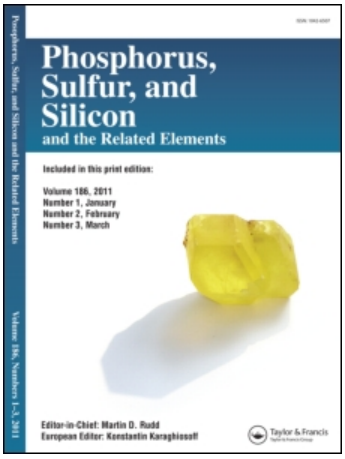

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Synthesis and Antitumor Activity of Novel 2-(Thymin-1'-ylmethoxy)ethyl Alkyl Sulfides and Their Oxidation Products

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Synthesis and Antitumor Activity of Novel 2-(Thymin-1′-ylmethoxy)ethyl Alkyl Sulfides and Their Oxidation Products

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A series of novel 2-(thymin-1′-ylmethoxy)ethyl alkyl sulfides have been synthesized in three steps from thymine. They have been oxidized into sulfoxide and sulfone derivatives by means of $NaIO_4$ and H_2O_2 30%/diethyl azodicarboxylate (DEAD), respectively, in high yields. All products were characterized by ^1H NMR and IR spectra and elemental analyses. The preliminary bioassay indicates that the compound ***6g*** *exhibited potential antitumor activity.*

Keywords Diethyl azodicarboxylate; sulfides; sulfones; sulfoxides; thymine

INTRODUCTION

A large number of sulfur nucleosides, nucleotides, and oligonucleotides were synthesized for the purpose of finding new chemical therapeutic agents and biological tools. Some of them were developed as important tools in the study of protein and nucleic acid structures, functions and interactions, and antisense modulation of gene expression.[1,2] The introduction of a single sulfur atom into the nucleosides led to efficient antiviral or antitumor agents. For example, Lamivudine ((-)-L-β-1,3-oxathiolanyl cytosine) is used in the treatment of AIDS and

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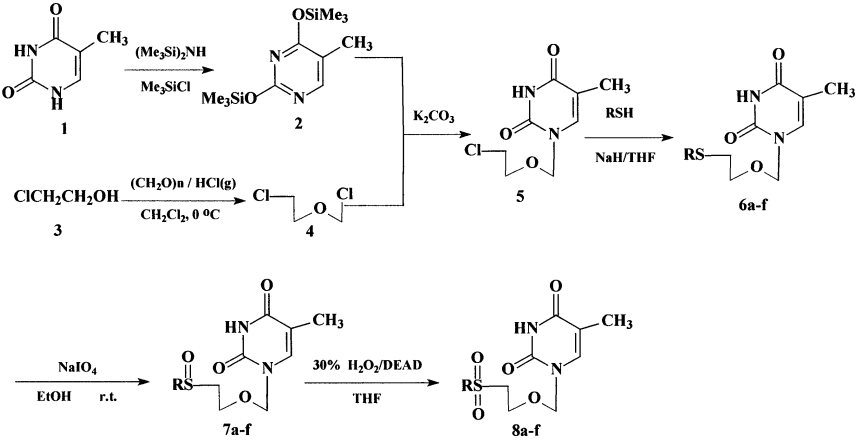
Chronic Hepatitis B; [3,4] and 4′-thioFAC (1-(2-deoxy-2-fluoro-β-D-4-thio-arabinopentofuranosyl) cytosine) is shown to be a promising orally active antitumor agent.[5]

Many pyrimidine thionucleoside analogues have exhibited antitumor properties.[6–8] As far as we know, there has been little research done on the thymine acyclic thionucleoside. As part of our research program,[9–13] we designed and synthesized the title compounds, 2-(thymin-1′-ylmethoxy)ethyl alkyl sulfides **6**, and its oxidation products **7** and **8**. The synthetic route is shown in Scheme 1.



	a	b	c	d	e	f
R	Me	Et	Pr	Bu	Pent	$C_{12}H_{25}$

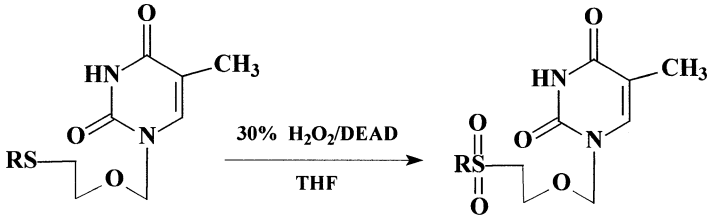
SCHEME 1

RESULTS AND DISCUSSION

Synthesis of 2-(Thymin-1′-ylmethoxy)ethyl Alkyl Sulfides (6), 2-(Thymin-1′-ylmethoxy)ethyl Alkyl Sulfoxides (7), and 2-(Thymin-1′-ylmethoxy)ethyl Alkyl Sulfones (8)

Thymine (**1**) reacted with hexamethyldisilylazane (HMDS) by means of an improved procedure of the literature[14] to give 2,4-di(trimethylsilyloxy)thymine **2**. According to the standard chloromethyl ether method,[15] the condensation of **2** with 2-chloromethoxyethyl

chlortide **4**, obtained from 2-chloroethanol (**3**), gave the key intermediate **5** (in a 76% yield) in the presence of anhydrate K_2CO_3. The compounds **6a–f** were obtained by the method for synthesis of unsymmetrical thioethers (NaH/RSH, THF) in yields of 91–97%; a slight excess of aqueous $NaIO_4$[16] was added to a solution of compound **6** in ethanol to afford compound **7**; the resultant **7** was oxidized by 30% H_2O_2 to produce the sulfone derivatives **8** at very slow rates. However, when DEAD ($EtO_2CN{=}NCO_2Et$) was added to this system, the reaction was considerably accelerated to give in high yields. The investigation of this reaction mechanism is under progress. The compound **8** also has been obtained directly by the oxidation of **6** with H_2O_2 30%/DEAD (Scheme 2).



SCHEME 2

All compounds **6–8** have been characterized by ^{1}H NMR, elemental analysis, and IR will be.

In the ^{1}H NMR spectra of the title compounds (**6–8**), the methylene protons of the methoxy appear as a set of characteristic singlet peaks in the range of δ 5.13~5.15. The protons of the ethylene group exhibit two sets of peaks at δ 2.67~2.68 and 3.68~3.72 (sulfides), 2.88~2.91 and 3.98~4.02 (sulfoxides), and 3.18~3.39 and 3.85~4.05 (sulfones). The hydrogens of another methylene (or methyl) linking with the sulfur atom display in the range of δ 2.10~2.53 (sulfides), 2.65~2.77 (sulfoxides), and 2.96~3.04 (sulfones). The ^{1}H NMR spectrum also reveals three sets of peaks at δ 1.90~1.92 (singlet), 7.12~7.14 (singlet), and 8.19~9.41 (singlet), supporting the thymine structure. The IR spectra of compounds (**6–8**) showed normal stretching absorption bands, indicating the existence of the groups NH (~3400 cm^{-1}), C=O (1709~1742 and 1652~1683), C=C (1622~1638), S=O (1033~1049), O=S=O (1165~1171 and 1340~1353), and C–O–C (1119~1137).

Biological Assays

The preliminary biological activities were determined for the title compounds **6–8**. The anticancer activities given in Table I indicate that

TABLE I Inhibitory Effects of Compounds 6–8 (10^{-5} M) on Cell Lines P-388 and BEL-7402

Compounds	**6a**	**6b**	**6c**	**6d**	**6e**	**6f**	**7a**	**7b**	**7c**	**7d**	**7e**	**8a**	**8b**	**8c**	**8d**	**8e**	**8f**
Inhibition rate																	
(A-549) %	59	68	75	88	67	61	43	41	52	22	35	40	36	17	23	31	25
(BEL-7402) %	56	43	42	45	49	38	49	51	42	44	35	37	33	41	29	36	40

compound **6d** has potential inhibitory activities on the A-549 (the human lung carcinoma) cell line. However, none of them has any significant inhibiting activities on the BEL-7402 (the human hepatocellular carcinoma) cell line. The inhibitory effect of compound **6d** on the A-549 cell line is more significant than that of Cisplatin, which is a clinic antitumor agent, but lower than that of Gleevec, a new antitumor drug.[17]

EXPERIMENTAL

Elemental analyses were performed with a CHNCORDERD MT-3 elementary analyzer. NMR spectra were recorded with a BRUKER AC-P200 spectrometer with TMS as the internal reference and $CDCl_3$ as the solvent. IR spectra were obtained on SHIMADZU-435. Melting Points were determined with a Thomas-Hoover melting point apparatus and are uncorrected. Column chromatography was performed on silica gel GF_{254} (Qing dao Hai yang Chemical Group Co. of China).

1-(2′-Chloroethoxy)methyl Thymine (5)

A suspension of 0.65 g (10 mmol) 2-chloroethanol and 0.70 g of paraformaldehyde in 18 mL of dry methylene chloride was cooled to 0°C. Dry hydrogen chloride was bubbled through the stirred suspension for 3 h until saturated. The mixture was allowed to stand in a refrigerator overnight and then dried over anhydrous $CaCl_2$. It was filtered and the solvent was removed under reduced pressure to give an oily residue, which was used directly in the next step to prepare 1-(2′-Chloroethoxy)methyl thymine (**5**).

To a mixture of thymine (10 mmol, 1.26 g), and HMDS (4 mL), trimethylsilyl chloride (1 mL) was added. The resultant suspension was refluxed for 3 h. The excess HMDS was removed from the reaction mixture in vacuo to give the crude silylation product of thymine as a solid, which was used in the next step without further purification.

A suspension of 0.2 g of anhydrous K_2CO_3 and 1.29 g (10 mmol) of $ClCH_2OCH_2CH_2Cl$ in 15 mL of dry CH_2Cl_2 was stirred at room

temperature for 5 min under a N_2 atmosphere. The crude silylation product of thymine was added into this system. The mixture was stirred overnight at room temperature. The resultant reaction mixture was adjusted to pH = 7 with 0.1 M HCl and was extracted with chloroform (3 × 60 mL). The organic extracts were combined and dried over $MgSO_4$ and were concentrated in vacuo. The residue was purified by silca-gel flash chromatography to give **5** as a white solid (1.70 g, 76%); m.p. 119–120°C; ^{1}H MNR ($CDCl_3$, δ) 1.91 (s, 3H) 3.60 (t, 2H, J = 5.4 Hz) 3.85 (t, 2H, J = 5.4 Hz) 5.19 (s, 2H) 7.14 (s, 1H) 9.70 (s, 1H).

General Procedure for the Preparation of 2-(Thymin-1′-ylmethoxy)ethyl Alkyl Sulfides (6)

To a suspension of 0.312 g (6.5 mmol) of 50% NaH in THF (15 mL), 6 mmol of RSH at 0°C was added dropwise. The reaction mixture was warmed to room temperature and stirred for 2 h, and then 0.67 g (3 mmol) of **5** was added to the reaction mixture and stirring was continued for 5 h. The resultant mixture was adjusted to pH = 6–7 with 1 M HCl and was extracted with $CHCl_3$ (3 × 50 mL). The organic layers were combined and dried over $MgSO_4$. The solvent was removed in vacuo and the residue then was purified by flash chromatography on silica-gel ($CHCl_3$: CH_3OH = 20:1) to give **6**.

6b

91% yield. m.p. 75–76°C. ^{1}H MNR ($CDCl_3$) δ: 1.22 (t, J = 7.30 Hz, 3H), 1.92 (s, 3H), 2.53 (q, J = 7.30 Hz, 2H), 2.69 (t, J = 6.5 Hz, 2H), 3.72 (t, J = 6.5 Hz, 2H), 5.14 (s, 2H), 7.13 (s, 1H), 8.80 (s, 1H). IR (KBr Disc): 3408, 3171, 3055, 2917, 2927, 2875, 1734, 1679, 1630, 1455, 1425, 1268, 1129, 831, 757 cm^{-1}. Anal. cacld. for $C_{10}H_{16}N_2O_3S$: C, 49.16; H, 6.60; N, 11.47. Found: C, 48.96; H, 6.49; N, 11.55.

6c

98% yield. m.p. 87–88°C. ^{1}H MNR ($CDCl_3$) δ: 0.93 (t, 3H), 1.57 (m, 2H), 1.91 (s, 3H), 2.47 (t, J = 7.3 Hz, 2H), 2.67 (t, J = 6.3 Hz, 2H), 3.68 (t, J = 6.3 Hz, 2H), 5.13 (s, 2H), 7.13 (s, 1H), 9.41 (s, 1H). IR (KBr Disc): 3414, 3170, 3051, 2960, 2874, 1732, 1675, 1628, 1455, 1426, 1269, 1125, 831, 555 cm^{-1}. Anal. cacld. for $C_{11}H_{18}N_2O_3S$: C, 51.14; H, 7.02; N, 10.65. Found: C, 51.13; H, 7.17; N, 10.48.

6d

95% yield. m.p. 99–100°C. ^{1}H MNR ($CDCl_3$) δ: 0.88 (t, J = 7.2 Hz, 3H), 1.24–1.65 (m, 4H), 1.92 (s, 3H), 2.51 (t, J = 7.5 Hz, 2H), 2.68 (t, J = 6.4 Hz, 2H), 3.70 (t, 2H, J = 6.4 Hz), 5.14 (s, 2H), 7.13 (s, 1H), 8.54

(s, 1H). IR (KBr Disc): 3408, 3177, 2956, 2866, 1739, 1662, 1629, 1454, 1425, 1133, 831, 757, 555 cm^{-1}. Anal. cacld. for $C_{12}H_{20}N_2O_3S$: C, 52.92; H, 7.40; N, 10.28. Found: C, 52.69; H, 7.18; N, 10.14.

6e

95% yield. m.p. 90–91°C. ^1H MNR ($CDCl_3$) δ: 0.87 (t, $J = 7.2$ Hz, 3H), 1.22–1.68 (m, 6H), 1.92 (s, 3H), 2.50 (t, $J = 7.4$ Hz, 2H), 2.68 (t, $J = 6.4$ Hz, 2H), 3.70 (t, 2H, $J = 6.4$ Hz), 5.14 (s, 2H), 7.13 (s, 1H), 8.41 (s, 1H). IR (KBr Disc): 3415, 3058, 2954, 2865, 1721, 1683, 1630, 1455, 1268, 1129, 831, 555 cm^{-1}. Anal. cacld. for $C_{13}H_{22}N_2O_3S$: C, 54.52; H, 7.74; N, 9.78. Found: C, 54.63; H, 7.75; N, 9.69.

6f

93% yield. m.p. 122–124°C. ^1H MNR ($CDCl_3$) δ: 0.86 (t, $J = 7.2$ Hz, 3H), 1.23–1.69 (m, 20H), 1.92 (s, 3H), 2.50 (t, $J = 7.3$ Hz, 2H), 2.68 (t, $J = 6.4$ Hz, 2H), 3.70 (t, 2H, $J = 6.4$ Hz), 5.14 (s, 2H), 7.13 (s, 1H), 8.45 (s, 1H). IR (KBr Disc): 3420, 3177, 3051, 2919, 2850, 1733, 1676, 1629, 1456, 1268, 1124, 1096, 947, 831, 757, 554 cm^{-1}. Anal. cacld. for $C_{20}H_{36}N_2O_3S$: C, 62.46; H, 9.43; N, 7.28. Found: C, 62.15; H, 9.82; N, 7.04.

When R = CH_3, chloride **5** was added to a solution of $NaSCH_3$ (5 mL), the mixture was stirred over 8 h, and then was adjusted to pH = 7. The reaction mixture was extracted with chloroform (3 × 50 mL). The organic phases were combined and dried over $MgSO_4$. The solvent was removed in vacuo and the residue then was purified by flash chromatography on silica-gel ($CHCl_3$: CH_3OH = 20:1) to give **6a**: 93% yield. m.p. 119–120°C. ^1H MNR ($CDCl_3$)δ: 1.92 (s, 3H), 2.10 (s, 3H) 2.67 (t, $J =$ 6.5 Hz, 2H), 3.72 (t, $J = 6.5$ Hz, 2H), 5.14 (s, 2H), 7.13 (s, 1H), 8.64 (s, 1H). IR (KBr Disc): 3417, 3140, 2921, 2878, 2812, 1731, 1669, 1622, 1460, 1400, 1258, 1135, 1097, 937 cm^{-1}. Anal. cacld. for $C_9H_{14}N_2O_3S$: C, 46.94; H, 6.13; N, 12.16. Found: C, 47.05; H, 6.14; N, 12.15.

General Procedure for the Preparation of 2-(Thymin-1′-ylmethoxy)ethyl Alkyl Sulfoxides (7)

To a solution of compounds **6** (2 mmol) in 5 mL of ethanol was added dropwise (0.46 g, 2.1 mmol) of aqueous saturated $NaIO_4$ at room temperature and the mixture was stirred overnight. The resultant mixture was poured into 10 mL of water and extracted with chloroform (3 × 30 mL). The organic layers were combined and dried over $MgSO_4$. The solvent was removed in vacuo and the residue was then purified by flash chromatography on silica-gel ($CHCl_3$: CH_3OH = 15:1) to give **7**.

7a

90% yield. m.p. 116–117°C. ^{1}H MNR ($CDCl_3$) δ: 1.92 (s, 3H), 2.65 (m, 2H), 2.91 (m, 2H), 4.02 (m, 2H), 5.15 (s, 2H), 7.13 (s, 1H), 9.04 (s, 1H). IR (KBr Disc): 3419, 3109, 3048, 2915, 1714, 1670, 1625, 1468, 1270, 1230, 1131, 1109, 1045, 968, 780, 611 cm^{-1}. Anal. cacld. for $C_9H_{14}N_2O_3S$: C, 43.89; H, 5.73; N, 11.37. Found: C, 43.62; H, 5.69; N, 11.42.

7b

95% yield. m.p. 99–100°C. ^{1}H MNR ($CDCl_3$) δ: 1.34 (t, $J = 7.5$ Hz, 3H), 1.92 (s, 3H), 2.77 (m, 2H), 2.89 (m, 2H), 4.00 (m, 2H), 5.14 (s, 2H), 7.13 (s, 1H), 8.54 (s, 1H). IR (KBr Disc): 3419, 3100, 2977, 2898, 2782, 1709, 1665, 1628, 1458, 1412, 1280, 1224, 1124, 1100, 1043, 977, 820, 769, 540, 547 cm^{-1}. Anal. cacld. for $C_{12}H_{20}N_2O_3S$: C, 52.92; H, 7.40; N, 10.28. Found: C, 52.69; H, 7.18; N, 10.14.

7c

92% yield. m.p. 95–96°C. ^{1}H MNR ($CDCl_3$) δ: 1.06 (t, $J = 7.3$ Hz, 3H), 1.79 (m, 2H), 1.90 (s, 3H), 2.75 (m, 2H), 2.88 (m, 2H), 3.98 (m, 2H), 5.15 (s, 2H), 7.12 (s, 1H), 9.32 (s, 1H). IR (KBr Disc): 3430, 3178, 3050, 2970, 2881, 1729, 1682, 1630, 1459, 1272, 1124, 1103, 1049, 881, 761, 415 cm^{-1}. Anal. cacld. for $C_{11}H_{18}N_2O_4S$: C, 46.14; H, 6.20; N, 10.76. Found: C, 46.01; H, 6.49; N, 10.60.

7d

94% yield. m.p. 103–104°C. ^{1}H MNR ($CDCl_3$) δ: 0.94 (t, $J = 7.2$ Hz, 3H), 1.56–1.73 (m, 4H), 1.91 (s, 3H), 2.75 (m, 2H), 2.89 (m, 2H), 3.98 (m, 2H), 5.15 (s, 2H), 7.13 (s, 1H), 8.97 (s, 1H). IR (KBr Disc): 3424, 3169, 3045, 2956, 2361, 1707, 1670, 1629, 1465, 1271, 1119, 1108, 1045, 856, 575 cm^{-1}. Anal. cacld. for $C_{12}H_{20}N_2O_4S$: C, 49.98; H, 6.99; N, 9.71. Found: C, 50.13; H, 6.81; N, 9.87.

7e

90% yield. m.p. 106–107°C. ^{1}H MNR ($CDCl_3$) δ: 0.89 (t, $J = 6.9$ Hz, 3H), 1.38–1.76 (m, 6H), 1.91 (s, 3H), 2.74 (m, 2H), 2.91 (t, $J = 6.4$ Hz, 2H), 4.00 (m, 2H), 5.15 (s, 2H), 7.13 (s, 1H), 8.86 (s, 1H). IR (KBr Disc): 3407, 3163, 3044, 2924, 2852, 1701, 1672, 1635, 1459, 1271, 1199, 1128, 1033, 867, 763, 593 cm^{-1}. Anal. cacld. for $C_{13}H_{22}N_2O_4S$: C, 51.64; H, 7.33; N, 9.26. Found: C, 51.46; H, 7.45; N, 9.02.

7f

90% yield. m.p. 119–120°C. ^{1}H MNR ($CDCl_3$) δ: 0.85 (t, $J = 7.2$ Hz, 3H), 1.20–1.77 (m, 20H), 1.92 (s, 3H), 2.74 (t, $J = 6.4$ Hz, 2H), 2.91 (m, 2H), 4.00 (m, 2H), 5.15 (s, 2H), 7.13 (s, 1H), 8.65 (s, 1H). IR (KBr

Disc): 3416, 3045, 2924, 2852, 1710, 1673, 1638, 1463, 1272, 1127, 1109, 1038, 875, 763, 718, 598 cm^{-1}. Anal. cacld. for $C_{20}H_{36}N_2O_4S$: C, 59.97; H, 9.06; N, 6.99. Found: C, 5.56; H, 8.79; N, 7.45.

General Procedure for the Preparation of 2-(Thymin-1′-ylmethoxy)ethyl Alkyl Sulfones (8)

0.5 mL of 30% H_2O_2 and 1.2 mmol of DEAD were added to a solution of 1 mmol of compounds **7** in THF (5 mL). The mixture was stirred at 50–55°C for 2 h. Additional DEAD was added, if necessary, to effect a complete reaction. The reaction mixture was stirred continuously at the same temperature for 1 h before pouring into H_2O (10 mL). The resultant mixture was extracted with chloroform (3 × 30 mL). The organic layers were combined and dried over $MgSO_4$. The solvent was removed in vacuo and the residue was purified by flash chromatography on silica-gel ($CHCl_3$: CH_3OH = 10:1) to give **8**.

8a

92% yield. m.p. 168–169°C. ^{1}H MNR ($CDCl_3$) δ: 1.92 (s, 3H), 2.96 (s, 3H), 3.39 (t, J = 5.5 Hz, 2H), 3.85 (t, J = 5.5 Hz, 2H), 5.15 (s, 2H), 7.14 (s, 1H), 8.95 (s, 1H). IR (KBr Disc): 3429, 3192, 3066, 2836, 1715, 1667, 1636, 1459, 1346, 1305, 1270, 1230, 1170, 1132, 1101, 959, 926, 861, 797, 733, 607, 543 cm^{-1}. Anal. cacld. for $C_{12}H_{20}N_2O_3S$: C, 40.89; H, 5.49; N, 10.52. Found: C, 41.01; H, 5.38; N, 10.68.

8b

92% yield. m.p. 152–153°C. ^{1}H MNR ($CDCl_3$) δ: 1.36 (t, J = 7.4 Hz, 3H), 1.92 (s, 3H), 3.01 (t, J = 7.4 Hz, 2H), 3.19 (t, J = 5.8 Hz, 2H), 4.02 (t, 2H, J = 5.8 Hz), 5.15 (s, 2H), 7.13 (s, 1H), 9.10 (s, 1H). IR (KBr Disc): 3425, 3105, 2874, 1725, 1664, 1630, 1468, 1431, 1349, 1279, 1234, 1168, 1131, 1078, 978, 845, 559 cm^{-1}. Anal. cacld. for $C_{12}H_{20}N_2O_3S$: C, 43.47; H, 5.84; N, 10.14. Found: C, 43.72; H, 5.65; N, 10.33.

8c

94% yield. m.p. 131–132°C. ^{1}H MNR ($CDCl_3$) δ: 1.08 (t, J = 7.5 Hz, 3H), 1.87 (m, 2H), 1.92 (s, 3H), 3.04 (t, J = 7.2 Hz, 2H), 3.18 (t, J = 5.9 Hz, 2H), 4.05 (t, 2H, J = 5.9 Hz), 5.15 (s, 2H), 7.13 (s, 1H), 8.84 (s, 1H). IR (KBr Disc): 3431, 3185, 2984, 2868, 1742, 1659, 1625, 1464, 1425, 1353, 1268, 1165, 1137, 1069, 845, 550 cm^{-1}. Anal. cacld. for $C_{12}H_{20}N_2O_3S$: C, 45.51; H, 6.25; N, 9.65. Found: C, 45.38; H, 6.49; N, 9.82.

8d

90% yield. m.p. 119–120°C. ^{1}H MNR ($CDCl_3$) δ: 0.95 (t, J = 7.2 Hz, 3H), 1.36–1.94 (m, 7H), 3.03 (t, J = 7.1 Hz, 2H), 3.22 (t, J = 6.5 Hz,

2H), 4.04 (t, 2H, $J = 6.5$ Hz), 5.15 (s, 2H), 7.13 (s, 1H), 8.19 (s, 1H). IR (KBr Disc): 3430, 3165, 3064, 2976, 2884, 1742, 1666, 1628, 1465, 1459, 1340, 1270, 1171, 1133, 1096, 946, 774, 546 cm^{-1}. Anal. cacld. for $C_{12}H_{20}N_2O_3S$: C, 47.32; H, 6.62; N, 9.20. Found: C, 47.60; H, 6.55; N, 9.31.

8e

93% yield. m.p. 135–136°C. ^1H MNR ($CDCl_3$) δ: 0.88 (t, $J = 7.2$ Hz, 3H), 1.24–1.89 (m, 6H), 1.92 (s, 3H), 2.99 (t, $J = 7.6$ Hz, 2H), 3.22 (t, $J = 5.7$ Hz, 2H), 4.03 (t, 2H, $J = 5.7$ Hz), 5.15 (s, 2H), 7.13 (s, 1H), 9.01 (s, 1H). IR (KBr Disc): 3432, 3108, 3034, 2945, 2843, 1730, 1674, 1625, 1460, 1349, 1279, 1169, 1130, 926, 747, 555 cm^{-1}. Anal. cacld. for $C_{12}H_{20}N_2O_3S$: C, 49.04; H, 6.96; N, 8.80. Found: C, 49.11; H, 6.81; N, 9.03.

8f

89% yield. m.p. 124–126°C. ^1H MNR ($CDCl_3$) δ: 0.86 (t, $J = 7.2$ Hz, 3H), 1.28–1.88 (m, 4H), 1.92 (s, 3H), 3.00 (t, $J = 7.5$ Hz, 2H), 3.21 (t, $J = 5.4$ Hz, 2H), 4.03 (t, 2H, $J = 5.4$ Hz), 5.15 (s, 2H), 7.13 (s, 1H), 8.99 (s, 1H). IR (KBr Disc): 3429, 3175, 3085, 2965, 2942, 2928, 2854, 1740, 1652, 1626, 1464, 1346, 1278, 1165, 1122, 934, 745, 645, 558 cm^{-1}. Anal. cacld. for $C_{12}H_{20}N_2O_3S$: C, 57.80; H, 8.73; N, 6.74. Found: C, 57.69; H, 8.98; N, 6.79.

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