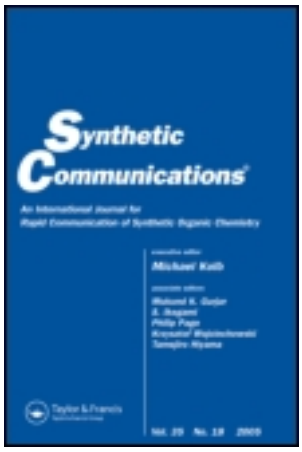

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# SYNTHETIC STUDIES ON THE SYNTHESIS OF PYRIDINE, α-PYRAN, α-THIOPYRAN, AND THIENOTHIOPYRANOPYRROL DERIVATIVES USING PTC TECHNIQUE

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SYNTHETIC COMMUNICATIONS, 31(4), 475–486 (2001)



# SYNTHETIC STUDIES ON THE SYNTHESIS OF PYRIDINE, $\alpha$-PYRAN, $\alpha$-THIOPYRAN, AND THIENOTHIOPYRANOPYRROL DERIVATIVES USING PTC TECHNIQUE

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## ABSTRACT

The reaction of *p*-chlorophenylmethylenemalononitrile **1** with some reactive halo compounds under phase-transfer catalysis conditions (PTC) afforded the corresponding alkylated or cyclized products **2–9** Thienothiopyranopyrrol $\mathbf{12_{a-c}}$ were synthesized from the reaction of compound **1** or **4** with $CS_2$ and ethyl chloroacetate in 1:1:2 molar ratio via the formation of the intermediates thiopyrans $\mathbf{10_{a-c}}$ and theinothiopyrans $\mathbf{11_{a-c}}$. Also, compound **1** or **4** reacted with phenylisocyanate or phenylisothiocyanate to give $\alpha$-pyran, $\alpha$-thiopyran pyridinone, and pyridine-2-thione derivatives **13–16**, respectively. The sequence of the reactions was studied.

In connection with our research program on the synthesis of pyridinone, pyridines, triazines (1), and thiopyrans (2) starting with arylmethylenemalononitriles, we report here the synthesis of some $\alpha$-pyran, cyclopentadienone,

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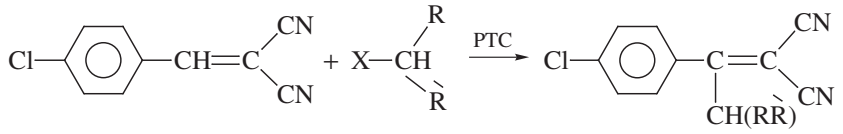
pyridinethione, thienothiopyran, thienothiopyranopyrrol, and pyridinone derivatives through consecutive reactions of *p*-chlorophenylmethylenemalononitrile with some reactive halo compounds followed by reacting the yielded intermediates with $CS_2$, PhNCO, or PhNCS.

The reaction of *p*-chlorophenylmethylenemalononitrile **1** with chloroacetonitrile (1) benzyl chloride, or bromomalononitrile under PTC conditions [dioxan/ $K_2CO_3$/tetrabutylammonium bromide (TBAB)], afforded the corresponding polyfunctional compounds $\mathbf{2_{a-c}}$, respectively. The IR and $^1$H-NMR spectra are consistent with their structures (cf. Scheme 1, Table I). MS of compound $\mathbf{2_a}$ showed the molecular ion peak at **m/e** 278.




**1** X = Cl, Br **$2_{a-c}$**

| Comp. No | R | R` |
|---|---|---|
| $\mathbf{2_a}$ | CN | H |
| $\mathbf{2_b}$ | Ph | H |
| $\mathbf{2_c}$ | CN | CN |

***Equation 1.***

The study was extended to the reaction of ylidenenitrile **1** or **3** with chloroacetaldehyde or phenacyl bromide under PTC conditions (DMF/ $K_2CO_3$/ tetrabutylammonium bromide TBAB) at 120 °C for 3 h to afford the corresponding $\alpha$-pyran derivatives $\mathbf{6_{a-c}}$ in a one-pot procedure. The control of time, temperature, and using different solvents gave the chance to follow up the sequence of the reaction. Thus, by the reaction of compound **1** or **3** with the same reactants under the PTC conditions [dioxan/$K_2CO_3$/ tetrabutylammonium bromide (TBAB)] at 60°–70 °C for 3–5 h, the corresponding alkylated derivatives $\mathbf{4_{a-c}}$ were separated. The IR spectra showed absorption bands at 1709 $cm^{-1}$ and1715 $cm^{-1}$ indicative of CHO and $CO_{ketone}$ groups. $^1$H-NMR spectra showed singlet signals at 9.5, 3.4, and 2.9 ppm for CHO, $\underline{CH_2}CHO$, and $\underline{CH_2}CO$ groups, respectively. MS ofcompound $\mathbf{4_a}$ showed the molecular ion peak at **m/e** 229. However, when the reaction was carried out at higher temperature 100 °–110 °C for a period of





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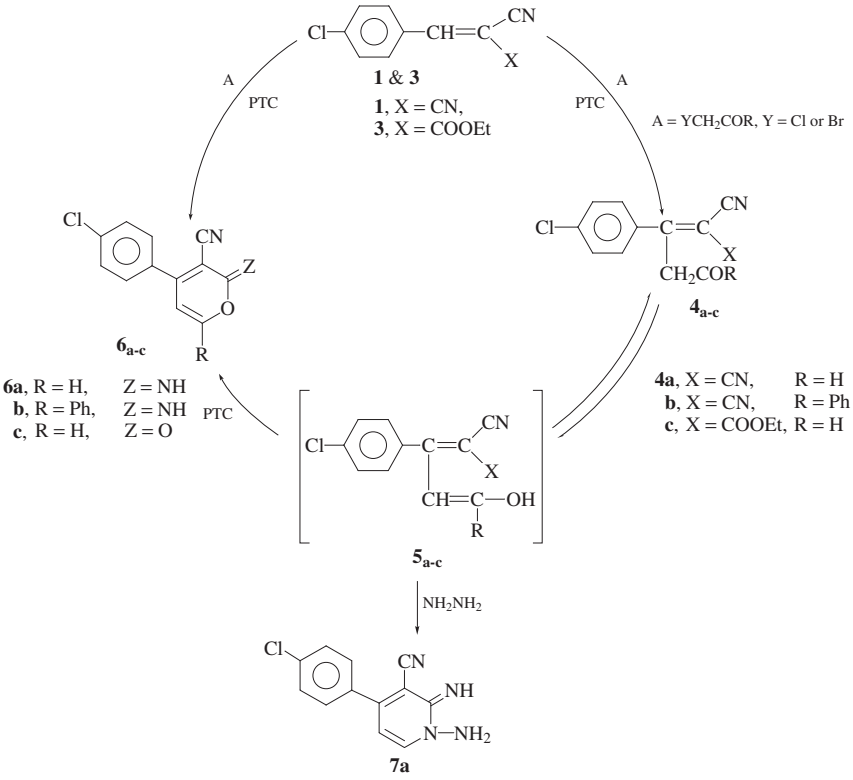


***Scheme 1.***

time 10–13 h using the same last conditions, the corresponding $\alpha$-pyran derivatives $\mathbf{6_{a-c}}$ were obtained. The cyclization step proceeded through formation of the enol form, which either added at the cyano group to form the imino derivatives $\mathbf{6_{a,b}}$ or attacked the carbonyl ester group with elimination of ethanol molecule to give $\mathbf{6_c}$. We were able to separate the intermediate enol form $\mathbf{5_a}$ [R = H, Y = CN] from the reaction of compound **1** with chloroacetaldehyde under PTC conditions [benzene/$K_2CO_3$/tetrabutylammonium bromide (TBAB)], which in turn cyclized to compound $\mathbf{6_a}$ in [dioxan/$K_2CO_3$/tetrabutylammonium bromide (TBAB)]. The IR spectrum of compound $\mathbf{5_a}$ showed an absorption band at 3390 $cm^{-1}$ indicative of −OH group. $^1$H-NMR spectra showed a broad peak at 6.00–5.80 ppm for CH═CH and singlet peak at 2.3 ppm for OH group. Also, compound $\mathbf{5_a}$ reacted with hydrazine hydrate in ethanol to afford the corresponding pyridine derivative $\mathbf{7_a}$ (Scheme 1, Table I).





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***Table I.*** Analytical and Spectral Data of the Prepared Compounds

| Prod. No. | React. Time (h) React. Temp. °C React. Solvent | M.P.[a] (Cryst. Solv.) | Yield % | Mol. Form. (Mol. wt.) | Analytical Data[b] Cal./(Found) C | H | N | S |
|---|---|---|---|---|---|---|---|---|
| **2b** | 5/70 (dioxan) | 230 (benzene) | 65 | $C_{17}H_{11}ClN_2$ (278.74) | 73.33 (73.02) | 3.97 (3.76) | 10.05 (10.29) | |
| **2c** | 6/65 (dioxan) | 300–302 (ethanol) | 50 | $C_{13}H_5ClN_4$ (252.66) | 61.80 (61.95) | 1.99 (1.76) | 22.17 (22.09) | |
| **4a** | 3/65 (benzene) | 271–273 (ethanol) | 75 | $C_{12}H_7ClN_2O$ (230.65) | 62.49 (62.74) | 3.06 (3.23) | 12.15 (12.39) | |
| **4b** | 4/65 (dioxan) | 218–220 (ethanol) | 52 | $C_{18}H_{11}ClN_2O$ (306.75) | 70.48 (70.60) | 3.61 (3.43) | 9.13 (9.48) | |
| **4c** | 4.5/60 (dioxan) | 210 (benzene) | 45 | $C_{14}H_{11}ClN_2O_2$ (274.71) | 61.21 (61.00) | 4.04 (4.23) | 10.20 (10.27) | |
| **6a** | 2.5/100 (DMF) | 311–313 (ethanol) | 65 | $C_{12}H_7ClN_2O$ (230.64) | 62.49 (62.64) | 3.06 (3.23) | 12.15 (12.39) | |
| **6b** | 4/110 (DMF) | 238–240 (ethanol) | 62 | $C_{18}H_{11}ClN_2O$ (306.75) | 70.48 (70.70) | 3.61 (3.83) | 9.13 (9.28) | |
| **6c** | 4/110 (DMF) | 288 (dioxan) | 60 | $C_{12}H_6NClO_2$ (231.64) | 62.22 (62.50) | 2.61 (2.41) | 6.05 (6.30) | |
| **5a** | 6/65 (benzene) | 192–194 (ethanol) | 77 | $C_{12}H_7ClN_2O$ (230.65) | 62.49 (62.20) | 3.06 (3.23) | 12.15 (12.42) | |
| **7a** | 2/79 (ethanol) | 302–304 (dioxan) | 87 | $C_{13}H_9ClN_2$ (228.68) | 86.28 (86.50) | 3.97 (3.73) | 12.57 (12.32) | |
| **8** | 3/80 (benzene) | 305 (benzene) | 90 | $C_{20}H_{10}ClN_3O_3$ (375.77) | 63.93 (63.61) | 2.68 (2.59) | 11.18 (11.42) | |
| **9** | 6.5/80 (benzene) | 140 (ethanol) | 70 | $C_{20}H_{10}ClN_3O_3$ (375.75) | 63.92 (63.60) | 2.68 (2.43) | 11.18 (11.38) | |
| **10a** | 3/50 (dioxan) | 265 (ethanol) | 65 | $C_{13}H_6ClN_3S_2$ (303.79) | 51.38 (51.10) | 1.99 (1.70) | 13.83 (13.67) | 21.11 (21.35) |
| **10b** | 4.5/75 (dioxan) | 320 (ethanol) | 60 | $C_{13}H_7ClN_2OS_2$ (306.79) | 50.90 (50.60) | 2.30 (2.25) | 9.13 (9.27) | 20.90 (20.68) |
| **10c** | 3/75 (dioxan) | 162 (ethanol) | 55 | $C_{19}H_{11}ClN_2OS_2$ (382.89) | 59.60 (59.90) | 2.90 (2.61) | 7.32 (7.50) | 16.75 (16.56) |
| **11a** | 4/75 (dioxan) | 271 (ethanol) | 35 | $C_{17}H_{12}ClN_3O_2S_2$ (389.88) | 52.37 (52.19) | 3.11 (3.35) | 10.78 (10.75) | 16.45 (16.75) |
| **11b** | 4/75 (dioxan) | 219 (ethanol) | 68 | $C_{17}H_{11}ClN_2O_2S$ (342.81) | 59.56 (59.79) | 3.23 (3.50) | 8.17 (8.37) | 9.35 (9.60) |
| **11c** | 5.5/77 (dioxan) | 295 (dioxan) | 75 | $C_{23}H_{15}ClN_2O_2S_2$ (450.97) | 61.26 (61.56) | 3.35 (3.51) | 6.21 (6.40) | 14.22 (14.54) |
| **12a** | 6/75 (dioxan) | 297 (ethanol) | 45 | $C_{21}H_{18}ClN_3O_4S_2$ (475.98) | 52.99 (52.72) | 3.81 (3.60) | 8.83 (8.65) | 13.47 (13.21) |
| **12b** | 6/75 (dioxan) | 315 (dioxan) | 80 | $C_{21}H_{17}ClN_2O_4S_2$ (460.96) | 54.72 (54.51) | 3.72 (3.90) | 6.07 (6.31) | 13.91 (13.77) |
| **12c** | 5/75 (dioxan) | 221 (benzene) | 85 | $C_{27}H_{21}ClN_2O_4S_2$ (537.10) | 60.38 (60.55) | 4.96 (4.83) | 5.21 (5.46) | 11.94 (11.70) |
| **13a** | 5/35 (acetonitrile) | 341 (benzene) | 75 | $C_{19}H_{11}ClN_4O$ (346.77) | 65.79 (65.91) | 3.19 (3.30) | 16.15 (16.45) | |





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***Table I.*** Continued

| Prod. No. | React. Time (h) React. Temp. °C React. Solvent | M.P.[a] (Cryst. Solv.) | Yield % | Mol. Form. (Mol. wt.) | Analytical Data[b] Cal./(Found) C | H | N | S |
|---|---|---|---|---|---|---|---|---|
| **13b** | 3/35 (acetonitrile) | 265 (dioxan) | 71 | $C_{24}H_{16}ClN_3O$ (397.86) | 72.44 (72.16) | 4.05 (4.30) | 16.56 (16.31) | |
| **13c** | 4/35 (acetonitrile) | 305 (ethanol) | 75 | $C_{25}H_{16}ClN_3O_2$ (425.86) | 70.49 (70.10) | 3.79 (3.53) | 9.87 (10.00) | |
| **14a** | 5/35 (acetonitrile) | >350 (ethanol) | 35 | $C_{19}H_{11}ClN_4S$ (362.84) | 62.88 (63.00) | 3.05 (2.90) | 15.44 (15.61) | 8.83 (9.00) |
| **14b** | 10/40 (acetonitrile) | 310 (ethanol) | 40 | $C_{24}H_{16}ClN_3S$ (413.93) | 70.20 (70.00) | 3.89 (4.60) | 10.15 (10.40) | 7.74 (7.55) |
| **14c** | 4/40 (acetonitrile) | >350 (ethanol) | 40 | $C_{25}H_{16}ClN_3OS$ (441.94) | 67.93 (67.73) | 3.64 (3.84) | 9.50 (9.30) | 7.25 (7.01) |
| **15a** | 2/38 (acetonitrile) | 138 (benzene) | 75 | $C_{19}H_{11}ClN_4O$ (346.77) | 65.79 (65.51) | 3.19 (3.30) | 16.15 (16.45) | |
| **15b** | 2/40 (acetonitrile) | 195 (ethanol) | 75 | $C_{24}H_{16}ClN_3O$ (397.86) | 72.44 (72.66) | 4.05 (4.30) | 16.56 (16.31) | |
| **15c** | 2/40 (acetonitrile) | 188 (dioxan) | 80 | $C_{25}H_{16}ClN_3O_2$ (425.87) | 70.49 (70.10) | 3.79 (3.93) | 9.87 (9.69) | |
| **16**a | 5/35 (acetonitrile) | 340 (ethanol) | 77 | $C_{19}H_{11}ClN_4S$ (362.84) | 62.88 (62.60) | 3.05 (3.20) | 15.44 (15.61) | 8.83 (8.76) |
| **16**b | 5/40 (acetonitrile) | 320 (ethanol) | 66 | $C_{24}H_{16}ClN_3S$ (413.93) | 70.20 (70.40) | 3.89 (3.99) | 10.15 (10.00) | 7.74 (7.95) |
| **16**c | 5/40 (acetonitrile) | 250 (ethanol) | 90 | $C_{25}H_{16}ClN_3OS$ (441.94) | 67.93 (67.70) | 3.64 (3.44) | 9.50 (9.70) | 7.25 (7.41) |

| Com. No. | I.R. ($cm^{-1}$)[c] | $^1$H-NMR[d] ($\delta$ ppm) |
|---|---|---|
| **2b** | 2979–2865 ($CH_{aliph}$), 2140 (C≡N) | 7.7–7.3 (s, 9H, aromatic), 3.4–3.2 (br, 2H, $CH_2$) |
| **2c** | 2950 ($CH_{aliph}$), 2190 (C≡N) | 7.7–7.4 (m, 4H, aromatic), 6.0 (s, 1H, CH) |
| **4a** | 2990–2895 ($CH_{aliph}$), 2250 (C≡N) 1709 (C=O) | 10.0 (s, 1H, CHO), 7.5–7.0 (m, 4H, aromatic), 3.3 (s, 2H, $CH_2$) |
| **4b** | 2980–2890 ($CH_{aliph}$), 2195 (C≡N) 1720 (C=O) | 7.6–7.3 (m, 9H, aromatic), 3.3 (s, 2H, $CH_2$) |
| **4c** | 2970–2850 ($CH_{aliph}$), 2189 (C≡N), 1755 (C=$O_{ester}$), 1710 (C=$O_{aldehyde}$) | 9.9 (s, 1H, CHO),7.5–7.2 (m, 4H, aromatic), 4.4–4.2 (q, 2H, $CH_2$), 3.4 (s, 2H, $CH_2$ CO), 1.3–1.0 (t, 3H, $CH_3$) |
| **5a** | 3440 (OH), 2900 ($CH_{aliph}$), 2190 (C≡N), 1090 (C–O) | 7.7–7.2 (m, 4H, aromatic), 6.6–6.4 (br, 2H, CH=CH), 2.3 (s, 1H, OH) |
| **6a** | 3310 (NH), 2171 (C≡N), 1100 (C–O–C) | 9.0 (s, 1H, NH), 7.7–7.3 (m, 4H, aromatic), 6.0–5.6 (m, 2H, CH=CH) |
| **6b** | 3321 (NH), 2180 (C≡N), 1155 (C–O–C) | 8.8 (s, IH, NH), 7.8–7.5 (m, 9H, aromatic), 5.6 (s, IH, =CH) |
| **6c** | 2190 (C≡N), 1700 (C=O), 1149 (C–O–C) | 7.9–7 (m, 4H, aromatic), 6.4–6.1 (br, 2H, CH=CH) |

(*continued*)





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***Table I.*** Continued

| | | |
|---|---|---|
| **$7_a$** | 3340, 3296, 3245 (NH, $NH_2$), 2187 (C≡N) | 10.0 (s, 1H, NH), 8.4–7.9 (m, 4H, aromatic), 6.8 (s, 1H, $NH_2$), 6.4–6.1 (br, 2H, CH=CH) |
| **8** | 2970–2810 ($CH_{aliph}$), 2184 (C≡N), 1720 (C=O), 1677 ($C=O_{amidie}$) | 7.7–7.3 (m, 8H, aromatic), 2.9 (s, 2H,$CH_2$) |
| **8** | 3368, 3290 ($NH_2$), 2189 (C≡N), 1714 (C=O), 1687 ($C=O_{amidie}$) | 7.9–7.2 (m, 8H, aromtic), 6.3–6.1 (br, 2H, $NH_2$) |
| **$10_a$** | 3390, 3285 ($NH_2$), 2210, 2200 (2C≡N), 1095 (C=S), 679 (C−S−C) | 7.7–7.2 (m, 4H, aromatic), 6.2–6.0 (s, 2H, $NH_2$) |
| **$10_b$** | 3230, 3150 ($NH_2$), 2190 (C≡N), 1730 (C=O), 1134 (C=S), 690 (C−S−C) | 9.6 (s, 1H, CHO), 7.7–7.0 (m, 4H, aromatic), 6.0 (s, 2H, $NH_2$). |
| **$10_c$** | 3260, 3150 ($NH_2$), 2190 (C≡N), 1700 (C=O), 1150 (C=S), 689 (C−S−C) | 7.9–7.0 (m, 9H, aromatic), 6.2–6.0 (s, 2H, $NH_2$) |
| **$11_a$** | 3343, 3290, 3160 (NH, $NH_2$), 2970–2810 ($CH_{aliph}$), 2178 (C≡N), 1740 ($C=O_{ester}$). | 9.2 (s, 1H, NH), 7.7–6.9 (m, 4H, aromatic), 6.6 (s, 2H, $NH_2$), 4.3–4.0 (q, 2H, $CH_2$), 1.3–1.0 (t, 3H, $CH_3$) |
| **$11_b$** | 3283 (NH), 2910–2880 ($CH_{aliph}$), 2182 (C≡N), 1740 ($C=O_{ester}$) | 9.2 (s, 1H, NH), 8.3–7.9 (m, 4H, aromatic), 5.8 (s, 1H, =CH), 4.4–4.1 (q, 2H, $CH_2$), 1.3–1.0 (t, 3H, $CH_3$) |
| **$11_c$** | 3160 (NH), 2940–2870 ($CH_{aliph}$), 2200 (C≡N), 1740 ($C=O_{ester}$) | 9.3 (s, 1H, NH), 8.4–7.7 (m, 9H, aromatic), 6.1 (s, 1H, =CH), 4.4–4.0 (q, 2H, $CH_2$), 1.4–1.2 (t, 3H, $CH_3$) |
| **$12_a$** | 3283, 3290, 3270, 3160 ($2NH_2$), 2970–2810 ($CH_{aliph}$), 1740 (C=O) | 7.7–6.9 (m, 4H, aromatic), 6.6–6.36 (br, 4H, $2NH_2$), 4.5–4.1 (q, 4H, $2CH_2$), 1.4–1.0 (t, 6H, $CH_3$) |
| **$12_b$** | 3290, 3180 ($NH_2$), 2970–2810 ($CH_{aliph}$), 1740 (C=O) | 7.7–6.9 (m, 4H, aromatic), 6.6 (s, 2H, $NH_2$), 5.9 (s, 1H, =CH), 4.3–4.1 (q, 4H, $2CH_2$), 1.3–1.0 (t, 6H, $2CH_3$) |
| **$12_c$** | 3343, 3250 ($NH_2$), 2970–2810 ($CH_{aliph}$) 2178 (C≡N), 1740 (C=O) | 7.7–6.8 (m, 9H, aromatic), 6.6 (s, 2H, $NH_2$), 5.5 (s, 1H, =CH), 4.4–4.1 (q, 4H, $2CH_2$), 1.5–1.2 (t, 6H, $2CH_3$) |
| **$13_a$** | 3280, 3170 ($NH_2$), 2209, 2200 (2C≡N) 1060 (C−O−C) | 8.0–7.6(m, 9H, aromatic), 6.4 (s, 2H, $NH_2$), |
| **$13_b$** | 3210, 3170 ($NH_2$), 2175 (C≡N), 1106 (C−O−C) | 8.2–7.8 (m, 14H, aromatic), 6.0 (s, 2H, $NH_2$) |
| **$13_c$** | 3200, 3150 ($NH_2$), 2170 (C≡N), 1705 (C=O) 1110 (C−O−C) | 8.0–7.2 (m, 14H, aromatic), 6.4–6.0 (br, $NH_2$) |
| **$14_a$** | 3280, 3170 ($NH_2$), 2200, 2180 (2C≡N), 679 (C−S−C) | 7.5–7.0 (m, 9H, aromatic), 6.4–6.0 (br, 2H, $NH_2$) |
| **$14_b$** | 3210, 3170 ($NH_2$), 2175 (C≡N), 686 (C−S−C) | 8.2–7.5 (m, 14H, aromatic), 6.0 (s, 2H, $NH_2$) |
| **$14_c$** | 3200, 3150 ($NH_2$), 2170 (C≡N), 1700 (C=O), 690 (C−S−C) | 8.0–7.4 (m, 14H, aromatic), 6.4–6.0 (br, 2H, $NH_2$) |
| **$15_a$** | 3280, 3170 ($NH_2$), 2200, 2180 (2C≡N), 1680 (C=O) | 8.4–7.9 (m, 9H, aromatic), 6.0 (s, 2H, $NH_2$) |
| **$15_b$** | 3210, 3170 ($NH_2$), 2175 (C≡N), 1696 (C=O) | 7.9–7.1 (m, 14H, aromatic), 5.5 (s, 2H, $NH_2$) |
| **$15_c$** | 3210, 3170 ($NH_2$), 2175 (C≡N), 1699 (C=O) | 8.2–7.9 (m, 14H, aromatic), 6.3 (s, 2H, $NH_2$) |





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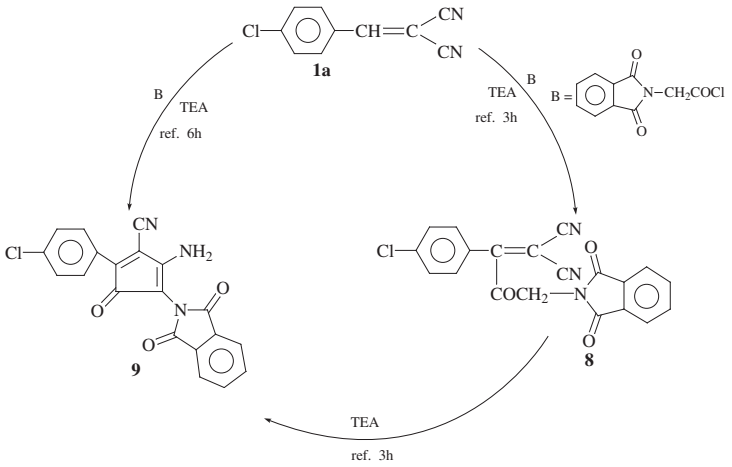
***Table I.*** Continued

| | | |
|---|---|---|
| **16$_a$** | 3321, 3210 ($NH_2$), 2200, 2195 (2C≡N), 1140 (C=S) | 8.4–8.0 (m, 9H, aromatic), 6.9 (s, 2H, $NH_2$) |
| **16$_b$** | 3321, 3210 ($NH_2$), 2195 (C≡N), 1140 (C=S) | 8.0–7.6 (m, 14H, aromatic), 6.5 (s, 2H, $NH_2$) |
| **16$_c$** | 3321, 3210 ($NH_2$), 2200 (C≡N), 1718 (C=O), 1140 (C=S) | 8.2–7.8 (m, 14H, aromatic), 6.6 (s, 2H, $NH_2$) |

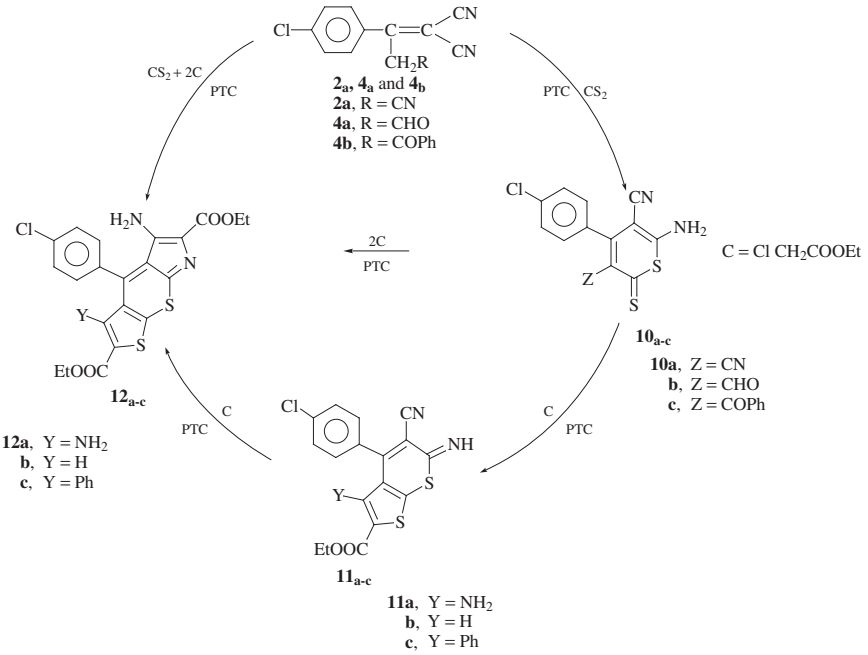
[a]Uncorrected.
[b]Satisfactory microanalysis obtained C; ±0.35; H; ±0.40, N; ±0.30.
[c]Measured by Nicolet FT-IR 710 spectrophotometer.
[d]Measured by a varian EM 360 L spectrometer at 60 MHz using TMS as internal standard and DMSO as a solvent.

Moreover, 4-amino-3-cyano-2-*p*-chlorophenylcyclopentadiene-4-one (**9**) was synthesized through the reaction of compound **1** with phthalylglycinyl chloride and triethylamine in 1:1:1 molar ratio in refluxing benzene for 6 h. On reducing the reaction time to 3 h, it is possible to separate the acylated compound **8**, which cyclized to compound **9** with an additional 3 h refluxing (Scheme 2, Table I).

5-Amino-2, 6-diethylcarboxy-3-substituted-4-*p*-chlorophenyl-6-iminothieno- [3,2:5,6]thiopyrano[2,3-b]pyrrols **12$_{a-c}$** were synthesized in a one-pot procedure via the reaction of compound **2$_a$**, **4$_a$**, or **4$_b$** with $CS_2$ and ethyl chloroacetate in 1:1:2 molar ratio under PTC conditions (dioxan/$K_2CO_3$/tetrabutylammonium bromide TBAB) in good yield. The formation sequence of compounds **12$_{a-c}$** was followed up by using stepwise reactions through the reaction of compound **2$_a$**, **4$_a$**,




***Scheme 2.***




***Scheme 3.***

or $\mathbf{4_b}$ with $CS_2$ under the same PTC conditions, in which thiopyran derivatives $\mathbf{10_{a-c}}$ were separated. IR spectra showed absorption bands at 3300, 3215 $cm^{-1}$ for $NH_2$ group, and at 1160 $cm^{-1}$ for C═S group. MS of compound $\mathbf{10_c}$ showed the molecular ion peak at m/e 382.

The compounds $\mathbf{10_{a-c}}$ were reacted with ethyl chloroacetate in 1:1 or 1:2 molar ratio using the current PTC conditions to afford thienothiopyrans $\mathbf{11_{a-c}}$ or thienothiopyranopyrrols $\mathbf{12_{a-e}}$, respectively. Moreover, when compounds $\mathbf{11_{a-c}}$ were treated with another mole of ethyl chloroacetate using the same PTC conditions, compounds $\mathbf{12_{a-c}}$ were obtained with fair yields (Scheme 3, Table I). Their stepwise reactions study revealed the priority of S-alkylation to N-alkylation according to the role of reactivity (3) (S > N > O).

In analogy, compound $\mathbf{2_a}$, $\mathbf{2_b}$, or $\mathbf{4_b}$ was treated with phenylisocyanate or phenylisothiocyanate under PTC conditions [$CH_3CN/K_2CO_3$/tetrabutylammonium bromide (TBAB)] to afford $\alpha$-pyran, $\alpha$-thiopyran, pyridinone, and pyridine-2-thione derivatives $\mathbf{13_{a-c}}$-$\mathbf{16_{a-c}}$, respectively. The reaction pathway is thus assumed to proceed via anucleophilic addition of the active methylene group at the N═C followed by the attack of the SH, NH or OH to the cyano group to give





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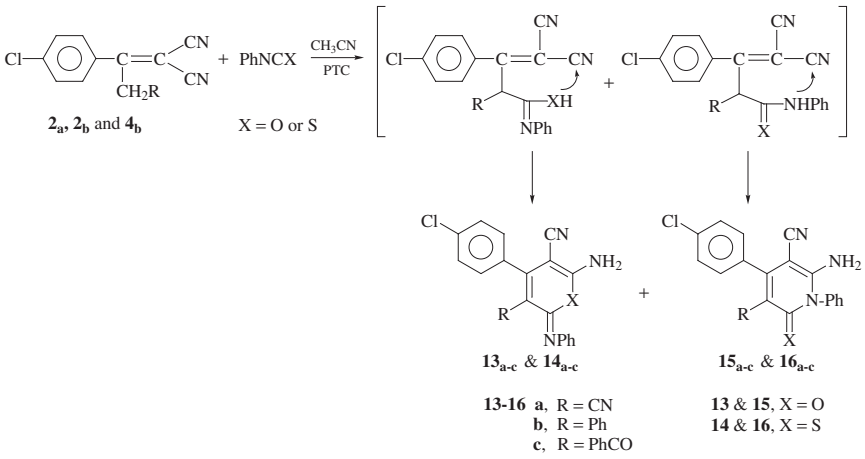


***Scheme 4.***

compounds **13–16** (Scheme 4, Table I). This is in accordance with the sequence of reactivity of anionic poles S > N > O ≈ C.

## EXPERIMENTAL

The MS were recorded on a Micromass 7070 E spectrometer operating at 70 eV, using direct inlet.

### Synthesis of Compounds $2_{b,c}$, $4_{a-c}$, and $6_{a-c}$ General Procedure

To a mixture of anhydrous potassium carbonate (3 g), dry benzene, dioxan, or DMF (40 mL), compound **1** (1.88 g, 0.01 mol) or **3** (2.35 g, 0.01 mol) and catalytic amount of tetrabutylammonium bromide (TBAB) was added to an equimolar amount 0.01 mol of benzyl chloride (1.15 mL), bromomalononitrile, (1.44 gm), chloroacetaldehyde (0.64 mL), or phenacyl bromide (1.99 g). The reaction mixtures were vigorously stirred over different periods of time at the appropriate temperatures (Table I), until completion of the reaction (TLC). The reaction mixtures were filtered off and the filtrate was evaporated in vacuo. The residual solid was washed with water and crystallized from the appropriate solvent, where compounds $\mathbf{2_{b,c}}$, $\mathbf{4_{a,c}}$, and $\mathbf{6_{a-c}}$ were obtained, respectively.

The solid potassium carbonate was dissolved in distilled water (50 mL). The separated solid was collected by filtration and crystallized from the proper solvent,

where compounds $\mathbf{4_b}$ and $\mathbf{5_a}$ were obtained (Tab. 1). MS of compound $\mathbf{2_b}$ : m/z. (relative intensity): 278 (18.23), 188 (3.64), 138 (8.9), 125 (100), 91 (59.24). MS of product $\mathbf{4_a}$: m/z (relative intensity): 230 (6.4), 184 (0.01), 163 (0.1), 124 (100), 86 (4.8), 63 (7.88).

### Synthesis of 4-*p*-Chlorophenyl-3-substituted-2-imino(oxo)-2H-3-pyrancarbonitrile $\mathbf{6_{a-c}}$ from the Intermediates $\mathbf{4_{a-c}}$ or $\mathbf{5_a}$

A mixture of compound $\mathbf{4_{a-c}}$ (0.01 mol) or $\mathbf{5_a}$ (2.3 g, 0.01 mol) in dry dioxan (20 mL) and anhydrous potassium carbonate (3 g) was treated with catalytic amount of tetrabutylammonium bromide (TBAB), and was vigorously stirred over different periods of time at the appropriate temperatures (Tab. I). The separation of the products was completed using the same previous procedure.

### Synthesis of 1-Amino-4-*p*-chlorophenyl-2-imino-1,2-dihydro-3-pyridinecarbonitrile $\mathbf{7_a}$

An equimolar mixture of compound $\mathbf{5_a}$ (0.69 g, 0.003 mol) and hydrazine hydrate (0.15 mL, 0.003 mol) in 30 mL of ethanol was refluxed for 2 h. The reaction mixture was evaporated in vacuo, and the residual solid was crystallized for ethanol (Tab. I).

### Synthesis of 4(1,3-Dioxo-2,3-dihydro-1H-2-isoindolyl)5-amino-2-*p* Chlorophenyl-3-oxo-1,4-cyclopentadiene-1-carbonitrile 8 and 2-[3(1,2-Dioxo-2,3-dihydro-H-2-isoindolyl)-2-oxo-1-phenylpropylidene]malononitrile 9

An equimolar mixture (0.01 mol) of compound **1** (1.88 g), phthalylglycinyl chloride (2.23 g) and triethylamine (1 mL) in 50 mL of dry benzene was refluxed for 3 h. The solvent was evaporated under reduced pressure and the residual solid was filtered off, washed with water, and crystallized from ethanol to give product **8**. Product **9** was obtained using the same procedure with 6-h reflux or by refluxing a benzene solution of compound **8** in presence of catalytic amount of triethylamine for 3 h. The desired product **9** was crystallized from ethanol (Tab. I).





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### Synthesis of 6-Amino-3-Substituted-4-*p*-Chlorophenyl-2-thioxo-2H-5-thiopyran Carbonitrile $10_{a-c}$

General Procedure

To a mixture of compound $\mathbf{2_a}$ (2.27 g, 0.01 mol), $\mathbf{4_a}$ (2.30 g, 0.01 mol), or $\mathbf{4_b}$ (3.06 g, 0.01 mol) and 3 g potassium carbonate in dry dioxan (40 mL), $CS_2$ (0.76 mL, 0.01 mol) was added. The reaction mixture was treated with a catalytic amount of TBAB and vigorously stirred over different periods of time at the appropriate temperature until completion of the reaction (TLC). The reaction mixtures were filtered off and the filtrate was evaporated in vacuo. The residual solid was washed with water and crystallized from the appropriate solvent, where compounds $\mathbf{10}_{a-c}$ were obtained (Tab. I). MS of compound $\mathbf{10_c}$ : m/z (relative intensity): 383 (25), 349 (16.66), 333 (21.75), 188 (7.47), 142 (9.73), 105 (100).

### Synthesis of 2-Ethylcarboxy-3-substituted-4-*p*-chlorophenyl-6-imino-6H-thieno-[2,3-c]thiopyran-5-carbonitrile $11_{a-c}$

Compounds $\mathbf{11_{a-c}}$ were prepared from the reaction of compound $\mathbf{2_a}$, $\mathbf{4_a}$, or $\mathbf{4_b}$ (0.01 mol) in dioxan (20 mL) and ethyl chloroacetate (1.06 mL, 0.01 mol) using the same previous procedure.

### Synthesis of 5-Amino-2,6-diethylcarboxy-3-substituted-4-*p*-chlorophenyl 6-iminothieno[3,2:5,6]thiopyrano[2,3-b]pyrrols $12_{a-c}$

Method A: General Procedure

To a mixture of anhydrous potassium carbonate (3 g) in dry dioxan (20 mL), compound $\mathbf{10_{a-c}}$ or $\mathbf{11_{a-c}}$ (0.01 mol) and ethy1 chloroacetate (1.06 mL, 0.01 mol) or (2.12 mL, 0.02 mol) were added. The reaction mixture was treated with a catalytic amount of TBAB and vigorously stirred over different periods of time at the appropriate termperatures until completion of the reaction (TLC). The reaction mixture was filtered off and the filtrate was evaporated in vacuo. The residual solid was washed with water and crystallized from the appropriate solvent, where compounds $\mathbf{12_{a-c}}$ were obtained (Tab. I).

Method B

Ethyl chloroacetate (0.02 mol) (2.12 mL) was added to a stirred mixture of compound $\mathbf{2_a}$ (2.27 g, 0.01 mol), $\mathbf{4_a}$(2.30 g, 0.01 mol), or $\mathbf{4_b}$ (3.06 g, 0.01 mol), $CS_2$





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(0.76 mL, 0.01 mol), anhydrous potassium carbonate (3 g), and catalytic amount of TBAB in dry dioxan (40 mL). The reaction mixture was treated as previously described in Method A.

### Synthesis of 6-Amino-3-substituted-2-iminophenyl-4-*p*-chlorophenyl-2H-5-pyrano(thiopyrano)carbonitrile 13&15 and 6-Amino-3-substituted-4-*p* chloro-phenyl-1-phenyl-2-oxo(thioxo)-1,2-dihydro-5-pyridinecarbonitrile 15&16

General Procedure

To a mixture of compound $\mathbf{2_a}$(2.27 g, 0.01 mol), $\mathbf{2_b}$ (2.78 g, 0.01 mol), or $\mathbf{4_b}$ (3.06 g, 0.01 mol) and 3 g potassium carbonate in acetonitrile (40 mL), phenylisocyanate (1.19 mL, 0.01 mol) or phenylisothiocyanate (1.35 mL, 0.01 mol) was added. The reaction mixture was treated with a catalytic amount of TBAB and vigorously stirred at the appropriate temperature untill completion of the reaction (TLC). The reaction mixture was filtered. The filtrate was evaporated in vacuo. The residual solid was crystallized from the appropriate solvent, where compounds $\mathbf{13_{a-c}}$ and $\mathbf{14_{a-c}}$ were obtained, respectively.

The solid potassium carbonate was dissolved in distilled water (50 mL). The separated solid was collected by filtration and crystallized from the proper solvent, where compounds $\mathbf{15_{a-c}}$ and $\mathbf{16_{a-c}}$ were obtained.(Tab. I, Scheme 4).

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