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NITRILIMINE CYCLOADDITIONS ONTO PARTIALLY SATURATED FURO[3,4-*c*]THIENO[2,3-*d*]PYRAZOLES. A PROBLEM IN SITE SELECTIVITY

Gianluigi Broggini,[b] Luisa Garanti,[a]* Giorgio Molteni[a], and Gaetano Zecchi[b]

[a]Dipartimento di Chimica Organica e Industriale dell'Università and Centro CNR, Via Golgi 19, 20133, Milano, Italy
[b]Dipartimento di Scienze Chimiche, Fisiche e Matematiche, Università dell'Insubria, via Lucini 3, 22100 Como, Italy

Abstract - Partially saturated furo[3,4-*c*]thieno[2,3-*d*]pyrazoles (**7**-**10**) have been submitted to 1,3-dipolar cycloaddition with a variety of nitrilimines. The competitive formation of products due to the dipolar attack at different dipolarophilic sites has been observed. The experimental evidence is discussed by taking into account electronic features of the reactive species as well as their steric encumbrance.

In the course of our research programme on intramolecular nitrilimine cycloadditions onto heteroaromatic rings,[1,2] we synthesised a number of strained tricyclic pyrazolines, including furo[3,4-*c*]thieno[2,3-*d*]-pyrazoles (FTP). The latter were capable of further intermolecular cycloaddition due to the presence of the dipolarophilic C=C and C=N bonds. Double cycloaddition products were actually obtained, but the observed site-preference revealed somewhat puzzling. Aimed at a better understanding of the factors governing the discrimination between the two dipolarophilic functionalities, we undertook a systematic investigation on the behavior of nitrilimines (**4**-**6**) towards FTP (**7**-**10**) as a function of the electron-withdrawing or -donating character of substituents R and R^1.

RESULTS AND DISCUSSION

As suitable precursors of the desired nitrilimines (**4**-**6**), we synthesised the hydrazonoyl chlorides (**1**-**3**) by coupling of the appropriate diazonium salts on benzyl 2-chloro-3-oxobutanoate (Scheme 1). In order to promote the *in situ* generation of the above-mentioned nitrilimines, base treatment of **1**-**3** was accomplished with a two-fold molar excess of silver carbonate in dry dioxane at 75°C in the presence of

Scheme 1

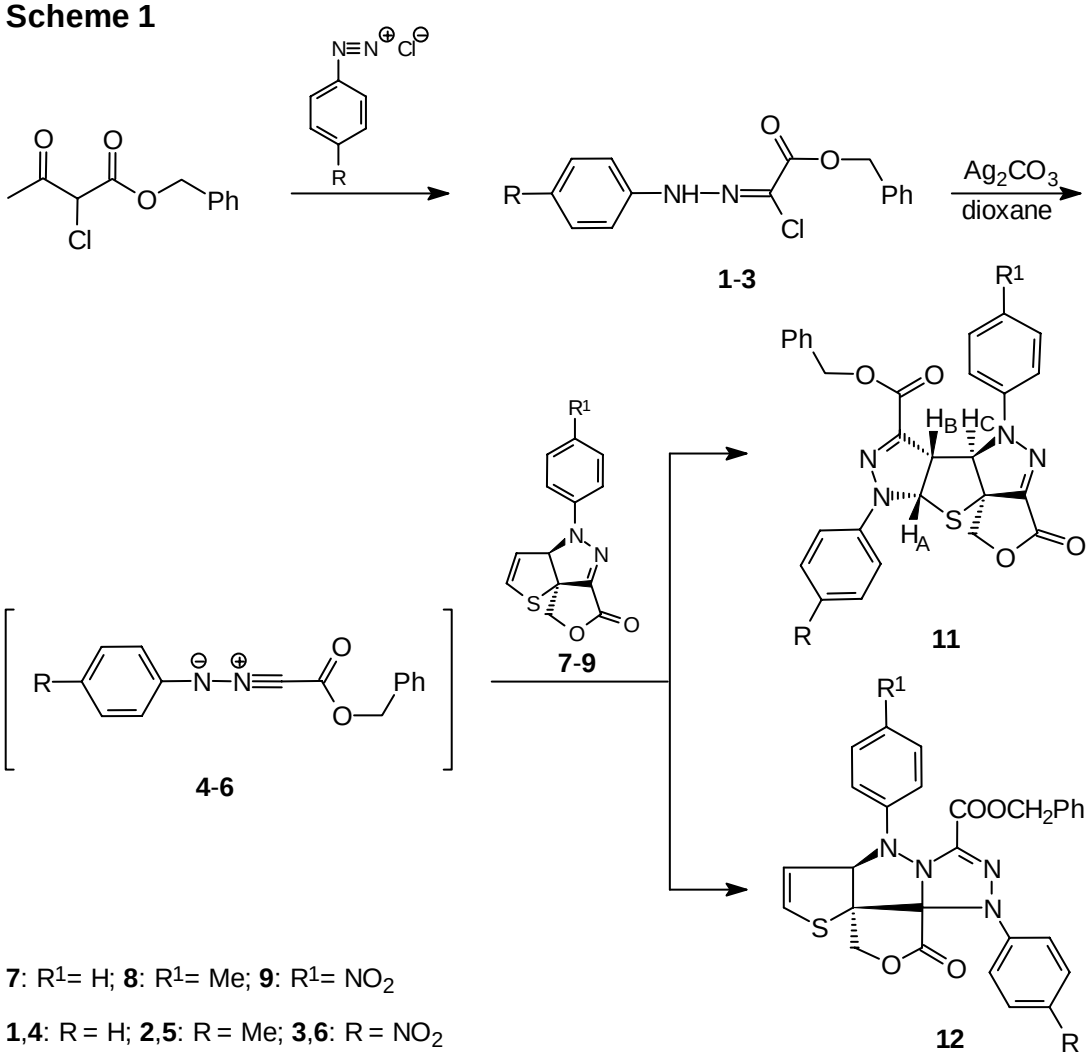

Table 1. Base-promoted reaction between hydrazonoyl chlorides (**1**-**3**) and TFP (**7**-**9**).

Entry	R	R^1	Time (h)	Product and Yield					Ratio of **12**/**11**	Eluent[b]
				7	**8**	**9**	**11**	**12**		
a	H	H	32	45	—	—	26	12	0.46	AcOEt-hexane 2:1
b	Me	H	19	28	—	—	35	12	0.34	Et_2O-LP 2:1
c	NO_2	H	26	25	—	—	10	10	1.0	Et_2O-LP 2:1
d	H	Me	28	—	40	—	21	7	0.33	Et_2O-LP 2:1
e	Me	Me	12	—	10	—	25	1[a]	0.04	Et_2O-LP 2:1
f	NO_2	Me	16	—	30	—	7	7	1.0	AcOEt-hexane 1:1
g	H	NO_2	30	—	—	22	10	12	1.2	Et_2O
h	Me	NO_2	30	—	—	11	27	41	1.5	Et_2O
i	NO_2	NO_2	29	—	—	39	0.5[a]	10	20	AcOEt-CH_2Cl_2 1:20

[a]Not isolated in the analytically pure state. [b]LP = light petroleum, bp 40-60°C.

Scheme 2

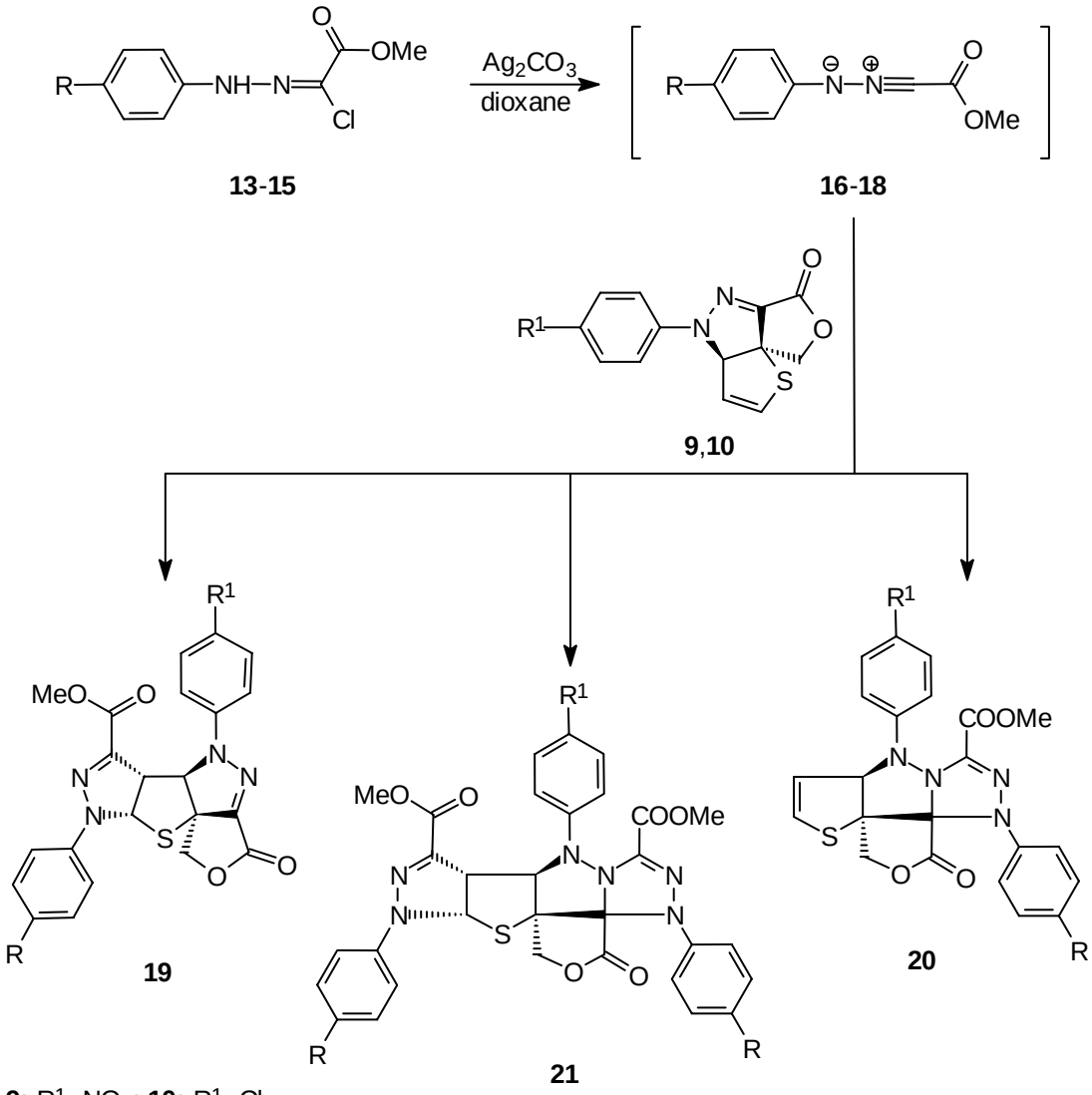

Table 2. Base-promoted reaction between hydrazonoyl chlorides (**13**-**15**) and TFP (**9**,**10**).

Entry	R	R^1	Time (h)	Product and Yield (%)[a]					Eluent
				9	**10**	**19**	**20**	**21**	
a	Me	NO_2	11	10	—	12	10	10	AcOEt - Hexane 2:1
b	NO_2	NO_2	40	20	—	15	15	10	AcOEt - CH_2Cl_2 1:19
c	Cl	Cl	24	—	10	20	20	10	AcOEt - Hexane 1:2

[a]Isolation yields.

equimolar amount of the appropriate FTP. Reaction times, products and eluants are collected in Table 1.

Structural assignment of products (**11**) and (**12**) are unambiguous and rely upon elemental analyses and spectral data, including ^{1}H-NMR, IR, and MS spectrometry (see experimental). As far as ^{1}H NMR spectra are concerned, the H_A hydrogen of **11** resonates as a doublet in the range of δ 6.28-6.36. Those values are fully coherent with the depicted regiochemistry, which requires that H_A is linked on the carbon connected with a nitrogen and a sulfur.[2] The reversed regiochemistry must be rejected on this basis. Furthermore, H_C resonates as a singlet in the range of δ 5.96-6.03 ppm; such chemical shifts and spin multiplicity agrees with those observed for structurally related tetracyclic pyrazolines.[2] In fact, the stereochemical relationship between H_B and H_C must be *anti* due to the apparent lack of vicinal coupling (J_{vic}< 1 Hz); the latter point is substantiated by several literature examples concerning the same kind of disposition in strained policyclic structures.[3,4] IR spectra of **12** also show diagnostic evidence; higher frequencies appeared for the unconjugated lactone carbonyl in comparison with the conjugated one of **11**.

As can be inferred from Table 1, sizable amounts of the starting FTP were recovered, thus evidencing their modest dipolarophilic reactivity. Furthermore, the extent of the cycloaddition depends upon the substituent R placed on the phenyl ring of the nitrilimine counterpart; the electron-donating methyl group of **5** generally works better than the electron-withdrawing nitro group of **6**. This behavior, as well as the regiochemical outcome, may be accounted by assuming the HOMO-dipole (LUMO-dipolarophile) controlled nature of the cycloaddition.[3,5]

The competition between the two dipolarophilic functionalities of FTP is fairly dependent on the R^1 substituent placed on the phenyl ring of the FTP. The electron-withdrawing nitro group of **9** works to favor the attack of the 1,3-dipolar intermediates to the C=N over the C=C bond, while the electron-donating methyl group of **8** just reverts this preference. When R^1=H, an intermediate behavior is operative. Furthermore, for a given R^1 on FTP, the site selectivity of the cycloaddition depends upon the electronic features of the nitrilimines. So, with respect to the results obtained with unsubstituted nitrilimine (**4**) (R=H), the nitro group of nitrilimine (**6**) somewhat facilitates the addition onto the C=N bond, while the methyl group of nitrilimine (**5**) shows the reversed effect. This selectivity is clearly observed by the ratio of **12**/**11** in Table 1.

To this point, we perceived the opportunity studying whether steric encumbrance on the C-terminus of the dipolar intermediates could have some influence on dictating the site-preference of the cycloaddition. Thus, we synthesised the hydrazonoyl chlorides (**13-15**) and submitted them to the silver carbonate treatment in the presence of equimolar amount of FTP (**9**) and (**10**) (Scheme 2). A lack of site selectivity was found, giving cycloadducts (**19**) and (**20**) in 1:1 ratio. The formation of products (**21**) arising from a double cycloaddition process is in line with this statement.

The cycloaddition outcomes of all the above reactions do not harmonise with the predictions based on the FMO theory[5,6] at the PM3[7] level (Figure 1). These calculations[8] indicates that the C=N site of FTP, although moderately sensitive to the R^1 substituent, should be more reactive than the C=C site towards electron-rich as well as electron-deficient nitrilimines.

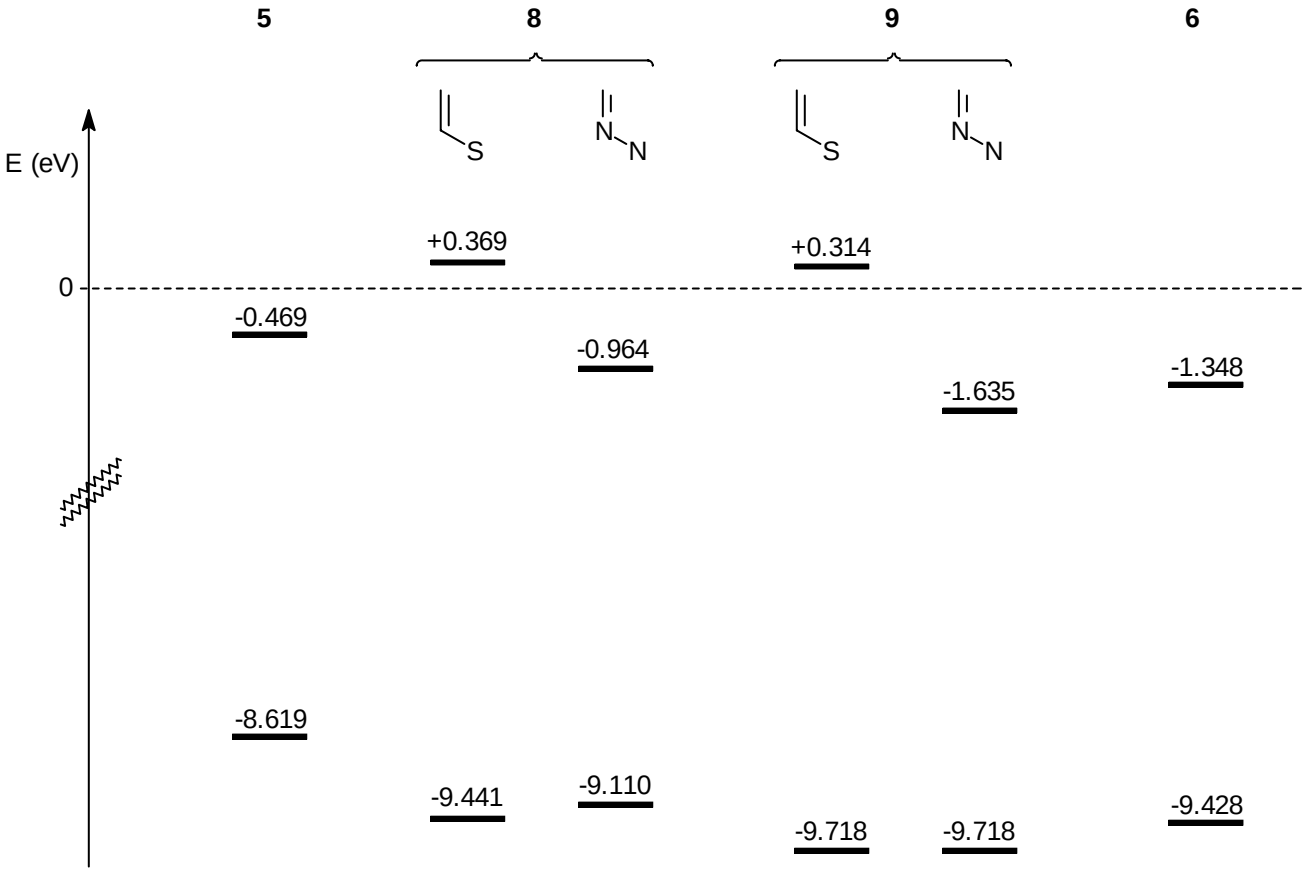

Figure 1. FMO energies for nitrilimines **5**,**6** and FTP **8**,**9** calculated with the PM3 method.

It remains to be added that an attempted reaction between **9** and **2** by the standard triethylamine method gave, besides some amounts of tarry material arising from the thermal decomposition of nitrilimine **5**, quantitatively unreacted **9**. Such kind of behavior is not surprising, since the fast generation of the nitrilimine intermediate, which occurs in the presence of triethylamine, can force intermolecular processes leading exclusively to resinous material. The effectiveness of silver carbonate in a heterogeneous medium is perhaps the consequence of a very slow generation of the nitrilimine.[9] Furthemore, one can tentatively suggest that the Ag^+ cation, due to its known complexating ability towards double-bonded functionalities,[10] might be involved in the transition state of the cycloaddition, so determining some kind of perturbation of the molecular orbitals of the reactants.

In conclusion, on the basis of our experimental findings, the site preference in nitrilimine cycloadditions to FTP seems to be dictated by a subtle interplay of electronic and steric factors. Notwithstanding, the

nitrilimine cycloaddition onto FTP constitutes an intriguing tool in the synthesis of fused tetra- and pentacyclic heterocycles not easily accessible by other routes.

EXPERIMENTAL

Melting points were determined with a Büchi apparatus and are uncorrected. IR spectra were recorded on an FT IR Perkin Elmer 1725 X spectrophotometer. MS spectra were determined with a VG-70EQ apparatus. ^{1}H-NMR spectra were taken with a Bruker AC 300 or AMX 300 instrument in $CDCl_3$ solutions; chemical shifts are given as δ ppm from Me_4Si and *J* values are given in Hz.

Benzyl 2-chloro-3-oxobutanoate[11] as well as compounds (**13**,[12] **14**,[13] and **15**[12]) was prepared according to literature procedures.

Preparation of hydrazonoyl chlorides (1-3); General Procedure. A solution of the proper aniline (7.5 mmol) in 6M hydrochloric acid (6.5 mL) and methanol (8 mL) was treated with sodium nitrite (0.73 g, 10.5 mmol) under vigorous stirring and ice cooling. After 10 min, the cold mixture was adjusted to pH 5 with sodium acetate and cold benzyl 2-chloro-3-oxobutanoate (1.70 g, 7.5 mmol) in methanol (1.5 mL) was added dropwise. The mixture was stirred under cooling for 2 h, then at rt for 15 h. The solvent was partly removed under reduced pressure, and the residue was taken up with ether (70 mL). The organic layer was washed firstly with 5% sodium hydrogencarbonate (25 mL), then with water (50 mL), and dried over sodium sulfate. The solvent was evaporated and the residue was crystallised from diisopropyl ether giving **1**-**3** in the analytically pure form.

Benzyl 2-Chloro-2-phenylhydrazonoacetate (**1**) (1.08 g, 50%) as pale yellow prisms having mp 116°C; IR (nujol): 3260, 1710 (cm^{-1}); ^{1}H-NMR: 5.37 (2H, s), 7.00-7.50 (10H, m), 8.37 (1H, br s); MS: *m/z* 288 (M^+). *Anal*. Calcd for $C_{15}H_{13}N_2O_2Cl$: C, 62.49; H, 4.55; N, 9.72. Found: C, 62.55; H, 4.51; N, 9.79.

Benzyl 2-Chloro-2-(4-tolylhydrazono)acetate **2** (1.22 g, 54%) as pale yellow prisms having mp 110°C; IR (nujol): 3285, 1710 (cm^{-1}); ^{1}H-NMR: 2.32 (3H, s), 5.37 (2H, s), 7.05-7.50 (9H, m), 8.35 (1H, br s); MS: *m/z* 302 (M^+). *Anal*. Calcd for $C_{16}H_{15}N_2O_2Cl$: C, 63.56; H, 5.00; N, 9.27. Found: C, 63.60; H, 5.02; N, 9.33.

Benzyl 2-Chloro-2-(4-nitrophenyl-hydrazono)acetate (**3**) (1.40 g, 56%) as yellow prisms having mp 146°C; IR (nujol): 3270, 2250, 1735, 1640 (cm^{-1}); ^{1}H-NMR: 5.40 (2H, s), 7.20-7.45 (7H, m), 8.20-8.25 (2H, m), 8.58 (1H, br s); MS: *m/z* 333 (M^+). *Anal*. Calcd for $C_{15}H_{12}N_3O_4Cl$: C, 54.05; H, 3.63; N, 12.61. Found: C, 54.11; H, 3.68; N, 12.70.

Reaction of hydrazonoyl chlorides (1-3) with FTP (7-9) in the presence of silver carbonate; General Procedure. A solution of the proper hydrazonoyl chloride (**1**,**2** or **3**) (5.0 mmol) and FTP (**7**,**8** or **9**) (5.0 mmol) in dry dioxane (250 mL) was treated with silver carbonate (2.76 g, 10.0 mmol). The mixture was stirred in the dark at 75°C for the time indicated in Table 1. The insoluble material was filtered off, the solvent was evaporated and the residue was chromatographed on a silica gel column. Eluents and isolation yields are collected in Table 1; the order of elution was **11**-**12**-unreacted FTP.

Compound (**11a**) (0.66 g, 26%) as white needles having mp 172°C (from diisopropyl ether); IR (nujol): 1765, 1700 (cm^{-1}); ^{1}H-NMR: 4.52 (1H, d, *J*=11.0), 4.60 (1H, d, *J*=11.0), 4.90 (1H, d, *J*=8.8), 5.38 (1H, d, *J*=12.5), 5.44 (1H, d, *J*=12.5), 5.98 (1H, s), 6.30 (1H, d, *J*=8.8), 7.10-7.30 (15H, m); MS: *m/z* 510 (M^+). *Anal*. Calcd for $C_{28}H_{22}N_4O_4S$: C, 65.86; H, 4.35; N, 10.98. Found: C, 65.92; H, 4.40; N, 11.06.

Compound (**11b**) (0.92 g, 35%) as white needles having mp 164°C (from diisopropyl ether); IR (nujol): 1765, 1700 (cm^{-1}); ^{1}H-NMR: 2.30 (3H, s), 4.54 (1H, d, *J*=11.2), 4.58 (1H, d, *J*=11.2), 4.89 (1H, d, *J*= 8.5), 5.40 (1H, d, *J*=12.4), 5.45 (1H, d, *J*=12.4), 5.99 (1H, s), 6.28 (1H, d, *J*=8.5), 7.07-7.50 (14H, m); MS: *m/z* 524 (M^+). *Anal*. Calcd for $C_{29}H_{24}N_4O_4S$: C, 66.39; H, 4.61; N, 10.69. Found: C, 66.44; H, 4.68; N, 10.77.

Compound (**11c**) (0.28 g, 10%) as pale yellow needles having mp 130°C (from diisopropyl ether-methanol); IR (nujol): 1765, 1700 (cm^{-1}); ^{1}H-NMR: 4.56 (1H, d, *J*=10.1), 4.61 (1H, d, *J*=10.1), 5.00 (1H, d, *J*=8.5), 5.45 (2H, s), 5.99 (1H, s), 6.31 (1H, d, *J*=8.5), 7.00-7.50 (12H, m), 8.22 (1H, d, *J*=9.1); MS: *m/z* 555 (M^+). *Anal*. Calcd for $C_{28}H_{21}N_5O_6S$: C, 60.53; H, 3.81; N, 12.61. Found: C, 60.48; H, 3.75; N, 12.69.

Compound (**11d**) (0.55 g, 21%) as white needles having mp 187°C (from hexane-benzene); IR (nujol): 1760, 1700 (cm^{-1}); ^{1}H-NMR: 2.33 (3H, s), 4.56 (2H, s), 4.88 (1H, d, *J*=8.5), 5.42 (2H, s), 5.96 (1H, s), 6.28 (1H, d, *J*=8.5), 7.05-7.50 (14H, m); MS: *m/z* 524 (M^+). *Anal*. Calcd for $C_{29}H_{24}N_4O_4S$: C, 66.39; H, 4.61; N, 10.69. Found: C, 66.47; H, 4.60; N, 10.61.

Compound (**11e**) (0.67 g, 25%) as white needles having mp 157°C (from diisopropyl ether-methanol); IR (nujol): 1760, 1700 (cm^{-1}); ^{1}H-NMR: 2.33 (3H, s), 2.37 (3H, s), 4.33 (2H, s), 4.88 (1H, d, *J*=8.5), 5.44 (2H, s), 5.97 (1H, s), 6.29 (1H, d, *J*=8.5), 7.00-7.55 (13H, m); MS: *m/z* 538 (M^+). *Anal*. Calcd for $C_{30}H_{26}N_4O_4S$: C, 66.89; H, 4.87; N, 10.41. Found: C, 66.96; H, 4.92; N, 10.51.

Compound (**11f**) (0.20 g, 7%) as yellow needles having mp 85°C (from diisopropyl ether-methanol); IR (nujol): 1770, 1715 (cm^{-1}); ^{1}H-NMR: 2.33 (3H, s), 4.53 (1H, d, *J*=9.6), 4.59 (1H, d, *J*=9.6), 4.96 (1H, d, *J*=8.5), 5.43 (2H, s), 5.97 (1H, s), 6.28 (1H, d, *J*=8.5), 6.95-7.50 (11 H, m), 8.18-8.29 (2H, m); MS: *m/z* 569 (M^+). *Anal*. Calcd for $C_{29}H_{23}N_5O_6S$: C, 61.15; H, 4.07; N, 12.30. Found: C, 61.20; H, 4.02; N, 12.41.

Compound (**11g**) (0.28 g, 10%) as pale yellow solid having mp 154°C (from diisopropyl ether); IR (nujol): 1765, 1720 (cm^{-1}); ^{1}H-NMR: 4.62 (1H, d, *J*=10.0), 4.68 (1H, d, *J*=10.0), 4.91 (1H, d, *J*=8.6), 5.44 (2H,

s), 6.03 (1H, s), 6.34 (1H, d, *J*=8.6), 7.00-7.60 (12 H, m), 8.15-8.22 (2H, m); MS: *m/z* 555 (M^+). *Anal*. Calcd for $C_{28}H_{21}N_5O_6S$: C, 60.53; H, 3.81; N, 12.61. Found: C, 60.45; H, 3.72; N, 12.66.

Compound (**11h**) (0.77 g, 27%) as pale yellow solid having mp 205°C (from diisopropyl ether); IR (nujol): 1765, 1690 (cm^{-1}); ^{1}H-NMR: 2.37 (3H, s), 4.58 (1H, d, *J*=10.0), 4.67 (1H, d, *J*=10.0), 4.90 (1H, d, *J*=8.3), 5.44 (2H, s), 5.97 (1H, s), 6.31 (1H, d, *J*=8.3), 6.90-8.35 (13 H, m); MS: *m/z* 569 (M^+). *Anal*. Calcd for $C_{29}H_{23}N_5O_6S$: C, 61.15; H, 4.07; N, 12.30. Found: C, 61.23; H, 4.12; N, 12.40.

Compound (**11i**) (15 mg, 0.5%) as oil; IR (nujol): 1780, 1720 (cm^{-1}); ^{1}H-NMR: 4.63 (1H, d, *J*=10.5), 4.72 (1H, d, *J*=10.5), 4.94 (1H, d, *J*=8.3), 5.46 (2H, s), 6.03 (1H, s), 6.36 (1H, d, *J*=8.3), 7.27-8.35 (13 H, m).

Compound (**12a**) (0.30 g, 12%) as white amorphous solid having mp 146°C (from diisopropyl ether); IR (nujol): 1785, 1695 (cm^{-1}); ^{1}H-NMR: 4.40 (1H, d, *J*=10.5), 4.52 (1H, d, *J*=10.5), 5.24 (1H, d, *J*=12.0), 5.38 (1H, d, *J*=12.0), 5.56 (1H, dd, *J*=2.5, 1.5), 5.65 (1H, dd, *J*=6.6, 2.5), 6.16 (1H, dd, *J*=6.6, 1.5), 7.00-7.40 (15H, m); MS: *m/z* 510 (M^+). *Anal*. Calcd for $C_{28}H_{22}N_4O_4S$: C, 65.86; H, 4.35; N, 10.98. Found: C, 65.92; H, 4.40; N, 11.06.

Compound (**12b**) (0.31 g, 12%) as white amorphous solid having mp 134°C (from diisopropyl ether); IR (nujol): 1785, 1695 (cm^{-1}); ^{1}H-NMR: 2.24 (3H, s), 4.37 (1H, d, *J*=10.6), 4.48 (1H, d, *J*=10.6), 5.28 (1H, d, *J*=12.1), 5.37 (1H, d, *J*=12.1), 5.54 (1H, dd, *J*=2.3, 1.7), 5.61 (1H, dd, *J*=6.0, 2.3), 6.12 (1H, dd, *J*=6.0, 1.7), 7.00-7.45 (14H, m); MS: *m/z* 524 (M^+). *Anal*. Calcd for $C_{29}H_{24}N_4O_4S$: C, 66.39; H, 4.61; N, 10.69. Found: C, 66.44; H, 4.68; N, 10.77.

Compound (**12c**) (0.28 g, 10%) as pale yellow needles having mp 183°C (from diisopropyl ether-acetone); IR (nujol): 1790, 1700 (cm^{-1}); ^{1}H-NMR: 4.40 (1H, d, *J*=10.5), 4.56 (1H, d, *J*=10.5), 5.32 (1H, d, *J*=12.5), 5.40 (1H, d, *J*=12.5), 5.65-6.22 (3H, m), 7.00-8.35 (14H, m); MS: *m/z* 555 (M^+). *Anal*. Calcd for $C_{28}H_{21}N_5O_6S$: C, 60.53; H, 3.81; N, 12.61. Found: C, 60.48; H, 3.75; N, 12.69.

Compound (**12d**) (0.18 g, 7%) as white amorphous solid having mp 137°C (from benzene-acetone); IR (nujol): 1790, 1700 (cm^{-1}); ^{1}H-NMR: 2.30 (3H, s), 4.37 (1H, d, *J*=10.3), 4.49 (1H, d, *J*=10.3), 5.28 (1H, d, *J*=7.9), 5.34 (1H, d, *J*=7.9), 5.51 (1H, dd, *J*=2.4, 2.0), 5.59 (1H, dd, *J*=6.0, 2.4), 6.09 (1H, dd, *J*=6.0, 2.0), 7.00-7.50 (14H, m); MS: *m/z* 524 (M^+). *Anal*. Calcd for $C_{29}H_{24}N_4O_4S$: C, 66.39; H, 4.61; N, 10.69. Found: C, 66.47; H, 4.60; N, 10.61.

Compound (**12e**) (27 mg, 1%) as oil; IR (nujol): 1785, 1700 (cm^{-1}); ^{1}H-NMR: 2.29 (3H, s), 2.33 (3H, s), 4.35 (1H, d, *J*=10.5), 4.50 (1H, d, *J*=10.5), 5.22 (1H, d, *J*=8.0), 5.33 (1H, d, *J*=8.0), 5.56-6.19 (3H, m), 7.00-7.35 (13H, m).

Compound (**12f**) (0.20 g, 7%) as pale yellow needles having mp 166°C (from diisopropyl ether); IR (nujol): 1785, 1700 (cm^{-1}); ^{1}H-NMR: 2.33 (3H, s), 4.34 (1H, d, *J*=10.0), 4.46 (1H, d, *J*=10.0), 5.24 (1H, d, *J*=8.2), 5.36 (1H, d, *J*=8.2), 5.53 (1H, dd, *J*=2.5, 2.0), 5.62 (1H, dd, *J*=6.0, 2.5), 6.11 (1H, dd, *J*=6.0,

2.0), 7.00-8.35 (13H, m); MS: *m/z* 569 (M^+). *Anal*. Calcd for $C_{29}H_{23}N_5O_6S$: C, 61.15; H, 4.07; N, 12.30. Found: C, 61.20; H, 4.02; N, 12.41.

Compound (**12g**) (0.33 g, 12%) as pale yellow amorphous solid having mp 140°C (from diisopropyl ether); IR (nujol): 1785, 1720 (cm^{-1}); ^{1}H-NMR: 4.48 (1H, d, *J*=11.5), 4.56 (1H, d, *J*=11.5), 5.29 (1H, d, *J*=12.1), 5.38 (1H, d, *J*=12.1), 5.62 (1H, dd, *J*=2.3, 1.6), 5.72 (1H, dd, *J*=6.2, 2.3), 6.29 (1H, dd, *J*=6.2, 1.6), 7.00-8.25 (14 H, m); MS: *m/z* 555 (M^+). *Anal*. Calcd for $C_{28}H_{21}N_5O_6S$: C, 60.53; H, 3.81; N, 12.61. Found: C, 60.45; H, 3.72; N, 12.66.

Compound (**12h**) (1.17 g, 41%) as pale yellow needles having mp 118°C (from diisopropyl ether); IR (nujol): 1790, 1700 (cm^{-1}); ^{1}H-NMR: 2.26 (3H, s), 4.28 (1H, d, *J*=10.3), 4.38 (1H, d, *J*=10.3), 5.30 (1H, d, *J*=12.1), 5.39 (1H, d, *J*=12.1), 5.62 (1H, dd, *J*=2.5, 1.5), 5.70 (1H, dd, *J*=6.3, 2.5), 6.30 (1H, dd, *J*=6.3, 1.5), 7.00-8.25 (13H, m); MS: *m/z* 569 (M^+). *Anal*. Calcd for $C_{29}H_{23}N_5O_6S$: C, 61.15; H, 4.07; N, 12.30. Found: C, 61.11; H, 4.00; N, 12.22.

Compound (**12i**) (0.30 g, 10%); as yellow prisms having mp 130°C (from diisopropyl ether-dichloromethane); IR (nujol): 1790, 1700 (cm^{-1}); ^{1}H-NMR: 4.48 (1H, d, *J*=10.9), 4.52 (1H, d, *J*=10.9), 5.28 (1H, d, *J*=11.7), 5.39 (1H, d, *J*=11.7), 5.61 (1H, dd, *J*=3.0, 1.5), 5.70 (1H, dd, *J*=6.7, 3.0), 6.21 (1H, dd, *J*=6.7, 1.5), 7.25-7.45 (9H, m), 8.05-8.25 (4H, m); MS: *m/z* 600 (M^+). *Anal*. Calcd for $C_{28}H_{20}N_6O_8S$: C, 55.99; H, 3.36; N, 14.00. Found: C, 60.05; H, 3.30; N, 13.91.

Reaction of hydrazonoyl chlorides (13-15) with FTP (9,10) in the presence of silver carbonate; General Procedure. A solution of the proper hydrazonoyl chloride (**13**,**14** or **15**) (5.0 mmol) and FTP (**9** or **10**) (5.0 mmol) in dry dioxane (250 mL) was treated with silver carbonate (2.76 g, 10.0 mmol). The mixture was stirred in the dark at 75°C for the time indicated in Table 2. The insoluble material was filtered off, the solvent was evaporated and the residue was chromatographed on a silica gel column. Eluents and isolation yields are collected in Table 2; the order of elution was **21**-**19**-**20**-unreacted FTP.

Compound (**19a**) (0.29 g, 12%) as white needles having mp 114°C (from diisopropyl ether); IR (nujol): 1770, 1725 (cm^{-1}); ^{1}H-NMR: 2.30 (3H, s), 3.96 (3H, s), 4.63 (1H, d, *J*=9.9), 4.78 (1H, d, *J*=9.9), 4.91 (1H, d, *J*=8.4), 6.01 (1H, s), 6.35 (1H, d, *J*=8.4), 7.10-8.45 (8H, m); MS: *m/z* 493 (M^+). *Anal*. Calcd for $C_{23}H_{19}N_5O_6S$: C, 55.97; H, 3.88; N, 14.20. Found: C, 56.03; H, 3.82; N, 14.27.

Compound (**19b**) (0.39 g, 15%) as yellow prisms having mp 176°C (from diisopropyl ether-acetone); IR (nujol): 1770, 1715 (cm^{-1}); ^{1}H-NMR: 4.05 (3H, s), 4.65 (1H, d, *J*=9.8), 4.80 (1H, d, *J*=9.8), 5.60 (1H, d, *J*=8.0), 6.10 (1H, s), 6.35 (1H, d, *J*=8.0), 7.55-8.35 (8H, m); MS: *m/z* 524 (M^+). *Anal*. Calcd for $C_{22}H_{16}N_6O_8S$: C, 50.37; H, 3.08; N, 16.03. Found: C, 50.30; H, 3.11; N, 16.11.

Compound (**19c**) (0.50 g, 20%) as pale yellow needles having mp 176°C (from diisopropyl ether); IR (nujol): 1765, 1710 (cm^{-1}); ^{1}H-NMR: 4.00 (3H, s), 4.62 (1H, d, *J*=10.1), 4.72 (1H, d, *J*=10.1), 4.88 (1H,

d, *J*=8.4), 6.02 (1H, s), 6.30 (1H, d, *J*=8.4), 7.10-7.40 (8H, m); MS: *m/z* 502 (M^+). *Anal*. Calcd for $C_{22}H_{16}N_4O_4Cl_2S$: C, 52.59; H, 3.21; N, 11.16. Found: C, 52.53; H, 3.17; N, 11.23.

Compound (**20a**) (0.24 g, 10%) as white prisms having mp 106°C (from diisopropyl ether); IR (nujol): 1790, 1740 (cm^{-1}); ^{1}H-NMR: 2.30 (3H, s), 3.99 (3H, s), 4.63 (1H, d, *J*=10.4), 4.76 (1H, d, *J*=10.4), 5.64 (1H, dd, *J*=2.4, 1.6), 5.74 (1H, dd, *J*=6.1, 2.4), 6.33 (1H, dd, *J*=6.1, 1.6), 6.95-8.10 (8H, m); MS: *m/z* 493 (M^+). *Anal*. Calcd for $C_{23}H_{19}N_5O_6S$: C, 55.97; H, 3.88; N, 14.20. Found: C, 55.92; H, 3.80; N, 14.23.

Compound (**20b**) (0.39 g, 15%) as yellow needles having mp 185°C (from diisopropyl ether); IR (nujol): 1787, 1735 (cm^{-1}); ^{1}H-NMR: 3.95 (3H, s), 4.50 (1H, d, *J*=8.6), 4.80 (1H, d, *J*=8.6), 5.65 (1H, dd, *J*=2.3, 1.9), 5.70-6.28 (2H, m), 7.20-8.30 (8H, m); MS: *m/z* 524 (M^+). *Anal*. Calcd for $C_{22}H_{16}N_6O_8S$: C, 50.37; H, 3.08; N, 16.03. Found: C, 50.27; H, 3.00; N, 15.99.

Compound (**20c**) (0.50 g, 20%) as yellow needles having mp 146°C (from diisopropyl ether); IR (nujol): 1790, 1730 (cm^{-1}); ^{1}H-NMR: 3.91 (3H, s), 4.47 (1H, d, *J*=10.6), 4.74 (1H, d, *J*=10.6), 5.53 (1H, dd, *J*=2.4, 1.9), 5.64 (1H, dd, *J*=6.3, 2.4), 6.17 (1H, dd, *J*=6.3, 1.9), 7.02-7.27 (8H, m); MS: *m/z* 502 (M^+). *Anal*. Calcd for $C_{22}H_{16}N_4O_4Cl_2S$: C, 52.59; H, 3.21; N, 11.16. Found: C, 52.66; H, 3.27; N, 11.20.

Compound (**21a**) (0.34 g, 10%) as white amorphous solid having mp 180°C (from methanol); IR (nujol): 1790, 1720, 1700 (cm^{-1}); ^{1}H-NMR: 2.30 (3H, s), 2.33 (3H, s), 3.95 (3H, s), 4.02 (3H, s), 4.41 (1H, d, *J*=10.8), 4.53 (1H, d, *J*=7.9), 4.70 (1H, d, *J*=10.8), 5.80 (1H, s), 6.25 (1H, d, *J*=7.9), 7.07-8.11 (12H, m); MS: *m/z* 683 (M^+). *Anal*. Calcd for $C_{33}H_{29}N_7O_8S$: C, 57.96; H, 4.28; N, 14.35. Found: C, 58.03; H, 4.32; N, 14.27.

Compound (**21b**) (0.37 g, 10%) as white amorphous solid having mp 204°C (from methanol); IR (nujol): 1790, 1735, 1730 (cm^{-1}); ^{1}H-NMR: 3.89 (3H, s), 3.96 (3H, s), 4.47 (1H, d, *J*=11.0), 4.60 (1H, d, *J*=7.6), 4.81 (1H, d, *J*=11.0), 5.88 (1H, s), 6.36 (1H, d, *J*=7.6), 7.28-8.45 (12H, m); MS: *m/z* 745 (M^+). *Anal*. Calcd for $C_{31}H_{23}N_9O_{12}S$: C, 49.42; H, 3.11; N, 16.91. Found: C, 49.47; H, 3.10; N, 17.00.

Compound (**21c**) (0.36 g, 10%) as white needles having mp 192°C (from methanol); IR (nujol): 1790, 1730, 1720 (cm^{-1}); ^{1}H-NMR: 4.00 (6H, s), 4.40 (1H, d, *J*=10.6), 4.45 (1H, d, *J*=8.0), 4.60 (1H, d, *J*=10.6), 5.95 (1H, s), 6.26 (1H, d, *J*=8.0), 7.10-8.00 (12H, m); MS: *m/z* 712 (M^+). *Anal*. Calcd for $C_{31}H_{23}N_6O_6Cl_3S$: C, 52.24; H, 3.26; N, 11.80. Found: C, 52.30; H, 3.27; N, 11.72.

Reaction between 2 and FTP (9) in the presence of triethylamine. A solution of **2** (0.68 g, 3.0 mmol) and **9** (1.04 g, 3.0 mmol) in dry dioxane (150 mL) was added with triethylamine (1.52 g, 15.0 mmol). The mixture was refluxed in the dark at for 48 h. The solvent was evaporated and the residue was chromatographed on a silica gel column with diethylether as eluant. Besides some amount of tarry material, unchanged **9** were recovered.

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