

Reaction of β -Nitro Enamines with Isocyanates, Isothiocyanates and Dimethyl Acetylenedicarboxylate

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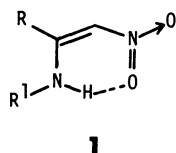
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(Received May 10, 1986)

β -Nitro enamines (**1**) reacted with isocyanates and isothiocyanates to give β -(substituted carbamoyl) and β -(substituted thiocarbamoyl) β -nitro enamines, respectively. The reaction of **1** with benzoyl isothiocyanate gave β -(benzoylthiocarbamoyl) β -nitro enamines (**8**) and/or a mixture of **8** and 4(1*H*)-pyrimidinethione derivatives (**9**) which were cyclization products of **8**. The isolated **8** afforded the corresponding **9** in high yields upon heating in DMF. The reaction of **1** with dimethyl acetylenedicarboxylate gave [2+2] cycloadducts (**12**) and/or a mixture of **12** and δ -nitro dienamino diesters (**13**) which were ring cleavage products of **12**. Compounds **12** afforded **13** upon heating in toluene or xylene.

β -Nitro enamines are useful synthetic intermediates, and their reactivities are of interest in connection with that of β -amino enones. In a previous paper, the author reported that the primary and secondary β -nitro enamines (**1**) reacted with electrophiles, *N*-halosuccinimides, *o*-nitrobenzenesulfonyl chloride and thiocyanogen, to give exclusively the β -substituted β -nitro enamines.¹⁾ The reaction of electrophiles such as isocyanates and isothiocyanates with **1** also is of interest because it may occur either at the nitrogen of the amino group or at the β -carbon. However, these reactions have been little studied: it has been reported only that 2-(nitromethylene)perhydroazepine reacts with benzoyl isothiocyanate to give a pyrimidine derivative.²⁾ On the other hand, it is known that tertiary β -nitro enamines react at the double bond with dipolar reagents such as nitrilimines, nitrile oxides and aryl azides to give azoles, [2+3] dipolar cycloaddition products.^{3,4)} However, there has been no report concerning the reaction of **1** with electrophilic alkynes.

In this paper, I wish to report the results of the reaction of **1** with isocyanates, isothiocyanates and dimethyl acetylenedicarboxylate.



	R	R ¹		R	R ¹
a:	Me	H	f:	Ph	H
b:	Me	Me	g:	Ph	Me
c:	Me	PhCH ₂	h:	Ph	PhCH ₂
d:	Me	Ph	i:	Ph	Ph
e:	Me	R ¹ -H=(CH ₂) ₅	j:	Ph	R ¹ -H=(CH ₂) ₅

Results and Discussion

Reaction of β -Nitro Enamines (1**) with Isocyanates and Isothiocyanates.** The reaction of **1a—d** with phenyl isocyanate (**2**) in acetonitrile afforded β -(phenylcarbamoyl) β -nitro enamines (**3a—d**) in 29—81% yields

and a small amount of the corresponding *N*-substituted ureas (**4**), which were considered to be decomposition products of an *N*-acylated product of **1**, respectively. In these reactions, tertiary β -nitro enamine, **1e**, decomposed. With methyl isocyanate, only **1b** at 90°C in a sealed tube gave *N*-methyl-3-methylamino-2-nitro-2-butanamide (**5b**) in a 35% yield. In the reaction of **1a—e** with phenyl isothiocyanate, only



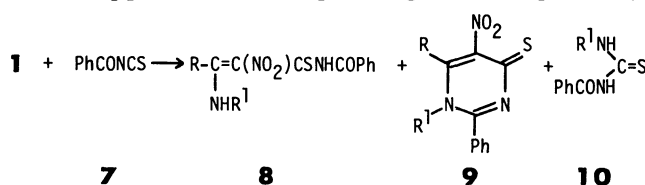
2



3a—d

4

1b and **1e** gave β -(phenylthiocarbamoyl) β -nitro enamines (**6b**) and (**6e**), in 25 and 5% yields, respectively. These results have revealed that the electrophilic addition of isocyanates and isothiocyanate to **1** takes place predominantly on the β -carbon of **1**; this reactivity is attributable to the enamine character of **1**.^{1,5)} New compounds **3a—d**, **5b** and **6b,e** were identified by spectral data and elemental analyses. In the IR spectra, **3a—d** and **5b** showed three and two weak absorptions, respectively, which were assigned to νNH . The absorptions in the carbonyl region were complex: **3a—d** and **5b** showed strong absorptions in the region 1602—1588 cm⁻¹, which may be assigned to $\nu\text{C}=\text{O}$ overlapped with a ring stretching that is shifted to a lower frequency by the enamino ketone conjugation and an intramolecular hydrogen bonding strengthened by the electron-withdrawing resonance effect of α -nitro group (as described below). A strong $\nu\text{C}=\text{S}$ absorption of **6b** and **6e** was found at 1168 and 1160 cm⁻¹,⁶⁾ respectively. The NMR spectra of **3a—d**, **5b**, and **6b,e** showed new peaks of NHCH_3 or NHC_6H_5 protons with a disappearance of a $=\text{CH}-$ proton signal near 6.5 ppm of the corresponding **1a—e**, respectively.



7

8

9

10

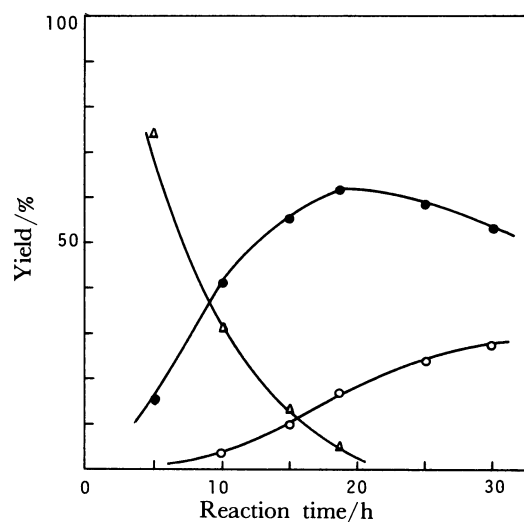
Table 1. Reaction of **1** with Benzoyl Isothiocyanate

	Reaction condition			Products					
	Temp/°C	Time/h	Separation ^{a)}	8	Yield/%	9	Yield/%	10	Yield/%
1a	50	100	C-CH ₂ Cl ₂	8a	17	9a	2		8
1b	rt	48	C-CH ₂ Cl ₂	8b	81	9b	0.5		0
1c	60	30	C-CCl ₄	8c	0	9c	9		26
1d	rt	120	CHCl ₃ /CCl ₄	8d	34	9d	2		0
1e	rt	30	C-CH ₂ Cl ₂	8e	84	9e	0		1
1g	rt	100	PhH/CCl ₄	8g	87	9g	0		0
1h	bp	18	C-CH ₂ Cl ₂	8h	60	9h	17		5
1i	bp	80	C-CH ₂ Cl ₂	8i	0	9i	16		6
1j	rt	45	C-CH ₂ Cl ₂	8j	50	9j	0		5

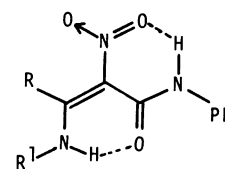
a) C: Silica-gel column chromatography.

In the reaction of **1** with benzoyl isothiocyanate (**7**), **1a,b,d,h** gave a mixture of corresponding β -(benzoylthiocarbamoyl) β -nitro enamines (**8a,b,d,h**) (17–81%), 4(1*H*)-pyrimidinethione derivatives (**9a,b,d,h**) (0.5–17%) and *N*-benzoyl *N'*-R¹-thioureas (**10**) (1–26%), and **1c,i** gave a mixture of corresponding **9c, i** (9 and 16%) and **10** (26 and 6%); **1e,g,j** and **1f** gave only corresponding **8e,g,j** (50–87%) and a small amount of *N*-benzoylthiourea, respectively. deStevens et al.⁵⁾ have reported that ethyl 3-amino-2-(benzoylthiocarbamoyl)-crotonate can be converted to the corresponding 4(1*H*)-pyrimidinethione derivative upon refluxing in THF. Therefore, compounds **9** appear to be produced by a thermal *Z-E* isomerization of the initially formed β -adducts, **8**, during the reaction, followed by a ring closure and dehydration. These results are also supported by the reaction of **1h** with **7**. Namely, plots of the yields of **8h** vs. the reaction times showed a maximum (about 60%) in about 18 h, while **9h** increased with increasing time. These results are shown in Fig. 1. On the other hand, the isolated primary and secondary **8a,b,d,g,h** afforded the corresponding **9a,b,d,g,h** in 90–96% yields upon heating in DMF for 5 min at 110 °C. Compounds **10** are the decomposition products of *N*-adducts of **7**. New compounds **8a,b,d,e,g,h,j** and **9a–d, g–i** were identified by the spectral data and elemental analyses. The IR spectra for **8** showed one, two and three absorptions assigned to ν NH in the region of 3500–3100 cm⁻¹, and ν C=O and ν C=S absorptions were observed at 1708–1706 and 1180–1162 cm⁻¹, respectively. In cyclic compounds **9b–d, g–i**, the ν C=O and ν NH absorptions disappeared, and **9a** showed a weak absorption of the ν NH at 3400 cm⁻¹. The absorptions of ν C=C+ ν C=N and ν C=S of **9a–d, g–i** were observed at 1677–1605 and 1172–1149 cm⁻¹ respectively. The NMR spectra also supported the structure of **8** and **9**, respectively.

As previously described, **3b–d** and **5b** showed two weak ν NH absorptions in the regions at 3350–3270 and 3180–3150 cm⁻¹; also, a strong absorption of ν C=O that overlapped with ν C=C of the aromatic ring was found in the lower-frequency region of 1602–1588 cm⁻¹, respectively. 4-(Monosubstituted amino)-3-nitro-3-penten-2-one (substituent: Me, PhCH₂, and

Fig. 1. Yields of **8h** and **9h** vs. reaction time in boiling benzene. ●: **8h**, ○: **9h**, Δ: recovered **1h**.

Ph) show a strong ν C=O in the lower-frequency region of 1605–1568 cm⁻¹. Such a low-frequency shift of the ν C=O absorption can be attributed to a delocalization of π -electrons of the chelate ring through an intramolecular hydrogen bonding, owing to the electron-withdrawing resonance effect of the α -nitro group.⁷⁾



[I]

The peaks of two NH protons for NMR were found for a lower magnetic field at δ 13.8–12.2 and 10.5–10.4 respectively. Compound **3a** was also similar to **3b–d**. Further, the peaks of NCH₃ and NCH₂- protons for **3b,c** and **5b** split into a doublet through a spin-spin coupling with the NH proton at δ 3.16–2.87 (*J*=5–6 Hz) and 4.6 (*J*=6 Hz), respectively. From these results, **3a–d** and **5b** appear to exist in a double intramolecular hydrogen-bonded structure [I].

In conclusion, it has been found that **1** reacts with

Table 2. Reaction of **1** with Dimethyl Acetylenedicarboxylate

	Reaction time/h	Separation ^{a)}	Product			
			12	Yield/%	13	Yield/%
1a	9	C-CH ₂ Cl ₂	12a	0	13a	71
1b	4	PhH	12b	72	13b	0
1d	4	C-CH ₂ Cl ₂	12d	47	13d	25
1f	48	C-CH ₂ Cl ₂	12f	64	13f	0
1g	7	PhH	12g	79	13g	0
1h	12	MeOH/CCl ₄	12h	58	13h	16
1i	72	C-CH ₂ Cl ₂	12i	26	13i	31
1j	100	C-CH ₂ Cl ₂	12j	0	13j	6

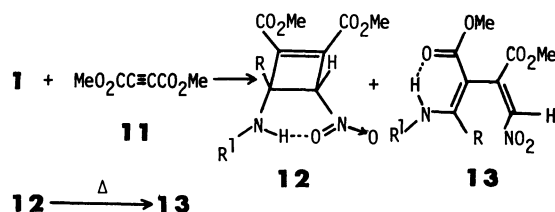
a) C: Silica-gel column chromatography.

Table 3. Ring Opening Reaction of **12**

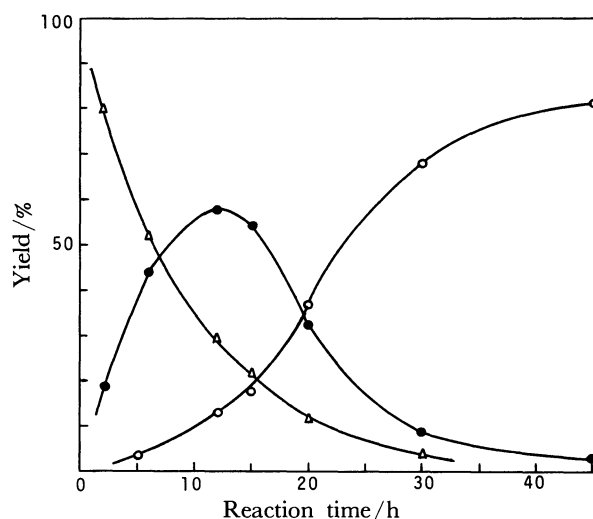
	Reaction condition				Product		
	Solvent	Temp/°C	Time/h	Separation ^{a)}	13	Yield/%	Mp(θ_m /°C)
12b	Toluene	bp	4	C-CH ₂ Cl ₂	13b	49	Liquid
12d	Toluene	bp	1	C-CH ₂ Cl ₂	13d	95	99—100
12f	Xylene	130	120	C-CH ₂ Cl ₂	13f	50	132—133
12g	Xylene	130	8	CCl ₄	13g	99	136—137
12h	Toluene	bp	2	CCl ₄	13h	99	167—168
12i	Toluene	bp	3	CCl ₄	13i	99	163—164

a) C: Silica-gel column chromatography.

isocyanates and isothiocyanates at β -carbon predominantly to give the β -adducts. With benzoyl isothiocyanate it gives 4(1*H*)-pyrimidinethiones by β -addition followed by cyclization.



Reaction of **1 with Dimethyl Acetylenedicarboxylate (**11**).** In a reaction of **1** with **11** in refluxing THF, **1d**, **h**, **i** gave a mixture of corresponding [2+2] cycloadducts (**12d,h,i**) and β,γ -bis(methoxycarbonyl) δ -nitro dienamines (**13d,h,i**), and **1b,f,g** gave only **12b,f,g**; **1a,j** and **1c, e** gave only the corresponding **13a, j** and decomposition products, respectively. These results are shown in Table 2. It is known that enamino ketones and esters also react similarly with **11** to give dienamino keto diesters and dienamino triesters, respectively, which are presumed to be produced via a rearrangement of unstable cyclobutene intermediates.⁸⁾ In a similar manner, **13** appears to be produced by a ring-cleavage of the initially formed cycloadducts **12**. This is also illustrated by the fact that plots of the yields of **12h** vs. the reaction times showed a maximum (58%) after about 12 h, while that of **13h** increased up to 81% with time (Fig. 2). The isolated **12** isomerized upon being heated in toluene or xylene to give the corresponding **13** in 49—99% yields. These results are summarized in Table 3. Compounds **12b,d,h,i** were

Fig. 2. Yields of **12h** and **13h** vs. reaction time in boiling THF. ●: **12h**, ○: **13h**, Δ: recovered **1h**.

easily cleaved by refluxing in toluene to give **13b,d,h,i**, respectively. **12f,g** were stable upon prolonged heating in toluene and required a long heating period at 130 °C in xylene. Such a difference in the thermal stability of **12** is consistent with the yield of **13** for the reaction described above.

The new compounds (**12** and **13**) were identified by spectral data and elemental analyses. The IR spectra of **12b,d, f—i** all showed a weak broad ν NH absorption at 3190—3120 cm^{-1} , and a strong ν C=O absorption was observed in the region of 1728—1720 cm^{-1} . A weak absorption at 1639—1625 cm^{-1} region was assigned to ν C=C absorption, and a strong absorption at 1603—

1561 cm^{-1} region was assigned to depend primarily on $\nu_{\text{as}}\text{NO}_2$ absorption. The NMR spectra for **12b,d,f-i** were also in agreement with the [2+2] cycloadducts, respectively, and a broad NH peak was observed at δ 12.37–9.9, respectively. These results suggested that **12b, d, f-i** have an intramolecular hydrogen-bonded structure of $\text{NH}\cdots\text{O}=\text{N}$ type. In the IR spectra of **13a,b,d,f-j** a weak broad absorption of νNH was observed in the region of 3200–3150 cm^{-1} except for **13j**, and a strong absorption of $\nu\text{C}=\text{O}$ and a medium absorption of $\nu\text{C}=\text{C}$ was observed at 1725–1718 and 1640–1618 cm^{-1} region, respectively. Strong absorptions of $\nu_{\text{as}}\text{NO}_2$ and $\nu_{\text{s}}\text{NO}_2$ were also observed at 1614–1544 and 1376–1351 cm^{-1} , respectively. The NMR spectra were also consistent with the ring-cleavage products, respectively, and a broad NH peak was observed at δ 12.49–9.95 as observed **12**. These results suggested that **13** were δ -nitro dienamino diester and that **13a,b,d,f-j** had an intramolecular hydrogen-bonded structure of the enamino ester type. Consequently, it is considered that the compounds **13** are produced via the conrotatory ring cleavage upon heating the corresponding cyclobutenes **12**.

In conclusion, it has been found that **1** reacts with the electrophilic dimethyl acetylenedicarboxylate at the double bond, in spite of the delocalization of π -electrons as a push-pull alkene,⁹ to give the [2+2] cycloadducts, and that their adducts afford the corresponding δ -nitro dienamino diesters by the ring opening reaction.

Experimental

Melting points were uncorrected. IR and UV spectra were recorded with a JASCO IRG and a Hitachi 124 spectrophotometers, respectively. NMR spectra were recorded with a Hitachi R24B (60 MHz) instrument using TMS as an internal standard. Isocyanates, isothiocyanates and dimethyl acetylenedicarboxylate were of commercial grade and used without further purification. The preparation of *N*-substituted β -nitro enamines, **1a-j**, was described in a previous paper.⁷⁾

General Procedure for the Reaction of 1 with Isocyanates and Phenyl Isothiocyanate. A solution containing **1** (5 mmol) and phenyl isothiocyanate or phenyl isocyanate (5.5 mmol) in acetonitrile 15 ml was refluxed for 9–90 h; then, the solvent was removed by a rotary evaporator. The residue was purified by recrystallization and/or column chromatography (silica-gel, benzene/acetone 5/1) to give **3a-d** and **6b,e**. The reaction of **1** with methyl isocyanate was performed in a sealed tube at 90 °C for 48 h, and purified in a similar manner as above. The results are as follows.

***N*-Phenyl-3-amino-2-nitro-2-butenamide (3a):** Reaction time 48 h; yield 29%; mp 177–178 °C (column chromatography); IR (CHCl_3) 3470m, 3300w, 3130w, 1658w, 1631m, 1591s, 1530s, 1444s, and 1322s cm^{-1} ; UV (EtOH) λ_{nm} ($10^{-3}\epsilon$) 252 (14.0) and 338 (21.1); ^1H NMR ($\text{DMSO}-d_6$) δ =10.35 (br, 1H), 9.5 (br, 1H), 9.05 (br, 1H), 7.4 (m, 5H), and 2.11 (s, 3H). Found: C, 54.30; H, 4.98; N, 19.09%. Calcd for $\text{C}_{10}\text{H}_{11}\text{N}_3\text{O}_3$: C, 54.29; H, 5.01; N, 18.99%.

***N*-Phenyl-3-methylamino-2-nitro-2-butenamide (3b):** Reaction time 9 h; yield 81%; mp 169–170 °C (EtOH); IR (CHCl_3) 3270w, 3150w, 1655w, 1611m, 1591s, 1532s, 1499s, and 1324s cm^{-1} ; UV (EtOH) λ_{nm} ($10^{-3}\epsilon$) 249 (14.4) and 350 (13.7); ^1H NMR (CDCl_3) δ =12.25 (br, 1H), 10.50 (br, 1H), 7.35 (m, 5H), 3.16 (d, J =6Hz, 3H), and 2.48 (s, 3H). Found: C, 56.03; H, 5.54; N, 17.80%. Calcd for $\text{C}_{11}\text{H}_{13}\text{N}_3\text{O}_3$: C, 56.16; H, 5.57; N, 17.86%.

***N*-Phenyl-3-benzylamino-2-nitro-2-butenamide (3c):** Reaction time 24 h; yield 58%; mp 144–145 °C (CCl_4); IR (CHCl_3) 3270w, 3160w, 1660w, 1618m, 1591s, 1583s, 1532s, 1444s, and 1323s cm^{-1} ; UV (EtOH) λ_{nm} ($10^{-3}\epsilon$) 249 (15.6) and 352 (15.4); ^1H NMR (CDCl_3) δ =12.48 (br, 1H), 10.4 (br, 1H), 7.3 (m, 10H), 4.6 (d, J =6Hz, 2H), and 2.47 (s, 3H). Found: C, 65.37; H, 5.47; N, 13.42%. Calcd for $\text{C}_{17}\text{H}_{17}\text{N}_3\text{O}_3$: C, 65.58; H, 5.50; N, 13.49%.

***N*-Phenyl-3-anilino-2-nitro-2-butenamide (3d):** Reaction time 18 h; yield 40%; mp 145–146 °C (CCl_4); IR (CHCl_3) 3300w, 3180w, 1665w, 1610m, 1588s, 1575s, 1490s, 1447s, and 1327s cm^{-1} ; UV (EtOH) λ_{nm} ($10^{-3}\epsilon$) 248 (14.6) and 355 (12.6); ^1H NMR (CDCl_3) δ =13.8 (br, 1H), 10.5 (br, 1H), 7.4 (m, 10H), and 2.45 (s, 3H). Found: C, 64.48; H, 5.05; N, 14.11%. Calcd for $\text{C}_{16}\text{H}_{15}\text{N}_3\text{O}_3$: C, 64.63; H, 5.08; N, 14.13%.

***N*-Methyl-3-methylamino-2-nitro-2-butenamide (5b):** Reaction time 48 h (at 90 °C in a sealed tube); yield 35%; mp 164–165 °C (column chromatography); IR (CHCl_3) 3350w, 3170w, 1602s, 1531m, and 1320s cm^{-1} ; UV (EtOH) λ_{nm} ($10^{-3}\epsilon$) $\approx$ 243 ($\approx$ 5.3) and 350 (14.9); ^1H NMR (CDCl_3) δ =12.3 (br, 1H), 10.4 (br, 1H), 3.11 (d, J =5Hz, 3H), 2.87 (d, J =5Hz, 3H), and 2.44 (s, 3H). Found: C, 41.59; H, 6.36; N, 24.36%. Calcd for $\text{C}_6\text{H}_{11}\text{N}_3\text{O}_3$: C, 41.61; H, 6.40; N, 24.26%.

***N*-Phenyl-3-methylamino-2-nitro-2-butenethioamide (6b):** Reaction time 90 h; yield 25%; mp 159–160 °C (column chromatography); IR (CHCl_3) 3350w, 3180w, 1609s, 1595s, 1495s, 1358s, and 1168s cm^{-1} ; UV (EtOH) λ_{nm} ($10^{-3}\epsilon$) 316 (14.1) and 366 (11.5); ^1H NMR ($\text{DMSO}-d_6$) δ =12.03 (br, 1H), 10.75 (br, 1H), 7.6 (m, 5H), 3.10 (d, J =6Hz, 3H), and 2.18 (s, 3H). Found: C, 52.11; H, 5.11; N, 16.66; S, 12.75%. Calcd for $\text{C}_{11}\text{H}_{13}\text{N}_3\text{O}_2\text{S}$: C, 52.45; H, 5.20; N, 16.68; S, 12.95%.

***N*-Phenyl-2-nitro-3-piperidino-2-butenethioamide (6e):** Reaction time 10 h; yield 7%; mp 163–164 °C (CCl_4); IR (CHCl_3) 3160w, 1632w, 1599w, 1550s, 1445s, 1365s, 1350s, and 1160s cm^{-1} ; UV (EtOH) λ_{nm} ($10^{-3}\epsilon$) 334 (15.8) and 355 (15.5); ^1H NMR (CDCl_3) δ =12.80 (br, 1H), 7.6 (m, 5H), 3.89 (m, 4H), 2.79 (s, 3H), and 1.85 (m, 6H). Found: C, 58.76; H, 6.29; N, 13.80; S, 10.52%. Calcd for $\text{C}_{15}\text{H}_{19}\text{N}_3\text{O}_2\text{S}$: C, 58.99; H, 6.27; N, 13.76; S, 10.50%.

General Procedure for the Reaction of 1 with Benzoyl Isothiocyanate (7). A solution containing **1** (5 mmol) and **7** (5.5 mmol) in benzene 15 ml was stirred at room temperature–boiling point. The solvent was then evaporated. The residue was separated by fractional crystallization and/or column chromatography (silica-gel, CH_2Cl_2) to give β -(benzoylthiocarbamoyl) β -nitro enamines (**8**), 4(1H)-pyrimidinethiones (**9**) and *N*-substituted *N'*-benzoylthioureas (**5**), which was the decomposition products of the *N*-adducts. The results are summarized in Table 1.

***N*-Benzoyl-3-amino-2-nitro-2-butenethioamide (8a):** Mp 136–137 °C; IR (CHCl_3) 3480m, 3380w, 3180w, 1708s, 1615s, 1465s, 1321s, and 1171s cm^{-1} ; UV (EtOH) λ_{nm} ($10^{-3}\epsilon$) 253 (11.0), 304 (16.8), and 357 (8.0); ^1H NMR ($\text{DMSO}-d_6$) δ =12.65 (br, 1H), 9.7 (br, 1H), 9.2 (br, 1H), 7.7 (m, 5H), and 2.15 (s, 3H). Found: C, 49.54; H, 4.11; N, 15.70; S, 11.80%. Calcd for

$C_{11}H_{11}N_3O_2S$: C, 49.80; H, 4.18; N, 15.84; S, 12.08%.

N-Benzoyl-3-methylamino-2-nitro-2-butenethioamide (8b): Mp 120–121 °C; IR (CHCl₃) 3370w, 3130w, 1706s, 1610s, 1600s, 1360s, and 1178s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) 248 (10.0), 310 (15.4), and 377 (10.8); ¹H NMR (DMSO-*d*₆) δ =12.8 (br, 1H), 10.9 (br, 1H), 7.7 (m, 5H), 3.19 (d, *J*=6Hz, 3H), and 2.28 (s, 3H). Found: C, 51.51; H, 4.70; N, 14.98; S, 11.53%. Calcd for C₁₂H₁₃N₃O₃S: C, 51.60; H, 4.69; N, 15.04; S, 11.48%.

N-Benzoyl-3-anilino-2-nitro-2-butenethioamide (8d): Mp 119–120 °C; IR (CHCl₃) 3380w, 3150w, 1708s, 1604s, 1582s, 1361s, and 1171s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) 243 (14.0), 308 (16.8), and 386 (13.2); ¹H NMR (CDCl₃) δ =12.52 (br, 1H), 10.30 (br, 1H), 7.6 (m, 10H), and 2.20 (s, 3H). Found: C, 59.39; H, 4.21; N, 12.25; S, 9.39%. Calcd for C₁₇H₁₅N₃O₃S: C, 59.79; H, 4.43; N, 12.31; S, 9.39%.

N-Benzoyl-2-nitro-3-piperidino-2-butenethioamide (8e): Mp 67–68 °C; IR (CHCl₃) 3140w, 1707s, 1639m, 1602m, 1525s, 1335s, and 1163s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) 242 (10.0), 312 (14.8), and 397 (12.4); ¹H NMR (CDCl₃) δ =14.06 (br, 1H), 7.8 (m, 5H), 3.95 (m, 4H), 2.75 (s, 3H), and 1.90 (m, 6H). Found: C, 57.51; H, 5.61; N, 12.39; S, 9.45%. Calcd for C₁₆H₁₉N₃O₃S: C, 57.64; H, 5.74; N, 12.60; S, 9.62%.

N-Benzoyl-3-methylamino-2-nitro-3-phenylpropenethioamide (8g): Mp 127–128 °C; IR (CHCl₃) 3370w, 3170w, 1703s, 1642m, 1598s, 1576s, 1320s, 1180s, and 1160s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) 247 (12.6), 309 (11.0), 378 (10.0), and $\approx$ 400 ($\approx$ 9.0); ¹H NMR (DMSO-*d*₆) δ =13.35 (br, 1H), 12.25 (br, 1H), 7.6 (m, 10H), and 2.91 (d, *J*=6Hz, 3H). Found: C, 59.72; H, 4.31; N, 12.40; S, 9.30%. Calcd for C₁₇H₁₅N₃O₃S: C, 59.79; H, 4.43; N, 12.31; S, 9.39%.

N-Benzoyl-3-benzylamino-2-nitro-3-phenylpropenethioamide (8h): Mp 147–148 °C; IR (CHCl₃) 3360w, 3160w, 1708s, 1604w, 1590s, 1580s, 1570s, 1368s, and 1173s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) 247 (15.2), 309 (14.0), 381 (11.8), and $\approx$ 400 ($\approx$ 10.0); ¹H NMR (DMSO-*d*₆) δ =13.4 (br, 1H), 12.5 (br, 1H), 7.6 (m, 15H), and 4.65 (d, *J*=6Hz, 2H). Found: C, 66.03; H, 4.35; N, 9.89; S, 7.70%. Calcd for C₂₃H₁₉N₃O₃S: C, 66.17; H, 4.58; N, 10.06; S, 7.68%.

N-Benzoyl-2-nitro-3-phenyl-3-piperidinopropenethioamide (8j): Mp 158–159 °C; IR (CHCl₃) 3140w, 1707s, 1610m, 1602s, 1525s, 1330s, and 1162s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) 242 (15.4), 308 (13.0), 368 (11.2), and $\approx$ 400 ($\approx$ 10.0); ¹H NMR (CDCl₃) δ =13.0 (br, 1H), 7.7 (m, 10H), 4.0 (m, 4H), and 1.1 (m, 6H). Found: C, 63.52; H, 5.33; N, 10.64; S, 8.02%. Calcd for C₂₁H₂₁N₃O₃S: C, 63.78; H, 5.35; N, 10.62; S, 8.10%.

1-Benzyl-6-methyl-5-nitro-2-phenyl-4(1H)-pyrimidinethione (9c): Mp 224–225 °C; IR (CHCl₃) 1618s, 1318s, 1294s, and 1149s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) $\approx$ 250 ($\approx$ 7.0) and 338 (18.8); ¹H NMR (DMSO-*d*₆) δ =7.6 (m, 10H), 5.30 (s, 2H), and 2.20 (s, 3H). Found: C, 63.86; H, 4.44; N, 12.45; S, 9.14%. Calcd for C₁₈H₁₅N₃O₂S: C, 64.07; H, 4.48; N, 12.45; S, 9.50%.

5-Nitro-1,2,6-triphenyl-4(1H)-pyrimidinethione (9i): Mp 260–261 °C; IR (CHCl₃) 1615s, 1593s, 1542s, 1329s, and 1170s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) 256 (10.2) and 342 (12.2); ¹H NMR (CDCl₃) δ =7.3 (m, 15H). Found: C, 68.08; H, 3.80; N, 10.65; S, 8.05%. Calcd for C₂₂H₁₅N₃O₂S: C, 68.55; H, 3.92; N, 10.90; S, 8.32%.

General Preparation of 4(1H)-Pyrimidinethione Derivatives (9) by the Cyclization of 8. A solution containing **8** in DMF (10 times) was heated at 110 °C for 5 min. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography (silica-gel, CH₂Cl₂) to

give corresponding **9**. The results are as follows.

6-Methyl-5-nitro-2-phenyl-4(1H)-pyrimidinethione (9a): Yield 90%; mp 238 °C; IR (CHCl₃) 3400w, 1675w, 1549s, 1328s, and 1155m cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) $\approx$ 270 ($\approx$ 10.0) and 305 (12.0); ¹H NMR (DMSO-*d*₆) δ =7.7 (m, 5H), 6.5 (br, 1H), and 1.29 (s, 3H). Found: C, 53.32; H, 3.54; N, 16.91; S, 12.82%. Calcd for C₁₁H₉N₃O₂S: C, 53.41; H, 3.67; N, 17.00; S, 12.91%.

1,6-Dimethyl-5-nitro-2-phenyl-4(1H)-pyrimidinethione (9b): Yield 93%; mp 219–220 °C; IR (CHCl₃) 1619s, 1517s, 1294s, and 1153s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) 251 (8.0) and 335 (18.0); ¹H NMR (DMSO-*d*₆) δ =7.6 (m, 5H), 3.45 (s, 3H), and 2.36 (s, 3H). Found: C, 55.15; H, 4.25; N, 15.95; S, 12.31%. Calcd for C₁₂H₁₁N₃O₂S: C, 55.16; H, 4.24; N, 16.08; S, 12.27%.

6-Methyl-5-nitro-1,2-diphenyl-4(1H)-pyrimidinethione (9d): Yield 92%; mp 252–253 °C; IR (CHCl₃) 1620s, 1592s, 1535s, 1320m, and 1172s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) 243 (14.0), 308 (16.8), and 386 (13.2); ¹H NMR (DMSO-*d*₆) δ =7.6 (m, 10H) and 1.92 (s, 3H). Found: C, 63.01; H, 3.99; N, 12.78; S, 9.86%. Calcd for C₁₇H₁₃N₃O₂S: C, 63.14; H, 4.02; N, 12.99; S, 9.91%.

1-Methyl-5-nitro-2,6-diphenyl-4(1H)-pyrimidinethione (9g): Yield 96%; mp 235–236 °C; IR (CHCl₃) 1613s, 1589m, 1540s, 1330s, and 1153s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) 245 (11.0) and 338 (19.0); ¹H NMR (CDCl₃) δ =7.6 (m, 10H) and 3.50 (s, 3H). Found: C, 63.00; H, 3.98; N, 13.00; S, 9.66%. Calcd for C₁₇H₁₃N₃O₂S: C, 63.14; H, 4.05; N, 12.99; S, 9.91%.

1-Benzyl-5-nitro-2,6-diphenyl-4(1H)-pyrimidinethione (9h): Yield 91%; mp 237–238 °C; IR (CHCl₃) 1605s, 1589s, 1552s, 1328s, and 1168s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) 248 (11.0) and 340 (16.0); ¹H NMR (CDCl₃) δ =7.6 (m, 15H) and 4.98 (s, 2H). Found: C, 69.02; H, 4.11; N, 10.38; S, 7.95%. Calcd for C₂₃H₁₇N₃O₂S: C, 69.15; H, 4.29; N, 10.52; S, 8.02%.

General Procedure for the Reaction of 1 with Dimethyl Acetylenedicarboxylate (11). A solution containing **1** (5 mmol) and **11** (5.5 mmol) in THF (15 ml) was refluxed until **1** was consumed as checked by TLC. The solvent was evaporated under reduced pressure. The residue was separated by fractional crystallization and/or column chromatography on silica-gel (CH₂Cl₂) to give [2+2] cycloadducts (**12**) and their ring opening products (**13**), respectively. The results are listed in Table 2.

Dimethyl 3-Methyl-3-methylamino-4-nitro-1-cyclobutene-1,2-dicarboxylate (12b): Mp 120–121 °C; IR (CHCl₃) 3150w, 1720s, 1630m, 1604m, 1578s, and 1364s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) $\approx$ 238 ($\approx$ 5.9) and 354 (6.7); ¹H NMR (CDCl₃) δ =11.0 (br, 1H), 6.01 (s, 1H), 3.73 (s, 6H), 3.12 (d, *J*=6Hz, 3H), and 2.19 (s, 3H). Found: C, 46.57; H, 5.43; N, 10.80%. Calcd for C₁₀H₁₄N₂O₆: C, 46.51; H, 5.46; N, 10.84%.

Dimethyl 3-Anilino-3-methyl-4-nitro-1-cyclobutene-1,2-dicarboxylate (12d): Mp 149–150 °C; IR (CHCl₃) 3120w, 1723s, 1639m, 1603s, and 1361s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) 230 (11.4) and 362 (12.4); ¹H NMR (CDCl₃) δ =12.37 (br, 1H), 7.3 (m, 5H), 6.20 (s, 1H), 3.78 (s, 6H), and 2.16 (s, 3H). Found: C, 56.02; H, 4.98; N, 8.73%. Calcd for C₁₅H₁₆N₂O₆: C, 56.25; H, 5.03; N, 8.74%.

Dimethyl 3-Amino-4-nitro-3-phenyl-1-cyclobutene-1,2-dicarboxylate (12f): Mp 154–155 °C; IR (CHCl₃) 3470w, 3290w, 3190w, 1728s, 1638m, 1599s, 1574s, and 1350s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) $\approx$ 240 ($\approx$ 8.6), $\approx$ 310 ($\approx$ 5.2), and 355 (11.7); ¹H NMR (DMSO-*d*₆) δ =9.8 (br, 1H), 9.46 (br, 1H), 7.4 (s, 5H), 5.61 (s, 1H), 3.60 (s, 3H), and 3.42 (s, 3H). Found: C, 54.83; H, 4.53; N, 9.07%. Calcd for C₁₄H₁₄N₂O₆: C, 54.90; H,

4.60; N, 9.14%.

Dimethyl 3-Methylamino-4-nitro-3-phenyl-1-cyclobutene-1,2-dicarboxylate (12g): Mp 164–165°C; IR (CHCl₃) 3180w, 1725s, 1630s, 1593s, 1572s, and 1366m cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) $\approx$ 240 ($\approx$ 7.3) and 362 (12.0); ¹H NMR (CDCl₃) δ =10.92 (br, 1H), 7.40 (s, 5H), 5.50 (s, 1H), 3.75 (s, 3H), 3.55 (s, 3H), and 2.90 (d, J =6Hz, 3H). Found: C, 56.44; H, 4.87; N, 8.64%. Calcd for C₁₅H₁₆N₂O₆: C, 56.25; H, 5.03; N, 8.74%.

Dimethyl 3-Benzylamino-4-nitro-3-phenyl-1-cyclobutene-1,2-dicarboxylate (12h): Mp 114–115°C; IR (CHCl₃) 3190w, 1724s, 1624m, 1590s, 1569s, and 1371s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) $\approx$ 240 ($\approx$ 7.8) and 362 (13.3); ¹H NMR (CDCl₃) δ =11.3 (br, 1H), 7.3 (m, 10H), 5.50 (s, 1H), 4.35 (d, J =6Hz, 2H), 3.75 (s, 3H), and 3.53 (s, 3H). Found: C, 63.39; H, 5.01; N, 7.07%. Calcd for C₂₁H₂₆N₂O₆: C, 63.62; H, 5.10; N, 7.07%.

Dimethyl 3-Anilino-4-nitro-3-phenyl-1-cyclobutene-1,2-dicarboxylate (12i): Mp 127–128°C; IR (CHCl₃) 3190w, 1724s, 1625s, 1590s, 1569s, and 1371s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) $\approx$ 231 ($\approx$ 13.5), $\approx$ 310 ($\approx$ 7.5), and 378 (16.0); ¹H NMR (CDCl₃) δ =12.25 (br, 1H), 7.3 (m, 10H), 5.50 (s, 1H), 3.80 (s, 3H), and 3.60 (s, 3H). Found: C, 62.72; H, 4.70; N, 7.12%. Calcd for C₂₀H₁₈N₂O₆: C, 62.81; H, 4.76; N, 7.33%.

Dimethyl 2-(1-Aminoethylidene)-3-(nitromethylene)-butanedioate (13a): Liquid; IR (CHCl₃) 3360w, 3272w, 3200w, 1720s, 1640m, 1614s, and 1355s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) 340 (6.4); ¹H NMR (CDCl₃) δ =9.95 (br, 1H), 7.58 (br, 1H), 6.95 (s, 1H), 3.81 (s, 3H), 3.73 (s, 3H), and 2.22 (s, 3H). Found: C, 43.99; H, 4.87; N, 11.25%. Calcd for C₉H₁₂N₂O₆: C, 44.26; H, 4.95; N, 11.47%.

Dimethyl 3-Nitromethylene-2-(α -piperidinobenzylidene)-butanedioate (13j): Mp 167–168°C; IR (CHCl₃) 1718s, 1618m, 1544s, and 1351s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) $\approx$ 287 ($\approx$ 8.2) and 404 (12.6); ¹H NMR (CDCl₃) δ =7.5 (m, 5H), 6.15 (s, 1H), 3.81 (s, 3H), 3.65 (s, 3H), 3.40 (m, 4H), and 2.88 (m, 6H). Found: C, 60.91; H, 5.93; N, 7.37%. Calcd for C₁₉H₂₂N₂O₆: C, 60.96; H, 5.92; N, 7.48%.

General Preparation of δ -Nitro Dienamino Diesters (13) by the Ring Opening Reaction of 12. A solution of **12** in toluene or xylene (10 times of **12**) was refluxed or stirred at 130°C until **12** was consumed as revealed by TLC. The solvent was evaporated in vacuo, and the residue was recrystallized from CCl₄ or column chromatographed (silica-gel, CH₂Cl₂) to give **13** in 49–99% yields. The results are summarized in Table 3.

Dimethyl 2-[1-(Methylamino)ethylidene]-3-(nitromethylene)-butanedioate (13b): IR (CHCl₃) 3150w, 1719m, 1608m, and 1363s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) 322 (6.4); ¹H NMR (CDCl₃) δ =11.26 (br, 1H), 6.84 (s, 1H), 3.75 (s, 3H), 3.70 (s, 3H), 3.16 (d, J =6Hz, 3H), and 2.12 (s, 3H). Found: C, 46.23; H, 5.28; N, 10.85%. Calcd for C₁₀H₁₄N₂O₆: C, 46.51; H, 5.46; N, 10.84%.

Dimethyl 2-(1-Anilinoethylidene)-3-(nitromethylene)-butanedioate (13d): IR (CHCl₃) 3150w, 1721s, 1638m, 1605m, 1583s, and 1364s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) 356

(6.6); ¹H NMR (CDCl₃) δ =12.49 (br, 1H), 7.4 (m, 5H), 6.98 (s, 1H), 3.80 (s, 3H), 3.75 (s, 3H), and 2.00 (s, 3H). Found: C, 56.24; H, 5.00; N, 8.80%. Calcd for C₁₅H₁₆N₂O₆: C, 56.25; H, 5.03; N, 8.84%.

Dimethyl 2-(α -Aminobenzylidene)-3-(nitromethylene)-butanedioate (13f): IR (CHCl₃) 3470w, 3280w, 3180w, 1725s, 1639m, 1601s, 1572m, and 1370s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) $\approx$ 240 ($\approx$ 8.6) and 350 (10.0); ¹H NMR (CDCl₃) δ =9.88 (br, 1H), 7.39 (m, 5H), 6.53 (s, 1H), 6.38 (br, 1H), 3.79 (s, 3H), and 3.58 (s, 3H). Found: C, 55.00; H, 4.61; N, 8.96%. Calcd for C₁₄H₁₄N₂O₆: C, 54.90; H, 4.60; N, 9.14%.

Dimethyl 2-[α -(Methylamino)benzylidene]-3-(nitromethylene)-butanedioate (13g): IR (CHCl₃) 3150w, 1724s, 1639m, 1600s, and 1375s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) 323 (6.6); ¹H NMR (CDCl₃) δ =10.95 (br, 1H), 7.30 (m, 5H), 6.50 (s, 1H), 3.78 (s, 3H), 3.68 (s, 3H), and 2.90 (d, J =5Hz, 3H). Found: C, 56.18; H, 5.05; N, 8.76%. Calcd for C₁₅H₁₆N₂O₆: C, 56.25; H, 5.03; N, 8.74%.

Dimethyl 2-[α -(Benzylamino)benzylidene]-3-(nitromethylene)-butanedioate (13h): IR (CHCl₃) 3180w, 1725s, 1638m, 1592s, 1571m, and 1376s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) 327 (6.1); ¹H NMR (CDCl₃) δ =11.19 (br, 1H), 7.3 (m, 10H), 6.50 (s, 1H), 4.33 (d, J =6Hz, 2H), 3.73 (s, 3H), and 3.63 (s, 3H). Found: C, 63.53; H, 5.01; N, 7.07%. Calcd for C₂₁H₂₀N₂O₆: C, 63.62; H, 5.10; N, 7.07%.

Dimethyl 2-(α -Anilinoethylidene)-3-(nitromethylene)-butanedioate (13i): IR (CHCl₃) 3160w, 1725s, 1639m, 1595m, 1568s, and 1380s cm⁻¹; UV (EtOH) λ_{nm} (10⁻³ ϵ) $\approx$ 233 ($\approx$ 12.8) and 378 (11.0); ¹H NMR (CDCl₃) δ =12.30 (br, 1H), 7.2 (m, 10H), 6.53 (s, 1H), 3.75 (s, 3H), and 3.55 (s, 3H). Found: C, 62.72; H, 4.73; N, 7.27%. Calcd for C₂₀H₁₈N₂O₆: C, 62.81; H, 4.76; N, 7.33%.

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