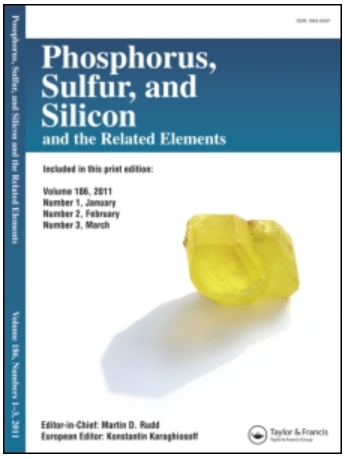


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# Studies on Organophosphorus Compounds: Synthesis and Reactions of Some New 5'-Cyano-2'-(4-methoxyphenyl)spiro[cycloalkane-1,6'-[1,3,2]thiazaphosphixane]-2',4'-disulfide Derivatives

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# STUDIES ON ORGANOPHOSPHORUS COMPOUNDS: SYNTHESIS AND REACTIONS OF SOME NEW 5′-CYANO-2′-(4-METHOXYPHENYL)-SPIRO[CYCLOALKANE-1,6′-[1,3,2]THIAZAPHOSPHIXANE]-2′,4′-DISULFIDE DERIVATIVES

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*2,4-Bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disulfide (Lawesson's Reagent, LR, **1**) reacts with cycloalkylidenecyanothioacetamides (**2** and **3**) to give 5′-cyano-2′-(4-methoxyphenyl)spiro[cyclopentane(cyclohexane)-1,6′-perhydro-[1,3,2]thiazaphosphixane]-2′,4′-disulfide (**4** and **5**). The reaction of compounds **4** and **5** with α-halo compounds led to the formation of the substituted thio-compounds **6a–e** and **7a–e**, respectively, these compounds, upon treatment with sodium ethoxide, produce the corresponding thienothiazaphosphixine derivatives **8a–e** and **9a–e** respectively. Compounds **8a–e** and **9a–e** react with LR under different reaction conditions to give polyfused heterocyclic compounds **10a–d** and **11a–d** respectively. Treatment of compounds **8b** and **9b** with $CS_2$ and $(CH_3)_2SO_4$ gave the corresponding dithiocarbamate methyl ester derivatives **12** and **13**, respectively, which on treating with hydrazine hydrate yielded compounds **14** and **15** respectively. Compounds **14** and **15** reacted with LR to yield compounds **16a,b** and **17a,b** respectively.*

*Keywords:* 2,4-Bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disulfide; cycloalkylidenecyanothioacetamides; P-heterocycles

Heterocycles containing phosphorus continue to attract considerable attention which mainly arises from the large variety of interesting pharmacological and biological activities observed with heterocycles containing phosphorus, which including, herbicidal,[1] insecticidal,[2–4] antibacterial,[5,6] antifungal,[5] and anticancer[7,8] properties. 2,4-Bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disulphide (Lawesson's reagent, LR, **1**), beside its effectiveness as

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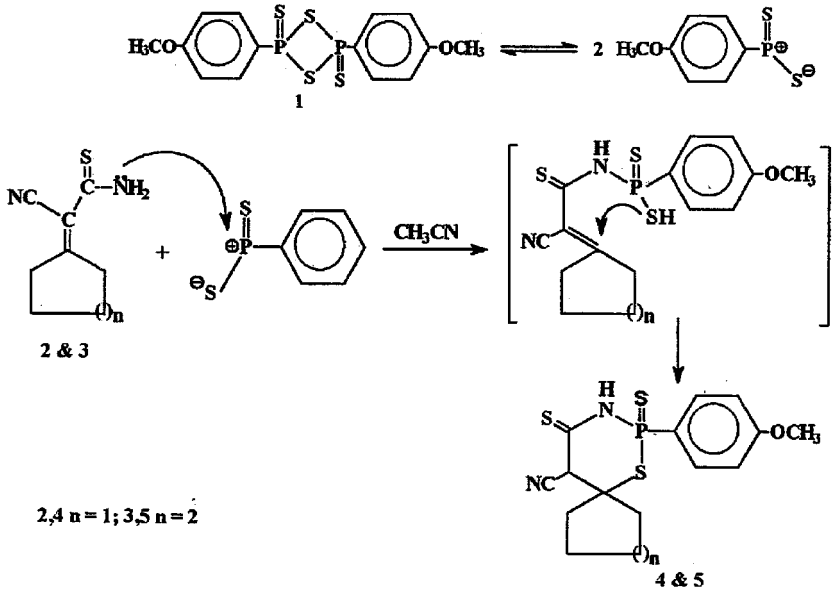
thiation reagent for different carbonyl compounds,[9–12] undergoes ring closure reactions with substrates containing two functional groups[13–19] forming phosphorus heterocycles. To extend the use of LR for the synthesis of new fused P-heterocycles its reaction with cycloalkylidenecyanothioacetamides and different substrates containing two functional groups has been investigated in this work.

## RESULTS AND DISCUSSION

The parent compounds cycloalkylidenecyanothioacetamide **2** and **3** were prepared in a good yield via the reaction of the corresponding cycloalkanone with cyanothioacetamide in the presence of piperidine.[20] Compounds **2** and **3** were allowed to react with LR in boiling acetonitrile to give 5′-cyano-2′-(4-methoxyphenyl)spiro[cyclopentane(cyclohexane)-1,6′-perhydro[1,3,2]thiazaphosphixane]- 2′,4′-disulfide (**4** and **5**). The reaction pathway was assumed to proceed via a nucleophilic attack of the amino group on LR followed by a P-SH addition to the ethylenic bond[21] (Scheme 1).

The structure of compounds **4** and **5** were confirmed on the basis of their elemental and spectral analyses (cf. Table I). The IR spectra of compounds **4** and **5** showed the absence of the absorption bands




**SCHEME 1**

**TABLE I** Analytical and Spectral Data of the New Compounds

| Comp. no. | M.P.[a] °C cryst. solvent | Yield % | $M_F(M_w)$ | Analytical data[b] calc./found % C | H | N | S | IR (KBr)[c] $\nu(cm^{-1})$ | $^1$H-NMR (DMSO-$d_6$)[d] ($\delta$ ppm) |
|---|---|---|---|---|---|---|---|---|---|
| **4** | 163 Ethanol | 59 | $C_{15}H_{17}N_2OPS_3$ (368.46) | 48.89 48.53 | 4.65 4.51 | 7.60 7.43 | 26.10 25.82 | 3310 (NH); 3060 (CH, arom); 2981 (CH, aliph); 2570 (SH); 2216(CN), 657 (P=S). | 11.5 (br, 1 H, NH); 7.7–7.1 (m, 4 H, arom), 3.9 (s, 3H, $CH_3$); 3.5 (s, 1H, CH); 1.95–1.40 (m, 8H, cyclic $CH_2$). |
| **5** | 172 Ethanol | 63 | $C_{16}H_{19}N_2OPS_3$ (382.48) | 50.23 49.95 | 5.00 4.82 | 7.32 7.17 | 25.15 24.88 | 3343 (NH); 3056 (CH, arom); 2950 (CH, aliph); 2539 (SH); 2211(CN), 644 (P=S). | 11.5 (br, 1 H, NH); 7.7–7.1 (m, 4 H, arom), 3.9 (s, 3H, $CH_3$); 3.5 (s, 1H, CH); 1.95–1.20 (m, 10 H, cyclic $CH_2$). |
| **6a** | 230–232 Dioxan | 71 | $C_{17}H_{19}N_2O_3PS_3$ (426.49) | 47.87 47.42 | 4.47 4.29 | 6.56 6.55 | 22.55 22.30 | 3012–2511 (broad band, OH) 1698 (C=O); 2218 (CN); 1293 (C–O); 659 (P=S). | 11.2 (br, 1H, OH); 7.7–7.1 (m, 4H, arom); 4.1 (s, 2H, $CH_2$); 3.9 (s, 3H, $CH_3$); 3.5 (s, 1H, CH); 1.95-1.40 (m, 8H, cyclic $CH_2$). |
| **6b** | 158 Ethanol | 88 | $C_{19}H_{23}N_2O_3PS_3$ (454.55) | 50.20 50.01 | 5.10 4.98 | 6.16 5.90 | 21.16 21.00 | 3011 (CH, arom); 2982, 2909 (CH, aliph); 2220 (CN); 1722 (C=O); 1303 (C–O); 649 (P=S). | 7.7–7.1 (m, 4H, arom); 4.5–4.1 (q, 2H, $OCH_2$) , 4.07 (s, 2H, $CH_2$); 3.9 (s, 3H, $CH_3$); 3.5 (s, 1H, CH); 1.95–1.10 (m, 11H, cyclic $CH_2$ + C–$CH_3$). |
| **6c** | 199 Ethanol | 78 | $C_{17}H_{20}N_3O_2PS_3$ (425.54) | 47.98 47.66 | 4.73 4.57 | 9.87 9.66 | 22.60 22.43 | 3321,3191 ($NH_2$); 3036 (CH, arom); 2906 (CH, aliph); 2213 (CN); 1659 (C=O); 665 (P=S). | 7.7–7.2 (m, 4H, arom); 6.1 (br, 2H, $NH_2$); 4.1 (s, 2H, $CH_2$); 3.9 (s, 3H, $CH_3$); 3.5 (s, 1H, CH); 1.9–1.4 (m, 8H, cyclic $CH_2$). |
| **6d** | 275–276 Ethanol | 84 | $C_{23}H_{24}N_3O_2PS_3$ (501.63) | 55.06 54.74 | 4.82 4.60 | 8.37 8.19 | 19.17 19.01 | 3211 (NH); 3052 (CH, arom); 2975 (CH, aliph); 2209 (CN); 1651 (C=O); 659 (P=S). | 8.7(br, 1H, NH); 7.8–7.0 (m, 9H, arom); 4.1 (s, 2H, $CH_2$); 3.9 (s, 3H, $CH_3$); 3.5 (s, 1H, CH), 1.9–1.4 (m, 8H, cyclic $CH_2$). |

*(Continued on next page)*

**TABLE I** Analytical and Spectral Data of the New Compounds *(Continued)*

| Comp. no. | M.P.[a] °C cryst. solvent | Yield % | $M_F(M_w)$ | Analytical data[b] calc./found % C | H | N | S | IR (KBr)[c] $\nu(cm^{-1})$ | $^1$H-NMR (DMSO-$d_6$)[d] ($\delta$ ppm) |
|---|---|---|---|---|---|---|---|---|---|
| **6e** | 198–200 Ethanol | 80 | $C_{17}H_{18}N_3OPS_3$ (407.49) | 50.10 49.80 | 4.45 4.27 | 10.31 9.99 | 23.60 23.43 | 3031(CH, arom); 2930 (CH, aliph) 2209, 2229 (2CN), 669 (P═S). | 7.7–7.2 (m, 4H, arom); 4.4 (s, 2H, $SCH_2$); 3.9 (s, 3H, $CH_3$); 3.5 (s, 1H, CH); 1.9–1.4 (m, 8H, cyclic $CH_2$). |
| **7a** | 230–232 Dioxan | 61 | $C_{18}H_{21}N_2O_3PS_3$ (440.52) | 49.07 48.72 | 4.80 4.69 | 6.36 6.55 | 21.83 21.60 | 3012–2511 (broad band, OH), 1698 (C═O); 2218 (CN); 1293 (C—O); 659 (P═S). | 11.2 (br, 1H, OH); 7.7–7.1 (m, 4H, arom); 4.1 (s, 2H, $CH_2$); 3.9 (s, 3H, $CH_3$); 3.5 (s, 1H, CH); 1.95–1.40 (m, 10H, cyclic $CH_2$). |
| **7b** | 156 Ethanol | 89 | $C_{20}H_{25}N_2O_3PS_3$ (468.57) | 51.26 50.91 | 5.37 5.18 | 5.97 5.77 | 20.52 20.24 | 3011 (CH, arom); 2982,2909 (CH, aliph); 2220 (CN); 1722 (C═O); 1303 (C—O); 649 (P═S). | 7.7–7.1 (m, 4H, arom); 4.5–4.1 (q, 2H, $OCH_2$); 4.07 (s, 2H, $CH_2$); 3.9 (s, 3H, $CH_3$); 3.5 (s, 1H, CH); 1.95–1.10 (m, 13H, cyclic $CH_2 + C—CH_3$). |
| **7c** | 219 Ethanol | 78 | $C_{18}H_{22}N_3O_2PS_3$ (439.54) | 49.18 48.91 | 5.04 4.87 | 9.56 9.66 | 21.88 21.53 | 3321, 3191 ($NH_2$); 3036 (CH, arom); 2906 (CH, aliph); 2213 (CN); 1659 (C═O); 665 (P═S). | 7.7–7.2 (m, 4H, arom); 6.1 (br, 2H, $NH_2$); 4.1 (s, 2H, $CH_2$); 3.9 (s, 3H, $CH_3$); 3.5 (s, 1H, CH); 1.9–1.4 (m, 10H, cyclic $CH_2$). |
| **7d** | 235–236 Dioxan | 84 | $C_{24}H_{26}N_3O_2PS_3$ (515.63) | 55.90 55.71 | 5.08 4.81 | 8.15 7.99 | 18.65 18.31 | 3211 (NH); 3052 (CH, arom); 2975 (CH, aliph); 2209 (CN); 1651 (C═O); 659 (P═S). | 8.7 (br, 1H, NH); 7.8–7.0 (m, 9H, arom); 4.1 (s, 2H, $CH_2$); 3.9 (s, 3H, $CH_3$); 3.5 (s, 1H, CH); 1.9–1.4 (m, 10H, cyclic $CH_2$). |
| **7e** | 231–233 Ethanol | 82 | $C_{18}H_{20}N_3OPS_3$ (421.52) | 51.28 50.89 | 4.78 4.57 | 9.96 9.79 | 22.82 22.43 | 3031 (CH, arom); 2930 (CH, aliph); 2209, 2229 (2CN), 669 (P═S). | 7.7–7.2 (m, 4H, arom); 4.4 (s, 2H, $SCH_2$); 3.9 (s, 3H, $CH_3$); 3.5 (s, 1H, CH); 1.9–1.4 (m, 10H, cyclic $CH_2$). |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **8a** | 259<br>Ethanol | 68 | $C_{17}H_{19}N_2O_3PS_3$<br>(426.49) | 47.87<br>47.50 | 4.47<br>4.33 | 6.56<br>6.34 | 22.55<br>22.33 | 3436, 3298 ($NH_2$); 3019–2509 (broad band, OH); 1697 (C=O); 659 (P=S). | 11.8 (br, 1H, OH); 7.6–7.2 (m, 4H, arom); 5.1 (br, 2H, $NH_2$); 3.9 (s, 3H, $CH_3$); 2.9 (s, 1H, CH); 1.85–1.35 (m, 8H, cyclic $CH_2$). |
| **8b** | 176<br>Ethanol | 66 | $C_{19}H_{23}N_2O_3PS_3$<br>(454.55) | 50.20<br>49.91 | 5.10<br>4.93 | 6.16<br>5.94 | 21.16<br>20.93 | 3405, 3320 ($NH_2$); 3011 (CH, arom); 2972 (CH, aliph); 1721 (C=O); 649 (P=S). | 7.7–7.1 (m, 4H, arom); 4.5–4.1 (q, 2H, $OCH_2$); 5.0 (br, 2H, $NH_2$); 3.9 (s, 3H, $CH_3$); 2.9 (s, 1H, CH); 1.95–1.10 (m, 11H, cyclic $CH_2$ + C–$CH_3$). |
| **8c** | 207<br>Dioxan | 59 | $C_{17}H_{20}N_3O_2PS_3$<br>(425.54) | 47.98<br>47.55 | 4.73<br>4.51 | 9.87<br>9.49 | 22.60<br>22.47 | 3441, 3269, 3197 ($2NH_2$); 3036 (CH, arom); 1656 (C=O); 671 (P=S). | 7.7–7.2 (m, 4H, arom); 6.1 (br, 2H, $NH_2$); 5.0 (br, 2H, $NH_2$); 3.9 (s, 3H, $CH_3$); 3.0 (s, 1H, CH); 1.9–1.4 (m, 8H, cyclic $CH_2$). |
| **8d** | 303–305<br>Ethanol | 65 | $C_{23}H_{24}N_3O_2PS_3$<br>(501.63) | 55.06<br>54.66 | 4.82<br>4.61 | 8.37<br>8.29 | 19.17<br>18.96 | 3411, 3259, 3198 (NH + $NH_2$); 3032 (CH, arom); 1670 (C=O); 666 (P=S). | 10.7 (br, 1H, NH); 7.8–7.0 (m, 9H, arom); 5.1 (br, 2H, $NH_2$); 3.9 (s, 3H, $CH_3$); 2.8 (s, 1H, CH); 1.9–1.4 (m, 8H, cyclic $CH_2$). |
| **8e** | 178–179<br>Ethanol | 56 | $C_{17}H_{18}N_3OPS_3$<br>(407.49) | 50.10<br>49.77 | 4.45<br>4.30 | 10.31<br>10.03 | 23.60<br>23.41 | 3439, 3301 ($NH_2$); 3031 (CH, arom); 2930 (CH, aliph); 2220 (CN), 655 (P=S). | 7.7–7.2 (m, 4H, arom); 5.4 (br, 2H, $NH_2$); 3.9 (s, 3H, $CH_3$); 3.0 (s, 1H, CH); 1.9–1.4 (m, 8H, cyclic $CH_2$). |
| **9a** | 215–217<br>Ethanol | 54 | $C_{18}H_{21}N_2O_3PS_3$<br>(440.52) | 49.07<br>48.66 | 4.80<br>4.77 | 6.36<br>6.19 | 21.83<br>21.57 | 3404, 3318 ($NH_2$); 3031–2511(broad band, OH); 1695 (C=O); 661 (P=S). | 12.5 (br, 1H, OH); 7.6–7.2 (m, 4H, arom); 5.3 (br, 2H, $NH_2$); 3.9 (s, 3H, $CH_3$); 2.9 (s, 1H, CH); 1.85–1.35 (m, 10H, cyclic $CH_2$). |
| **9b** | 177<br>Ethanol | 73 | $C_{20}H_{25}N_2O_3PS_3$<br>(468.57) | 51.26<br>50.93 | 5.37<br>5.19 | 5.97<br>5.61 | 20.52<br>20.19 | 3411, 3332 ($NH_2$); 3051 (CH, arom); 2952 (CH, aliph); 1717 (C=O); 659 (P=S). | 7.7–7.1 (m, 4H, arom); 5.0 (br, 2H, $NH_2$); 4.5–4.1 (q, 2H, $OCH_2$); 3.9 (s, 3H, $CH_3$); 2.9 (s, 1H, CH); 1.95–1.10 (m, 13H, cyclic $CH_2$ + C–$CH_3$). |

*(Continued on next page)*

**TABLE I** Analytical and Spectral Data of the New Compounds *(Continued)*

| Comp. no. | M.P.[a] °C cryst. solvent | Yield % | $M_F(M_w)$ | Analytical data[b] calc./found % C | H | N | S | (KBr)[c] $\nu(cm^{-1})$ | $^1$H-NMR (DMSO-$d_6$)[d] ($\delta$ ppm) |
|---|---|---|---|---|---|---|---|---|---|
| **9c** | 248–249 Ethanol | 67 | $C_{18}H_{22}N_3O_2PS_3$ (439.54) | 49.18 48.83 | 5.04 4.89 | 9.56 9.32 | 21.88 21.60 | 3441, 3350, 3211 ($2NH_2$); 3036 (CH, arom); 1665 (C=O); 656 (P=S). | 7.7–7.2 (m, 4H, arom); 5.9 (br, 2H, $NH_2$); 5.0 (br, 2H, $NH_2$); 3.9 (s, 3H, $CH_3$); 3.0 (s, 1H, CH); 1.9–1.4 (m, 10H, cyclic $CH_2$). |
| **9d** | 271–273[e] Dioxan | 58 | $C_{24}H_{26}N_3O_2PS_3$ (515.63) | 55.90 55.61 | 5.08 4.89 | 8.15 7.93 | 18.65 18.55 | 3411, 3299,3198 ($NH+NH_2$); 3032 (CH, arom); 1673 (C=O); 663 (P=S). | 11.0 (br, 1H, NH); 7.8–7.0 (m, 9H, arom); 5.1 (br, 2H, $NH_2$); 3.9 (s, 3H, $CH_3$); 2.8 (s, 1H, CH); 1.9–1.4 (m, 10H, cyclic $CH_2$). |
| **9e** | 196–198 Ethanol | 55 | $C_{18}H_{20}N_3OPS_3$ (421.52) | 51.28 50.90 | 4.78 4.57 | 9.96 9.81 | 22.82 22.49 | 3419, 3301 ($NH_2$); 3056 (CH, arom); 2930 (CH, aliph); 2217 (CN), 660 (P=S). | 7.7–7.2 (m, 4H, arom); 5.6 (br, 2H, $NH_2$); 3.9 (s, 3H, $CH_3$); 3.0 (s, 1H, CH); 1.9–1.4 (m, 10H, cyclic $CH_2$). |
| **10a** | 234–236 Ethanol | 58 | $C_{24}H_{24}N_2O_4P_2S_4$ (594.64) | 48.47 47.99 | 4.07 4.00 | 4.71 4.49 | 21.56 21.39 | 3249 (NH); 3055 (CH, arom); 1739 (C=O); 1236 (P–O–C); 659, 672 (2 P=S). | 9.8 (br, 1H, NH) ; 7.7–7.1 (m, 8H, arom); 3.9 (s, 6H, $2CH_3$); 2.9 (s, 1H, CH); 1.8–1.4 (m, 8H, cyclic $CH_2$). |
| **10b** | 267–268 Methanol | 63 | $C_{24}H_{24}N_2O_2P_2S_6$ (626.77) | 45.98 45.59 | 3.86 3.66 | 4.47 4.30 | 30.69 30.39 | 3266 (NH); 3085 (CH, arom); 1156 (C=S); 639, 969 (2P=S). | 10.3 (br, 1H, NH); 7.7–7.1 (m, 8H, arom); 3.9 (s, 6H, $2CH_3$); 2.9 (s, 1H, CH); 1.8–1.4 (m, 8H, cyclic $CH_2$). |
| **10c** | 215–216 $CH_3CN$ | 70 | $C_{24}H_{25}N_3O_2P_2S_5$ (609.72) | 47.27 46.95 | 4.13 4.00 | 6.89 6.83 | 26.29 25.98 | 3312, 3134 (2 NH); 3077 (CH, arom); 1170 (C=S); 644, 669 (2 P=S). | 10.3 (br, 1H, NH); 9.7 (br, 1H, NH); 7.7–7.1 (m, 8H, arom); 3.9 (s, 6H, $2CH_3$); 2.9 (s, 1H, CH); 1.8–1.4 (m, 8H, cyclic $CH_2$). |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **10d** | 305–307<br>DMF | 78 | $C_{30}H_{29}N_3O_2P_2S_5$<br>(685.81) | 52.53<br>52.14 | 4.26<br>4.07 | 6.12<br>5.93 | 23.37<br>23.11 | 3340 (NH); 3057 (CH, arom); 1170 (C═S); 639, 659 (2 P═S). | 10.3 (br, 1H, NH); 7.7–7.0 (m, 13H, arom); 3.9 (s, 6H, $2CH_3$); 2.9 (s, 1H, CH); 1.8–1.4 (m, 8H, cyclic $CH_2$). |
| **11a** | 233–234<br>Ethanol | 53 | $C_{25}H_{26}N_2O_4P_2S_4$<br>(608.67) | 49.33<br>88.90 | 4.30<br>4.14 | 4.60<br>4.38 | 21.07<br>20.81 | 3199 (NH); 3055 (CH, arom); 1728 (C═O); 1233 (P—O—C); 644, 662 (2 P═S). | 9.6 (br, 1H, NH); 7.7–7.1 (m, 8H, arom); 3.9 (s, 6H, $2CH_3$); 3.0 (s, 1H, CH); 1.8–1.4 (m, 10H, cyclic $CH_2$). |
| **11b** | 293–295<br>Ethanol | 78 | $C_{25}H_{26}N_2O_2P_2S_6$<br>(640.79) | 46.85<br>46.52 | 4.09<br>3.85 | 4.37<br>4.09 | 30.02<br>29.78 | 3216 (NH); 3075 (CH, arom); 1156 (C═S); 648, 967 (2P═S). | 10.9 (br, 1H, NH) ; 7.7–7.1 (m, 8H, arom); 3.9 (s, 6H, $2CH_3$); 2.9 (s, 1H, CH); 1.8–1.4 (m, 10H, cyclic $CH_2$). |
| **11c** | 230<br>Methanol | 76 | $C_{25}H_{27}N_3O_2P_2S_5$<br>(623.75) | 48.13<br>47.79 | 4.36<br>4.15 | 6.73<br>6.66 | 25.70<br>25.47 | 3229, 3189 (2 NH); 3077 (CH, arom); 1167 (C═S); 646, 671 (2 P═S). | 11.2 (br, 1H, NH); 9.6 (br, 1H, NH); 7.7–7.1 (m, 8H, arom); 3.9 (s, 6H, $2CH_3$); 2.9 (s, 1H, CH); 1.8–1.4 (m, 10H, cyclic $CH_2$). |
| **11d** | 321–323<br>Dioxan | 69 | $C_{31}H_{31}N_3O_2P_2S_5$<br>(699.84) | 53.20<br>52.86 | 4.46<br>4.19 | 6.00<br>5.74 | 22.90<br>22.69 | 3311 (NH); 3057 (CH, arom); 1170 (C═S); 640, 662 (2 P═S). | 10.3 (br, 1H, NH); 7.7–7.0 (m, 13H, arom); 3.9 (s, 6H, $2CH_3$); 2.9 (s, 1H, CH); 1.8–1.4 (m, 10H, cyclic $CH_2$). |
| **12** | 149<br>Ethanol | 66 | $C_{21}H_{25}N_2O_3PS_5$<br>(544.71) | 46.30<br>45.90 | 4.62<br>4.44 | 5.14<br>5.01 | 29.43<br>29.14 | 3204 (NH); 3057 (CH, arom); 1723 (C═O), 1123 (C═S); 639 ( P═S). | 10.3 (br, 1H, NH); 7.7–7.1 (m, 4H, arom); 4.4–4.0 (q, 2H, $OCH_2$); 3.9 (s, 3H, $OCH_3$); 3.1 (s, 3H, $SCH_3$); 2.9 (s, 1H, CH); 1.8–1.2 (m, 11H, cyclic $CH_2 + CH_3$). |
| **13** | 156<br>Ethanol | 63 | $C_{22}H_{27}N_2O_3PS_5$<br>(558.74) | 47.29<br>46.83 | 4.87<br>4.59 | 5.01<br>4.82 | 28.96<br>28.66 | 3233 (NH); 3033 (CH, arom); 1721 (C═O), 1112 (C═S); 643 (P═S). | 11.6 (br, 1H, NH); 7.7–7.1 (m, 4H, arom); 4.4–4.0 (q, 2H, $OCH_2$); 3.9 (s, 3H, $OCH_3$); 3.1 (s, 3H, $SCH_3$); 2.9 (s, 1H, CH); 1.8–1.2 (m, 13H, cyclic $CH_2 + CH_3$). |

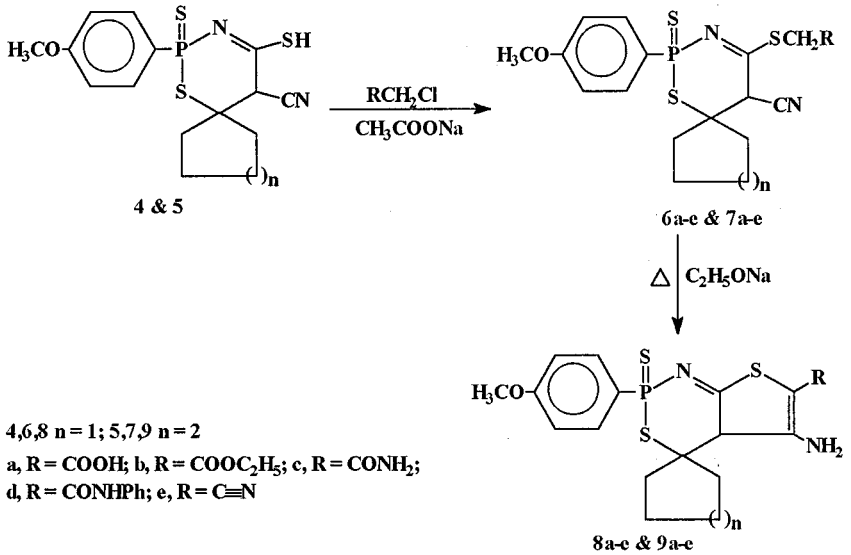


*(Continued on next page)*

**TABLE I** Analytical and Spectral Data of the New Compounds *(Continued)*

| Comp. no. | M.P.[a] °C cryst. solvent | Yield % | $M_F(M_w)$ | Analytical data[b] calc./found % C | H | N | S | (KBr)[c] $\nu(cm^{-1})$ | $^1$H-NMR (DMSO-$d_6$)[d] ($\delta$ ppm) |
|---|---|---|---|---|---|---|---|---|---|
| **14** | 193–195 Ethanol | 66 | $C_{18}H_{19}N_4O_2PS_4$ (482.58) | 44.79 44.37 | 3.97 3.77 | 11.61 11.40 | 26.57 26.27 | 3336, 3235, 3187 ($NH_2$, NH); 3033 (CH, arom);1679 (C=O), 1112 (C=S); 643 (P=S). | 10.3 (br, 1H, NH); 7.7–7.1 (m, 4H, arom); 5.0–4.7 (br, 2H, $NH_2$); 3.9 (s, 3H, $OCH_3$); 2.9 (s, 1H, CH); 1.8–1.4 (m, 8H, cyclic $CH_2$). |
| **15** | 211 Ethanol | 69 | $C_{19}H_{21}N_4O_2PS_4$ (496.61) | 45.95 45.53 | 4.26 4.09 | 11.28 11.03 | 25.82 25.52 | 3367, 3277, 3187 ($NH_2$, NH); 3050 (CH, arom); 1681 (C=O), 1132 (C=S); 649 (P=S). | 10.9 (br, 1H, NH); 7.7–7.1 (m, 4H, arom); 5.0–4.7 (br, 2H, $NH_2$); 3.9 (s, 3H, $OCH_3$); 2.9 (s, 1H, CH); 1.8–1.3 (m, 10H, cyclic $CH_2$). |
| **16a** | 243 Ethanol | 49 | $C_{25}H_{24}N_4O_3P_2S_5$ (650.73) | 46.14 45.72 | 3.71 3.56 | 8.61 8.40 | 24.63 24.47 | 3350 (NH); 3087 (CH, arom); 1693 (C=O); 623, 659 (2 P=S). | 10.9 (br, 1H, NH); 7.7–7.1 (m, 8H, arom); 3.9 (s, 6H, 2 $OCH_3$); 2.9 (s, 1H, CH); 1.8–1.3 (m, 8H, cyclic $CH_2$). |
| **16b** | 266–268 Dioxan | 33 | $C_{25}H_{24}N_4O_2P_2S_6$ (666.79) | 45.03 44.70 | 3.62 3.57 | 8.40 8.19 | 28.85 28.61 | 3323 (NH); 3069 (CH, arom); 1113 (C=S); 631, 659 (2 P=S). | 10.9 (br, 1H, NH); 7.7–7.1 (m, 8H, arom); 3.9 (s, 6H, 2 $OCH_3$); 2.9 (s, 1H, CH); 1.8–1.3 (m, 8H, cyclic $CH_2$). |
| **17a** | 239 Ethanol | 53 | $C_{26}H_{26}N_4O_3P_2S_5$ (664.75) | 46.97 46.59 | 3.94 3.84 | 8.42 8.31 | 24.11 23.94 | 3263 (NH); 3066 (CH, arom); 1687 (C=O); 641, 669 (2 P=S). | 11.7 (br, 1H, NH); 7.7–7.1 (m, 8H, arom); 3.9 (s, 6H, 2 $OCH_3$); 2.9 (s, 1H, CH); 1.8-1.2 (m, 10H, cyclic $CH_2$). |
| **17b** | 311 Dioxan | 31 | $C_{26}H_{26}N_4O_2P_2S_6$ (680.81) | 45.86 45.41 | 3.85 3.66 | 8.23 8.09 | 28.25 27.96 | 3239 (NH); 3043 (CH, arom); 1151 (C=S); 622, 656 (2 P=S) | 11.3 (br, 1H, NH); 7.7–7.1 (m, 8H, arom); 3.9 (s, 6H, $CH_3$); 2.9 (s, 1H, CH); 1.8-1.2 (m, 10H, cyclic $CH_2$). |

[a]Uncorrected.
[b]Satisfactory microanalyses obtained: C, ±0.4%, H ± 0.2%, N ± 0.3%, S ± 0.2%.
[c]Measured on a Nicolet 710 FT-IR spectrophotometer.
[d]Measured on a Varian 360 A spectrometer using TMS as internal standard.



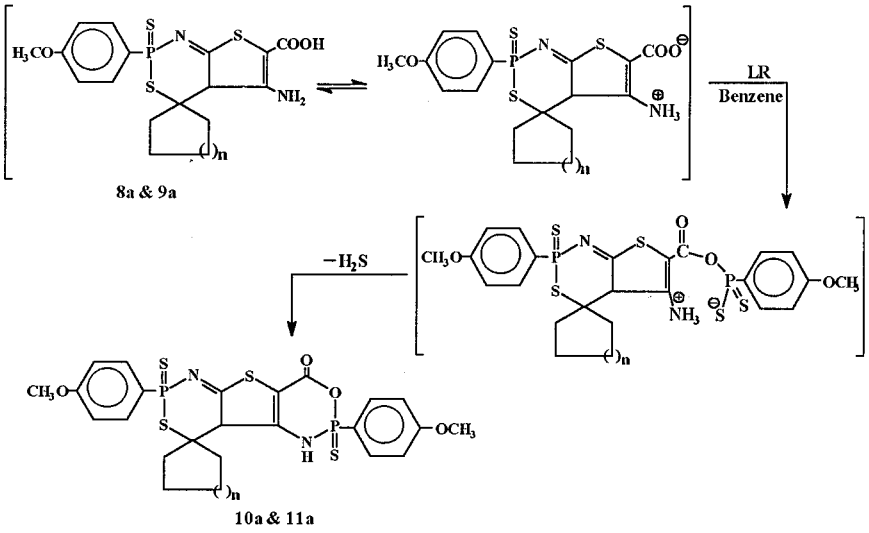

**SCHEME 2**

corresponding to the amino groups while exhibiting characteristic bands corresponding to P=S at 657 and 644 $cm^{-1}$ respectively. The $^1$H-NMR (DMSO) spectra of compounds **4** and **5** showed the absence of a signal corresponding to $NH_2$ groups while exhibiting new signals corresponding to four aromatic protons at $\delta$ 7.7–7.1, four aliphatic protons at $\delta$3.9 ($OCH_3$, s) and 3.5 (CH, s).

Reaction of compounds **4** and **5** with different $\alpha$-halo compounds, namely chloroacetic acid, ethyl chloroacetate, chloroacetamide, chloroacetanilide, and chloroacetonitrile in the presence of anhydrous sodium acetate led to the formation of the corresponding thioethers **6a–e** and **7a–e** respectively. On refluxing compounds **6a–e** and **7a–e** with sodium ethoxide in absolute ethanol gave the thienothiazaphosphixine derivatives **8a–e** and **9a–e** respectively (Scheme 2).

IR spectra of compounds **6a–e** and **7a–e** exhibited the absorption bands corresponding to CN (2209–2229 $cm^{-1}$) while the IR spectra of compounds **8a–d** and **9a–d** showed the absence of the absorption bands corresponding to CN groups and appearance of new bands corresponding to $NH_2$ groups (3197–3441 $cm^{-1}$). The $^1$H-NMR spectra of compounds **6a–e**–**9a–e** are in agreement with the proposed structures (cf. Table I).

Compounds **8a** and **9a** react with LR in anhydrous benzene at 80°C to give 3,1,2-oxazaphosphixin-4-one derivatives **10a** and **11a** respectively. The formation of **10a** and **11a** is believed to occur via a




**SCHEME 3**

nucleophilic attack of the carboxylate of the betaine on LR to give a new betaine followed by ring closure through elimination of an $H_2S$ molecule[13] (Scheme 3).

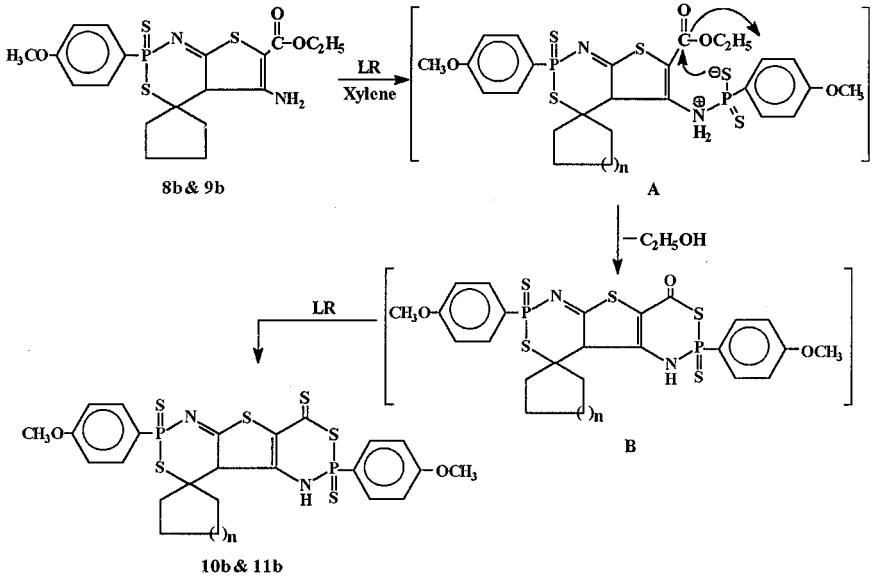
The structures of products **10a** and **11a** were determined by elemental analysis, IR and $^1$H-NMR spectra (cf. Table I).

On the other hand, the reaction of compounds **8b** and **9b** with LR at elevated temperature (140°C) produced 3,1,2-thiazaphosphixine-4-thione derivatives **10b** and **11b** in moderate yield. As to the mechanism for the formation of the P-heterocycles (**10b** and **11b)**, it is suggested that a nucleophilic attack on LR gives A, followed by ring closure and elimination of ethanol molecule to give B, subsequent thiation produce **10b** and **11b** (Scheme 4).

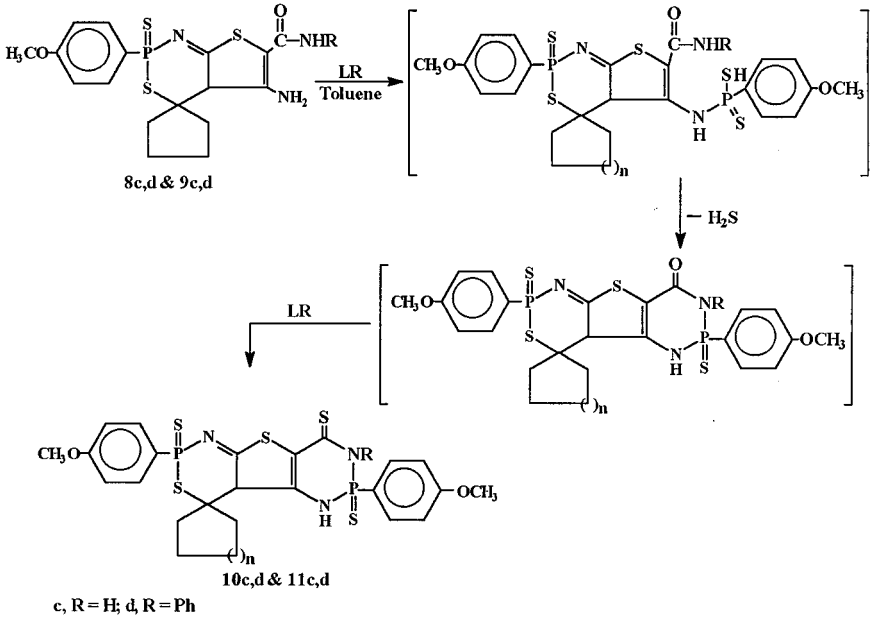
1,3,2-Diazaphosphixine-4-thione-2-sulfide derivatives **10c**,**d** and **11c**,**d** were formed by reacting compounds **8c**,**d** and **9c**,**d** with LR in refluxing toluene. The mechanism for the formation of compounds **10c**,**d** and **11c**,**d** is suggested as follows (Scheme 5).

The reaction of compounds **8e** and **9e** with LR in toluene at 110°C yielded compounds which are identical in all respects with authentic samples of compounds **10c** and **11c** respectively. It was suggested that nucleophilic attack of the amino group on the phosphorus of LR, followed by P-SH addition to the nitrile group and subsequent rearrangement,[22] yielded compounds **10c** and **11c** (Scheme 6, Table I).

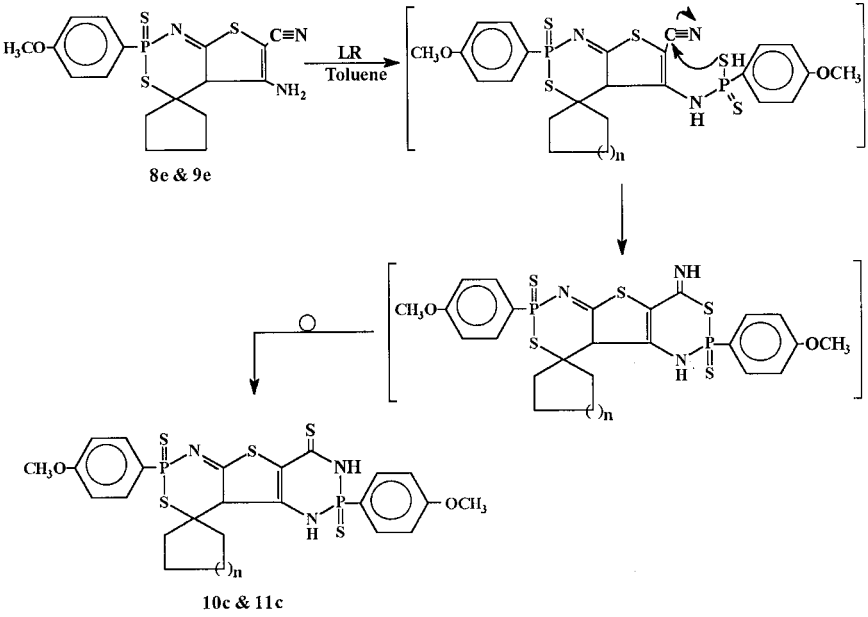
Treatment of compounds **8b** or **9b** with NaOH, $CS_2$ and $(CH_3)_2SO_4$ afforded the corresponding dithiocarbamate methyl ester derivatives




**SCHEME 4**




**SCHEME 5**




**SCHEME 6**

**12** and **13**, respectively, which on treating with hydrazine hydrate yielded compounds **14** and **15** respectively (Scheme 7). Compounds **14** and **15** were allowed to react with Lawesson's reagent (LR) in refluxing toluene to afford compounds **16a**,**b** and **17a**,**b** respectively. As to the concerted mechanism[23] for the formation of compounds **16a**,**b** and **17a**,**b**, it is suggested that a nucleophilic attack by $NH_2$ group on LR gives the transient intermediate which underwent intramolecular cyclization via elimination of $H_2S$ molecule to give **16a** and **17a**. Subsequent thiation of compounds **16a** and **17a** produced compounds **16b** and **17b**, respectively (Scheme 7).

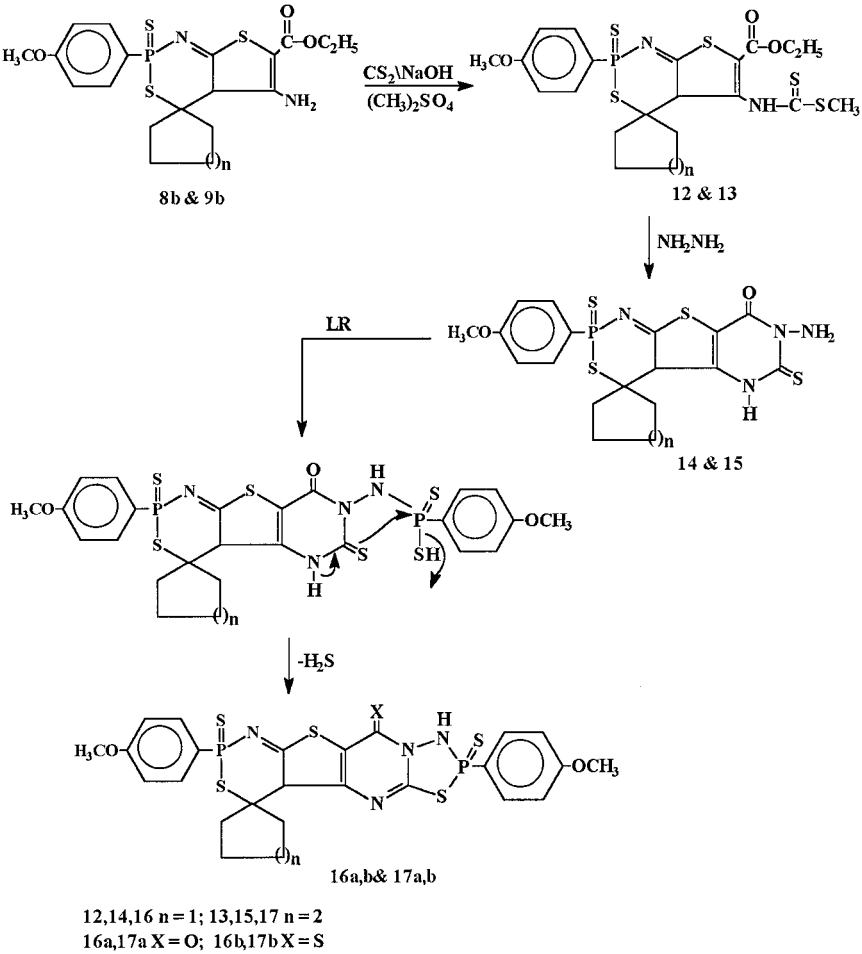
The structures of compounds **12–17** were determined by elemental analysis, IR and $^1$H-NMR spectra (cf. Table I).

## EXPERIMENTAL

### Synthesis of Compounds 4 and 5

#### *General Procedure*

A mixture of 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disulfide LR (0.005 mmol) and compound **2** or **3** (0.01 mmol) in dry acetonitrile (70 ml) was refluxed until no more of the reactants could




**SCHEME 7**

be detected (TLC) (≈7 h). The reaction mixture was concentrated and cooled. The resultant precipitate was collected by filtration and recrystallized from the suitable solvent to give compounds **4** and **5** respectively (cf. Table I).

## Synthesis of Compounds 6a–e and 7a–e

### *General Procedure*

A mixture of compound **4** and/or **5** (0.01 mmol), anhydrous sodium acetate (0.01 mmol), and a proper chloro compound (0.01 mmol) in ethanol

(70 ml) was refluxed for 2 h. The reaction mixture was filtered while hot, concentrated, and cooled. The resultant precipitate was collected by filtration and the filter cake was washed with water. The crude product was purified by recrystallization from an appropriate solvent to give compounds **6a–e** and **7a–e** respectively (cf. Table I).

## Synthesis of Compounds 8a–e and 9a–e

### *General Procedure*

The sulfide (**6a–e** and/or **7a–e**) (0.01 mmol) was refluxed in absolute ethanol (60 ml) in the presence of sodium ethoxide (0.23 g of Na in 5 ml ethanol) for 5 h. The mixture was concentrated and cooled. The resultant precipitate was collected by filtration and the filter cake was washed with water. The crude product was purified by recrystallization from an appropriate solvent to give compounds **8a–e** and **8a–e** respectively (cf. Table I).



## Synthesis of Compounds 10a and 11a

### *General Procedure*

A mixture of compound **8a** or **9a** (0.005 mmol) and LR (0.005 mmol) in dry benzene (70 ml) was refluxed for 10 h. The reaction mixture was concentrated and cooled. The resultant precipitate was collected by filtration. The crude product was purified by recrystallization from the suitable solvent to give compounds **10a** and **11a** respectively (cf. Table I).

## Synthesis of Compounds 10b and 11b

### *General Procedure*

A mixture of compound **8b** or **9b** (0.005 mmol) and LR (0.005 mmol) in dry xylene (40 ml) was refluxed for 24 h. The solvent was evaporated to dryness under reduced pressure, and the residue was triturated with methanol. The separated solid was collected by filtration. The crude product was purified by recrystallization from an appropriate solvent to give **10b** and **11b** respectively (cf. Table I).

## Synthesis of Compounds 10c,d and 11c,d

### *General Procedure*

A mixture of compound **8c–e** or **9c–e** (0.005 mmol) and LR (0.005 mmol) in dry toluene (60 ml) was refluxed for 12 h. The solvent was evaporated to dryness under reduced pressure, and the residue was triturated with methanol. The separated solid was collected by filtration. The crude product was purified by recrystallization from the

suitable solvent to give **10c**,**d** and **11c**,**d** respectively. Compounds **8e** and **9e** yielded compounds which are identical in all respects with authentic samples of compounds **10c** and **11c** respectively (cf. Table I).

## Synthesis of Compounds 12 and 13

### *General Procedure*

To a vigorously stirred solution of compound **8b** or **9b** (0.01 mmol) in DMSO (10 ml) at room temperature was added $CS_2$ (0.013 mmol) and aq. solution of NaOH (0.013 mmol). After stirring for 30 min at room temperature, the reaction mixture was cooled in ice-bath (5–10°C) and dimethyl sulfate (0.013 mmol) was added with stirring. The stirring was continued for additional 3 h; then the reaction mixture was poured into ice-water mixture (500 ml). The separated solid was collected by filtration and dried. The crude product was purified by recrystallization from an appropriate solvent to give compounds **12** and **13** respectively (cf. Table I).



## Synthesis of Compounds 14 and 15

### *General Procedure*

To a stirred solution of compound **12** or **13** (0.005 mmol) in ethanol (30 ml) hydrazine hydrate (0.0052 mmol) was added dropwise. After the addition, the reaction mixture was refluxed for 3 h. On cooling, the solid that separated out was collected by filtration and the filter cake was washed with water. The crude product was purified by recrystallization from an appropriate solvent to give compounds **14** and **15** respectively (cf. Table I).

## Synthesis of Compounds 16a,b and 17a,b

### *General Procedure*

A mixture of compound **14** or **15** (0.005 mmol), LR (0.005 mmol), and dry toluene (60 ml) was refluxed for 12 h. The reaction mixture was filtered while hot. The resultant precipitate was collected by filtration and crystallized from ethanol, where compounds **16a** and **17a** were obtained. The filtrate was concentrated and the separated solid was collected by filtration. The crude product was purified by recrystallization from dioxan to give compounds **16b** and **17b** respectively.

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