmad-Juhan, S. A.; Whiting, D. A. *J. Chem. Soc., Perkin Trans. 1* **1990**, 418. (b) Beckwith, A. L. J.; Blair, I. A.; Phillipou, G. *Tetrahedron Lett.* **1974**, *15*, 2251. (c) Ponaras, A. A.; Zaim, O. *Tetrahedron Lett.* **1993**, *34*, 2879.

(13) Beckwith, A. L. J. *J. Chem. Soc., Chem. Commun.* **1976**, 738.

(14) (a) Takano, S.; Suzuki, M.; Kijima, S.; Ogasawara, K. *Tetrahedron Lett.* **1990**, *31*, 2315. (b) Ishibashi, H.; Kato, I.; Takeda, Y.; Kogure, M.; Tamura, O. *Chem. Commun.* **2000**, 1527. (c) Ishibashi, H.; Ohata, K.; Niihara, M.; Sato, T.; Ikeda, M. *J. Chem. Soc, Perkin Trans. 1* **2000**, 547.

(15) Majumdar, K. C.; Basu, P. K.; Mukhopadhyay, P. P.; Sarkar, S.; Ghosh, S. K.; Biswas, P. *Tetrahedron* **2003**, *59*, 2151.

(16) Miyasaka, T.; Tanaka, H.; Baba, M.; Hayakawa, H.; Walker, R. T.; Balzarini, J.; DeClercq, E. *J. Med. Chem.* **1989**, *32*, 2507.

(17) Baba, M.; Tanaka, H.; DeClercq, E.; Pauwels, R.; Balzarini, J.; Schols, D.; Nakashima, H.; Perno, C. F.; Walker, R. T.; Miyasaka, T. *Biochem. Biophys. Res. Commun.* **1989**, *165*, 1375.

(18) DeClercq, E. *Med. Res. Rev.* **1993**, *13*, 229.

(19) (a) Gallo, R. C. *Sci. Am.* **1986**, *255*, 78. (b) Gallo, R. C. *Sci. Am.* **1987**, *256*, 38.

(20) Kundu, N. G.; Das, P. *J. Chem. Soc., Chem. Commun.* **1995**, 99.

(21) Botta, M.; Saladino, R.; Lamba, D.; Nicoletti, R. *Tetrahedron* **1993**, *49*, 6053.

(22) (a) Majumdar, K. C.; Mukhopadhyay, P. P. *Synthesis* **2003**, 920. (b) Majumdar, K. C.; Das, U.; Jana, N. K. *J. Org. Chem.* **1998**, *63*, 3550.

Downloaded by: University of Liverpool. Copyrighted material.