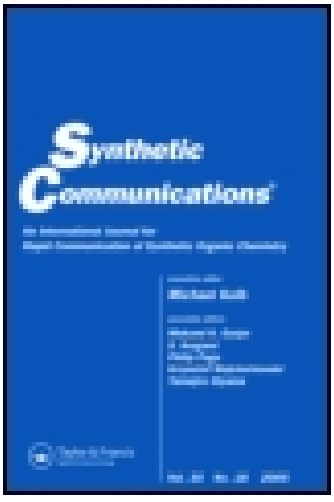

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Antibacterial Activities of New (E) 2-Cyano-3-(3′,4′-dimethoxyphenyl)-2-propenoyla Derivatives

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Antibacterial Activities of New (E) 2-Cyano-3-(3′,4′-dimethoxyphenyl)-2-propenoylamide Derivatives

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Abstract: (E) 2-Cyano-3-(3′,4′-dimethoxyphenyl)-2-propenoyl chloride (**2**) underwent mono- and binucleophilic displacement with hydrazines, amines, ureas, and aromatic bifunction amines to give new 2-propenoyl hydrazines (**4** and **5**), 2-propenoylamide (**6**, **7**, **12**, **13**, **15**, **17**, **19**, **21**), and 2-thiol propenoate (**22**–**24**). Some of these products were cyclized to give novel heterocyclic derivatives (**8**, **10**, **14**, **16**, and **20**).

Keywords: benzimidazole, benzoxazine, 1,3,5-oxadiazine-2,4-dione

INTRODUCTION

In the present study, we continue our investigation of the 2-propenoyl chloride derivative's chemistry.[1–4] Synthesis and reactivity of new (E) 2-cyano-3-(3′,4′-dimethoxyphenyl)-2-propenoyl chloride (**2**) toward some aliphatic and/or aromatic nitrogen, oxygen and sulfur nucleophilic reagents are the main targets in this report, and we aim to produce some new derivatives and study their biological activities.

RESULTS AND DISCUSSION

Condensation of acid chloride (**2**) with hydrazine hydrate afforded a mixture of the 3,4-dimethoxybenzaldehyde azine[5] (**3**) and N,N′-dipropenoyl

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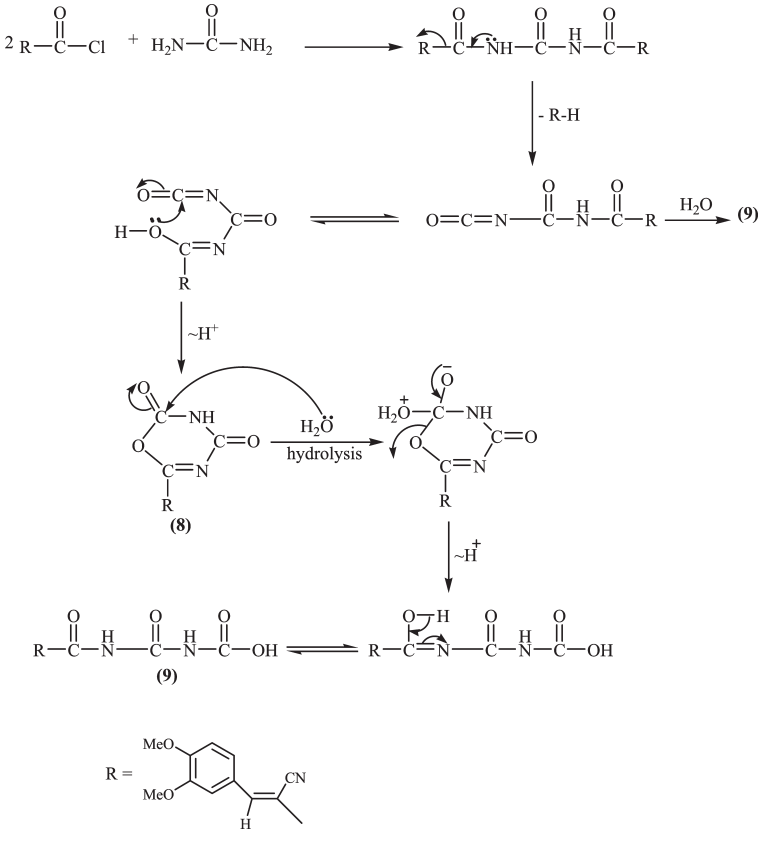
hydrazine derivative (**4**), whereas with benzoylhydrazine, the expected *N*-benzoyl-*N*′-propenoyl hydrazine derivative (**5**) was obtained. On the other hand, reaction of (**2**) with p-anisidine yielded the corresponding amide (**6**) (Scheme 1). Treatment of **2** with ethanol amine gave the unexpected N,N-dipropenoyl ethanol amine (**7**) (Scheme 1).

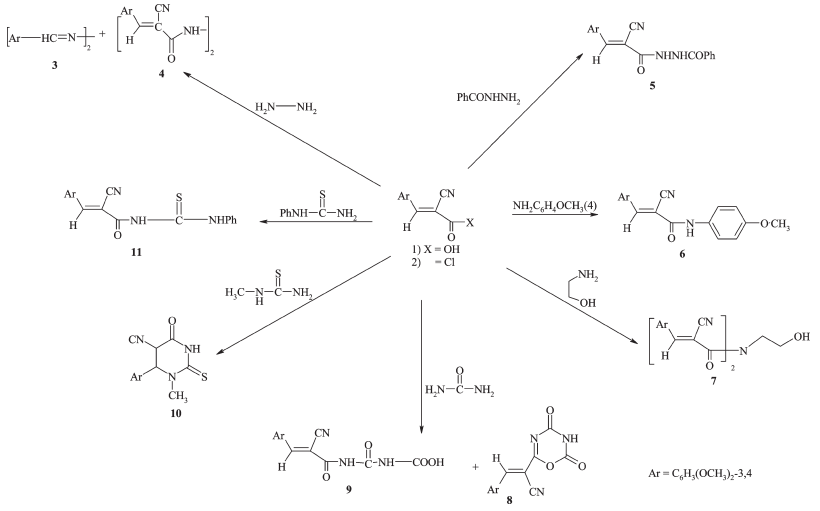
Condensation of **2** with urea produced a mixture of the unexpected 1,3,5-oxadiazine-2,4-dione (**8**) and N-carboxy N′-[2- cyano -3 (3′,4′-dimethoxyphenyl)-2-propenoyl]urea (**9**) (Scheme 1), which might be formed according to the following mechanism:



With methylthiourea and/or phenylthiourea, acid chloride (**2**) condensed to give the probable pyrimidine derivative (**10**) and/or the thiourea derivative (**11**) (Scheme 1).

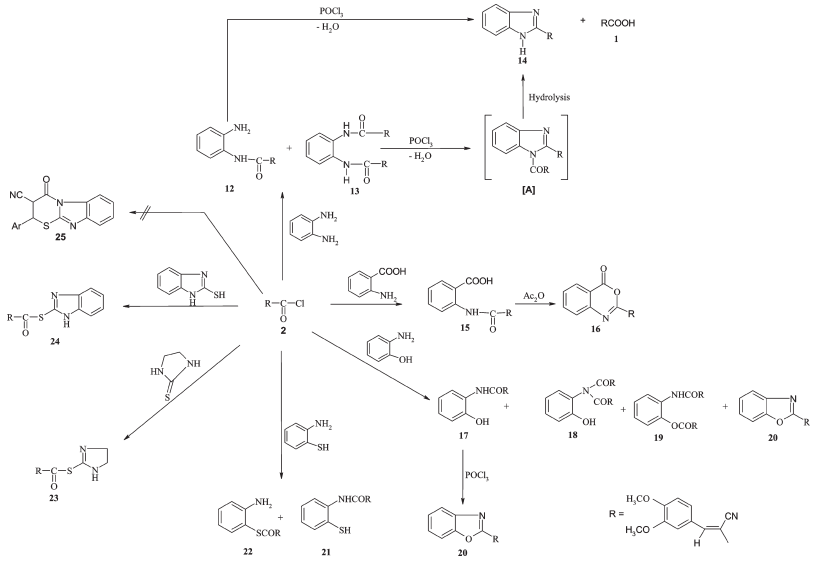
Furthermore, treatment of acid chloride (**2**) with bifunction aromatic compounds, such as o-phenylenediamine, o-aminophenol, and/or o-amino-thiophenol, produced varieties of mono- and bisubstituted derivatives as shown in Scheme 2.

With o-phenylenediamine (1:1 mol), acid chloride (**2**) gave a mixture of monosubstituted derivative (**12**) and N,N′-disubstituted derivative (**13**),



Scheme 1.

whereas at 1:2 mol, only the disubstituted derivative (**13**) was obtained in fairly good yield (Scheme 2). Treatment of both **12** and **13** with $POCl_3$ yielded the same benzimidazole derivative (**14**), via the normal cyclodehydration[6] of **12** or dehydration with subsequent hydrolysis of the intermediate [A] to give the acid (**1**) as shown in Scheme 2.



Scheme 2.

Condensation of **2** with anthranilic acid yielded the N-propenoyl anthranilic acid derivative (**15**), which upon treatment with Ac_2O cyclized to the benzoxazinone derivative (**16**) (Scheme 2).

Condensation of **2** with o-aminophenol gave a surprising mixture of products: N-propenoyl derivative (**17**), N,N-dipropenoyl derivative (**18**), N-propenoyl-O-propenoyl derivative (**19**), and the benzoxazole derivative (**20**) (Scheme 2). Formation of benzoxazole derivative (**20**) was also supported by dehydration of **17** with $POCl_3$ (Scheme 2). On the other hand, (N) vs (S) substitution was confirmed by condensation of (**2**) with o-aminothiophenol to give a mixture of N-propenoyl derivative (**21**) (minor yield) and S-propenoyl derivative (**22**) (Scheme 2).

In contrast to the results of Britsun,[7,8] acid chloride (**2**) reacted with 2-imidazolidinethione and/or 2-benzimidazolthiol in different conditions to give only the S-substituted derivatives (**23**, **24**) rather than the thiazino [3,2-a]benzimidazole derivatives (**25**) (Scheme 2).

The structure of all products (**2**–**24**) was confirmed by elemental analysis, (Table 1) and IR, ^{1}HNMR, and MS spectroscopy (Tables 2 and 3).

Biological Activity

The recent importance of 2-propenoyl amides,[9] 2-propenoates,[10,11] pyrimidines,[12–14] benzimidazoles,[15–17] benzoxazine,[18] benzoxazoles,[15,17,19] and oxadiazine[20] derivatives as biologically and pharmacologically active compounds makes them worthy of synthesis to obtain new structures of potentially enhanced potency.

Experimental Determination of Biological Activity

The antibacterial activity of 14 synthesized products were determined using hole plate and filter-paper disc method.[21] The tested compounds (100 μg) were loaded on Whatman No. 1 filter-paper discs in sterile conditions. The discs were evaporated to dryness; after that, the discs were placed on the surface of nutrient agar media inoculated with the tested organisms. The plates were incubated for 2 h in the refrigerator, then incubated for 24 h at 37°C. A variety of species of gram-positive and gram-negative bacteria such as Bacillus subtilis, Staphylococcus, Escherichia coli, and Pseudomonas aurignosa were used. The inhibition zones were measured in mm. The results are summarized in Table 4.

EXPERIMENTAL

Melting points are uncorrected. IR spectra were recorded on a Pye Unicam SP 1200 spectrophotometer using the KBr wafer technique. ^{1}H NMR spectra were

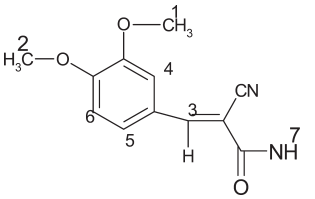
Table 1. Physical data of the synthesized compounds

Comp. no.	Mp (°C)	Yield (%)	Molecular formula	Molecular weight	Analysis calc. (found)		
					C	H	N
2	138–140	95	$C_{12}H_{10}ClNO_3$	251.66	57.27 (57.07)	4.01 (3.98)	5.57 (5.54)
4	250–252	40	$C_{24}H_{22}N_4O_6$	462.44	62.28 (62.25)	4.79 (4.77)	12.11 (12.09)
5	182–184	50	$C_{19}H_{17}N_3O_4$	351.34	64.95 (64.92)	4.87 (4.83)	11.96 (11.94)
6	180–182	70	$C_{19}H_{18}N_2O_4$	338.34	67.45 (67.08)	5.36 (5.32)	8.28 (8.19)
7	220–222	30	$C_{26}H_{25}N_3O_7$	491.25	63.52 (63.29)	5.13 (5.10)	8.56 (8.52)
8	200–202	65	$C_{14}H_{11}N_3O_5$	301.13	55.79 (55.60)	3.68 (3.62)	13.96 (13.89)
9	200–202	12	$C_{14}H_{13}N_3O_6$	319.14	52.65 (52.60)	4.11 (4.02)	13.17 (12.95)
10	188–190	50	$C_{14}H_{15}N_3O_3S$	305.20	55.10 (55.07)	4.95 (4.89)	13.77 (13.70)
11	142–144	50	$C_{19}H_{17}N_3O_3S$	367.41	62.11 (62.07)	4.66 (4.56)	11.44 (11.42)
12	150–152	35	$C_{18}H_{17}N_3O_3$	323.33	66.87 (66.72)	5.30 (5.27)	13.00 (12.89)
13	218–220	60	$C_{30}H_{26}N_4O_6$	538.53	66.91 (66.72)	4.86 (4.81)	10.40 (10.33)
14	224–226	92	$C_{18}H_{15}N_3O_2$	305.32	70.81 (70.72)	4.95 (4.90)	13.76 (13.72)
15	256	70	$C_{19}H_{16}N_2O_5$	352.33	64.75 (64.71)	4.57 (4.52)	7.95 (7.92)
16	226–228	88	$C_{19}H_{14}N_2O_4$	334.32	68.26 (68.23)	4.22 (4.15)	8.38 (8.35)
17	190–192	44	$C_{18}H_{16}N_2O_4$	324.32	66.66 (66.59)	4.97 (4.91)	8.64 (8.61)
18	180–182	15	$C_{30}H_{25}N_3O_7$	539.52	66.79 (66.77)	4.67 (4.62)	7.79 (7.78)
19	190–192	16	$C_{30}H_{25}N_3O_7$	539.52	66.79 (66.69)	4.67 (4.60)	7.79 (7.69)
20	186–188	10	$C_{18}H_{14}N_2O_3$	306.33	70.52 (70.32)	4.61 (4.57)	9.15 (9.09)
21	208–210	15	$C_{18}H_{16}N_2O_3S$	340.38	63.52 (63.51)	4.73 (4.69)	8.23 (8.19)
22	220–222	75	$C_{18}H_{16}N_2O_3S$	340.38	63.52 (63.49)	4.73 (4.70)	8.23 (8.16)
23	156–158	50	$C_{15}H_{15}N_3O_3S$	317.35	76.77 (76.75)	4.76 (4.74)	13.24 (13.20)
24	160–162	60	$C_{19}H_{15}N_3O_3S$	365.40	62.45 (62.39)	4.13 (4.10)	11.50 (11.46)

Table 2. IR and mass spectral data of compounds prepared

Comp.	IR (cm^{-1}) OH, NH	C=O	C≡N	MS, m/z (abundance, %)
1	3000–3550 br	1685	2210	233$[M]^+$, (100), 216 (22.5), 188 (9.3), 189 (28), 162 (12.7), 128 (10.3), 145 (11), 119 (8.5), 103 (15.4)
2	—	1734	2219	—
3	—	—	—	—
4	3383	1631	2210	462 $[M]^{+\cdot}$ (7.5), 231 (40.2), 216 (100), 162 (11.28), 119 (7.5)
5	3265	1692, 1660	2213	—
6	3358	1676	2204	—
7	3420	1794, 1722	2215	$[M]^{+\cdot}$ not detected, 446 (33), 233 (27), 216 (100), 188 (17.7)
8	3424	1753, 1709	2210	301 $[M]^{+\cdot}$ (8.7), 285 (20), 259 (100), 232 (31.7), 217 (28), 189 (20)
9	3100–3600 br	1660, 1690	2212	318 $[M^{+\cdot}-1]$ (22.6), 301 (10), 259 (80), 216 (100), 188 (26.2)
10	3195	1731	2262	—
11	3319	1681	2215	367 $[M]^{+\cdot}$ (5.9), 308 (42.5), 231 (22.2), 151 (20.3), 135 (15)
12	3359–3315	1681	2204	—
13	3405	1690	2202	—
14	3290	—	2227	305 $[M]^{+\cdot}$ (50), 304 (100), 188 (20), 116 (32), 216 (14), 91 (12)
15	3400–2638 br	1683	2203	—
16	—	1767	2220	334 $[M]^{+\cdot}$ (100), 291 (26.9), 265 (27.1), 260 (9.5), 216 (8.9), 188 (6.3)
17	3379–3284	1665	2205	324 $[M]^{+\cdot}$ (27.3), 216 (100), 188 (13)
18	3350	1793, 1725	2217	539 $[M]^{+\cdot}$ (17.41), 306 (32.9), 216 (100), 188 (11.6)
19	3240	1710, 1695	2212	539 $[M]^{+\cdot}$ (10.2), 538 $[M^{+\cdot}-1]$ (100), 307 (23.4), 231 (25.4), 188 (13.2)
20	—	—	2220	306 $[M^{+\cdot}]$ (15.2), 290 (10.8), 214 (82.0), 74 (52), 188 (100)
21	3324	1682	2201	340 $[M^{+\cdot}]$ (100), 188 (64.9), 152 (33), 216 (16.5), 109 (30.9)
22	3378, 3298	1687	2201	340 $[M^{+\cdot}]$ (10.9), 322 (29.8), 296 (10.1), 216 (100), 188 (18.3)
23	3246	1681	2222	317 $[M^{+\cdot}]$ (40.27), 232 (10.9), 216 (100), 188 (6.2)
24	3154	1689	2219	365 $[M^{+\cdot}]$ (30.8), 339 (28.5), 216 (27.7), 149 (26.2)

Table 3. ^{1}H NMR of prepared compounds



Comp. no.	C_1-H or C_2 H(s)	C_3-H(s)	C_4-H(s)	C_5-H(d)	C_6-H(d)	NH(s)	Others
2	3.97, 3.99	8.24	7.88	7.60 ($J = 28$)	7.01 ($J = 28$)	—	—
4	3.88, 3.81	8.17	7.70	7.62 ($J = 28$)	7.1 ($J = 28$)	10.56	—
6	3.88, 3.85	8.16	7.71	7.60 ($J = 28$)	7.17 ($J = 28$)	10.17	3.81 (s, OCH_3), 6.92 (d, $J = 21$, 2H), 7.55 (d, $J = 20$, 2H (anisyl protons)
10	3.79, 3.77	—	7.72	7.72 ($J = 28$)	7.31 ($J = 28$)	—	5.17 (dd, 2H), 3.74 (s, 3H, CH_3), 10.4 (s, 1H, NH)
12	3.98, 3.97	8.33	7.74	7.53 ($J = 28$)	6.95 ($J = 28$)	8.04	7.37 (d, 1H, $J = 28$), 7.12 (t, 1H), 6.87 (tt, 2H)

(*continued*)

Table 3. Continued

Comp. no.	C_1-H or C_2 H(s)	C_3-H(s)	C_4-H(s)	C_5-H(d)	C_6-H(d)	NH(s)	Others
13	3.97, 3.95	8.4	7.73	7.64 ($J = 28$)	6.9 ($J = 28$)	8.67	7.33 (dd, 2H, $J = 28$), 7.52 (dd, 2H, $J = 28$)
14	3.89	8.28	7.75	7.61 ($J = 28$)	6.92 ($J = 28$)	—	7.18–7.28 (m,5H), 4H Ar H & NH
15	3.87, 3.83	8.36	7.76	7.71 ($J = 28$)	7.21 ($J = 28$)	10.17	7.18 (t, 2H), 8.04 (d, 1H, $J = 25$), 8.64 (d, 1H, $J = 38$, 12.19 (s, 1H, COOH)
17	3.89, 3.83	8.18	7.72	7.67 ($J = 28$)	7.17 ($J = 28$)	10.18	6.85–7.38 (m, 4H, Ar-H), 9.17 (s, 1H, OH)
21	3.88, 3.82	8.22	7.69	7.65 ($J = 28$)	7.16 ($J = 28$)	10.11	7.28–7.53 (m, 4H, Ar), 6.7 (s, 1H, SH)
22	3.87, 3.81	8.22	7.70	7.65 ($J = 28$)	7.18 ($J = 28$)	—	7.28–7.54 (m, 4H, Ar-H), 10.11 (s_{br}, 2H, NH_2)
23	3.81, 3.82	8.25	7.76	7.70 ($J = 28$)	7.20 ($J = 28$)	—	3.5–3.65 (m, 4H, $2CH_2$), 7.98 (s_{br}, 1H, NH)

Table 4. Antibacterial activity of the tested compounds

Compound no.	*Staphylococcus*	*Escherichia coli*	*Pseudomonas aurignosa*	*Bacillus subtilis*
1	—	—	—	—
2	—	—	—	—
6	—	—	16	—
7	—	—	—	3.5
11	—	4.5	—	—
12	—	—	—	—
13	—	—	—	—
14	—	—	—	—
15	4.5	—	—	—
16	—	—	—	—
19	6.5	—	—	—
21	—	—	—	—
22	—	—	—	—
23	—	—	—	—

Note. Diameter of an inhibition zones is measured in mm.

determined on a Varian FT−200 and Brucker AC-200 MHz using TMS as internal standard. All chemical shifts (δ) are expressed in parts per million (ppm). All NH or OH protons disappeared by deuterium exchange (addition of D_2O). Mass spectra were determined on MP model MS-5988 and Shimadzu single-focusing mass spectrophotometer (70 eV) (Scheme 3).

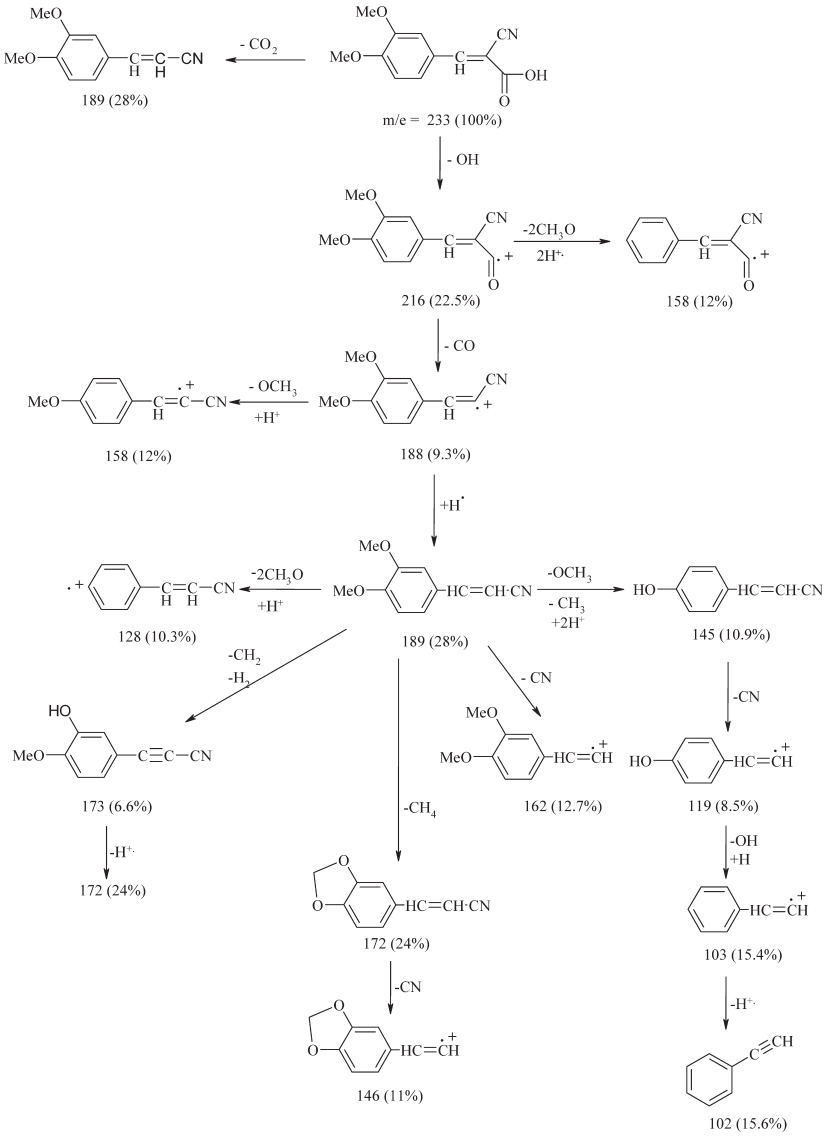
Synthesis of the Compounds

2-Cyano-3-(3′,4′-dimethoxyphenyl)-2-propenoyl chloride (**2**)

A mixture of acid[22] (**1**) (5 g) and thionyl chloride (20 mL) was heated in a water bath for 6 h. The excess thionyl chloride was distilled, and the residue was collected and washed with petroleum ether (40−60°C) to give (**2**) as yellow crystals.

3,4-Dimethoxybenzaldehydeazine (**3**) and N,N′-Bis[2-cyano-3-(3′,4′-dimeth-oxyphenyl)-2-propenoyl]-hydrazine (**4**)

A mixture of **2** (2.51 g, 0.01 mol), triethylamine (1.01 g, 0.01 mol), and hydrazine hydrate (0.5 g, 0.01 mol) in dry benzene (50 mL) was stirred at room temperature for 30 min. The solid formed was filtered, washed with warm water, dried, and crystallized from ethanol−dioxane mixture to give **4**



Scheme 3. Mass fragmentation of acid 1.

as pale yellow crystals. The benzene layer was concentrated, and the solid separated was collected and crystallized from petroleum ether (80–100°C) to give **3** as pale yellow crystals. Compound **3** was compared with an authentic sample,[5] which gave the same melting point, mixed melting point (mmp), and thin layer chromatography (TLC).

N-Benzoyl-N′-[2-cyano-3-(3′,4′-dimethoxyphenyl)-2-propenoylhydrazine (**5**)

A mixture of **2** (2.51 g, 0.01 mol), triethylamine (1.01 g, 0.01 mol), and benzoylhydrazine, (1.39 g, 0.01 mol) in dry benzene (50 mL) was stirred at room temperature for 30 min. The solid formed was filtered, washed with water, dried, and crystallized from a toluene–ethanol mixture to give **5** as grey crystals.

N-(p-Anisyl)2-cyano-3-(3′,4′-dimethoxyphenyl)-2-propenamide (**6**)

A mixture of **2** (2.51 g, 0.01 mol), triethylamine (1.01 g, 0.01 mol), and p-anisidine (1.23 g, 0.01 mol) in dry benzene (50 mL) was stirred at room temperature for 30 min. The solid formed was filtered, washed with warm water, dried, and crystallized from a toluene–ethanol mixture to give (**6**) as canary yellow crystals.

N,N-Bis-[2-cyano-3-(3′,4′-dimethoxyphenyl)-2-prpenoyl]-ethanolamine (**7**)

A mixture of **2** (2.51 g, 0.01 mol), triethylamine (1.01 g, 0.01 mol), and ethanolamine (0.61 g, 0.01 mol) in dry benzene (50 mL) was stirred at room temperature for 30 min. The solid separated was filtered, washed with warm water, dried, and crystallized from a toluene–ethanol mixture to give **7** as pale yellow crystals.

6-[1′-Cyano-2′-(3″,4″-dimethoxyphenyl)-1′-ethenyl]-(3H)-1,3,5-oxadiazin-2,4-dione (**8**) and N-Carboxy N′-[2-cyano -3(3′,4′-dimethoxyphenyl)-2-propenoyl] Urea (**9**).

A mixture of **2** (2.51 g, 0.01 mol), triethylamine (1.01 g, 0.01 mol), and urea (0.44 g, 0.01 mol) was refluxed in dioxane (50 mL) for 30 min. The reaction mixture was concentrated, and the solid formed was collected and crystallized from toluene to give **8** as yellow crystals. The mother liquor was poured on ice-cold water, and the residue was collected, dried, and crystallized from an ethanol–dioxane mixture to give (**9**) as colorless crystals.

5-Cyano-6-(3′,4′-dimethoxyphenyl)-1-methyl-5,6-dihydropyrimidine-4-one-2-thione (**10**)

A mixture of **2** (2.51 g, 0.01 mol), triethylamine (1.01 g, 0.01 mol), and methylthiourea (0.76 g, 0.01 mol) was refluxed in dioxane (40 mL) for 4 h. The reaction mixture was concentrated, and the solid formed was collected and crystallized from an ethanol–dioxane mixture to give **10** as yellow crystals.

N-[2-Cyano-3-(3′,4′-dimethoxyphenyl)-2-propenoyl]-N′-phenylthiourea (**11**)

A mixture of **2** (2.51 g, 0.01 mol), triethylamine (1.01 g, 0.01 mol), and phenylthiourea (1.38 g, 0.01 mol) was refluxed in dioxane (40 mL) for 4 h. The reaction mixture was concentrated, and the solid formed was collected and crystallized from an ethanol–dioxane mixture to give **11** as yellow crystals.

N-[2-Cyano-3-(3′,4′-dimethoxyphenyl)-2-propenoyl]-1,2-diaminobenzene (**12**) and N,N′-Bis-[2′-cyano-3′-(3″,4″-dimethoxyphenyl)-2′-propenoyl]-1,2-diaminobenzene (**13**)

Procedure 1

A mixture of **2** (2.51 g, 0.01 mol), triethylamine (1.01 g, 0.01 mol), and o-phenylenediamine (1.08 g, 0.01 mol) in dry benzene (50 mL) was stirred at room temperature for 45 min. The precipitate formed was filtered, washed with water, dried, and crystallized from toluene to give **13** as pale yellow crystals. The benzene layer was concentrated and the residue was collected and crystallized from a petroleum ether (80–100°C)–benzene mixture to give **12** as yellow crystals.

Procedure 2

A mixture of **2** (5.02 g, 0.02 mol), triethylamine (2.02 g, 0.02 mol), and o-phenylenediamine (1.08 g, 0.01 mol) in dry benzene (100 mL) was stirred at room temperature for 45 min. The precipitate formed was filtered, washed with water, dried, and crystallized from toluene to give **13** as pale yellow crystals.

2-[1′-Cyano-2′-(3″,4″-dimethoxyphenyl)-1′-ethenyl]-[1H]-benzimidazole (**14**) and 2-Cyano-3-(3′,4′-dimethoxyphenyl)-2-propenoic Acid (**1**)

A mixture of **12** and/or **13** (1 g) and phosphoryl chloride (10 mL) was heated on a water bath for 4 h. After cooling, the reaction mixture was poured onto crushed ice. The precipitate was filtered, washed with water, dried, and crystallized from toluene to give **14** as brown crystals. The insoluble residue from treatment of **13** was crystallized from ethanol to give **1** as yellow crystals.

2-N-[2-Cyano-3-(3′,4′-dimethoxyphenyl)-2-propenoyl]aminobenzoic Acid (**15**)

To a solution of anthranilic acid (1.37 g, 0.01 mol) in dry pyridine (30 mL), **2** (2.51 g, 0.01 mol) was added portionwise with stirring for 30 min. The reaction mixture was stirred for a further 30 min, then poured onto cold dil. HCL. The precipitate formed was filtered, washed with water, dried, and crystallized from toluene to give **15** as pale yellow crystals.

2-[1′-Cyano-2′-(3″,4″-dimethoxyphenyl)-1-ethenyl]-3,1-benzoxazin-4-one (**16**)

A mixture of **15** (3 g) and acetic anhydride (15 mL) was heated on a water bath for 2 h. After cooling, the precipitated was filtered, washed with dry petroleum-ether (40–60°C), dried, and crystallized from petroleum ether (80–100°C)–benzene mixture to give **16** as yellow crystals.

2-N-[2′-Cyano-3′-(3″,4″-dimethoxyphenyl)-2′-propenoyl] aminophenol (**17**), 2-N,N-Bis[2′-cyano-3′-(3″,4″-dimethoxyphenyl)-2′-propenoyl]-aminophenol (**18**), 2-N-[2′-Cyano-3′-(-3″,4″-dimethoxyphenyl)-2′-propenoyl]-aminophenyl]-2-cyano-3-(3′,4′-dimethoxyphenyl)-2-propenoate (**19**), and 2-[1′-cyano-2′-(3″,4″-dimethoxyphenyl)-1′-ethenyl]-benzoxazole (**20**)

A mixture of **2** (2.51 g, 0.01 mol), triethylamine (1.01 g, 0.01 mol), and *o*-aminophenol, (1.09 g, 0.01 mol) in dry benzene (50 mL) was stirred at room temperature for 30 min. The solid separated was filtered, washed with water, dried, and crystallized from an ethanol–dioxane mixture to give **17** as yellow crystals. The mother liquor was concentrated to dryness, and the residue was crystallized from petroleum ether (80–100°C) to give **18** as yellow crystals. The benzene layer was concentrated, and the residue was crystallized from petroleum ether (80–100°C)–benzene mixture to give **20** as a pale yellow crystals. The mother liquor was concentrated to give **19** as yellow crystals.

Conversion of 17 into 20

A mixture of **17** (0.5 g) and phosphoryl chloride (5 mL) was heated on a water bath for 2 h. After cooling, the crushed ice was added to the mixture and left overnight. The solid separated was collected, washed with water, dried, and crystallized from a petroleum ether (80–100°C)–benzene mixture to give **20** as pale yellow crystals, which were identified by mp, mmp, TLC, and spectral data with that obtained in the previous experiment.

2-N-[2′-Cyano-3′-(3″,4″-dimethoxyphenyl)-2′propenoyl]-aminothiophenol (**21**) and S-(2′-aminophenyl)2-cyano-3-(3′,4′-dimethoxyphenyl)-2-thiolpropenoate (**22**)

A mixture of **2** (2.51 g, 0.01 mol), triethylamine (1.01 g, 0.01 mol), and *o*-aminothiophenol (1.25 g, 0.01 mol) in dry benzene (50 mL) was stirred at room temperature for 30 min. The solid separated was filtered, washed with water, dried, and crystallized from a toluene–ethanol mixture to give **21** as yellow crystals. The benzene layer was concentrated and the residue was collected and crystallized from a petroleum ether (80–100°C)–benzene mixture to give **22** as pale yellow crystals.

S-[2′-Imidazolidin]2-cyano-3-(3′,4′-dimethoxyphenyl)-2-thiolpropenoate (**23**)

A mixture of **2** (2.51 g, 0.01 mol), triethylamine (1.01 g, 0.01 mol), and 2-imidazolidinthion, (1.02 g, 0.01 mol) was refluxed in dioxane (50 mL) for 4 h. The solvent was concentrated, and the solid precipitated was filtered and crystallized from ethanol to give **23** as brown crystals.

S-[2′-Benzimidazole]2-cyano-3-(3′,4′-dimethoxyphenyl)-2-thiolpropenoate (**24**)

Fusion of **2** (2.51 g, 0.01 mol), 2-benzimidazolethiol (1.5 g, 0.01 mol), and triethylamine (1.01 g, 0.01 mol) was heated at 140°C without solvent for 15 min. After cooling, the residue was triturated with warm water. The solid separated was filtered, dried, and crystallized from an ethanol–dioxane mixture to give **24** as yellow crystals. This reaction at room temperature and in dioxane at reflux gave no change.

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