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Note

Reactions of bis-2, 2-(3, 1-benzoxazin-4-one)phenylene (*m*-) with some nitrogen nucleophiles: Synthesis of new oxadiazole, triazole, pyrazole, pyrazolone and quinazolone derivatives

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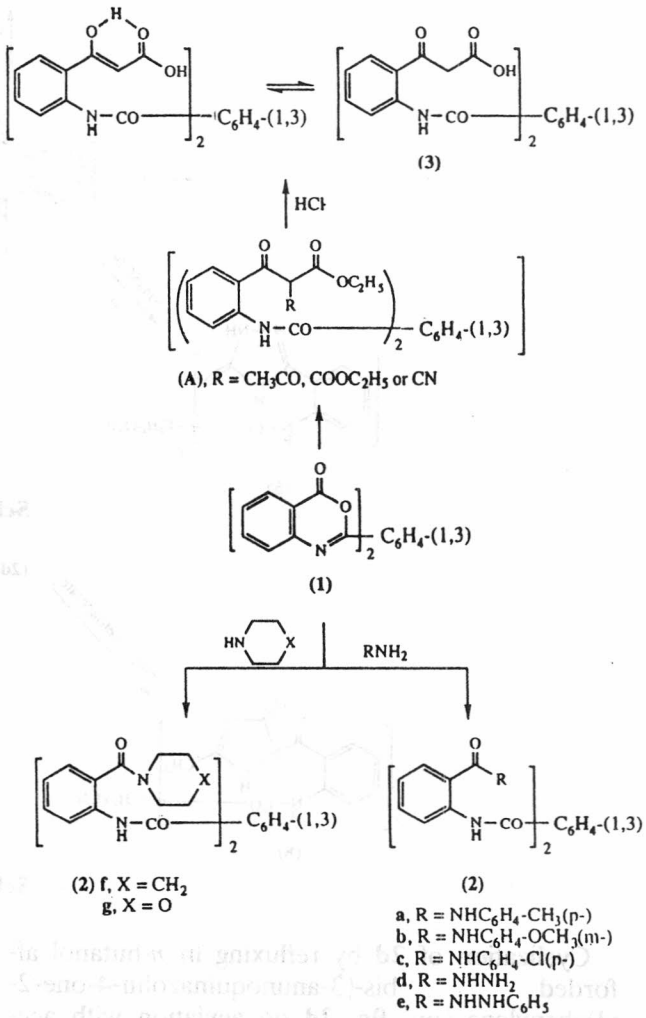
The bis-benzoxazinone **1** respond to nucleophilic attacks of either primary or secondary amines to give the benzamidoisophthalamide derivatives **2**. The hitherto unknown *N,N'*-bis(2, 2-benzoylhydrazine)isophthalamide **2d** in reaction with CS_2, NH_4SCN and/ or KSCN afford the corresponding oxadiazolethione **4**, triazolethione **5** and/ or the semi-carbazide derivative **6**, respectively. Reaction of **2d** with acetylacetone and/ or ethyl acetoacetate furnish the pyrazole **7** and/ or the pyrazolone derivative **8**, respectively. The Schiff's base **10b** and Schiff's base of the quinazolinone derivative **9c** are obtained when **2d** is condensed with *p*-anisaldehyde.

In continuation of our work on the preparation of biologically active compounds[1-3] heterocycles with azole moities, such as pyrazole,[4,5] triazole,[6,7] oxadiazole[8,9] and quinazolinone[10] derivatives were prepared. Study was also made on the susceptibility of new benzoxazinones to ring-opening reaction under the influence of both nitrogen and carbon nucleophiles.

The aminolysis of bis-benzoxazinone **1** with primary amines, such as, *p*-toludine, *m*-anisidine and *p*-chloroaniline, hydrazine hydrate and phenyl hydrazine in ethanol at reflux gave the corresponding *N,N'*-bis-2,2[*N''*-aryl/amino or aminophenyl)benzamide]isophthalamides **2a-e** (Scheme I). Similarly the reaction of **1** with secondary amines namely, piperidine and/ or morpholine provided the expected isophthalamide derivatives **2f** and **g** (Scheme I).

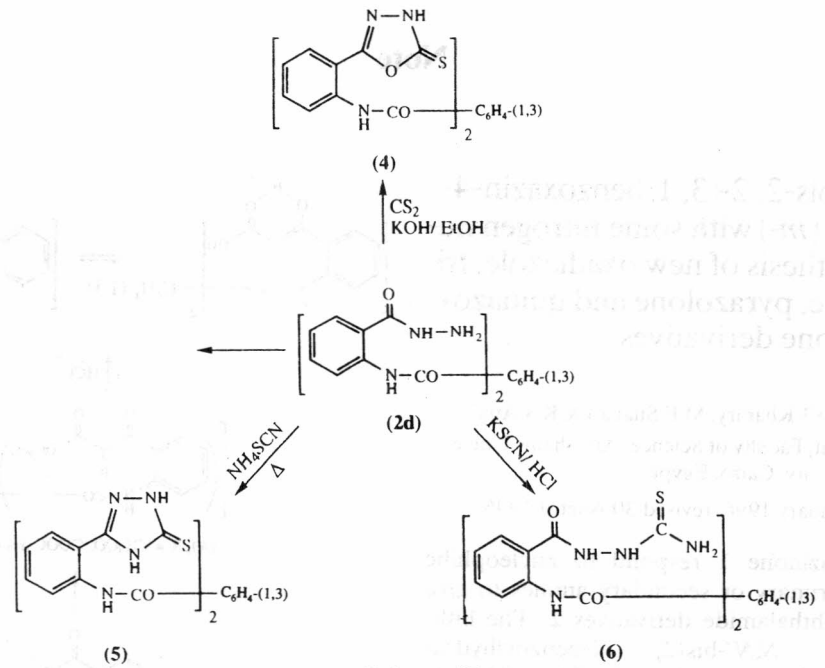
As reported in a previous study,[11,12] benzoxazinone **1**, reacts with ethyl acetoacetate, diethyl malonate and/ or ethyl cyanoacetate in pyridine at reflux to give one and the same product N, N'-bis-(2, 2-benzoylacetic)isophthalamide **3** (Scheme I).



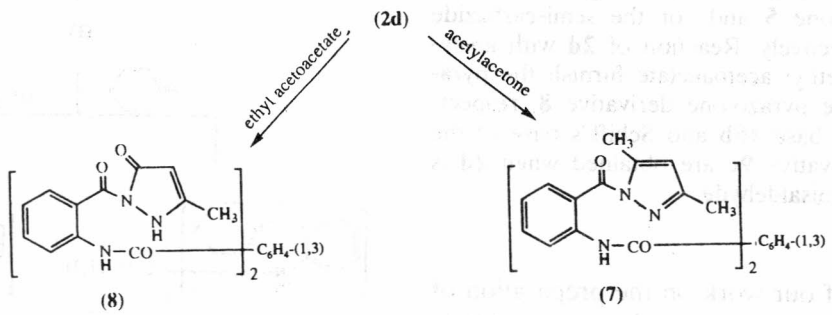
Scheme I

Condensation of hydrazide **2d** with carbon disulphide in ethanolic KOH afforded *N,N'*-bis-[2, 2-(1', 3', 4'-oxadiazolin-2'-thion-5'-yl)phenyl]isophthalamide **4** (Scheme II) while on fusion with ammonium thiocyanate *N, N'*-bis[2, 2-(1', 2', 4'-triazolin-5'-thione-3'-yl)phenyl]isophthalamide **5** was obtained (Scheme II). On the other hand, treatment of **2d** with potassium thiocyanate in acidic medium yielded the thiosemicarbazide derivative **6** (Scheme II).

Condensation of **2d** with acetylacetone and/ or ethyl acetoacetate afforded the pyrazole derivative **7** and pyrazolone derivative **8** respectively (Scheme III).

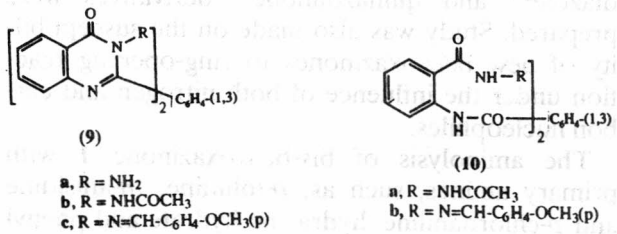


Scheme II



Scheme III

Cyclization of **2d** by refluxing in *n*-butanol afforded bis-(3-aminoquinazolin-4-one-2-yl)phenylene (*m*-) **9a**. **2d** on acylation with acetylchloride gave mainly the N-acylated derivative **10a** beside bis-(3-*N*-acetylaminoquinazolin-4-one)phenylene (*m*-) **9b** in low yield. Furthermore, condensation of **2d** with *p*-anisaldehyde provided the corresponding Schiff's base **10b**, beside the corresponding Schiff's base of the 3-aminoquinazolinone derivative **9c**.



Experimental Section

Melting points reported are uncorrected. IR spectra (ν_{max} in cm^{-1}) were recorded on a Pye Unicam Sp 1200 spectrophotometer using KBr Wafer technique, ^1H PMR spectra on a varian Gimine 200 MHz, Brucker Ac-200 MHz using TMS as an internal standard (chemical shifts in δ, ppm) and mass spectra using HP Model MS-5988 at electron energy 70 ev.

***N, N'*-Bis[2, 2-(arylbenzamide/benzhydrazides and/ or benzoylimine)]isophthalamides 2a-g: General procedure.** A mixture of bis-(3, 1-benzoxazin-4-one-2-yl)phenylene (*m*-)[13] **1** (0.01 mole) and primary amines, hydrazines[5] and/ or secondary amines, namely, *p*-toludine, *m*-anisidine, *p*-chloroaniline, hydrazine hydrate, phenyl hydrazine, piperidine and/ or morpholine (0.02 mol), respectively, in ethanol (50 mL) was refluxed in a period 2-10 h. The solid separated during reflux or after concentration of the solvent was collected

Table I—Characterization data of compounds prepared

Compd.	m.p. (°C)	Yield (%) (solvent)	Mol. formula (Mol. wt.)	Calcd. (Found) (%) C	H	N
2a	183-85	52 (E)	$C_{36}H_{30}N_4O_4$ (582.66)	74.21 (74.39	5.19 4.93	9.62 9.66)
2b	275-78	78 (M)	$C_{36}H_{30}N_4O_6$ (614.66)	70.35 (70.56	4.92 5.01	9.12 8.98)
2c	252-53	82 (*n*-Bu)	$C_{34}H_{24}Cl_2N_4O_4$ (623.49)	65.55 (65.41	3.88 3.72	8.99 9.12)
2d	296-98	95 (E)	$C_{22}H_{20}N_6O_4$ (432.44)	61.12 (60.90	4.66 4.54	19.43 19.67)
2e	240-43	92 (*n*-Bu)	$C_{34}H_{28}N_6O_4$ (584.69)	69.84 (69.59	4.83 4.60	14.37 14.22)
2f	150-52	45 (E)	$C_{32}H_{34}N_4O_4$ (538.65)	71.36 (71.60	6.36 6.41	10.40 10.62)
2g	191-93	66 (E)	$C_{30}H_{30}N_4O_6$ (542.59)	66.40 (66.30	5.57 5.87	10.33 10.45)
3	277-78	60 (T-E)	$C_{26}H_{20}N_2O_8$ (488.45)	63.93 (63.62	4.12 4.15	5.73 5.86)
4	262-63	40 (T-E)	$C_{24}H_{16}N_6O_4S_2$ (516.56)	56.02 (55.88	2.74 2.61	16.33 16.54)
5	256-59	82 (*n*-Bu)	$C_{24}H_{18}N_8O_2S_2$ (514.56)	56.02 (56.08	3.53 3.44	21.78 21.97)
6	278-79	65 (M)	$C_{24}H_{22}N_8O_4S_2$ (550.62)	52.35 (52.55	4.03 3.80	20.35 20.60)
7	293-96	15 (M)	$C_{32}H_{28}N_6O_4$ (560.61)	68.85 (68.82	5.03 4.96	14.99 15.12)
8	308-10	22 (M)	$C_{30}H_{24}N_6O_4$ (564.56)	63.83 (63.54	4.28 4.18	14.89 15.01)
9a	219-22	95 (EA)	$C_{22}H_{16}N_6O_2$ (396.40)	66.66 (66.54	4.07 3.91	21.20 21.50)
9b	307-09	15 (M)	$C_{26}H_{20}N_6O_4$ (480.49)	64.99 (65.20	5.06 5.12	16.79 16.88)
9c	253.55	45 (T-E)	$C_{38}H_{28}N_6O_4$ (632.34)	72.14 (71.81	4.46 4.42	13.28 13.20)
10a	258-60	35 (T-E)	$C_{26}H_{24}N_6O_6$ (516.52)	60.46 (60.65	4.68 4.90	16.27 16.01)
10b	247-48	33 (M)	$C_{38}H_{32}N_6O_6$ (668.34)	68.29 (68.38	4.79 4.60	12.57 12.79)

E = Ethanol, T = Toluene, M = Methanol, *n* = Bu = *n*-Butanol, EA = Ethyl acetate.

and crystallized from suitable solvent to give **2a-g**. IR: 3000-3450 cm^{-1} (br ν NH), 1650-1700 cm^{-1} (C=O); PMR (DMSO-d_6) of **2a**: δ 2.36(s, 6H, 2×CH_3), centered at 8.00 (m, 20H, Ar-H), 10.62(s, 1H, NH), 11.60(s, 1H, NH), 11.84(s, 1H, NH), 11.93(s, 1H, NH); **2f**: δ1.21 (m, 12H, 2×3(CH_2), 4.35(m, 8H, 2×N (CH_2)$_2$), centered at 8.11 (m, 12H, Ar-H), 11.61 (s, 2H, 2×NH); **2g**: δ 3.82(m, 8H, 2×O(CH_2)$_2$), centered at 8.35 (m, 12H, Ar-H), 11.75(s, 1H, NH), 11.83(s, 1H, NH); MS (m/z%) of **2b**: M^+ (614, 25%), 368 (5%), 149 (100%), 122 (3%), 119 (22%); **2c**: $[M-1]^+$ (622, 3%), 388 : 386 (1:3.15%), 551(12%), 129 : 127 (1 : 3, 100%), 120 (12%), 92 (13%); **2e**: $[M+1]^+$ (586, 7%), 548 (6%), 366 (4%), 268 (29%), 252 (62%), 149 (100%), 119 (51%), 108 (57%).

***N, N'*-Bis(2, 2-benzoylacetic)isophthalamide (3).** A mixture of **1** (0.01 mole) and active methylene compounds, namely, ethyl acetoacetate, diethyl malonate and/ or ethyl cyanoacetate (0.02 mole) in pyridine (10 mL) was refluxed for 10 h. The reaction mixture was poured onto crushed ice and acidified with cold dil. HCl (50 mL), 10%). The solid separated was collected, washed with water (2 × 10 mL), dried and crystallized to give **3** as colourless crystals. IR: 3500-2750 (br, OH), 1700-1680 cm^{-1} (C=O); PMR (DMSO-d_6) : δ 3.80 (s_{br}, 2H, 2×NH), 7.10(m, 4H, 2×C*H*=(Ċ−O*H*), centered at 8.40 (m, 12H, Ar-H) and 12.2 (s, 2H, 2×COOH); MS (m/z%) : M^+ (488, 16%), 398 (5%), 370 (50%), 342 (70%), 222 (3%), 119 (5%).

***N, N'*-Bis[2, 2-(1', 3', 4'-oxadiazolin-2'-thione-5'-yl)phenyl]isophthalamide 4.** To a suspension of hydrazide **2d** (0.01 mole) in ethanol (50 mL) containing KOH (1 g), carbon disulphide (20 mL) was added dropwise at room temperature within 30 min. The reaction mixture was refluxed on a water-bath for 4 h. The solvent was removed and the residue neutralized with conc. HCl (20 mL). The solid separated was filtered, washed with water (2 × 10 mL), dried and crystallized to give **4** as colourless crystals. IR: 3350 (br, νNH), 1680 (C=O), 1170 cm^{-1} (C=S); MS (m/z%) : M^+ (516, 9%), 192 (8%), 149 (100%), 119 (50%), 101 (15%).

***N, N'*-Bis[2, 2-(1', 2', 4'-triazolin-5'-thione-3'-yl)phenyl]isophthalamide 5.** A mixture of hydrazide **2d** (1 g) and ammoniumthiocyanate (2 g) was heated at 210°C for an hour. After cooling solid mass was triturated with warm water and the solid suspended was collected, dried and crystallized to give **5** as colourless crystals. IR: 3420, 3210 cm^{-1} (br, NH), 1670 (C=O), 1140 cm^{-1} (C=S): MS (m/z%) : $[M+1]^+$ (515, 10%), 396 (32%), 395 (100%), 366 (36%), 119 (73%), 100 (25%), 92 (35%).

***N* ,*N'*-Bis[2, 2-(thiosemicarbazide-4'-yl)benzoyl] isophthalamide 6.** A mixture of **2d** (0.01 mole), potassium thiocyanate (0.02 mole) and conc. HCl (2 mL) in ethanol (50 mL) was refluxed for 8 h. The solid produced after concentration of the solvent was filtered and crystallized to give **6** as colourless crystals. IR: 3425, 3340 (br, NH), 1690, 1670 (C=O), 1150 cm^{-1}) (C=S); MS (m/z%): M^+ (550, 15%), 396 (5%), 149 (100%), 119 (40%).

***N, N'*-Bis[2, 2-(3', 5'-dimethylpyrazole and/ or 3'-methyl-5-'pyrazolone-1'-yl)benzoyl]-isophthalamides 7 and 8.** A mixture of **2d** (0.01 mole) and active methylene compounds, namely, acetylacetone and/ or ethyl acetoacetate (0.02 mole) in ethanol (50 mL) was heated on water-bath for 2 h. The solid separated was collected, washed with pet. ether (40-60°C) (3 × 15 mL) and crystallized to give **7** and/ or **8** as colourless crystals. IR : 3420, 3280 (br, NH), 1700, 1685, 1680 cm^{-1} (C=O); PMR (DMSO-d_6) of **7**: δ 2.22 (s, 12H, 4 × CH_3), 5.82 (s_{br}, 2H, 2 × NH), 5.95 (s, 2H, 2 × CH) centered at 8.20 (m, 12H, Ar-H); **8**: δ2.30 (s, 6H, 2 × CH_3), 5.45 (s, 2H, 2 × CH), 5.92 (s_{br}, 2H, 2 × NH) centered at 8.40 (m, 14H, Ar-H and 2 × NH); MS (m/z%) of **8**: M^+ not observed, 396 (73%), 395 (100%) 97 (10%), 69 (13%).

Bis-(3-aminoquinazolin-4-one-2-yl)phenylene (*m*-) (9a). A solution of hydrazide **2d** (1 g) in *n*-butanol (30 mL) was refluxed for 30 h. The solid separated was collected and crystallized to give **9a** s yellow crystals. IR: 3400, 3180 (NH), 1690 cm^{-1} (C=O); PMR (DMSO-d_6) : δ 5.75 (br, 4H, 2 × NH_2), centered at 8.00 (m, 12H, Ar-H); MS (m/z%): M^+ (396, 75%), 380 (80%), 366 (75%), 149(45%), 119(60%).

***N, N'*-Bis[2, 2-(*N*-acetyl)benzoylhydrazine]isophthalamide 10a and bis-(3-N-acetamidoquinazolin-4-one-2-yl)phenylene (m-) 9b.** A mixture of hydrazide **2d** (1 g) and acetyl chloride (20 mL) was heated on a water-bath for 3 h. The solution was then added to crushed ice, and the solid separated was collected, washed with water (2 × 10 mL), dried and subjected to fractional crystallization (toluene-ethanol mixture) to give **9b** and **10a** as faint yellow crystals. IR : 3460, 3340 (br, NH), 1685, 1670 cm^{-1} (C=O); MS (m/z%) of **9b**: $[M+2]^+$ (482, 6%), M^+ (480, 7%), 438 (3%), 394 (13%), 366 (17%), 119 (73%), 72 (28%), 55 (100%); **10a**: M^+ (516, 9%), 268 (100%), 192 (15%), 162 (65%), 149 (70%), 144 (25%), 119 (33%).

Schiff's bases 10b and 9c. A mixture of **2d** (0.01 mole) and *p*-anisaldehyde (0.02 mole) in ethanol (50 mL) was refluxed for 2 h. The solid separated during reflux was filtered and crystallized to give **10b** as colourless crystals. The filtrate was concentrated till dryness and the residue crystallized to give **9c** as yellow crystals. IR of **9c** : 1705 cm^{-1} (C=O); **10b**: 3500 (br, NH), 1690, 1680 cm^{-1} (C=O); MS (m/z%) of **10b**: M^+ (668, 3%), 400 (7%), 266 (100%), 222 (22%), 149 (5%), 120 (16%), 119 (75%).

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