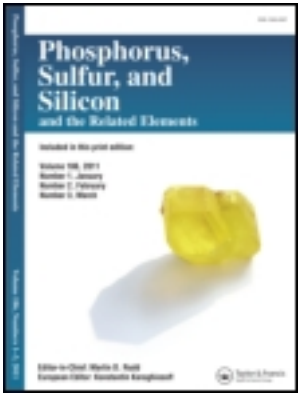

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Part 7: Synthesis of Some New 1,5-Benzodiazepines Fused with Different Heterocyclic Moieties

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Part 7: Synthesis of Some New 1,5-Benzodiazepines Fused with Different Heterocyclic Moieties

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3-cyano-1,11-dihydro-4,5-diphenyl-2-thioxopyrido[2,3-b](1,5)benzodiazepine ***2*** *and 3-(2′-cyano-1′-phenyl-2′-ethanethiocarboxamide)-4-phenyl-1(H)(1,5)benzodiazepin-2-one* ***3*** *were prepared via the reaction of 1,3-dihydro-4-phenyl-(1,5)benzodiazepin-2-one* ***1*** *with benzylidenecyanothioacetamide. Compound* ***2*** *was treated with halo compounds to give the corresponding S-alkylated compounds* $\mathbf{4_{a-c}}$*, which underwent as intramolecular ring closure to thieno[3,2.5,6]pyrido[2,3-b](1,5)benzodiazepines* $\mathbf{5_{a-c}}$ *under PTC conditions. One-pot syntheis of compounds* $\mathbf{5_{a-c}}$ *was achieved via the reaction of compound* ***2*** *with the appropriate halo compound under PTC conditions. Compound* ***1*** *and 1-ethyl-4-phenyl-(1,5)benzodiazepin-2-one* ***9*** *were treated with carbon disulfide or phenylisothiocyanate and active nitriles to afford 4-thioxothiopyrano[4,3-b](1,5)benzodiazepines* ***8*** *and* ***10–14****. Treatment of compound* ***10*** *with phenylisothiocyanate or acetic anhydride yielded oxazino- and pyrimido[4,5-b]thiopyrano-[4′,3′-b′](1,5)benzodiazepine* ***15*** *and* ***17****. The reaction of compound* ***1*** *with elemental sulfur and active nitriles yielded thieno[3,2-b](1,5)benzodiazepines* ***18–21****, respectively.*

Keywords 3-cyano-1,11-dihydro-4,5-diphenyl-2-thioxopyrido[2,3-b](1,5)benzodiazepine; 1-ethyl-1(H)-4-phenyl-1,5-benzodiazepin-2-one; PTC

INTRODUCTION

Benzodiazepines and their polycyclic derivatives are used in pharmaceutical and biological chemistry,[1] where they are used as antitumor agents,[2] nevirapine analgnes,[3] and anti–HIV-1 (Human Immunodeficiency Virus) agents.[3] They also are screened for in vitro cytotoxicity against a number of cancer cell lines,[4] such as colon cancer, breast cancer, lung cancer, and bladder cancer.[5] For all these reasones, we continue our laboratory work on the synthesis of fused and spiro

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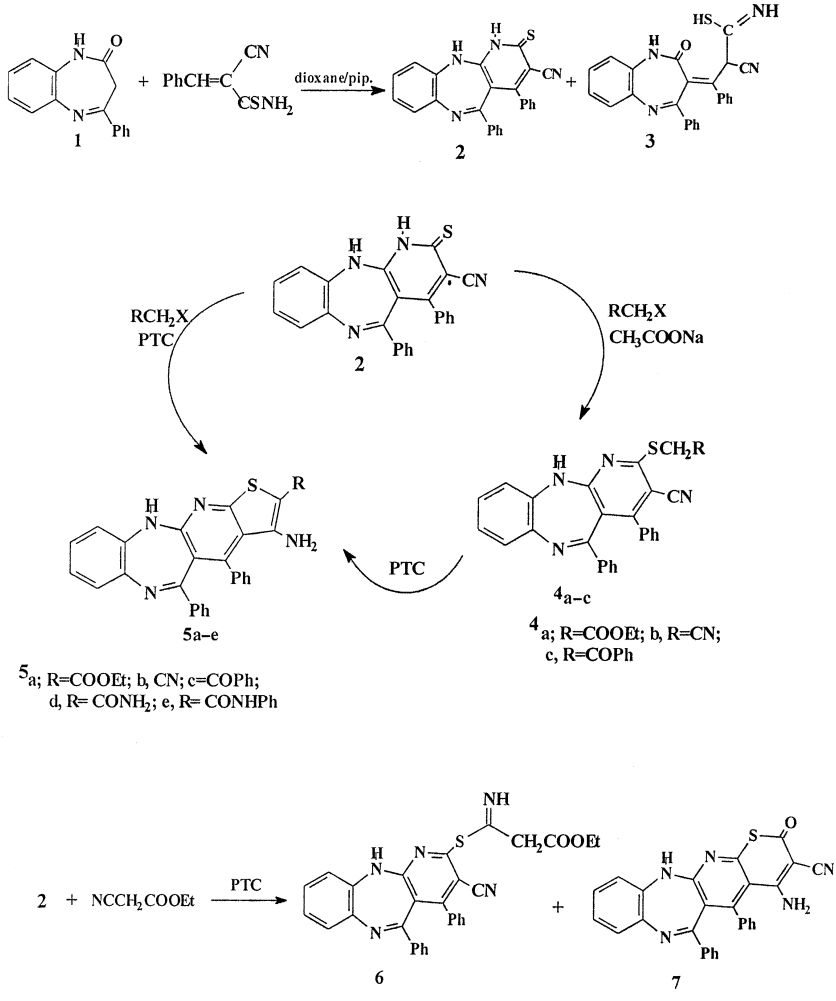
benzodiazepines.[6–11] So herein we report the synthesis of pyrido[2,3-b]-,thiopyrano[4,3-b]-, and thieno[3,2-b](1,5)benzodiazepines.

RESULTS AND DISCUSSION

Recently, Khodairy[10] reported that the reaction of 1,3-dihydro-4-phenyl-1,5-benzodiazepin-2-one **1**[12] with some ylidenecyanothioacetamides and sodium ethoxide gave corresponding 3-cyano-2-thioxopyrido[2,3-b][1,5]-benzodiazepines. We report herein other trials for the synthesis of 3-cyano-1,11-dihydro-4,5-diphenyl-2-thiopyrido [2,3-b][1,5]benzodiazepine via the reaction of 1,3-dihydro-4-phenyl-1,5-benzodiazepin-2-one **1** with benzylidenecyanothioacetamide and piperidine as a basic catalyst, where a mixture of 3-cyano-1,11-dihydro-4,5-diphenyl-2-thioxopyrido[2,3-b](1,5)-benzodiazepine **2** and 2-cyano-3(4-phenyl-2-oxo-1,2-dihydro-3H-(1,5)benzodiazepin-3-ylidene)-3-phenylpropanimidothioic acid **3** was obtained in a 20% and 70% yield, respectively. The IR spectrum of compound **2** showed new absorption bands at 3385 cm^{-1} and 2214 cm^{-1} corresponding to NH and CN groups, respectively, while its ^1H NMR spectrum revealed the presence of multiplet signals at δ 8.70–7.00 ppm for the 14 H aromatic protons and a singlet signal at δ 9.50 ppm for the new NH group.

Treatment of compound **2** with active halo compounds, namely ethyl chloroacetate, chloroacetonitrile, and phenacyl bromide in the presence of odium acetate as a catalyst, afforded 2-carbethoxymethylthio-3-cyano-4,5-diphenyl-11(H)pyrido[2,3-b](1,5)benzodiazepine $\mathbf{4_a}$, 3-cyano-2-cyanomethy-Ithio-4,5-diphenyl-11(H)pyrido[2,3-b](1,5) benzodiazepine $\mathbf{4_b}$, and 2-benzoyl-methylthio-3-cyano-4,5-diphenyl-11(H)pyrido [2,3-b](1,5)benzodiazepine $\mathbf{4_c}$, respectively. Using the PTC technique (dioxane/potassium carbonate/tetrabutyl-ammonium bromide [TBAβ]), compounds $\mathbf{4_{a-c}}$ underwent intramolecular cyclization into 3-amino-2-carbethoxy-4,5-diphenyl-11(H)thieno[2,3-b]pyrido-[2′,3′-b′](1,5)benzodiazepine $\mathbf{5_a}$, 3-amino-2-cyano-4,5-diphenyl-11(H)thieno-[2,3-b]pyrido [2′,3′-b′](1,5)benzodiazepine $\mathbf{5_b}$, and 3-amino-2-benzoyl-4,5-diphenyl-11(H)thieno[2,3-b]pyrido[2′,3′-b′](1,5)benzodiazepine $\mathbf{5_c}$, respectively. Compounds $\mathbf{5_{a-c}}$, 3-amino-2-carboxamido-4,5-diphenyl-11(H)thieno [2,3-b]pyrido [2′,3′-b′](1,5)benzodiazepine $\mathbf{5_d}$, and 3-amino-2-phenylcarboxamido-4,5-diphenyl-11(H)thieno[2,3-b]pyrido[2′,3′-b′](1,5)benzodiazepine $\mathbf{5_e}$ were synthesized directly in a one-pot step via the reaction of compound **2** with ethyl chloroacetate, chloroacetonitrile, phenacyl bromide, chloroacetamide, and chloroacetanilide, respectively, under PTC conditions (dioxane/potassium carbonate/TBAB). IR spectra of compounds $\mathbf{5_{a-e}}$ showed characteristic absorption bands at 3463–3215 cm^{-1} due to the NH_2 group and at 1721 cm^{-1} and 1671 cm^{-1}

for the CO groups, with disappearance of the absorption band for the CN group. ^{1}HNMR spectra of compounds $\mathbf{5_{a-e}}$ represented the characteristic broad signal at δ 5.70–5.10 ppm due to the NH_2 group along with two singlet signals at δ 8.10 and δ 4.60 ppm due to the NH and $CONH_2$ groups. The reaction of compound **2** with ethyl cyanoacetate under PTC conditions yielded a mixture of ethyl 3-{[3-cyano-4,5-diphenyl-11H-pyrido(2,3-b)(1,5)benzodiazepin-2-yl]thio}-3-iminopropanoate **6** and 4-amino-3-cyano-5,6-diphenyl-2-oxo-12(H)thiopyrano[2,3-b]pyrido [2′,3′b′](1,5)benzo-diazepine **7**, respectively (c.f. Scheme 1 and Table I).



SCHEME 1

TABLE I Analytical and Spectral Data of the New Compounds

Product No.	M.P. (°C)[a]	Yield (%)	Mole. Form. (Mol. Wt.)	Analytical Data[b] Calcd/Found				IR (cm^{-1})[c]	^{1}HNMR ∂ (ppm)[d]
				C	H	N	S		
2	180 dioxane	66	$C_{25}H_{16}N_4S$ (404.49)	74.23 74.50	3.99 3.86	13.85 13.96	7.93 7.89	3309, 3196 (2NH); 2214 (CN); 1119 (C=S)	10.00 (s, 1H, NH); 9.50 (s, 1H, NH); 8.70–7.00 (m, 14H, arom.)
3	214 dioxane	42	$C_{25}H_{18}N_4OS$ (422.50)	71.07 71.26	4.29 4.42	13.26 13.00	7.59 7.34	3385, 3290, 3184 (NH, NH_2); 2205 (CN); 1669 (CO), 1122 (C=S)	10.20 (s, 1H, NH); 8.30–7.00 (m, 14H, arom.); 6.60–6.50 (br, 1H, NH); 3.50 (s, 1H, CH), 1.7(s, 1H, SH)
4$_a$	200 ethanol	70	$C_{29}H_{22}N_4O_2S$ (490.58)	71.00 71.23	4.52 4.70	11.42 11.23	6.54 6.41	3218 (NH); 2978, 2922 ($CH_{aliph.}$); 2210 (CN); 1719 (CO)	7.55 (s, 1H, NH); 7.40–6.80 (m, 14H, arom.); 4.25–3.80 (q, 2H, CH_2): 3:20 (s, 2H, CH_2); 1.45–1.00 (t, 3H, CH_3)
4$_b$	240 $CHCl_3$	74	$C_{27}H_{17}N_5S$ (443.53)	73.12 73.15	3.86 3.93	15.79 15.86	7.23 7.50	3221 (NH); 2980 ($CH_{aliph.}$); 2205 (CN)	10.55 (s, 1H, NH); 8.65–7.60 (m, 14H, arom.); 4.50 (s, 2H, CH_2)
4$_c$	222 ethanol	55	$C_{33}H_{22}N_4OS$ (522.62)	75.84 75.89	4.24 4.38	10.72 10.84	6.13 6.22	3343(NH); 2921 ($CH_{aliph.}$); 2208 (CN); 1677 (CO)	8.30–7.15 (m, 20H, arom. + NH); 4.85 (s, 2H, CH_2)
5$_a$	220 ethanol	82	$C_{29}H_{22}N_4O_2S$ (490.58)	71.00 71.16	4.52 4.39	11.42 11.56	6.54 6.32	3415, 3345, 3221 (NH, NH_2); 2934 ($CH_{aliph.}$); 1710 (CO)	8.30 (s, 1H, NH); 7.65–6.40 (m, 14H, arom.); 5.20 (s, 2H, NH_2); 4.20–3.80 (q, 2H, CH_2); 1.50–0.80 (t, 3H, CH_3)
5$_b$	268 benzene	60	$C_{27}H_{17}N_5S$ (443.53)	73.12 73.26	3.86 3.74	15.79 15.66	7.23 7.42	3415, 3334, 3233 (NH, NH_2); 2192 (CN)	8.40 (s, 1H, NH); 8.10–6.95 (m, 14H, arom.); 5.20 (s, 2H, NH_2)
5$_c$	230 $CHCI_3$	43	$C_{33}H_{22}N_4OS$ (522.62)	75.84 75.69	4.24 4.29	10.72 10.78	6.13 6.29	3456, 3356, 3240 (NH, NH_2); 1670 (CO)	10.35 (s, 1H, NH); 8.00–7.20 (m, 19H, arom.); 5.30 (s, 2H, NH_2)

5$_d$	204 pet. Ether	80	$C_{27}H_{19}N_5OS$ (461.54)	70.26 70.39	4.15 4.28	15.17 15.32	6.95 6.87	3463, 3370, 3329, 3197 (NH, $2NH_2$); 1683 (2CO)	10.20 (s, 1H, NH); 8.30–6.90 (m, 14H, arom.); 5.70 (s, 2H, NH_2); 4.65 (s, 2H, NH_2).
5$_e$	280 ethanol	60	$C_{33}H_{23}N_5OS$ (537.64)	73.72 73.91	4.31 4.50	13.03 13.23	5.96 5.72	3461, 3392, 3316, 3215 (2NH, NH_2); 1680 (CO)	9.15 (s, 1H, NH); 8.10 (s, 1H, NH); 7.80–6.90 (m, 19H, arom.); 5.75 (s, 2H, NH_2)
6	124 benzene	40	$C_{30}H_{23}N_5O_2S$ (517.60)	69.61 69.83	4.48 4.91	13.53 13.26	6.19 6.02	3397, 3202 (2NH); 2204 (CN); 1700 (CO)	8.40 (s, 1H, NH); 7.45 (s, 1H, NH); 7.30–6.60 (m, 14H, arom.); 4.30–3.60 (q, 2H, CH_2); 3.10(s, 2H, CH_2), 1.15–0.95 (t, 3H, CH_3)
7	188 dioxane	23	$C_{28}H_{17}N_5OS$ (471.53)	71.32 71.51	3.63 3.83	14.85 14.50	6.80 6.84	3424, 3318, 3215 (NH, NH_2); 2216 (CN); 1636 (CO)	
8	189 dioxane	78	$C_{19}H_{12}N_4S_2$ (360.45)	63.31 63.53	3.35 3.11	15.54 15.77	17.79 17.59	3430, 3330, 3194 (NH, NH_2); 2202 (CN)	8.02(s, 1H, NH); 7.85–6.90 (m, 9H, arom.); 5.20–4.60 (br, 2H, NH_2
10	200 ethanol	50	$C_{21}H_{16}N_4S_2$ (388.51)	64.92 64.83	4.15 4.00	14.42 14.60	16.51 16.55	3304, 3163 (NH_2); 2211 (CN)	9.60 (s, 2H, NH_2); 8.00–6.95 (m, 9H, arom.); 3.25–2.85 (q, 2H, CH_2); 1.40–1.05 (t, 3H, CH_3)
11	185 benzene	43	$C_{21}H_{18}N_4OS_2$ (406.52)	62.05 62.15	4.46 4.55	13.78 13.50	15.77 15.43	3427, 3340, 3258 ($2NH_2$); 1645 (CO)	9.50 (s, 2H, NH_2); 8.25–7.05 (m, 9H, arom.); 4.65 (s, 2H, NH_2); 1.50–1.15 (q, 2H, CH_2); 1.00–0.80 (t, 3H, CH_3)
12	130 benzene	48	$C_{21}H_{15}N_3OS_2$ (389.49)	64.76 64.88	3.88 3.49	10.79 10.96	16.46 16.51	2209 (CN); 1667 (CO)	7.90–7.15 (m, 9H, arom.); 4.50 (s, 1H, CH); 4.00–3.80 (q, 2H, CH_2); 1.30–1.10 (t, 3H, CH_3)
13	140 methanol	.72	$C_{27}H_{21}N_5S$ (447.55)	72.46 72.31	4.73 4.85	15.65 15.69	7.16 7.09	3315, 3210 (NH_2); 2206 (CN)	8.00–7.00 (m, 14H, arom.); 4.90 (s, 2H, NH_2); 2.90–2.40 (q, 2H, CH_2); 1.10–0.80 (t, 3H, CH_3)
14	170 pet. ether	66	$C_{27}H_{20}N_4S_2$ (464.60)	69.80 69.71	4.34 4.30	12.06 12.18	13.80 13.77	2209 (CN)	8.20–6.85 (m, 14H, arom.); 4.40 (s, 1H, CH); 2.75–2.35 (q, 2H, CH_2); 1.15–0.90 (t, 3H, CH_3)
15	218 ethanol	89	$C_{23}H_{18}N_4OS_2$ (430.54)	64.16 64.30	4.21 4.09	13.01 13.30	14.89 14.67	3290 (NH); 2930 ($CH_{aliph.}$); 2203 (CN); 1696 (CO)	8.80 (s, 1H, NH); 8.30–7.05 (m, 9H, arom.); 3.90–3.50 (q, 2H, CH_2); 2.50 (s, 3H, CH_3); 1.45–1.00 (t, 3H, CH_3)

(Continued on next page)

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

Product No.	M.P. (°C)[a]	Yield (%)	Mole. Form. (Mol. Wt.)	Analytical Data[b] Calcd/Found				IR (cm^{-1})[c]	^{1}HNMR ∂ (ppm)[d]
				C	H	N	S		
16	272 ethanol	61	$C_{23}H_{18}N_4OS_2$ (430.54)	64.16 64.00	4.21 4.33	13.01 13.21	14.89 15.04	3270 (NH); 2924 ($CH_{aliph.}$)	8.95 (s, 1H, NH); 8.20–7.25 (m, 9H, arom.), 4.00–3.50 (q, 2H, CH_2); 2.35 (s, 3H, CH_3); 1.50–1.10 (t, 3H, CH_3)
17	243 methanol	59	$C_{28}H_{21}N_5S_3$ (523.69)	64.22 64.07	4.04 4.31	13.37 13.01	18.37 18.52	3200, 3140 (2NH); 2926($CH_{aliph.}$)	8.70 (s, 1H, NH); 8.30–6.90 (m, 15H, arom. + NH); 3.80–3.15 (q, 2H, CH_2); 1.60–1.05 (t, 3H, CH_3)
18	360 benzene	30	$C_{18}H_{12}N_4S$ (316.38)	68.33 68.52	3.82 4.00	17.71 17.95	10.13 10.01	3416, 3310, 3240 (NH, NH_2); 2201 (CN)	9.00–7.25 (m, 10H, arom.+ NH); 4.45–4.00 (br, 2H, NH_2)
19	212 ethanol	67	$C_{18}H_{14}N_4OS$ (334.39)	64.65 64.35	4.22 4.00	16.75 16.94	9.59 9.89	3436, 3320, 3200, 3105 (NH, $2NH_2$); 1669 (CO)	10.60 (s, 1H, NH); 8.25–7.20 (m, 9H, arom.); 5.50 (s, 2H, NH_2); 5.00 (s, 2H, NH_2)
20	180 ethanol	57	$C_{20}H_{17}N_3O_2S$ (363.43)	66.10 66.32	4.71 4.52	11.56 11.71	8.82 8.97	3220, 3205, 3110 (NH, NH_2); 2918 ($CH_{aliph.}$); 1681 (CO)	11.05 (s, 1H, NH); 8.30–7.00 (m, 9H, arom.); 4.30 (s, 2H, NH_2); 3.70–3.20 (q, 2H, CH_2); 1.60–1.10 (t, 3H, CH_3)
21	120 benzene	20	$C_{18}H_{11}N_3OS$ (317.36)	68.12 68.41	3.49 3.60	13.24 13.10	10.10 10.31	3196 (NH); 2926 ($CH_{aliph.}$); 2203 (CN); 1700 (CO)	8.85 (s, 1H, NH); 8.30–7.05 (m, 9H, arom.); 4.40 (s, 1H, CH)

[a]Uncorrected.

[b]Satisfactory microanalysis obtained, C, ±0.35; H, ±0.4; N, ±0.2; S, ±0.2.

[c]Measured by a Nicolet FT-IR 710 spectrophotometer.

[d]Measured by a Varian EM 360 L spectrometer at 60 MHZ using TMS as a internal standard and DMSO as a solvent.

Compound **1** was allowed to react with carbon disulfide and malononitrile in the presence of triethylamine as a basic catalyst to afford 2-amino-1-cyano-11(H)-5-phenyl-4-thioxothiopyrano[4,3-b](1,5)benzodiazepine **8**. Moreover, the reaction of 1-ethyl-3H-4-phenyl-1,5-benzodiazepin-2-one **9**[10] with carbon disulfide and active nitriles, namely malononitrile, cyanothioacetamide, cyanoacetamide, or ethyl cyanoacetate in the presence of triethylamine as a basic catalyst, yielded 2-amino-1-cyano-11-ethyl-5-phenyl-4-thioxothiopyrano[4,3-b](1,5)benzodiazepine **10**, 2-amino-11-ethyl-5-phenyl-4-thioxo-thiopyran[4,3-b](1,5)benzodiazepine-1-carboxamide **11**, and 1-cyano-11-ethyl-2-oxo-5-phenyl-4-thioxothiopyrano[4,3-b](1,5)benzodiazepine **12**, respectively. In analogy, compound **9** was treated with a mixture of phenyl isothiocyanate and malononitrile or cyanothioacetamide in presence of triethylamine as a basic catalyst to give 2-amino-1-cyano-3,5-diphenyl-11-ethyl-4-thioxopyrido[4,3-b](1,5)benzodiazepine **13** and 1-cyano-3,5-diphenyl-2,4-dithioxo-11-ethyl-pyrido[4,3-b](1,5)benzodiazepine **14**, respectively. The reaction pathway was suggested to be a preliminary formation of carbanion of the $CH_{2\ \text{benzodiazepine}}$ group, which was added to the C=S bond followed by a nucleophilic attack of the SH group or the NH group at the CN, CO, and CS groups followed by condensation of the active methylene and the $C{=}O_{\text{benzodiazepine}}$ group with the eliminaton of H_2S molecule in case of cyanothioacetamide, water molecule in case of cyanoacetamide, or ethanol molecule in case of ethyl cyanoacetate. The IR spectra of compounds **8** and **10–14** exhibited new absorption bands at 3430–3163 cm^{-1} for the NH_2 group and 2211–2202 cm^{-1} for the CN group. The ^{1}HNMR spectra of these compounds showed the disappearance of the signal corresponding to the $CH_{2\ \text{benzodiazepine}}$ group and exihibted multiplet signals at δ 8.00–7.00 for aromatic protons, a broad signal at δ 5.20–4.30 ppm for the NH_2 group, and a singlet signal at δ 4.1 for the CH group, respectively.

Treatment of compound **10** with acetic anhydride along with pyridine gave 2-acetylamino-1-cyano-11-ethyl-5-phenyl-4-thioxothiopyrano[4,3-b](1,5)-benzodiazepine **15**, which was converted into 13-ethyl-1-imino-3-methyl-7-phenyl-6-thioxo(1,3)oxazino[4,5-b]thiopyrano[4′,3′-b′] (1,5) benzodiazepine **16** in boiling pyridine. The cyclization of compound **10** into 2,7-diphenyl-3,6-dithioxo-13-ethyl-1-imino-4(H)-pyrimido[4,5-b]thiopyrano[4′,3-b,](1,5)benzodiazepine **17** was achieved by treating it with phenylisothiocyanate. The IR spectra of compounds **16** and **17** showed the absence of absorption bands corresponding to the NH_2 and CN groups and revealed a new absorption band at 3270–3140 cm^{-1} corresponding to NH groups. ^{1}HNMR spectra were consistent of the proposed structures.

Furthermore, the reaction of elemental sulfur and active methylene, namely malononitrile, cyanothioacetamide, cyanoacetamide, or ethyl cyanoacetate with compound **1** in presence of triethylamine as a basic catalyst, gave 2-amino-1-cyano-4-phenyl-10(H)thieno[3,2-b](1,5)benzodiazepine **18**,[10] 2-amino-1-carboxamido-4-phenyl-10(H)thieno[3,2-b](1,5)benzodiazepine **19**, 2-amino-1-carbethoxy-4-phenyl-10(H)thieno[3,2-b](1,5)benzodiazepine **20**, and 1-cyano-1, 10-dihydro-2-oxo-4-phenylthieno[3,2-b](1,5)benzodiazepine **21**, respectively. IR spectra of compounds **18–21** exhibited new absorption bands at 3436–3105 cm^{-1} for the NH_2 group, 2201 and 2203 cm^{-1} for the CN group in compounds **18** and **20**, and 1700–1669 cm^{-1} for C=O groups in compounds **19–21**. ^{1}HNMR spectra of these compounds showed the disappearance of the signal specific for the $CH_{2\ \text{benzodiazepine}}$ group.

EXPERIMENTAL

Synthesis of Compounds 2 and 3: General Procedure

A mixture of compound **1** (0.01 mol, 2.36 g), benzylidenecyanothioacetamide (0.01 mol, 1.88 g), and piperidine (1 mL) was refluxed in dioxane (20 mL) for 4 h. On cooling, the formed precipitate was filtered off and crystallized to give compound **3**. The filtrate was poured into a mixture of water and HCl (50: 3 v/v), and the solid product was filtered off, washed with water, and crystallized to give compound **2** (cf. Scheme 1, Table I).

Synthesis of Compounds 4_{a-c}: General Procedure

A mixture of compound **2** (0.005 mol, 2.02 g); 0.005 mol of the appropriate halocompound; ethyl chloroacetate (0.54 mL), chloroacetonitrile (0.31 mL), or phenacyl bromide (0.99 g); and sodium acetate (0.005 mol, 0.41 gm) in ethanol (20 mL) was refluxed for 2 h. The precipitate that obtained on cooling was filtered off, washed with water, and crystallized from the appropirate solvent (cf. Scheme 1, Table I).

Synthesis of Compounds 5_{a-c}: Method A (General Procedure)

To a solution of the appropriate compound $\mathbf{4_{a-c}}$ (0.01 mol) in dioxane (20 mL), anhydrous potassium carbonate (3 g), and TBAB (0.003 g) were added. The reaction mixture was stirred for 5 h at 60°C until the completion of the reaction (TLC). The reaction mixture was filtered off, and the filtrate evaporated in vacuo. The residual solid was washed with water and crystallized from the appropriate solvent (cf. Scheme 1, Table I).

Synthesis of Compounds 5_{a-e}: Method B (General Procedure)

A mixture of anhydrous potassium carbonate (3 g); dry dioxane (30 mL); compound **2** (0.005 mol, 2.02 g); the appropirate halocompound; ethylchloroacetate (0.54 mL), chloroacetonitrile (0.31 mL), phenacyl bromide (0.99 g) chloroacetamide (0.46 g), or chloroacetanilide (0.85 g); and TBAB (0.003 g) was stirred for 5 hr at 60°C until the completion of the reaction (TLC). The reaction mixture was filtered off, and the filtrate evaporated in vacuo. The residual solid was washed with water and crystallized from the appropriate solvent (cf. Scheme 1, Table I).

Synthesis of Compounds 6 and 7: General Procedure

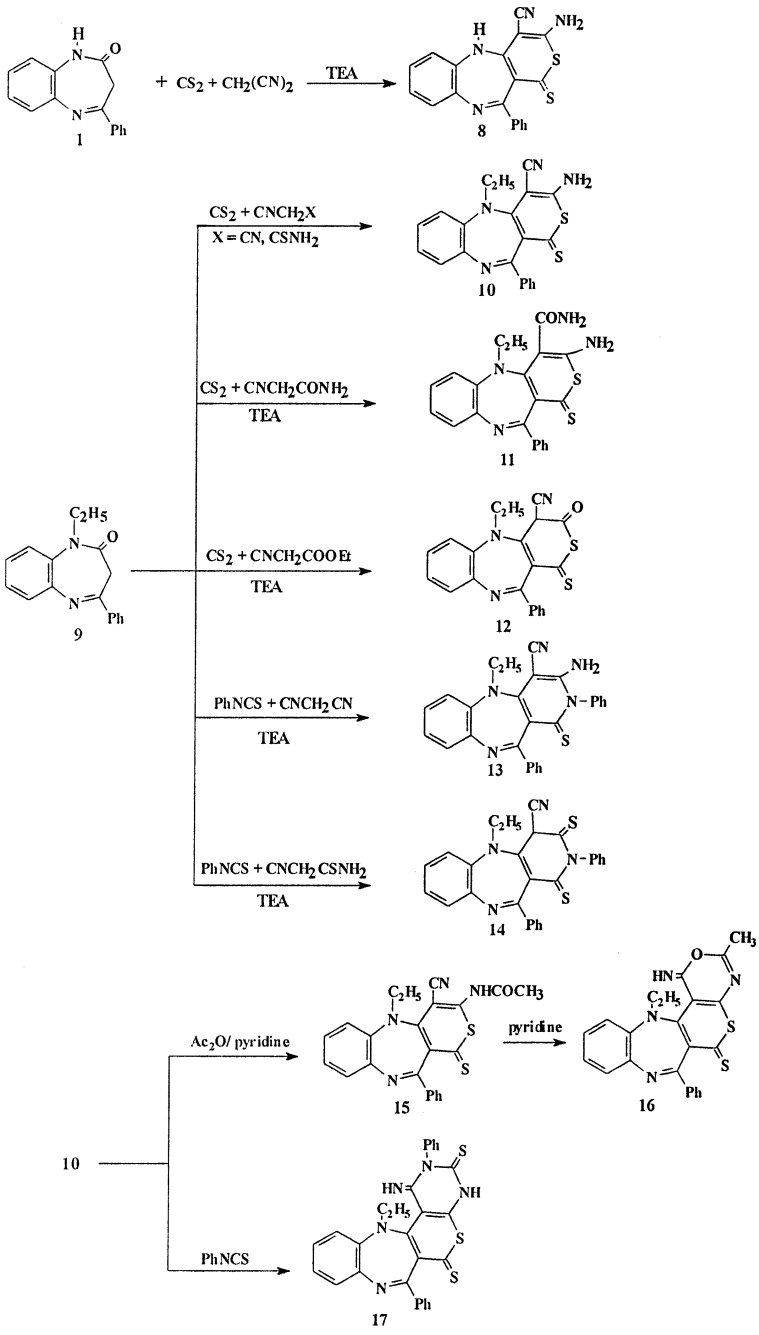
A mixture of anhydrous potassium carbonate (3 g), dry dioxane (30 mL), compound **2** (0.005 mol, 2.02 g), ethyl cyanoacetate (0.005 mol, 0.53 mL), and TBAB (0.003 g) was stirred for 4 h at 60°C until the completion of the reaction (TLC). The reaction mixture was filtered off, and the filtrate evaporated in vacuo. The residual solid was washed with water and crystallized to give compound **6**. The precipitate (carbonate layer) was dissolved in water (50 mL) and acidified by HCl, and the solid product was filtered off, washed with water, and crystallized to give compound **7** (cf. Scheme 1, Table I).

Synthesis of Compounds 8 and 10–14: General Procedure

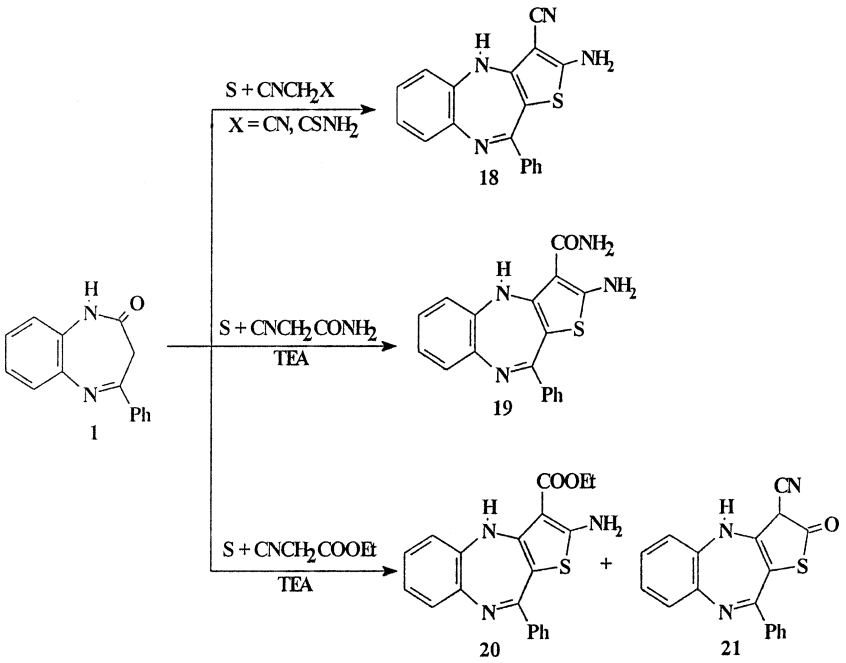
An equimolar amount (0.01 mole) of compound **1** (2.36 g) or compound **9** (2.64 g) in ethanol (20 mL), carbondisulfide (1.14 mL), or phenylisothiocyanate (1.3 mL), along with triethylamine (2 mL) were added. The reaction mixture was stirred at r. t. for 2 h, and the suitable active methylene, namely malononitrile (0.66 g), cyanothioacetamide (1 g), cyanoacetamide (0.8 g), ethyl cyanoacetate (1.1 mL), and dimethylformamide (2 mL), was added. The reaction mixture was refluxed for 4 h. After cooling, the reaction mixture was poured into water and HCl (100: 5 v/v). The solid product was filtered off, washed with water, and crystallized from the appropirate sovent (cf. Scheme 2, Table I)

Synthesis of Compound 15

A mixture of compound **10** (0.001 mol, 0.388 g), acetic anhydride (0.001 mol, 0.1 mL), and dry pyridine (20 mL) was refluxed for 1 h The reaction mixture was poured into ice-cold water. The separated solid was collected by filtration, washed with water, and crystallized (cf. Scheme 2, Table I).



SCHEME 2



SCHEME 3

Synthesis of Compound 16

A solution of compound **15** (0.001 mol, 0.43 g) in dry pyridine (20 mL) was refluxed for 5 h. The reaction mixture was poured into ice-cold water containing few drops of HCl. The separated solid was collected by filtration and crystallized (cf. Scheme 2, Table I).

Synthesis of Compound 17

A mixture of compound **10** (0.001 mol, 0.388 g), phenyl isothiocyanate (0.001 mol, 0.12 mL), and dry pyridine (20 mL) was refluxed for 10 h. The reaction mixture was poured into ice-cold water. The separated solid was collected by filtration and crystallized (cf. Scheme 2, Table I)

Synthesis of Compounds 18–21: General Procedure

To a stirred solution of compound **1** (0.01 mol, 2.36 g) in dry dioxane (20 mL), sulphur (0.01 mol, 0.32 g) and triethylamine (0.4 mL) were added. The reaction mixture was refluxed for 1 h, and then 0.01 mol of the appropirate active methylene, namely malononitrile (0.66 g),

cyanothioacetamide (1 g), cyanoacetamide (0.88 g), or ethyl cyanoacetate (1.13 mL), was added. The reaction mixture was refluxed for 4 h. After cooling, the solid precipitate was filtered off, washed with water, and crystallized from the appropirate solvent. The filtrate was evaporated in vacuo, and the residual solid was washed with water, filtered off, dried, and crystallized to give compound **20** (cf. Scheme 2, Table I).

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