Pergamon

SCIENCE DIRECT®

Tetrahedron 59 (2003) 2151–2157

TETRAHEDRON

Regioselective synthesis of 1*H*,3*H*,6*H*[2]benzopyrano[4,3-*d*]pyrimidine-2,4-diones and 12*H*-benzopyrano[3,2-*c*][1]benzopyran-5-ones by radical cyclization

K. C. Majumdar,* P. K. Basu, P. P. Mukhopadhyay, S. Sarkar, S. K. Ghosh and P. Biswas

Department of Chemistry, University of Kalyani, Kalyani 741 235, West Bengal, India

Received 21 June 2002; revised 6 January 2003; accepted 30 January 2003

Abstract—5-Hydroxy uracils or 4-hydroxy[1]benzopyran-2-ones were refluxed with 2-bromobenzyl bromides in acetone in the presence of anhydrous potassium carbonate to afford a number of 5-(2′-bromobenzyloxy) pyrimidine-2,4-dione (80–92%) or 4-(2′-bromobenzyloxy) benzopyran-7-ones (70–82%) respectively. These were then refluxed with tri-*n*-butyltin chloride and sodium cyanoborohydride in the presence of a catalytic amount of azobisisobutyronitrile (AIBN) for 3–4 h to give 1*H*,3*H*,6*H* [2]benzopyrano[4,3-*d*]pyrimidine-2,4-diones (75–85%) or 12*H*-benzopyrano[3,2-*c*][1]benzopyran-5-ones (70–85%) respectively.

Aryl radical cyclization has recently emerged as a valuable tool for organic synthesis.[1] During our work on the synthesis of heterocycles by the application of sigmatropic rearrangements[2] we recently observed the unusual formation of [6,6] pyranopyrans in the case of substrates containing 5-hydroxypyrimidine[3] and 3-hydroxy coumarin,[4] in the second Claisen rearrangement step. The generation and subsequent reactions of radicals formed from aryl halides using tri-*n*-butyltin hydride and azobisisobutyronitrile (AIBN) is now well established[1] and a wide range of natural product synthesis based on aryl radical cyclizations have been reported.[5] The literature reveals only a few examples of heteroaryl radicals: several examples, by Snieckus [5a,b,6a] and Harrowven,[6b,c] involve pyridine and pyridyl radicals; one reported example of an indonyl radical was offered by Sundberg[7] in the synthesis of Iboga alkaloids. The cyclization of radicals derived from *N*-(*o*-bromobenzyl) anilines to phenanthridine was very recently reported.[8] Aryl radical cyclization normally has a 5-*exo*; 6-*endo* ratio indicating a stronger preference for *exo* cyclization than alkyl radicals. However, this preference is found to be reversed by cyclization to stabilised radicals.[9–11] This is examplified by the radical cyclization of *N*-(*o*-bromobenzyl)enamide precursors which exclusively undergo '6-*endo*-*trig*' cyclization to afford tetrahydroisoquinolone derivatives via stable α-aminoalkyl radical intermediates.[9] As part of our ongoing work we became interested in building the 6-membered fused pyran ring by radical cyclization. Recently there has been a flurry of activity in the synthesis of pyrimidine derivatives due to their proven biological activity and medicinal utility. 5-Substituted uracils and their nucleosides are of immense biological significance because of their use in the chemotherapy of cancer,[12] e.g. 5-fluorouracil (FU), 5-fluoro-2′-deoxyuridine (FUDR) and viral diseases[13–17] e.g. trifluorothymidine (F_3TDR), E-5-(2-bromovinyl-2′-deoxyuridine) (BVDU), 3′-azido-3′-deoxythy-midine (AZT) and 5-(2-chloroethyl)-2′-deoxyuridine (CEDU). Both BVDU and CEDU effectively inhibit herpes simplex type 1 virus (HSV-1) and varicella zoster virus (VZU) replication in vitro[13,18–20] and AZT, CNT are anti-AIDS compounds.[21] Also, many 5-substituted uracils have been developed as enzyme inhibitors[22] and have been used in the synthesis of modified nucleotides.[23] Recently, a 6-substituted uracil derivative 1-(2-hydroxyethoxymethyl)-6-phenylthio thymine (HEPT)[24–26] has attained considerable significance as a specific inhibitor for HIV-1,[27] a causative agent of AIDS. Functionalisation 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.[28–30] We have recently reported the synthesis of a number of pyrimidine-annelated heterocycles fused at the C-5 and C-6 positions of uracil.[3,31–33] Herein we report results of our efforts on the formation of fused pyran ring annulated pyrimidines. Similarly the importance of physiological activity[34] of coumarin and its derivatives prompted

Keywords: 2-bromobenzyl bromide; azobisisobutyronitrile; sodium cyanoborohydride; tri-*n*-butyltin chloride; radical cyclization.

* Corresponding author. Tel.: +91-33-2582-7521; fax: +91-33-2582-8282; e-mail: kcm@klyuniv.ernet.in

0040–4020/03/$ - see front matter
doi:10.1016/S0040-4020(03)00182-0

us to undertake the synthesis of 12*H*-benzopyrano[3,2-*c*][1]benzopyran-5-ones by aryl radical cyclization.

1. Results and discussion

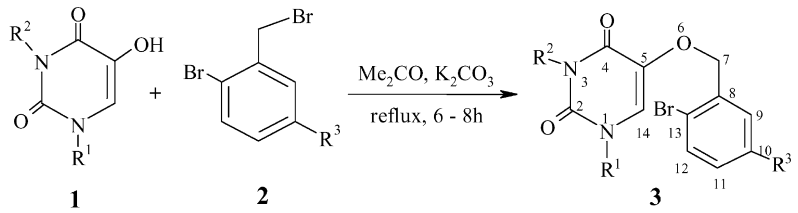
The compounds **1a–c** or **4a–d** were refluxed with either 2-bromobenzyl bromide **2a** or 2-bromo-5-methoxy benzyl bromide **2b** in acetone in the presence of anhydrous potassium carbonate for 6–8 h to afford a number of 5-(2′-bromobenzyloxy)pyrimidine-2,4-diones **3a–f** or 4-(2′-bromobenzyloxy) benzopyran-7-ones **5a–h** (Scheme 1).

Compounds **3a–f** and **5a–h** were characterized from their elemental analyses and spectroscopic data. The substrates **3a** or **5a** were refluxed in benzene under a nitrogen atmosphere with tri-*n*-butyltin chloride and sodium cyanoborohydride in the presence of a catalytic amount of azobisisobutyronitrile (AIBN) respectively, for 3–4 h to give cyclic product **6a** (yield 80%) or **7a** (yield 75%). Compounds **6a** and **7a** were also characterized from their elemental analyses and spectroscopic data. The IR spectrum of **6a** and **7a** showed ν_{max} at 2925 and 2920 cm^{-1}, respectively, due to aromatic C–H stretching and at 1703 and 1710 cm^{-1}, respectively, due to a carbonyl group. The ^1H NMR spectra of the products **6a** and **7a** displayed a two proton singlet at δ 4.21 and 4.55, respectively, due to $-OCH_2$.

The two $N-CH_3$ peaks in compound **6a** appeared as singlets each at δ 3.44 and 3.48. The mass spectra of compounds **6a** and **7a** showed molecular ion peaks at *m*/*z* 244 (M^+) and 250 (M^+) respectively. To test the generality of the reaction, five other 5-(2′-bromobenzyloxy) pyrimidine-2,4-diones **3b–f** and seven other 4-(2′-bromobenzyloxy) benzopyran-7-one derivatives **5b–h** were treated similarly to give products **6b–f** (75–85%) and **7b–h** (70–85%) respectively (Scheme 2).

The exact reason why the '6-*endo*' cyclization product is exclusive in the system **3a–f** or **5a–h** is not clear at present but the formation of products **6a–f** from **3a–f** may be explained by the generation of an aryl radical **8**. Subsequent '5-*exo*' cyclization may give spiroheterocyclic radical[35] **9** (not isolated) followed by neophyl rearrangement[36] to give the more stable intermediate radical **10** (benzylic radical) or by a '6-*endo*' route directly to give the intermediate radical **10** which then rearomatises to yield the products **6a–f** by an unknown mechanism which is usual for this synthetic sequence, i.e. an oxidation step in *n*-Bu_3SnH mediated cyclizations[37] (Scheme 3). A similar mechanism would explain the formation of **7a–h** from **5a–h**.

The mildness of the reaction conditions and the high level of chemoselectivity allow this radical cyclization to serve as a powerful synthetic tool. The methodology described here for the synthesis of 1*H*,3*H*,6*H*-[2]benzopyrano[4,3-*d*]pyrimidine-2,4-dione and 12*H*-benzopyrano [3,2-*c*][1] benzopyran-5-ones appears to be a general one.



1

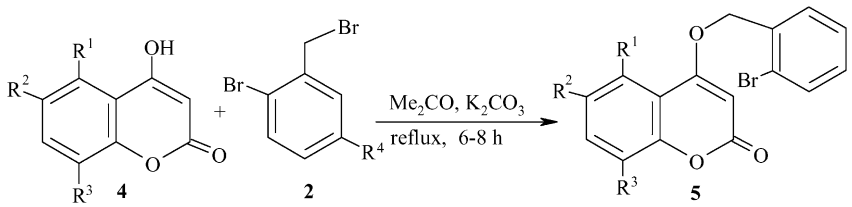
1. a) $R^1 = R^2 = CH_3$
b) $R^1 = R^2 = C_2H_5$
c) $R^1 = C_2H_5$, $R^2 = CH_3$

2

2.a) $R^3 = H$
b) $R^3 = OCH_3$

3

3. a) $R^1 = R^2 = CH_3$, $R^3 = H$ (82%)
b) $R^1 = R^2 = CH_3$, $R^3 = OCH_3$ (85%)
c) $R^1 = R^2 = C_2H_5$, $R^3 = H$ (88%)
d) $R^1 = R^2 = C_2H_5$, $R^3 = OCH_3$ (92%)
e) $R^1 = C_2H_5$, $R^2 = CH_3$, $R^3 = H$ (90%)
f) $R^1 = C_2H_5$, $R^2 = CH_3$, $R^3 = OCH_3$ (80%)



4

4.a) $R^1 = R^2 = R^3 = H$,
b) $R^1 = R^3 = H$, $R^2 = CH_3$
c) $R^1 = R^3 = CH_3$, $R^2 = H$
d) $R^1 = R^2 = H$, $R^3 = CH_3$

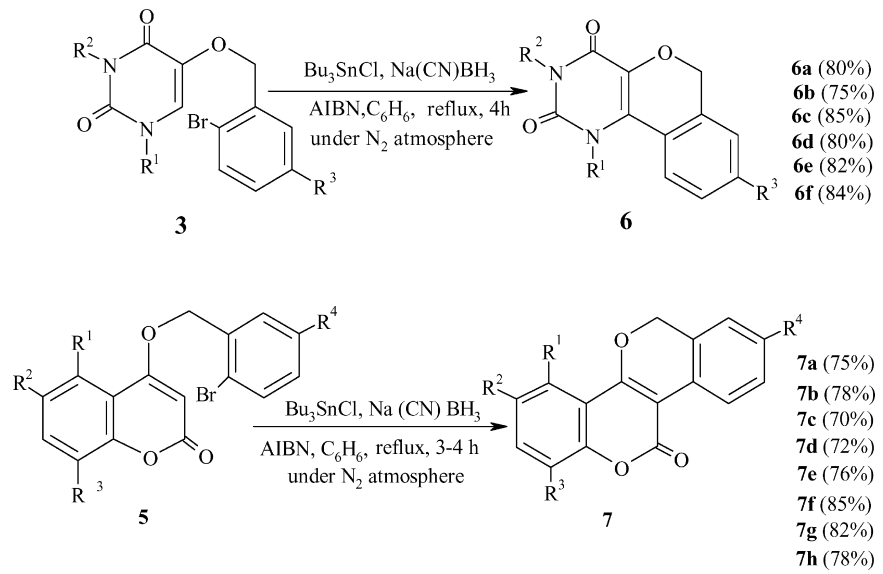
2

2.a) $R^4 = H$
b) $R^4 = OCH_3$

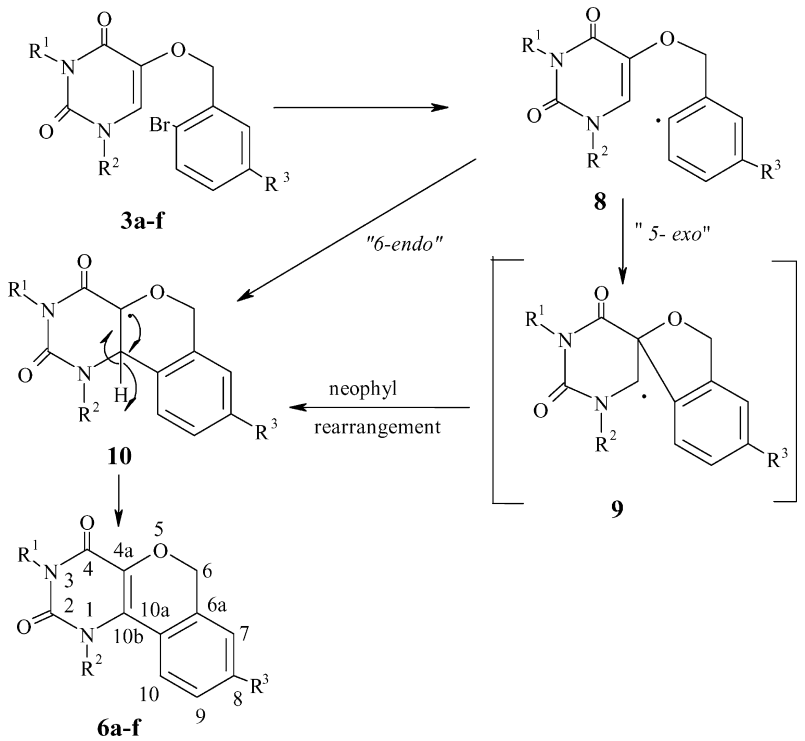
5

5.a) $R^1 = R^2 = R^3 = R^4 = H$ (72%)
b) $R^1 = R^2 = R^3 = H$, $R^4 = OCH_3$ (75%)
c) $R^1 = R^3 = R^4 = H$, $R^2 = CH_3$ (80%)
d) $R^1 = R^3 = H$, $R^2 = CH_3$, $R^4 = OCH_3$ (70%)
e) $R^1 = R^3 = CH_3$, $R^2 = R^4 = H$ (76%)
f) $R^1 = R^3 = CH_3$, $R^2 = H$, $R^4 = OCH_3$ (71%)
g) $R^1 = R^2 = R^4 = H$, $R^3 = CH_3$ (82%)
h) $R^1 = R^2 = H$, $R^3 = CH_3$, $R^4 = OCH_3$ (74%)

Scheme 1.



Scheme 2.



Scheme 3.

2. Experimental

Melting points were determined in a sulfuric acid bath and are uncorrected. UV absorption spectra were recorded in EtOH on a Shimadzu UV-2401 PC spectrophotometer (λ_{max} in nm) and IR spectra on KBr discs on a Perkin Elmer L 120-000A apparatus (ν_{max} in cm^{-1}). ^1H, ^{13}C NMR spectra were run in $CDCl_3$ with TMS as an internal standard on a Bruker DPX-300 (300 MHz) instrument at the Indian Institute of Chemical Biology, Kolkata (chemical shifts in δ ppm). Elemental analyses and mass spectra were recorded by RSIC (CDRI), Lucknow on a JEOL D-300 (E1) instrument. Silica gel (60–120 mesh) was obtained from Spectrochem, India. Extracts were dried over anhydrous sodium sulfate. Petroleum ether refers to the fraction boiling between 60 °C and 80 °C.

2.1. General procedure for the preparation of 5-(2′-bromobenzyloxy)pyrimidine-2,4-diones (3a–f) and 4-(2′-bromobenzyloxy)benzopyran-7-ones (5a–h)

A mixture of 5-hydroxy uracil (**1a–c**) or 4-hydroxy[1]benzopyran-2-ones (**4a–d**) (4 mmol) and either 2-bromobenzyl bromide **2a** (4 mmol, 1.0 g) or 2-bromo-5-methoxy benzyl

bromide **2b** (4 mmol, 1.12 g) and anhydrous potassium carbonate (4 g) was refluxed in dry acetone (100 mL) on a water bath for 6–8 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 to remove unreacted 5-hydroxy uracil or 4-hydroxy[1]benzopyran-2-ones; 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 benzene or petroleum ether–benzene (1:1) as eluant to give compounds **6a–f** or **7a–h**, respectively, which were then recrystallized from chloroform–petroleum ether.

2.1.1. 1,3-Dimethyl-5-(2′-bromobenzyloxy)pyrimidine-2,4-dione (3a). (82%) as a white solid, mp 124 °C; [Found: C, 47.97; H, 4.05; N, 8.68. $C_{13}H_{13}N_2O_3Br$ requires C, 48.02; H, 4.02; N, 8.61%]; ν_{max} (KBr) 2886, 1707, 1655, 1472 cm^{-1}; λ_{max} 216, 237, 243, 261, 279 nm; δ_H (300 MHz, $CDCl_3$) 3.33 (s, 3H, *N*–C*H*$_3$), 3.38 (s, 3H, *N*–C*H*$_3$), 5.09 (s, 2H, O–C*H*$_2$), 6.87 (s, 1H, =C*H*), 7.16–7.22 (m, 1H, Ar*H*), 7.28–7.38 (m, 2H, Ar*H*), 7.52–7.60 (m, 1H, Ar*H*); *m*/*z* 324, 326 (M^+).

2.1.2. 1,3-Dimethyl-5-(2′-bromobenzyloxy-5′-methoxy)-pyrimidine-2,4-dione (3b). (85%) as a white solid, mp 92 °C; [Found: C, 47.39; H, 4.18; N, 7.80. $C_{14}H_{15}N_2O_4Br$ requires C, 47.34; H, 4.25; N, 7.89%]; ν_{max} (KBr) 2881, 1698, 1661, 1478 cm^{-1}; λ_{max} 215, 238, 243, 261, 281 nm; δ_H (300 MHz, $CDCl_3$) 3.34 (s, 3H, *N*–C*H*$_3$), 3.39 (s, 3H, *N*–C*H*$_3$), 3.80 (s, 3H, O–C*H*$_3$), 5.05 (s, 2H, O–C*H*$_2$), 6.74–6.77 (m, 1H, Ar*H*), 6.86 (s, 1H, =C*H*), 7.12 (s, 1H, Ar*H*), 7.42–7.45 (m, 1H, Ar*H*); δ_c (75.5 MHz, $CDCl_3$) 28.7 and 37.4 (*N*–*C*H$_3$), 56.0 (O–*C*H$_3$), 73.1 (C_7), 113.4 (C_5), 115.5 (C_{11}), 116.2 (C_9), 129.2 (C_{14}), 133.7 (C_{12}), 134.1 (C_{13}), 136.8 (C_8), 151.0 (C_2), 159.7 (C_{10}), 160.6 (C_4); *m*/*z* 354, 356 (M^+).

2.1.3. 1,3-Diethyl-5-(2′-bromobenzyloxy)pyrimidine-2,4-dione (3c). (88%) as a white solid, mp 82 °C; [Found: C, 50.92; H, 4.90; N, 7.98. $C_{15}H_{17}N_2O_3Br$ requires C, 51.00; H, 4.85; N, 7.93%]; ν_{max} (KBr) 2927, 1703, 1644, 1461 cm^{-1}; λ_{max} 216, 237, 243, 261, 279 nm; δ_H (300 MHz, $CDCl_3$) 1.21–1.24 (t, 3H, *J*=6.9 Hz, C–C*H*$_3$), 1.25–1.28 (t, 3H, *J*=6.9 Hz, C–C*H*$_3$), 3.69–3.76 (q, 2H, *J*=6.9 Hz, *N*–C*H*$_2$), 4.01–4.08 (q, 2H, *J*=6.9 Hz, *N*–C*H*$_2$), 5.10 (s, 2H, O–C*H*$_2$), 6.81 (s, 1H, =C*H*), 7.17–7.22 (m, 1H, Ar*H*), 7.31–7.37 (m, 1H, Ar*H*), 7.54–7.59 (m, 2H, Ar*H*); *m*/*z* 352, 354 (M^+).

2.1.4. 1,3-Diethyl-5-(2′-bromobenzyloxy-5′-methoxy)-pyrimidine-2,4-dione (3d). (92%) as a white solid, mp 70 °C; [Found: C, 50.18; H, 5.01; N, 7.24. $C_{16}H_{19}N_2O_4Br$ requires C, 50.15; H, 5.00; N, 7.31%]; ν_{max} (KBr) 2937, 1702, 1645, 1464 cm^{-1}; λ_{max} 215, 237, 243, 260, 282 nm; δ_H (300 MHz, $CDCl_3$) 1.22–1.25 (t, 3H, *J*=6.9 Hz, C–C*H*$_3$), 1.26–1.29 (t, 3H, *J*=6.9 Hz, C–C*H*$_3$), 3.70–3.77 (q, 2H, *J*=6.9 Hz, *N*–C*H*$_2$), 3.80 (s, 3H, O–C*H*$_3$), 4.01–4.08 (q, 2H, *J*=6.9 Hz, *N*–C*H*$_2$), 5.03 (s, 2H, O–C*H*$_2$), 6.74–6.77 (dd, 1H, *J*=8.7, 3.0 Hz, Ar*H*), 6.83 (s, 1H, =C*H*), 7.11 (s, 1H, Ar*H*), 7.42–7.45 (d, 1H, *J*=8.7 Hz, Ar*H*); *m*/*z* 382, 384 (M^+).

2.1.5. 1-Ethyl-3-methyl-5-(2′-bromobenzyloxy)pyrimidine-2,4-dione (3e). (90%) as a white solid, mp 78 °C; [Found: C, 49.62; H, 4.35; N, 8.18. $C_{14}H_{15}N_2O_3Br$ requires C, 49.58; H, 4.46; N, 8.26%]; ν_{max} (KBr) 2935, 1698, 1645, 1453 cm^{-1}; λ_{max} 215, 238, 243, 261, 280 nm; δ_H (300 MHz, $CDCl_3$) 1.22–1.27 (t, 3H, *J*=6.9 Hz, C–C*H*$_3$), 3.33 (s, 3H, *N*–C*H*$_3$), 4.01–4.08 (q, 2H, *J*=6.9 Hz, *N*–C*H*$_2$), 5.09 (s, 2H, O–C*H*$_2$), 6.85 (s, 1H, =C*H*), 7.18–7.23 (m, 1H, Ar*H*), 7.32–7.38 (t, 1H, *J*=7.3 Hz, Ar*H*), 7.55–7.59 (m, 2H, Ar*H*); *m*/*z* 338, 340 (M^+).

2.1.6. 1-Ethyl-3-methyl-5-(2′-bromobenzyloxy-5′-methoxy)pyrimidine-2,4-dione (3f). (80%) as a white solid, mp 64 °C; [Found: C, 48.84; H, 4.66; N, 7.50. $C_{15}H_{17}N_2O_4Br$ requires C, 48.80; H, 4.64; N, 7.59%]; ν_{max} (KBr) 2937, 1704, 1660, 1478 cm^{-1}; λ_{max} 215, 238, 243, 261, 282 nm; δ_H (300 MHz, $CDCl_3$) 1.22–1.27 (t, 3H, *J*=6.9 Hz, C–C*H*$_3$), 3.33 (s, 3H, *N*–C*H*$_3$), 3.80 (s, 3H, O–C*H*$_3$), 4.01–4.08 (q, 2H, *J*=6.9 Hz, *N*–C*H*$_2$), 5.05 (s, 2H, O–C*H*$_2$), 6.74–6.78 (m, 1H, Ar*H*), 6.84 (s, 1H, =C*H*), 7.12 (s, 1H, Ar*H*), 7.42–7.45 (d, 1H, *J*=7.3 Hz, Ar*H*); *m*/*z* 368, 370 (M^+).

2.1.7. Compound 5a. (72%) as a white solid, mp 142 °C; [Found: C, 58.09; H, 3.22. $C_{16}H_{11}O_3Br$ requires C, 58.03; H, 3.35%]; ν_{max} (KBr) 3050, 1710, 1620, 1380 cm^{-1}; λ_{max} 215, 265, 302 nm; δ_H (300 MHz, $CDCl_3$) 5.28 (s, 2H, –OC*H*$_2$), 5.80 (s, 1H, =C*H*), 7.28–7.32 (m, 2H, Ar*H*), 7.36–7.39 (m, 2H, Ar*H*), 7.50–7.57 (m, 2H, Ar*H*), 7.63–7.66 (m, 1H, Ar*H*), 7.87–7.90 (m, 1H, Ar*H*); *m*/*z* 330, 332 (M^+).

2.1.8. Compound 5b. (75%) as a white solid, mp 122 °C; [Found: C, 56.69; H, 3.77. $C_{17}H_{13}O_4Br$ requires C, 56.53; H, 3.63%]; ν_{max} (KBr) 3030, 1700, 1600, 1450, 1360 cm^{-1}; λ_{max} 215, 266, 302 nm; δ_H (300 MHz, $CDCl_3$) 3.84 (s, 3H, O–C*H*$_3$), 5.25 (s, 2H, –OC*H*$_2$), 5.81 (s, 1H, =C*H*), 6.82–6.85 (m, 1H, Ar*H*), 7.08–7.09 (m, 1H, Ar*H*), 7.28–7.37 (m, 2H, Ar*H*), 7.53–7.61 (m, 2H, Ar*H*), 7.89–7.91 (m, 1H, Ar*H*); *m*/*z* 360, 362 (M^+).

2.1.9. Compound 5c. (80%) as a white solid, mp 158 °C; [Found: C, 59.03; H, 3.72. $C_{17}H_{13}O_3Br$ requires C, 59.15; H, 3.80%]; ν_{max} (KBr) 3030, 1700, 1570, 1430, 1360 cm^{-1}; λ_{max} 215, 268, 311 nm; δ_H (300 MHz, $CDCl_3$) 2.44 (s, 3H, C–C*H*$_3$), 5.29 (s, 2H, –OC*H*$_2$), 5.80 (s, 1H, =C*H*), 7.24–7.32 (m, 3H, Ar*H*), 7.38–7.44 (m, 1H, Ar*H*), 7.53–7.55 (m, 2H, Ar*H*), 7.67–7.69 (m, 1H, Ar*H*); *m*/*z* 344, 346 (M^+).

2.1.10. Compound 5d. (70%) as a white solid, mp 168 °C; [Found: C, 57.68; H, 4.11. $C_{18}H_{15}O_4Br$ requires C, 57.62; H, 4.03%]; ν_{max} (KBr) 3020, 1700, 1570, 1440, 1360 cm^{-1}; λ_{max} 215, 268, 310 nm; δ_H (300 MHz, $CDCl_3$) 2.46 (s, 3H, C–C*H*$_3$), 3.86 (s, 3H, O–C*H*$_3$), 5.27 (s, 2H, –OC*H*$_2$), 5.80 (s, 1H, =C*H*), 6.86–6.89 (m, 1H, Ar*H*), 7.09–7.11 (m, 1H, Ar*H*), 7.29–7.31 (m, 1H, Ar*H*), 7.40–7.43 (m, 1H, Ar*H*), 7.56–7.59 (m, 1H, Ar*H*), 7.69–7.70 (m, 1H, Ar*H*); *m*/*z* 374, 376 (M^+).

2.1.11. Compound 5e. (76%) as a white solid, mp 165 °C; [Found: C, 59.22; H, 3.69. $C_{17}H_{13}O_3Br$ requires C, 59.15; H, 3.80%]; ν_{max} (KBr) 3020, 1720, 1550, 1420, 1350 cm^{-1}; λ_{max} 215, 269, 305 nm; δ_H (300 MHz, $CDCl_3$) 2.46 (s, 3H,

C–CH_3), 5.27 (s, 2H, –OCH_2), 5.79 (s, 1H, =C*H*), 7.17–7.20 (t, 1H, *J*=7.6 Hz, Ar*H*), 7.25–7.29 (m, 1H, Ar*H*), 7.37–7.42 (m, 2H, Ar*H*), 7.51–7.53 (d, 1H, *J*=7.6 Hz, Ar*H*), 7.63–7.65 (d, 1H, *J*=7.9 Hz, Ar*H*), 7.73–7.74 (d, 1H, *J*=7.9 Hz, Ar*H*); *m/z* 344, 346 (M^+).

2.1.12. Compound 5f. (71%) as a white solid, mp 170 °C; [Found: C, 57.50; H, 3.88. $C_{18}H_{15}O_4Br$ requires C, 57.62; H, 4.03%]; ν_{max} (KBr) 3030, 1700, 1570, 1400, 1300 cm^{-1}; λ_{max} 215, 270, 305 nm; δ_H (300 MHz, $CDCl_3$) 2.47 (s, 3H, C–CH_3), 3.81 (s, 3H, O–CH_3), 5.23 (s, 2H, –OCH_2), 5.78 (s, 1H, =C*H*), 6.80–6.83 (dd, 1H, *J*=2.9, 8.8 Hz, Ar*H*), 7.06–7.07 (d, 1H, *J*=2.9 Hz, Ar*H*), 7.17–7.20 (t, 1H, *J*=7.6 Hz, Ar*H*), 7.41–7.43 (d, 1H, *J*=7.1 Hz, Ar*H*), 7.51–7.53 (d, 1H, *J*=8.8 Hz, Ar*H*), 7.73–7.75 (d, 1H, *J*=7.1 Hz, Ar*H*); *m/z* 374, 376 (M^+).

2.1.13. Compound 5g. (82%) as a white solid, mp 116 °C; [Found: C, 60.10; H, 4.29. $C_{18}H_{15}O_3Br$ requires C, 60.18; H, 4.21%]; ν_{max} (KBr) 3060, 1700, 1560, 1430, 1350 cm^{-1}; λ_{max} 214, 279, 308 nm; δ_H (300 MHz, $CDCl_3$) 2.41 (s, 3H, C–CH_3), 2.56 (s, 3H, C–CH_3), 5.24 (s, 2H, –OCH_2), 5.76 (s, 1H, =C*H*), 6.92–6.94 (d, 1H, *J*=8.1 Hz, Ar*H*), 7.24–7.29 (m, 2H, Ar*H*), 7.35–7.39 (t, 1H, *J*=7.5 Hz, Ar*H*), 7.46–7.48 (d, 1H, *J*=7.5 Hz, Ar*H*), 7.64–7.66 (d, 1H, *J*=8.1 Hz, Ar*H*); *m/z* 358, 360 (M^+).

2.1.14. Compound 5h. (74%) as a white solid, mp 144 °C; [Found: C, 58.76; H, 4.51. $C_{19}H_{17}O_4Br$ requires C, 58.63; H, 4.40%]; ν_{max} (KBr) 3050, 1690, 1580, 1440, 1310 cm^{-1}; λ_{max} 212, 281, 310 nm; δ_H (300 MHz, $CDCl_3$) 2.41 (s, 3H, C–CH_3), 2.60 (s, 3H, C–CH_3), 3.80 (s, 3H, O–CH_3), 5.19 (s, 2H, –OCH_2), 5.75 (s, 1H, =C*H*), 6.81–6.83 (dd, 1H, *J*=8.8, 2.9 Hz, Ar*H*), 6.93–6.94 (d, 1H, *J*=7.6 Hz, Ar*H*), 7.02–7.03 (d, 1H, *J*=2.9 Hz, Ar*H*), 7.25 (s, 1H, Ar*H*), 7.51–7.53 (d, 1H, *J*=8.8 Hz, Ar*H*); *m/z* 388, 390 (M^+).

2.2. General procedure for the preparation of 1*H*,3*H*, 6*H*-[2]benzopyrano[4,3-*d*]pyrimidine-2,4-dione (6a–f) and 12*H*-benzopyrano[3,2-*c*][1]benzopyran-5-ones (7a–h)

A suspension of the compounds **3a–f** or **5a–h** (0.04 mmol), *n*-Bu_3SnCl (0.04 ml.), $Na(CN)BH_3$ (100 mg) and AIBN (catalytic) in dry benzene (7–8 mL) was refluxed for 3–4 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% aqueous NH_4OH (2×10 mL) and brine, and dried (Na_2SO_4). Evaporation of the solvent furnished the residual mass which was then magnetically stirred with saturated solution of potassium fluoride 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 benzene–ethyl acetate (9:1) as eluant to give cyclized products **6a–f** or **7a–h**.

2.2.1. 1,3-Dimethyl-6*H*-[2]benzopyrano[4,3-*d*]pyrimidine-2,4-dione (6a). (80%), as a white solid, mp 142 °C; [Found: C, 63.87; H, 4.84; N, 11.44. $C_{13}H_{12}N_2O_3$ requires C, 63.93; H, 4.95; N, 11.47%]; ν_{max} (KBr) 2925, 1703, 1631, 1457 cm^{-1}; λ_{max} 215, 238, 243, 261, 279 nm; δ_H (300 MHz, $CDCl_3$) 3.44 (s, 3H, *N*–CH_3), 3.48 (s, 3H, *N*–CH_3), 4.21 (s, 2H, O–CH_2), 7.14–7.15 (d, 1H, *J*=7.3 Hz, Ar*H*), 7.33–7.36 (t, 1H, *J*=7.3 Hz, Ar*H*), 7.41–7.44 (t, 1H, *J*=7.3 Hz, Ar*H*), 7.53–7.54 (d, 1H, *J*=7.3 Hz, Ar*H*); *m/z* 244 (M^+).

2.2.2. 1,3-Dimethyl-6*H*-[2]benzopyrano[4,3-*d*]8-methoxypyrimidine-2,4-dione (6b). (75%) as a white solid, mp 105 °C; [Found: C, 61.24; H, 5.20; N, 10.27. $C_{14}H_{14}N_2O_4$ requires C, 61.31; H, 5.14; N, 10.21%]; ν_{max} (KBr) 2924, 1706, 1645, 1497 cm^{-1}; λ_{max} 215, 238, 243, 260, 276 nm; δ_H (300 MHz, $CDCl_3$) 3.43 (s, 3H, *N*–CH_3), 3.47 (s, 3H, *N*–CH_3), 3.85 (s, 3H, O–CH_3), 4.38 (s, 2H, O–CH_2), 6.85–6.89 (m, 1H, Ar*H*), 7.04–7.08 (m, 1H, Ar*H*), 7.21 (s, 1H, Ar*H*); *m/z* 274 (M^+).

2.2.3. 1,3-Diethyl-6*H*-[2]benzopyrano[4,3-*d*]pyrimidine-2,4-dione (6c). (85%) as a white solid, mp 95 °C; [Found: C, 66.28; H, 5.75; N, 10.38. $C_{15}H_{16}N_2O_3$ requires C, 66.16; H, 5.92; N, 10.29%]; ν_{max} (KBr) 2935, 1704, 1645, 1469 cm^{-1}; λ_{max} 215, 238, 243, 260, 279 nm; δ_H (300 MHz, $CDCl_3$) 1.25–1.29 (t, 3H, *J*=6.9 Hz, C–CH_3), 1.35–1.40 (t, 3H, *J*=6.9 Hz, C–CH_3), 3.85–3.92 (q, 2H, *J*=6.9 Hz, *N*–CH_2), 4.06–4.13 (q, 2H, *J*=6.9 Hz, *N*–CH_2), 4.42 (s, 2H, O–CH_2), 7.15–7.17 (d, 1H, *J*=7.3 Hz, Ar*H*), 7.32–7.37 (t, 1H, *J*=7.3 Hz, Ar*H*), 7.40–7.45 (t, 1H, *J*=7.3 Hz, Ar*H*), 7.52–7.55 (d, 1H, *J*=7.3 Hz, Ar*H*); *m/z* 272 (M^+).

2.2.4. 1,3-Diethyl-6*H*-[2]benzopyrano[4,3-*d*]8-methoxypyrimidine-2,4-dione (6d). (80%) as a white solid, mp 102 °C; [Found: C, 63.45; H, 5.90; N, 9.22. $C_{16}H_{18}N_2O_4$ requires C, 63.57; H, 6.00; N, 9.27%]; ν_{max} (KBr) 2940, 1702, 1652, 1459 cm^{-1}; λ_{max} 215, 237, 243, 260, 277 nm; δ_H (300 MHz, $CDCl_3$) 1.24–1.28 (t, 3H, *J*=6.9 Hz, C–CH_3), 1.34–1.39 (t, 3H, *J*=6.9 Hz, C–CH_3), 3.84 (s, 3H, O–CH_3), 3.86–3.95 (q, 2H, *J*=6.9 Hz, *N*–CH_2), 4.05–4.12 (q, 2H, *J*=6.9 Hz, *N*–CH_2), 4.38 (s, 2H, O–CH_2), 6.85–6.89 (m, 1H, Ar*H*), 7.05–7.08 (m, 1H, Ar*H*), 7.21 (s, 1H, Ar*H*); *m/z* 302 (M^+).

2.2.5. 1-Ethyl-3-methyl-6*H*-[2]benzopyrano[4,3-*d*]pyrimidine-2,4-dione (6e). (82%) as a white solid, mp 98 °C; [Found: C, 65.17; H, 5.47; N, 10.80. $C_{14}H_{14}N_2O_3$ requires C, 65.11; H, 5.46; N, 10.85%]; ν_{max} (KBr) 2920, 1686, 1653, 1445 cm^{-1}; λ_{max} 215, 238, 244, 261, 279 nm; δ_H (300 MHz, $CDCl_3$) 1.24–1.29 (t, 3H, *J*=6.9 Hz, C–CH_3), 3.47 (s, 3H, *N*–CH_3), 4.06–4.13 (q, 2H, *J*=6.9 Hz, *N*–CH_2), 4.42 (s, 2H, O–CH_2), 7.14–7.16 (d, 1H, *J*=7.3 Hz, Ar*H*), 7.32–7.36 (t, 1H, *J*=7.3 Hz, Ar*H*), 7.40–7.45 (t, 1H, *J*=7.3 Hz, Ar*H*), 7.52–7.55 (d, 1H, *J*=7.3 Hz, Ar*H*); δ_c (75.5 MHz, $CDCl_3$) 12.6 (*C*H_3), 36.8 (*N*–*C*H_2), 36.9 (*N*–*C*H_3), 63.4 (C_6), 113.9 (C_{4a}), 127.9 (C_7), 128.9 (C_{10}), 130.0 (C_9), 130.3 (C_8), 131.6 (C_{10b}), 140.3 (C_{10a}), 142.2 (C_{6a}), 150.8 (C_2), 163.3 (C_4); *m/z* 258 (M^+).

2.2.6. 1-Ethyl-3-methyl-6*H*-[2]benzopyrano[4,3-*d*]8-methoxypyrimidine-2,4-dione (6f). (84%) as a white solid, mp 92 °C; [Found: C, 62.57; H, 5.51; N, 9.75. $C_{15}H_{16}N_2O_4$ requires C, 62.49; H, 5.59; N, 9.72%]; ν_{max} (KBr) 2940, 1706, 1645, 1451 cm^{-1}; λ_{max} 215, 238, 243, 261, 276 nm; δ_H (300 MHz, $CDCl_3$) 1.24–1.28 (t, 3H,

J=6.9 Hz, C–CH_3), 3.46 (s, 3H, N–CH_3), 3.85 (s, 3H, O–CH_3), 4.07–4.10 (q, 2H, J=6.9 Hz, N–CH_2), 4.38 (s, 2H, O–CH_2), 6.86–6.89 (d, 1H, J=7.3 Hz, ArH), 7.05–7.08 (m, 1H, ArH), 7.19 (s, 1H, ArH); m/z 288 (M^+).

2.2.7. Compound 7a. (75%) as a white solid, mp 137 °C; [Found: C, 76.87; H, 4.12. $C_{16}H_{10}O_3$ requires C, 76.79; H, 4.03%]; ν_{max} (KBr) 2920, 1710, 1560, 1400 cm^{-1}; λ_{max} 215, 279 nm; δ_H (300 MHz, $CDCl_3$) 4.55 (s, 2H, –OCH_2), 7.30–7.34 (m, 2H, ArH), 7.39–7.42 (m, 1H, ArH), 7.43–7.45 (m, 2H, ArH), 7.47–7.50 (m, 1H, ArH), 7.54–7.59 (m, 1H, ArH), 7.61–7.77 (m, 1H, ArH); m/z 250 (M^+).

2.2.8. Compound 7b. (78%) as a white solid, mp 142 °C; [Found: C, 72.70; H, 4.20. $C_{17}H_{12}O_4$ requires C, 72.85; H, 4.32%]; ν_{max} (KBr) 2900, 1710, 1590, 1380 cm^{-1}; λ_{max} 218, 292 nm; δ_H (300 MHz, $CDCl_3$) 3.87 (s, 3H, O–CH_3), 4.51 (s, 2H, –OCH_2), 6.90–6.94 (dd, 1H, J=2.5, 8.4 Hz, ArH), 7.13–7.14 (d, 1H, J=2.5 Hz, ArH), 7.20–7.23 (d, 1H, J=8.4 Hz, ArH), 7.31–7.36 (m, 1H, ArH), 7.39–7.42 (m, 1H, ArH), 7.53–7.59 (m, 1H, ArH), 7.73 (s, 1H, ArH); m/z 280 (M^+).

2.2.9. Compound 7c. (70%) as a white solid, mp 165 °C; [Found: C, 77.18; H, 4.42. $C_{17}H_{12}O_3$ requires C, 77.26; H, 4.58%]; ν_{max} (KBr) 2905, 1705, 1570, 1380 cm^{-1}; λ_{max} 218, 290 nm; δ_H (300 MHz, $CDCl_3$) 2.44 (s, 3H, C–CH_3), 4.53 (s, 2H, –OCH_2), 7.30–7.33 (m, 4H, ArH), 7.37–7.59 (m, 2H, ArH), 7.71 (s, 1H, ArH); m/z 264 (M^+).

2.2.10. Compound 7d. (72%) as a white solid, mp 152 °C; [Found: C, 73.51; H, 4.84. $C_{18}H_{14}O_4$ requires C, 73.46; H, 4.79%]; ν_{max} (KBr) 2900, 1710, 1550, 1400 cm^{-1}; λ_{max} 219, 279 nm; δ_H (300 MHz, $CDCl_3$) 2.43 (s, 3H, C–CH_3), 3.87 (s, 3H, O–CH_3), 4.90 (s, 2H, –OCH_2), 6.90–6.93 (dd, 1H, J=2.5, 8.4 Hz, ArH), 7.12–7.13 (d, 1H, J=2.5 Hz, ArH), 7.19–7.22 (d, 1H, J=8.4 Hz, ArH), 7.28–7.38 (m, 2H, ArH), 7.67 (s, 1H, ArH); m/z 294 (M^+).

2.2.11. Compound 7e. (76%) as a white solid, mp 185 °C; [Found: C, 77.36; H, 4.69. $C_{17}H_{12}O_3$ requires C, 77.26; H, 4.58%]; ν_{max} (KBr) 2900, 1700, 1560, 1390 cm^{-1}; λ_{max} 218, 290 nm; δ_H (300 MHz, $CDCl_3$) 2.43 (s, 3H, C–CH_3), 4.54 (s, 2H, –OCH_2), 7.29–7.32 (m, 2H, ArH), 7.37–7.40 (m, 2H, ArH), 7.44–7.49 (m, 1H, ArH), 7.57–7.59 (m, 1H, ArH), 7.70 (s, 1H, ArH); m/z 264 (M^+).

2.2.12. Compound 7f. (85%) as a white solid, mp 175 °C; [Found: C, 73.59; H, 4.67. $C_{18}H_{14}O_4$ requires C, 73.46; H, 4.79%]; ν_{max} (KBr) 2900, 1720, 1590, 1440 cm^{-1}; λ_{max} 219, 285 nm; δ_H (300 MHz, $CDCl_3$) 2.51 (s, 3H, C–CH_3), 3.87 (s, 3H, O–CH_3), 4.49 (s, 2H, –OCH_2), 6.91–6.94 (m, 1H, ArH), 7.20–7.22 (m, 2H, ArH), 7.36–7.43 (m, 2H, ArH), 7.71 (s, 1H, ArH); m/z 294 (M^+).

2.2.13. Compound 7g. (82%) as a white solid, mp 134 °C; [Found: C, 77.79; H, 4.94. $C_{18}H_{14}O_3$ requires C, 77.68; H, 5.07%]; ν_{max} (KBr) 2950, 1710, 1580, 1390 cm^{-1}; λ_{max} 218, 291 nm; δ_H (300 MHz, $CDCl_3$) 2.47 (s, 3H, C–CH_3), 2.51 (s, 3H, C–CH_3), 4.55 (s, 2H, –OCH_2), 7.04–7.07 (d, 1H, J=7.5 Hz, ArH), 7.29–7.31 (d, 1H, J=7.5 Hz, ArH), 7.36–7.50 (m, 2H, ArH), 7.58–7.60 (m, 1H, ArH), 7.95 (s, 1H, ArH); m/z 278 (M^+).

2.2.14. Compound 7h. (78%) as a white solid, mp 172 °C; [Found: C, 73.96; H, 5.27. $C_{19}H_{16}O_4$ requires C, 74.01; H, 5.23%]; ν_{max} (KBr) 2890, 1720, 1590, 1420 cm^{-1}; λ_{max} 218, 285 nm; δ_H (300 MHz, $CDCl_3$) 2.46 (s, 3H, C–CH_3), 2.50 (s, 3H, C–CH_3), 3.87 (s, 3H, O–CH_3), 4.51 (s, 2H, –OCH_2), 6.92–6.94 (dd, 1H, J=2.5, 8.4 Hz, ArH), 7.04–7.05 (d, 1H, J=7.5 Hz, ArH), 7.13–7.14 (d, 1H, J=2.5 Hz, ArH), 7.22–7.23 (d, 1H, J=8.4 Hz, ArH), 7.28–7.30 (d, 1H, J=7.5 Hz, ArH); m/z 308 (M^+).

Acknowledgements

We thank the CSIR (New Delhi) for financial assistance. P. K. B is grateful to UGC (New Delhi) for a Junior Research Fellowship. P. P. M and S. S are grateful to CSIR (New Delhi) for Junior Research Fellowships.

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. see also pp 489. (c) Jasperse, C. P.; Curran, D. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237.
2. Majumdar, K. C.; Balasubramanium, K. K.; Thyagarajan, B. S. *J. Heterocycl. Chem.* **1973**, *10*, 159.
3. Majumdar, K. C.; Das, U. *J. Org. Chem.* **1998**, *63*, 9997.
4. (a) Majumdar, K. C.; Chatterjee, P.; Saha, S. *Tetrahedron Lett.* **1998**, *39*, 7147. (b) Majumdar, K. C.; Chatterjee, P.; Saha, S.; Samanta, S. K. *Indian J. Chem.* **2001**, *40B*, 915.
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) Parker, K. A.; Spero, D. M.; Inman, K. C. *Tetrahedron Lett.* **1986**, *27*, 2833. (d) Jones, K.; Willkinson, J. A. *J. Chem. Soc., Chem. Commun.* **1992**, 1767.
6. (a) Snieckus, V. *Bull. Soc. Chim. Fr.* **1988**, 67. (b) Harrowven, D. C. *Tetrahedron Lett.* **1993**, *34*, 5653. (c) Harrowven, D. C.; Browne, R. *Tetrahedron Lett.* **1994**, *35*, 5301.
7. Sundberg, R. J.; Cherney, R. J. *J. Org. Chem.* **1990**, *55*, 6028.
8. Rosa, A. M.; Prabhakar, S.; Lobo, A. M. *Tetrahedron Lett.* **1990**, *13*, 1881.
9. Ishibashi, H.; Kato, I.; Takeda, Y.; Kogure, M.; Tamura, O. *Chem. Commun.* **2000**, 1527.
10. Ponaras, A. A.; Zaim, O. *Tetrahedron Lett.* **2000**, *41*, 2279.
11. Cid, M. M.; Dominguez, D.; Castedo, L.; Va'zquez-Lopez, E. M. *Tetrahedron* **1999**, *55*, 5599.
12. Heidelberger, C. In *Pyrimidine and Pyrimidine Antimetabolites in Cancer Medicine*; Holland, J. F., Frei, E., Eds.; Lea and Febiger: Philadelphia, 1984; p 801.
13. DeClercq, E.; Descamps, J.; Somer, P. De.; Barr, P. J.; Jones, A. S.; Walker, R. T. *Proc. Natl Acad. Sci. USA* **1979**, *76*, 2947.
14. Heidelberger, C.; King, D. H. *Antiviral Agents in Pharmacology and Therapeutics*; Shugar, D., Ed.; Pergamon: Oxford, 1979; Vol. 6, p 427.
15. Mitsuya, H.; Weinhold, K. J.; Furman, P. A.; St. Clair, M. H.; Lehrman, S. N.; Gallo, R. C.; Bolognesi, D.; Barry, D. W.; Broder, S. *Proc. Natl Acad. Sci. USA* **1985**, *82*, 7096.
16. Fischl, M. A.; Richman, D. D.; Grieco, M. H.; Gottlieb, M. S.; Volberdin, P. A.; Laskin, O. L.; Leedom, J. M.; Groopman,

J. E.; Mildvan, D.; Schooley, R. T.; Jackson, G. G.; Durack, D. T.; King, D. N. *N. Engl. J. Med.* **1987**, *317*, 185.
17. Griengl, H.; Bodenteich, M.; Hayden, W.; Wanek, E.; Streicher, W.; Stutz, P.; Bachmayer, H.; Ghazzo-uli, I.; Rosenwirth, B. *J. Med. Chem.* **1985**, *28*, 1679.
18. DeClercq, E.; Descamps, J.; Ogata, M.; Shigeta, S. *Antimicrob. Agents Chemother.* **1982**, *21*, 33.
19. DeClercq, E.; Rosenwirth, B. *Antimicrob. Agents Chemother.* **1985**, *28*, 246.
20. Rosenwirth, B.; Griengl, H.; Wanek, E.; DeClercq, E. *Antiviral Res.* **1985**, *Suppl. I*, 21.
21. MacIlwain, C. *Nature* **1993**, *365*, 378.
22. (a) DeClercq, E.; Balzarini, J.; Torrence, P. F.; Mertes, M. P.; Schmidt, C. L.; Shugar, D.; Barr, P. J.; Jones, A. S.; Verhelst, G.; Walker, R. T. *Mol. Pharmacol.* **1981**, *19*, 321. (b) Danenberg, V.; Bhatt, R. S.; Kundu, N. G.; Danenberg, K.; Heidelberger, C. *J. Med. Chem.* **1981**, *24*, 1537. (c) Chu, C. K.; Schinagi, R. F.; Ahn, M. K.; Ulas, G. V.; Gu, Z. P. *J. Med. Chem.* **1989**, *32*, 612.
23. (a) Prober, J. M.; Trainer, G. L.; Dam, R. J.; Hobbs, F. W.; Robertson, C. W.; Zagursky, R. J.; Cocuzza, A. J.; Jehnsen, M. A.; Banmeister, K. *Science* **1987**, *238*, 336. (b) Povsic, T. J.; Dervan, P. B. *J. Am. Chem. Soc.* **1990**, *112*, 9428.
24. Miyasaka, T.; Tanaka, H.; Baba, M.; Hayakawa, H.; Walker, R. T.; Balzarini, J.; DeClercq, E. *J. Med. Chem.* **1989**, *32*, 2507.
25. 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.
26. DeClercq, E. *Med. Res. Rev.* **1993**, *13*, 229.
27. (a) Gallo, R. C. *Sci. Am.* **1986**, *255*, 78. (b) Gallo, R. C. *Sci. Am.* **1987**, *256*, 38.
28. Kundu, N. G.; Das, P. *J. Chem. Soc., Chem. Commun.* **1995**, 99.
29. Botta, M.; Saladino, R.; Lamba, D.; Nicoletti, R. *Tetrahedron* **1993**, *49*, 6053.
30. Kundu, N. G.; Dasgupta, S. K. *J. Chem. Soc., Perkin Trans 1* **1993**, 2657.
31. (a) Majumdar, K. C.; Das, U. *J. Chem. Res. (S)* **1997**, 309. (b) Majumdar, K. C.; Das, U. *J. Chem. Res. (M)* **1997**, 2062.
32. Majumdar, K. C.; Das, U. *Synth. Commun.* **1997**, *27*, 4013.
33. Majumdar, K. C.; Das, U.; Jana, N. K. *J. Org. Chem.* **1998**, *63*, 3550.
34. (a) Feur, G. In *Progress in Medicinal Chemistry*; Ellis, G. P., West, G. B., Eds.; North-Holland: New York, 1974. (b) Lauger, V. P.; Martin, H.; Muller, P. *Helv. Chim. Acta* **1994**, *27*, 892. (c) Soine, T. *J. Pharm. Sci.* **1964**, *53*, 231.
35. Ishibashi, H.; Kawanami, H.; Nakagawa, H.; Ikeda, M. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2291.
36. Abeywickrema, A. N.; Beckwith, A. L. J.; Gerba, S. *J. Org. Chem.* **1987**, *52*, 4072.
37. (a) Rosa, A. M.; Lobo, A. M.; Branco, P. S.; Prabhakar, S.; Sa-da-Costa, S. M. *Tetrahedron* **1997**, *53*, 299. (b) Aldabbagh, F.; Bowman, W. R. *Tetrahedron Lett.* **1997**, *38*, 3793. (c) Curran, D. P.; Ko, S.-B.; Josien, H. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2683. (d) Bowman, W. R.; Cloonan, M. O.; Krintel, S. L. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2885.