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

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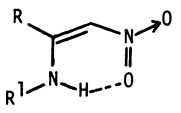
β-Nitro enamines (**1**) reacted with isocyanates and isothiocyanates to give β-(substituted carbamoyl) and β-(substituted thiocarbamoyl) β-nitro enamines, respectively. The reaction of **1** with benzoyl isothiocyanate gave β-(benzoylthiocarbamoyl) β-nitro enamines (**8**) and/or a mixture of **8** 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*-nitrobenzenesulfenyl 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.

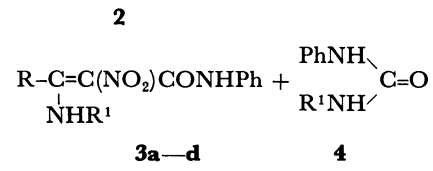


1

	R	R¹		R	R¹
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

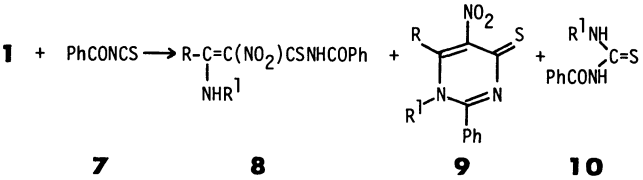


1a—d + PhNCO ⟶ **2**

R–C=C(NO_2)CONHPh + $PhNH(R^1NH)C{=}O$

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** and **3b—d**, **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 νC=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 νC=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 =CH- proton signal near 6.5 ppm of the corresponding **1a—e**, respectively.



1 + PhCONCS ⟶ R–C(NHR¹)=C(NO_2)CSNHCOPh + + PhCONH(R¹NH)C=S

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_2Cl_2	**8a**	17	**9a**	2		8
1b	rt	48	C-CH_2Cl_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_2Cl_2	**8e**	84	**9e**	0		1
1g	rt	100	PhH/CCl_4	**8g**	87	**9g**	0		0
1h	bp	18	C-CH_2Cl_2	**8h**	60	**9h**	17		5
1i	bp	80	C-CH_2Cl_2	**8i**	0	**9i**	16		6
1j	rt	45	C-CH_2Cl_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'*-R^1-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 νNH in the region of 3500—3100 cm^{-1}, and νC=O and νC=S absorptions were observed at 1708—1706 and 1180—1162 cm^{-1}, respectively. In cyclic compounds **9b—d, g—i**, the νC=O and νNH absorptions disappeared, and **9a** showed a weak absorption of the νNH at 3400 cm^{-1}. The absorptions of νC=C+νC=N and νC=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 νNH absorptions in the regions at 3350—3270 and 3180—3150 cm^{-1}; also, a strong absorption of νC=O that overlapped with νC=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, $PhCH_2$, and Ph) show a strong νC=O in the lower-frequency region of 1605—1568 cm^{-1}. Such a low-frequency shift of the νC=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]

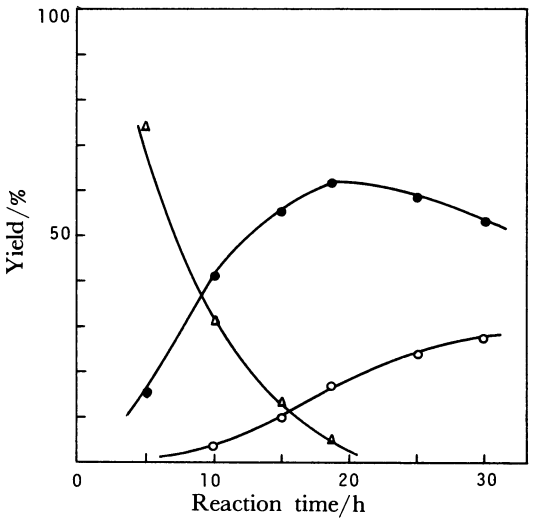
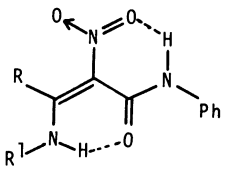


Fig. 1. Yields of **8h** and **9h** vs. reaction time in boiling benzene. ●: **8h**, ○: **9h**, △: recovered 1h.



[**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 NCH_3 and NCH_2- 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_2Cl_2	**12a**	0	**13a**	71
1b	4	PhH	**12b**	72	**13b**	0
1d	4	C-CH_2Cl_2	**12d**	47	**13d**	25
1f	48	C-CH_2Cl_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_2Cl_2	**12i**	26	**13i**	31
1j	100	C-CH_2Cl_2	**12j**	0	**13j**	6

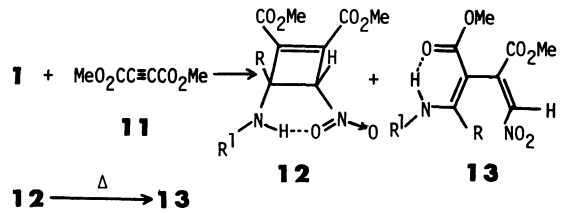
a) C: Silica-gel column chromatography.

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_2Cl_2	**13b**	49	Liquid
12d	Toluene	bp	1	C-CH_2Cl_2	**13d**	95	99—100
12f	Xylene	130	120	C-CH_2Cl_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

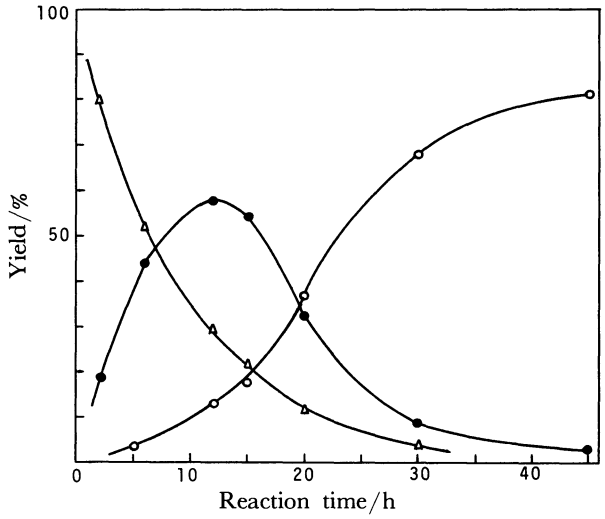


Fig. 2. Yields of **12h** and **13h** vs. reaction time in boiling THF. ●: **12h**, ○: **13h**, △: recovered 1h.

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 νNH absorption at 3190—3120 cm^{-1}, and a strong νC=O absorption was observed in the region of 1728—1720 cm^{-1}. A weak absorption at 1639—1625 cm^{-1} region was assigned to νC=C absorption, and a strong absorption at 1603—

1561 cm^{-1} region was assigned to depend primarily on $\nu_{as}NO_2$ 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 NH ··· O=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 νC=O and a medium absorption of νC=C was observed at 1725—1718 and 1640—1618 cm^{-1} region, respectively. Strong absorptions of $\nu_{as}NO_2$ and ν_sNO_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 isocyanate or phenyl isothiocyanate (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} ($10^{-3}\varepsilon$) 252 (14.0) and 338 (21.1); ^1H NMR (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 $C_{10}H_{11}N_3O_3$: 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} ε) 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 $C_{11}H_{13}N_3O_3$: 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} ($10^{-3}\varepsilon$) 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 $C_{17}H_{17}N_3O_3$: 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} ε) 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 $C_{16}H_{15}N_3O_3$: 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} ε) ≈243 (≈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 $C_6H_{11}N_3O_3$: 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} ε) 316 (14.1) and 366 (11.5); ^1H NMR (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 $C_{11}H_{13}N_3O_2S$: 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} ε) 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 $C_{15}H_{19}N_3O_2S$: 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(1*H*)-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} ε) 253 (11.0), 304 (16.8), and 357 (8.0); ^1H NMR (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 ($CHCl_3$) 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 $C_{12}H_{13}N_3O_3S$: 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 ($CHCl_3$) 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 ($CDCl_3$) 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 $C_{17}H_{15}N_3O_3S$: 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 ($CHCl_3$) 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 ($CDCl_3$) 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 $C_{16}H_{19}N_3O_3S$: 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 ($CHCl_3$) 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 ≈400 (≈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 $C_{17}H_{15}N_3O_3S$: 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 ($CHCl_3$) 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 ≈400 (≈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 $C_{23}H_{19}N_3O_3S$: 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 ($CHCl_3$) 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 ≈400 (≈10.0); ^1H NMR ($CDCl_3$) 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 $C_{21}H_{21}N_3O_3S$: C, 63.78; H, 5.35; N, 10.62; S, 8.10%.

1-Benzyl-6-methyl-5-nitro-2-phenyl-4(1*H*)-pyrimidinethione (9c): Mp 224—225 °C; IR ($CHCl_3$) 1618s, 1318s, 1294s, and 1149s cm^{-1}; UV (EtOH) λ_{nm} (10^{-3} ε) ≈250 (≈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 $C_{18}H_{15}N_3O_2S$: C, 64.07; H, 4.48; N, 12.45; S, 9.50%.

5-Nitro-1,2,6-triphenyl-4(1*H*)-pyrimidinethione (9i): Mp 260—261 °C; IR ($CHCl_3$) 1615s, 1593s, 1542s, 1329s, and 1170s cm^{-1}; UV (EtOH) λ_{nm} (10^{-3} ε) 256 (10.2) and 342 (12.2); ^1H NMR ($CDCl_3$) δ=7.3 (m, 15H). Found: C, 68.08; H, 3.80; N, 10.65; S, 8.05%. Calcd for $C_{22}H_{15}N_3O_2S$: C, 68.55; H, 3.92; N, 10.90; S, 8.32%.

General Preparation of 4(1*H*)-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, CH_2Cl_2) to give corresponding **9**. The results are as follows.

6-Methyl-5-nitro-2-phenyl-4(1*H*)-pyrimidinethione (9a): Yield 90%; mp 238 °C; IR ($CHCl_3$) 3400w, 1675w, 1549s, 1328s, and 1155m cm^{-1}; UV (EtOH) λ_{nm} (10^{-3} ε) ≈270 (≈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 $C_{11}H_9N_3O_2S$: C, 53.41; H, 3.67; N, 17.00; S, 12.91%.

1,6-Dimethyl-5-nitro-2-phenyl-4(1*H*)-pyrimidinethione (9b): Yield 93%; mp 219—220 °C; IR ($CHCl_3$) 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 $C_{12}H_{11}N_3O_2S$: C, 55.16; H, 4.24; N, 16.08; S, 12.27%.

6-Methyl-5-nitro-1,2-diphenyl-4(1*H*)-pyrimidinethione (9d): Yield 92%; mp 252—253 °C; IR ($CHCl_3$) 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 $C_{17}H_{13}N_3O_2S$: C, 63.14; H, 4.02; N, 12.99; S, 9.91%.

1-Methyl-5-nitro-2,6-diphenyl-4(1*H*)-pyrimidinethione (9g): Yield 96%; mp 235—236 °C; IR ($CHCl_3$) 1613s, 1589m, 1540s, 1330s, and 1153s cm^{-1}; UV (EtOH) λ_{nm} (10^{-3} ε) 245 (11.0) and 338 (19.0); ^1H NMR ($CDCl_3$) 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 $C_{17}H_{13}N_3O_2S$: C, 63.14; H, 4.05; N, 12.99; S, 9.91%.

1-Benzyl-5-nitro-2,6-diphenyl-4(1*H*)-pyrimidinethione (9h): Yield 91%; mp 237—238 °C; IR ($CHCl_3$) 1605s, 1589s, 1552s, 1328s, and 1168s cm^{-1}; UV (EtOH) λ_{nm} (10^{-3} ε) 248 (11.0) and 340 (16.0); ^1H NMR ($CDCl_3$) 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 $C_{23}H_{17}N_3O_2S$: 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 (CH_2Cl_2) 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 ($CHCl_3$) 3150w, 1720s, 1630m, 1604m, 1578s, and 1364s cm^{-1}; UV (EtOH) λ_{nm} (10^{-3} ε) ≈238 (≈5.9) and 354 (6.7); ^1H NMR ($CDCl_3$) 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 $C_{10}H_{14}N_2O_6$: C, 46.51; H, 5.46; N, 10.84%.

Dimethyl 3-Anilino-3-mehtyl-4-nitro-1-cyclobutene-1,2-dicarboxylate (12d): Mp 149—150 °C; IR ($CHCl_3$) 3120w, 1723s, 1639m, 1603s, and 1361s cm^{-1}; UV (EtOH) λ_{nm} (10^{-3} ε) 230 (11.4) and 362 (12.4); ^1H NMR ($CDCl_3$) 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 $C_{15}H_{16}N_2O_6$: 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 ($CHCl_3$) 3470w, 3290w, 3190w, 1728s, 1638m, 1599s, 1574s, and 1350s cm^{-1}; UV (EtOH) λ_{nm} (10^{-3} ε) ≈240 (≈8.6), ≈310 (≈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 $C_{14}H_{14}N_2O_6$: 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 ($CHCl_3$) 3180w, 1725s, 1630s, 1593s, 1572s, and 1366m cm^{-1}; UV (EtOH) λ_{nm} (10^{-3} ε) ≈240 (≈7.3) and 362 (12.0); ^1H NMR ($CDCl_3$) 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 $C_{15}H_{16}N_2O_6$: 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 ($CHCl_3$) 3190w, 1724s, 1624m, 1590s, 1569s, and 1371s cm^{-1}; UV (EtOH) λ_{nm} (10^{-3} ε) ≈240 (≈7.8) and 362 (13.3); ^1H NMR ($CDCl_3$) 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 $C_{21}H_{26}N_2O_6$: 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 ($CHCl_3$) 3190w, 1724s, 1625s, 1590s, 1569s, and 1371s cm^{-1}; UV (EtOH) λ_{nm} (10^{-3} ε) ≈231 (≈13.5), ≈310 (≈7.5), and 378 (16.0); ^1H NMR ($CDCl_3$) 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 $C_{20}H_{18}N_2O_6$: C, 62.81; H, 4.76; N, 7.33%.

Dimethyl 2-(1-Aminoethylidene)-3-(nitromethylene)-butanedioate (13a): Liquid; IR ($CHCl_3$) 3360w, 3272w, 3200w, 1720s, 1640m, 1614s, and 1355s cm^{-1}; UV (EtOH) λ_{nm} (10^{-3} ε) 340 (6.4); ^1H NMR ($CDCl_3$) 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 $C_9H_{12}N_2O_6$: C, 44.26; H, 4.95; N, 11.47%.

Dimethyl 3-Nitromethylene-2-(α-piperidinobenzylidene)-butanedioate (13j): Mp 167—168 °C; IR ($CHCl_3$) 1718s, 1618m, 1544s, and 1351s cm^{-1}; UV (EtOH) λ_{nm} (10^{-3} ε) ≈287 (≈8.2) and 404 (12.6); ^1H NMR ($CDCl_3$) 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 $C_{19}H_{22}N_2O_6$: 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 CCl_4 or column chromatographed (silica-gel, CH_2Cl_2) to give **13** in 49—99% yields. The results are summarized in Table 3.

Dimethyl 2-[1-(Methylamino)ethylidene]-3-(nitromethylene)butanedioate (13b): IR ($CHCl_3$) 3150w, 1719m, 1608m, and 1363s cm^{-1}; UV (EtOH) λ_{nm} (10^{-3} ε) 322 (6.4); ^1H NMR ($CDCl_3$) 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 $C_{10}H_{14}N_2O_6$: C, 46.51; H, 5.46; N, 10.84%.

Dimethyl 2-(1-Anilinoethylidene)-3-(nitromethylene)-butanedioate (13d): IR ($CHCl_3$) 3150w, 1721s, 1638m, 1605m, 1583s, and 1364s cm^{-1}; UV (EtOH) λ_{nm} (10^{-3} ε) 356 (6.6); ^1H NMR ($CDCl_3$) 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 $C_{15}H_{16}N_2O_6$: C, 56.25; H, 5.03; N, 8.84%.

Dimethyl 2-(α-Aminobenzylidene)-3-(nitromethylene)-butanedioate (13f): IR ($CHCl_3$) 3470w, 3280w, 3180w, 1725s, 1639m, 1601s, 1572m, and 1370s cm^{-1}; UV (EtOH) λ_{nm} (10^{-3} ε) ≈240 (≈8.6) and 350 (10.0); ^1H NMR ($CDCl_3$) 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 $C_{14}H_{14}N_2O_6$: C, 54.90; H, 4.60; N, 9.14%.

Dimethyl 2-[α-(Methylamino)benzylidene]-3-(nitromethylene)butanedioate (13g): IR ($CHCl_3$) 3150w, 1724s, 1639m, 1600s, and 1375s cm^{-1}; UV (EtOH) λ_{nm} (10^{-3} ε) 323 (6.6); ^1H NMR ($CDCl_3$) 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 $C_{15}H_{16}N_2O_6$: C, 56.25; H, 5.03; N, 8.74%.

Dimethyl 2-[α-(Benzylamino)benzylidene]-3-(nitromethylene)butanedioate (13h): IR ($CHCl_3$) 3180w, 1725s, 1638m, 1592s, 1571m, and 1376s cm^{-1}; UV (EtOH) λ_{nm} (10^{-3} ε) 327 (6.1); ^1H NMR ($CDCl_3$) 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 $C_{21}H_{20}N_2O_6$: C, 63.62; H, 5.10; N, 7.07%.

Dimethyl 2-(α-Anilinobenzylidene)-3-(nitromethylene)-butanedioate (13i): IR ($CHCl_3$) 3160w, 1725s, 1639m, 1595m, 1568s, and 1380s cm^{-1}; UV (EtOH) λ_{nm} (10^{-3} ε) ≈233 (≈12.8) and 378 (11.0); ^1H NMR ($CDCl_3$) 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 $C_{20}H_{18}N_2O_6$: C, 62.81; H, 4.76; N, 7.33%.

References

1) T. Tokumitsu and T. Hayashi, *J. Org. Chem.*, **50**, 1547 (1985).

2) D. Rajappa, *Heterocycles*, **7**, 507 (1977).

3) S. Maiorana, D. Pocar, and P. D. Croce, *Tetrahedron Lett.*, **1966**, 6043.

4) D. Pocar, S. Maiorana, and P. D. Croce, *Gazz. Chim. Ital.*, **98**, 949 (1968).

5) G. deStevens, B. Smolinsky, and L. Dorfman, *J. Org. Chem.*, **29**, 1115 (1964).

6) L. J. Bellamy, "Advances in Infrared Group Frequencies," Methuen & Co. Ltd., London (1968), p. 213.

7) T. Tokumitsu and T. Hayashi, *Nippon Kagaku Kaishi*, **1983**, 88.

8) K. C. Brannock, R. D. Burpitt, V. W. Goodlett, and J. G. Thweatt, *J. Org. Chem.*, **28**, 1464 (1963); G. A. Berchtold, and G. F. Uhlig, *ibid.*, **28**, 1459 (1963); C. F. Huebner, L. Dorfman, M. M. Robinson, E. Donoghue, W. G. Pierson, and P. Strachan, *ibid.*, **28**, 3139 (1963).

9) D. Lloyd and H. McNab, *Ang. Chem. Int. Ed. Engl.*, **15**, 459 (1976).