Tetrahedron Vol. 42, No. 1, pp. 305 to 314, 1986
Printed in Great Britain.

0040-4020/86 $3.00 + .00

PALLADIUM-CATALYZED CYCLIZATION REACTIONS. UNIQUE SYNTHESIS OF CONDENSED THIAZOLES

MASATO MIZUTANI* and YUZURU SANEMITSU

Takarazuka Research Center, Sumitomo Chemical Co. Ltd.,
Takatsukasa, Takarazuka, Hyogo 665, Japan

YOSHINAO TAMARU and ZEN-ICHI YOSHIDA*

Department of Synthetic Chemistry, Faculty of Engineering,
Kyoto University, Yoshida, Kyoto 606, Japan

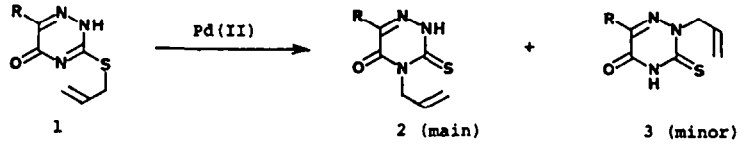
(*Received in Japan* 31 *August* 1985)

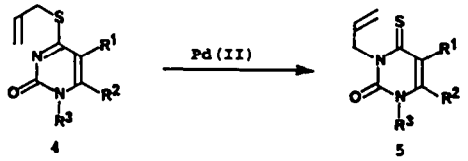
Abstract: The facile synthesis of 3-methylene-2,3-dihydro-5H-thiazolo-[3,2-c]pyrimidin-5-ones (9) has been performed by the catalytic action of a Pd(II) salt on 4-propargylthiopyrimidin-2(1H)-ones (6). Similar Pd(II)-catalyzed cyclization of 3-propargylthio-1,2,4-triazin-5(2H)-ones (10) gives 6-methylene-6,7-dihydro-4H-thiazolo[2,3-c][1,2,4]-triazin-4-ones (11) as a main product. 3-Methylene-2,3-dihydro-7H-thiazolo[3,2-b][1,2,4]triazin-7-ones (12), the regioisomers of 11, are provided by a base-catalyzed cyclization of 10.

Many efforts have been devoted to prepare a variety of heterocyclic systems by using palladium-catalyzed intramolecular functionalization of olefins as the ring-forming step.[1] Such a functionalization by use of acetylenic moiety seems to be very attractive because the remaining double bond might be used for the further manipulations after cyclization. However, only a few reports, e.g. 1-amino-3-alkyn-2-ols to pyrroles[2] and homoalkynyl alcohol to α-methylene lactones via carbonylation,[3] have been recorded. Recently we have disclosed that the S → N allylic transformation of 3-allylthio-1,2,4-triazin-5(2H)-ones[4] and 4-allylthiopyrimidin-2(1H)-ones[5] are effectively catalyzed by Pd(II) salts (Scheme I).

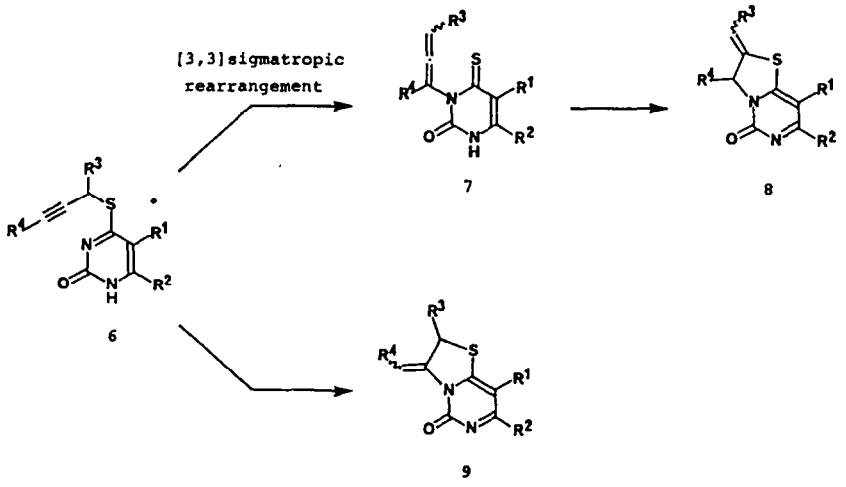
Since the addition of amines and amides to acetylenes is a well-known process,[6] it is of interest to know, not only from a mechanistic but also a synthetic point of view whether 4-propargylthiopyrimidin-2(1H)-ones 6 undergo the [3,3]sigmatropic rearrangement or a direct nucleophlic addition of amide function to acetylenes (Scheme II).[7] The former process might provide 2-methylene-2,3-dihydro-5H-thiazolo-

Scheme I





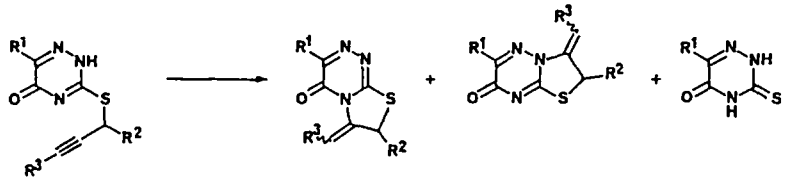
Scheme II



6 7 8 9

[3,2-c]pyrimidin-5-ones 8 and the latter process 3-methylene-2,3-dihydro-5H-thiazolo[3,2-c]pyrimidin-5-ones 9, both of which are exo methylene regioisomers of thiazolopyrimidones. In this paper[8] we describe that by the catalysis of Pd(II) salts 6 specifically undergoes the cyclization via a nucleophilic addition of amide to acetylene to provide 9 in a reasonable yield. 3-Propargylthio-1,2,4-triazin-5(2H)-ones 10 undergo the similar Pd(II)-catalyzed cyclization to give 6-methylene-6,7-dihydro-4H-thiazolo[2,3-c][1,2,4]triazin-4-ones 11 together with a small amount of their regioisomer 3-methylene-2,3-dihydro-7H-thiazolo[3,2-b][1,2,4]triazin-7-ones 12 (Scheme III). This regioisomer 12 could be obtained specifically by the NaOH catalyzed cyclization of 10.

Scheme III



10 11 12 13

Results and Discussion

Cyclization of 6 to Thiazolopyrimidones 9

The palladium-catalyzed reaction was performed for the typical eight kinds of 4-propargylthiopyrimidin-2(1H)-ones 6 (6a-h; Table I) using 1-10 mol% of bis(benzonitrile)palladium chloride as a catalyst in a wide range of solvents at their refluxing temperatures. Protic (e.g., methanol) and aprotic (e.g., acetonitrile, 1,2-dimethoxyethane DME, tetrahydrofuran THF, dioxane, etc) are applicable, but judging from the yield of 9, reaction times and conversions, acetonitrile and methanol were mostly employed (cf. entries 3, 4 and 5). In every case (except for entry 14), 3-methylene-2,3-dihydro-5H-thiazolo[3,2-c]pyrimidin-5-ones 9 was formed cleanly and in a reasonable yield. From Table I, it is apparent that the R^1 and/or R^3 methyl substituent(s) accelerate the reaction. For the steric reasons,

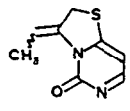
Table I. The Cyclization of 4-Propargylthiopyrimidin-2(1H)-ones (6) to 3-Methylene-2,3-dihydro-5H-thiazolo[3,2-c]pyrimidin-5-ones (9)

entry	4-propargylthiopyrimidone 6	R^1	R^2	R^3	R^4	Pd[a] (mol%)	reaction condition[b]	conversion (%)	product 9	yield[c] (%)
1	6a	H	H	H	H	5	DME, 5 h	76	9a	88
2	6a	H	H	H	H	none	CH_3OH, 18 h	100	9a	0
3	6b	CH_3	H	H	H	5	CH_3CN, 2 h	100	9b	78
4	6b	CH_3	H	H	H	5	CH_3OH, 2 h	100	9b	76
5	6b	CH_3	H	H	H	5	DME, 8 h	100	9b	57
6	6b	CH_3	H	H	H	none	CH_3OH, 30 h	66	9b	39
7	6c	F	H	H	H	10	CH_3CN, 7 h	100	9c[d]	35
8	6d	H	CH_3	H	H	2	CH_3OH, 1 h	100	9d	93
9	6e	Br	CH_3	H	H	5	CH_3CN, 3 h	100	9e	80
10	6f	H	H	CH_3	H	1	CH_3OH, 1 h	100	9f	82
11	6f	H	H	CH_3	H	none	CH_3OH, 48 h	76	9f	88
12	6g	CH_3	H	CH_3	H	2	CH_3OH, 1 h	100	9g	75
13	6g	CH_3	H	CH_3	H	none	CH_3OH, 37 h	80	9g	75
14	6h	H	H	H	CH_3	5	dioxane, 37 h	58	9h	e

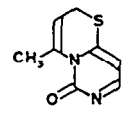
a) $PdCl_2(PhCN)_2$ was used and the amount of catalyst is not optimized. b) At the refluxing temperature of the solvent indicated. c) Yields refer to the isolated ones based on conversion. d) Product 9c is unstable. Low yield might be due to the decomposition during reaction and purification. e) The exact structure of products could not be determined (see text).

the R^1 and R^3 substituents seem to operate to orient the propargyl group to the close proximity of the pyrimidone N-3 center and accelerate the cyclization.

Cyclization of 6h ($R^1 = R^2 = R^3 = H$, $R^4 = CH_3$) was slow and gave many products. Among them 3-ethylidene-5H-thiazolino[3,2-c]pyrimidin-5-one 9h and 4-methyl-2H,6H-[1,3]thiazino[3,2-c]pyrimidin-6-one 9h', whose structures were assigned tentatively, were isolated in 11% yield as a chromatographically non-separable 1:1 mixture.



9h



9h'

The fluorinated substrate 6c showed the similar or a slightly reduced reactivity compared with 6a. In this case the modest isolated yield of 9c may be probably due to instability of the product, which seems to decompose during reaction and chromatography purification.

The smooth cyclization of 6d may be attributed to an enhanced nucleophilicity of the pyrimidone N-3 nitrogen atom by the R^2 methyl group and/or to the stability of the product 9b.[9]

Interestingly, even in the absence of Pd(II) salts, the relatively reactive 6b, 6f and 6g could be cyclized at the methanol refluxing temperature to give 9b, 9f and 9g, respectively. These reactions, however, are very slow and hardly attain the completion. In order to get rid of drawbacks (sluggishness, low yield, limited applicability, cf. entry 2) in the thermal cyclization, many reaction conditions were tried, but all attempts resulted in either complete decomposition (6b: cat. CH_3ONa, cat. p-toluenesulfonic acid, or 1.2 equiv of BF_3-etherate in refluxing CH_3OH or DMF, 120 °C) or complete recovery of 6b (1.2 equiv of BF_3-etherate in refluxing THF).

Cyclization of 10 to thiazolo-1,2,4-triazinones (11 and 12)

For the Pd(II)-catalyzed reaction of 3-propargylthio-1,2,4-triazin-5(2H)-ones 10, in addition to the problem of the course of the reaction (a [3,3]sigmatropic

rearrangement vs. direct nucleophilic addition of amide to acetylene, cf. Scheme II), there exists another problem of regiochemistry, i.e., alkylation at the N-2 vs. N-4 nitrogen atoms of triazinone ring. Again in this triazinone case, only the direct nucleophilic addition of amide function to the propargyl triple bond took place.

Results, together with the reaction conditions for six kinds of 10, are summarized in Table II. As seen from this Table, 1-5 mol% of a Pd(II) salt is sufficient for the complete cyclization of 10. The reaction could be undertaken both in aprotic (CH_3CN, DME, THF) and protic (CH_3OH) solvents at their refluxing temperatures. Generally Pd-catalyzed reaction provides 6-methylene-6,7-dihydro-4H-thiazolo[2,3-c][1,2,4]triazin-4-ones 11 as a main product together with small amounts of 3-methylene-2,3-dihydro-7H-thiazolo[3,2-b][1,2,4]triazin-7-ones 12 and depropargylated product 13 (Scheme III). There seems to be a general trend that the product 13 is formed in large amounts in the cases where the reactions are reluctant to proceed (entries 1 and 7 in Table II). The methyl substituent as R^2 accelerates the reaction and diminishes the formation of 13 (entries 9 and 12), which can be explained from the steric effect of R^2 substituent (vide supra). The reaction of 10f ($R^1 = R^2 = H$, $R^3 = CH_3$) provided many products in which no traces of desirable fused compounds were detected.

Thermal cyclization of 10 was then followed, but no reaction took place and the starting material was recoverd (e.g., 10b: in refluxing CH_3OH for 20 h). Surprisingly, the addition of a base was found to catalyze the cyclization of 10, although 6 decomposed under bacic condition. The reaction proceeded in the presence of small amounts of base (e.g., NaOH, NaH) in protic (CH_3OH) and aprotic (DMF) solvents at 65-80 °C, and gave 12 as a single product when the reaction was stopped at an appropriate conversion time (Table II). Further reaction caused decomposition of the product. Both the exclusive cyclization on the N-2 nitrogen

Table II. The Cyclization of 3-Propargylthio-1,2,4-triazin-5(2H)-ones (10) to 6-Methylene-6,7-dihydro-4H-thiazolo[2,3-c][1,2,4]triazin-4-ones (11) and/or 3-Methylene-2,3-dihydro-7H-thiazolo[3,2-b][1,2,4]triazin-7-ones (12)

entry	propargylthiotriazine 10	R^1	R^2	R^3	catalyst[a] (mol%) Pd[b]	NaOH[c]	reaction condition[d]	conversion (%)	product yield[e] (%) 11	12	13
1	10a	H	H	H	5	-	CH_3CN, 6 h	94	56	0	14
2	10a	H	H	H	-	50	CH_3OH, 4 h	59	0	76	0
3	10b	CH_3	H	H	2	-	DME, 2 h	100	64	26	4
4	10b	CH_3	H	H	1	-	THF, 3 h	100	44	6	-
5	10b	CH_3	H	H	2	-	CH_3OH, 10 h	90	58	11	-
6	10b	CH_3	H	H	-	20	CH_3OH, 4 h	68	0	74	0
7	10c	Ph	H	H	5	-	DME, 6 h	100	43	8	25
8	10c	Ph	H	H	-	10	CH_3OH, 9 h	62	23	73	0
9	10d	CH_3	CH_3	H	2	-	CH_3OH, 2 h	100	70	10	5
10	10d	CH_3	CH_3	H	-	10	CH_3OH, 4.5 h	88	0	87[f]	0
11	10d	CH_3	CH_3	H	-	10[g]	DMF, 80 °C, 3 h	79	0	54[h]	0
12	10e	Ph	CH_3	H	2	-	DME, 2 h	100	70	15	3
13	10f	CH_3	H	CH_3	5	-	CH_3CN, 2 h	93		i	
14	10f	CH_3	H	CH_3	-	160	CH_3OH, 22 h	0	-	-	-

a) The amount of catalyst is not optimized. b) $PdCl_2(PhCN)_2$ was used. c) Indicated amounts of 1 N NaOH was added to the 10 M reaction solution. d) At the refluxing temperature of the solvent indicated (except entry 11). e) Yields refer to the isolated ones based on conversion. f) The product is a mixture of 2,6-dimethyl-3-methylene-2,3-dihydro-7H-thiazolo[3,2-b][1,2,4]triazin-7-one (12d) and 2,3,6-trimethyl-7H-thiazolo[3,2-b][1,2,4]triazin-7-one (14) (52 : 48). g) Sodium hydride was used in place of NaOH. h) The product ratio of 12d to 14 is 78 : 22. i) The structure of products could not be determined.

atom (entries 2, 6 and 10), and the exceptional concomitant cyclization on N-4 in 10c (entry 8) are reminiscent of the selective alkylation of 3-methylthio-1,2,4-triazin-5(2H)-ones with alkyl halides under basic condition.[10] Meanwhile the product in entry 10 and 11 in Table II was a mixture of 2,6-dimethyl-3-methylene-2,3-dihydro-7H-thiazolo[3,2-b][1,2,4]triazin-7-one (12d) and 2,3,6-trimethyl-7H-thiazolo[3,2-b][1,2,4]triazin-7-one (14) which can be undertaken to be the base-assisted isomerization product of 12d from the following experiment: Treatment of isolated 12d with 0.1 equiv of NaOH in refluxing CH_3OH for 1 h afforded 14 in 90 % yield.

Reaction Mechanism and Structural Study of Fused Heterocycles

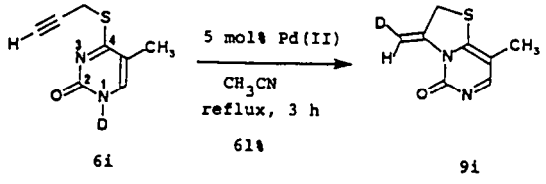
The structure of 9 follows from its analytical and spectral data. The mass spectra of 9 showed the same parent peak as the corresponding starting material 6. The methylidene thiazoline structure of 9a was indicated by the well separated allylic methylene protons (δ 4.05, triplet, J = 1.8 Hz) and two kinds of exo methylene protons (δ 5.15, quartet, J = 1.8 Hz, δ 6.58, quartet, J = 1.8 Hz). The large differnce in the ^1H chemical shifts of exo methylene protons may be due to the anisotropy of the C-2 carbonyl group and the deshielded resonance was assigned to the methylene proton syn to the C-2 carbonyl. This assignment was also supported by the $Eu(dpm)_3$ experiments. By the gradual addition of $Eu(dpm)_3$, the lower field resonance shifted downfield 2.4 times larger than the higher field resonance.

The two exo methylene protons and the aliphatic methyl doublet in 9f and 9g (9f: δ 1.63, doublet, J = 7.2 Hz; 9g: δ 1.62, doublet, J = 7.2 Hz), as well as the regio- and stereospecific deuterization (vide infra, Scheme IV), clearly support the structure of 9 and exclude the possibility of the structure 8.

The exo methylene structures of 11 and 12 were determined similarly, especially based on their ^1H NMR spectra: The ^1H NMR spectra of 11 showed a close resemblance to those of 9 and the splitting of the exo methylene chemical shifts of 12 was smaller than that of 9 and 11 (e.g., 11a: 1.25 ppm; 12a: 0.63 ppm).

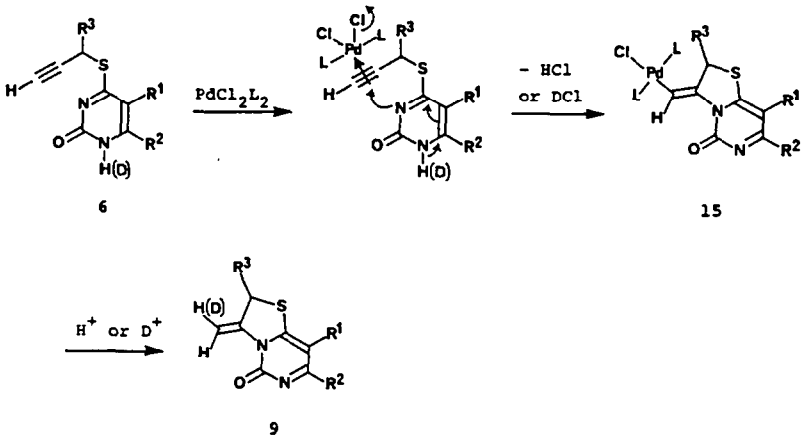
Based on these structures of 9, 11 and 12, the reaction pathway involving a [3,3]sigmatropic rearrangement can be excluded . In order to get a further insight to the reaction mechanism, the N-1 monodeuterated 6b (=6i) was subjected to the Pd-catalyzed cyclization (Scheme IV-1). The specific monodeuteration at the methylene proton anti to the C-2 carbonyl was evident on the bases of the disappearance of the higher field resonance of the methylene protons.

Scheme IV



This regio- and stereospecific deuteration and the catalytic behavior of Pd(II) species seem to be reconciled with the mechanism shown in Scheme V, which involves the coordination of Pd(II) to the propargyl triple bond and a nucleophilic trans attack of the N-3 nitrogen atom to the thus activated triple bond to form a vinylpalladium complex (15). Protonolysis of 15 may

Scheme V

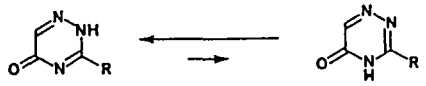


provide 9 and $PdCl_2$.[11]

The same monodeuterated methylidenethiazoline 9i was also obtained, though in a very low conversion despite of the larger reaction times, by the reaction of 6b in refluxing d_4-CH_3OH (Scheme IV-2). This is rationalized as a result of a simple trans nucleophilic addition of the N-3 nitrogen to the triple bond. Similar trans addition was observed in the base-catalyzed cylization of 12d (Scheme IV-3).

3-Substituted-1,2,4-triazin-5(2H)-ones are known to exist as a mixture of tautomers 16A and 16B (Scheme VI). It is indicated spectroscopically[12] and chemically[4,10,13] that the equilibrium lies heavily to the left. Accordingly the results of cyclization of 10 indicate that the C=N nitrogen atom, by the conjugation with the N-2 nitrogen atom, reacts favorably with the triple bond activated by the coordination of Pd(II), on the other hand, the N-2 nitrogen, under basic conditions, exclusively reacts with the unactivated triple bond. Although these are very controversial, it is premature to discuss them in detail.

Scheme VI



16A 16B

R = H, Me, Ph, SMe, NMe_2

The structures of 11 and 12 were also carefully discriminated by the comparison of their ^1H NMR and UV spectra. In the ^1H NMR spectra of 11, the exo methylene proton syn to carbonyl group resonates at 1.26 - 1.37 ppm lower field than the anti one owing to the deshielding effect of carbonyl group. In contrast with this, the difference between two kinds of exo methylene protons of 12 is small (0.48 - 0.74 ppm). Another basis for distinguishing 11 and 12 is comparison of their UV spectra. 3,4-Disubstituted-1,2,4-triazin-5(4H)-ones are known to show the absorption maxima at the longer wavelengths compared with 2,3-disubstituted compounds.[10b] The bicyclic derivatives 11b and 12b showed the extremely similar absorption shapes and maxima, respectively.

In the synthetic viewpoint of thiazolo[3,2-c]pyrimidones, only two methods, i.e., acid-catalyzed isomerization of 2,3-dihydro-5H-thiazolo[3,2-a]pyrimidin-5-ones[14] and the reaction of 4-thiouraciles with α-haloaldehyde,[15] have been reported. Our method is very unique and effective from the standpoint of the availability of starting material, ease of operation and the possibility of introducing an exo methylene group in good yield. For the preparation of thiazolo-1,2,4-triazinones, the presently available synthetic methods show drawbacks in yield,[16] limited availability of the starting materials[17] or low selectivity.[18] In comparison with these, the efficiency of the present method is apparent because each of 11 and 12 can be prepared at will by Pd(II)-catalyzed or base-catalyzed cyclization by using a sole starting material 10.

Experimental Section

Melting points were determined in capillary tubes with a Mettler FP 61 instrument and Yanagimito Micro Melting Point apparatus, and are uncorrected. Microanalyses were obtained with a Perkin-Elmer 240 or 240B instrument. Measurement of infrared spectra were made on a Hitachi 260-10 spectrometer. Proton magnetic resonances (^{1}H NMR) spectra were measured at 60 MHz on a Hitachi R-24B NMR spectrometer and at 90 MHz on a Hitachi R-900 spectrometer taking Me_4Si as an internal standard. ^{13}C NMR spectra at 22.6 MHz were taken on a Hitachi R-900 spectrometer with $CDCl_3$ as an internal standard. Mass spectra were run on a Shimadzu LKB-9000B instrument. Ultraviolet spectra were obtained with a Hitachi 220 spectrometer.

(A) General Procedure for Preparation of 4-Propargylthiopyrimidin-2(1H)-ones (6a-e,h) and 3-Propargylthio-1,2,4-triazin-5(2H)-ones (10b,c,f): Into a stirred solution of 4-thiouracil [$R^1 = R^2 = H$ (6a, 6h), $R^1 = CH_3$, $R^2 = H$ (6b), $R^1 = F$, $R^2 = H$ (6c), $R^1 = H$, $R^2 = CH_3$ (6d), $R^1 = Br$, $R^2 = CH_3$ (6e); 10 mmol] or 3-thio-1,2,4-triazine-3,5(2H,4H)-dione [$R^2 = CH_3$ (10b, 10f), $R^2 = Ph$ (10c); 10 mmol] and NaOMe (11 mmol) in MeOH (30 ml) was added alkynyl bromide [propargyl bromide (6a-e, 10b,c), 1-bromo-2-butyne (6h, 10f); 13 mmol] at room temperature. The reaction mixture was stirred for 3 days at the same temperature. After removal of an excess of alkynyl bromide and MeOH, the residue was filtered and the precipitate was thoroughly washed with water. Recrystallization of the precipitate from EtOH (except 10b) or MeOH (10b) provided pure compound 6a-e,h or 10b,c,f.

6a: yield 57.1%; mp 170.8 °C (dec.); IR (nujol, cm^{-1}) 3240m, 3100w, 1645s, 1600s, 1410m, 1230m, 1090m; ^{1}H NMR (DMSO-d_6) δ 3.09 (t, J = 2.4 Hz, 1 H), 3.90 (d, J = 2.4 Hz, 2 H), 6.23 (d, J = 7.2 Hz, 1 H), 7.59 (d, J = 7.2 Hz, 1 H); Mass m/e (relative intensity) 166 (M^+, 100), 138 (18), 72 (77), 71 (79). Anal. Calcd for $C_7H_6N_2OS$: C, 50.58; H, 3.64; N, 16.86; S, 19.29. Found: C, 50.68; H, 3.72; N, 16.68; S, 19.18.

6b: 60.0%; mp 199-202 °C (dec.); IR 3200m, 3110w, 1640s, 1620s, 1400m, 1205m, 1070s; ^{1}H NMR (DMSO-d_6) δ 1.91 (s, 3 H), 3.14 (t, J = 1.8 Hz, 1 H), 3.97 (d, J = 1.8 Hz, 2 H), 7.54 (s, 1 H), 11 50 (br.s, 1 H); m/e 180 (M^+, 100), 152 (24), 125 (46), 72 (75), 71 (66). Anal. Calcd for $C_8H_8N_2OS$: C, 53.32; H, 4.48; N, 15.55; S, 17.79. Found: C, 53.55; H, 4.48; N, 15.51; S, 17.57.

6c: 62.5%; mp 165.9 °C (dec.); IR 3290w, 3240m, 3080w, 1720m, 1630s, 1295m, 760m; ^{1}H NMR ($CDCl_3$ - DMSO-d_6) δ 2.84 (t, J = 2.4 Hz, 1 H), 4.01 (d, J = 2.4 Hz, 2 H), 7.87 (d, J = 4.2 Hz, 1 H); m/e 184 (M^+, 100), 156 (77), 72 (43), 71 (49), 39 (61). Anal. Calcd for $C_7H_5N_2OSF$: C, 45.64; H, 2.74; N, 15.21; S, 17.41. Found: C, 45.66; H, 2.60; N, 15.18; S, 17.50.

6d: 73.6%; mp 199.5-202.5 °C; IR 3240w, 1650s, 1600s, 1260m, 1090m; ^{1}H NMR ($CDCl_3$ - DMSO-d_6) δ 2.16 (s, 3 H), 2.55 (t, J = 2.4 Hz, 1 H), 3.94 (d, J = 2.4 Hz, 2 H), 6.04 (s, 1 H); m/e 180 (M^+, 100), 80 (29), 72 (70), 71 (62). Anal. Calcd for $C_8H_8N_2OS$: C, 53.32; H, 4.48; N, 15.55; S, 17.79. Found: C, 52.62; H, 4.36; N, 15.28; S, 18.02.

6e: 49.4%; mp 197-200 °C (dec.); IR 3230w, 1665s, 1580s, 1275m, 1150m; ^{1}H NMR ($CDCl_3$ - DMSO-d_6) δ 2.27 (s, 3 H), 2.79 (t, J = 2.4 Hz, 1 H), 3.78 (d, J = 2.4 Hz, 2 H); m/e 260 (M^+, 6), 258 (M^+, 6), 179 (3), 98 (29), 80 (100), 52 (59). Anal. Calcd for $C_8H_7N_2OSBr$: C, 37.08; H, 2.72; N, 10.81; S, 12.38. Found: C, 37.10; H, 2.68; N, 10.89; S, 12.66.

6h: 62.2%; mp 205.9 °C (dec.); IR 1650s, 1605s, 1230m, 1085m, 780m; ^{1}H NMR ($CDCl_3$ - DMSO-d_6) δ 1.80 (t, J = 2.1 Hz, 3 H), 3.88 (q, J = 2.1 Hz, 2 H), 6.15 (d, J = 6.6, 1 H), 7.49 (d, J = 6.6 Hz, 1 H); m/e 180 (M^+, 100), 179 (90), 147 (78), 85 (55), 53 (98), 45 (46). Anal. Calcd for $C_8H_8N_2OS$: C, 53.32; H, 4.48; N, 15.55; S, 17.79. Found: C, 53.83; H, 4.43; N, 15.56; S, 17.30.

10b: 66.7%; mp 210-212 °C (dec.); IR 3230m, 1610s, 1490m, 1260m, 1225m, 1010m; ^{1}NMR (DMSO-d_6) δ 2.10 (s, 3 H), 3.15 (t, J = 2.1 Hz, 1 H), 3.94 (d, J = 2.1 Hz, 2 H); m/e 181 (M^+, 51), 140 (56), 112 (63), 72 (66), 69 (100), 39 (65). Anal. Calcd for $C_7H_7N_3OS$: C, 46.40; H, 3.89; N, 23.19; S, 17.70. Found: C, 46.51; H, 3.94; N, 23.03; S, 17.89.

10c: 53.4%; mp 175-177 °C; IR 3270w, 1610s, 1560m, 1485m, 1285m; ^{1}NMR (DMSO-d_6) δ 3.28 (t, J = 2.4 Hz, 1 H), 4.07 (d, J = 2.4 Hz, 2 H), 7.35 - 7.55 (m, 3 H), 7.91 - 8.11 (m, 2 H); m/e 243 (M^+, 59), 214 (20), 140 (100), 112 (24), 103 (36), 72 (75). Anal. Calcd for $C_{12}H_9N_3OS$: C, 59.23; H, 3.73; N, 17.27; S, 13.18. Found: C, 59.23; H, 3.58; N, 17.16; S, 13.25.

10f: 57.9%; mp 197-199 °C; IR 1620s, 1495m, 1270m, 1235m; ^{1}NMR (DMSO-d_6) δ 1.84 (t, J = 2.1 Hz, 3 H), 2.16 (s, 3 H), 3.98 (q, J = 2.1 Hz, 2 H); m/e 195 (M^+, 12), 136 (74), 85 (44), 69 (70), 53 (100), 42 (70). Anal. Calcd for $C_8H_9N_3OS$: C, 49.22; H, 4.65; N, 21.53; S, 16.43. Found: C, 49.03; H, 4.63; N, 21.67; S, 16.45.

(B) General Procedure for Preparation of 4-Propargylthiopyrimidin-2(1H)-ones (6f,g) and 3-Propargylthio-1,2,4-triazin-5(2H)-ones (10d,e): To a suspension of NaH (11 mmol) in DMF (30 ml) was added 4-thiouracil [$R^1 = R^2 = H$ (6f), $R^1 = CH_3$, $R^2 = H$ (6g); 10 mmol] or 3-thio-1,2,4-triazine-3,5(2H,4H)-dione [$R^1 = CH_3$ (10d), $R^1 = Ph$ (10e); 10 mmol] at room temperature. After stirring for 30 min at the same temperature under the nitrogen atmosphere, 3-bromo-1-butyne[19] (13 mmol) was added. The reaction mixture was stirred overnight. Usual extractive workup with $CHCl_3$ and removal of the solvent gave a yellow solid (6g, 10d) or a yellow liquid (6f, 10e). Recrystallization of crude 6g and 10d from EtOH afforded pure material 6g and 10d, respectively. Crude 6f and 10e were purified by column chromatography (silica gel, $CHCl_3$ - MeOH gradient) to furnish the spectroscopically pure compound 6f and 10e, respectively. Analytically pure materials were obtained by recystallization from EtOH.

6f: 44.4%; mp 164-166 °C; IR 3270m, 1630s, 1400m, 1235m, 1090m; ^{1}H NMR (DMSO-d_6) δ 1.60 (d, J = 7.2 Hz, 3 H), 3.31 (d, J = 2.4 Hz, 1 H), 4.76 (dq, J = 2.4, 7.2 Hz, 1 H), 6.35 (d, J = 7.2 Hz, 1 H), 7.74 (d, J = 7.2 Hz, 1 H); m/e 180 (M^+, 100), 165 (47), 86 (42), 85 (25), 71 (75). Anal. Calcd for $C_8H_8N_2OS$: C, 53.32; H, 4.48; N, 15.55; S, 17.79. Found: C, 53.26; H, 4.51; N, 15.41; S, 17.84.

6g: 28.4%; mp 166-168 °C (dec.); IR 3230w, 1650s, 1620s, 1085m; ^{1}H NMR (DMSO-d_6) δ 1.61 (d, J = 7.2 Hz, 3 H), 1.95 (s, 3 H), 3.37 (d, J = 2.4 Hz, 1 H), 4.82 (dq, J = 2.4, 7.2 Hz, 1 H), 7.62 (s, 1 H); m/e 194 (M^+, 80), 179 (32), 139 (41), 86 (42), 71 (100), 53 (48). Anal. Calcd for $C_9H_{10}N_2OS$: C, 55.66; H, 5.19; N, 14.43; S, 16.51. Found: C, 55.47; H, 5.41; N, 14.27; S, 16.60.

10d: 40.1%; mp 150.5-152.5 °C; IR 3230w, 1610s, 1500m, 1255m; ^{1}H NMR (DMSO-d_6) δ 1.64 (d, J = 7.2 Hz, 3 H), 2.18 (s, 3 H), 3.43 (d, J = 2.4 Hz, 1 H), 4.64 (dq, J = 2.4, 7.2 Hz, 1 H); m/e 195 (M^+, 100), 167 (64), 154 (51), 139 (70), 85 (67), 53 (89). Anal. Calcd for $C_8H_9N_3OS$: C, 49.22; H, 4.65; N, 21.53; S, 16.43. Found: C, 49.38; H, 4.95; N, 21.29; S, 16.16.

10e: 58.3%; mp 160-162 °C; IR 1630s, 1605s, 1290m; ^{1}H NMR ($CDCl_3$) δ 1.52 (d, J = 7.2 Hz, 3 H), 2.23 (d, J = 2.4 Hz, 1 H), 4.66 (dq, J = 2.4, 7.2 Hz, 1 H), 7.16 - 7.37 (m, 3 H), 7.81 - 8.08 (m, 2 H); m/e 257 (M^+, 100), 154 (87), 139 (75), 103 (54), 86 (57), 53 (80). Anal. Calcd for $C_{13}H_{11}N_3OS$: C, 60.68; H, 4.31; N, 16.33; S, 12.46. Found: C, 60.72; H, 4.30; N, 16.31; S, 12.63.

Preparation of 3-Propargylthio-1,2,4-triazin-5(2H)-one 10a: Into a stirred solution of thiosemicarbazide (12.8 g, 0.14 mol) in 80% aqueous EtOH (360 ml) at 70 °C was added glyoxylic acid (1.28 g, 0.12 mol) in 80% aqueous EtOH (70 ml). After the reaction mixture was stirred at the same temperature for 5 min, a solution of NaOH (6.24 g, 0.16 mol) dissolved in H_2O (40 ml) and propargyl bromide (12.5 ml, 0.14 mol) were added. The reaction mixture was refluxed for 3 h. The solvent was removed in vacuo. The residue was filtrated and the precipitate was thoroughly washed with H_2O and EtOH. Recrystallization of the precipitate from EtOH gave pure compound 10a (4.84 g, 23.7% yield): mp 166.9 °C (dec.); IR 3230m, 1610s, 1555m, 1490m, 1180m, 1010m; ^{1}NMR (DMSO-d_6) δ 3.14 (t, J = 2.4 Hz, 1 H), 3.91 (d, J = 2.4 Hz, 2 H), 7.51 (s, 1 H); m/e 167 (M^+, 69), 140 (46), 108 (80), 72 (64), 69 (100), 39 (93). Anal. Calcd for $C_6H_5N_3OS$: C, 43.10; H, 3.01; N, 25.13; S, 19.18. Found: C, 43.14; H, 3.07; N, 25.43; S, 18.91.

Cyclization Reactions of 6 to Thiazolopyrimidones 9

(A) Pd(II)-Catalyzed Cyclization of 6: General Procedure: A solution of 6 (1 mmol) and $PdCl_2(PhCN)_2$ (indicated amounts in Table I) in indicated solvent (10 ml) was refluxed for indicated period of time under nitrogen atmosphere. After evaporation of the solvent, the residue was directly subjected to column chromatography (silica gel, $CHCl_3$ - MeOH gradient) to give spectroscopically pure material 9a-g. Analytically pure samples were obtained by recrystallization. In the case of entry 14 in Table I, many reaction products were formed. After the column purification, 9h and 9h' were obtained as a non-separable 1:1 mixture, whose structures were determined tentatively by their ^{1}H NMR spectra.

(B) Thermal Cyclization of 6: General Procedure: A MeOH (10 ml) solution of 6 (1 mmol) was refluxed for indicated period of time under nitrogen atmosphere. After removal of the solvent, the residue was directly subjected to column chromatography (silica gel, $CHCl_3$ - MeOH gradient) to provide spectroscopically pure compound 9 and the starting material 6 (9 was eluded first). In the case of entry 2 in Table I, the absence of the cyclized product (9a) and complete conversion of the starting material were thoroughly checked by TLC.

9a: mp 180.8 °C (dec. n-hexane - acetone); IR 1660s, 1490m, 1330m, 780m; ^{1}H NMR ($CDCl_3$) δ 4.05 (t, J = 1.8 Hz, 2 H), 5.15 (q, J = 1.8 Hz, 1 H), 6.20 (d, J = 4.8 Hz, 1 H), 6.58 (q, J = 1.8 Hz, 1 H), 8.13 (d, J = 4.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 32.20 (C_9), 99.77, 105.51 (C_8, CH_2=), 141.26 (C_7), 154.79, 157.75 (C_5, C_9), 162.96 (C_7); m/e 166 (M^+, 100), 72 (68), 71 (61). Anal. Calcd for $C_7H_6N_2OS$: C, 50.58; H, 3.64; N, 16.86; S, 19.29. Found: C, 50.74; H, 3.59; N, 16.70; S, 19.08.

9b: mp 160-163 °C (dec. EtOH); IR 1665s, 1420m, 1350s, 1245m, 1220m; ^{1}H NMR ($CDCl_3$) δ 2.02 (s, 3 H), 4.10 (t, J = 1.8 Hz, 2 H), 5.20 (q, J = 1.8 Hz, 1 H), 6.69 (q, J = 1.8 Hz, 1 H), 8.09 (s, 1 H); by doping of Eu(dpm)$_3$, the resonance at δ 6.69 shifted downfield 2.4 times larger than the one at δ 5.20; m/e 180 (M^+, 100), 125 (35), 72 (73), 71 (61). Anal. Calcd for $C_8H_8N_2OS$: C, 53.32; H, 4.48; N, 15.55; S, 17.79. Found: C, 53.13; H, 4.58; N, 15.55; S, 17.80.

9c: ^{1}H NMR ($CDCl_3$) δ 4.13 (t, J = 1.8 Hz, 2 H), 5.20 (q, J = 1.8 Hz, 1 H), 6.65 (q, J = 1.8 Hz, 1 H), 8.24 (s, 1 H).

9d: mp 208-210 °C (dec. EtOH); IR 1655s, 1580m, 1480m, 770m; ^{1}H NMR ($CDCl_3$) δ 2.28 (s, 3 H), 4.00 (t, J = 1.8 Hz, 2 H), 5.10 (q, J = 1.8 Hz, 1 H), 6.11 (s, 1 H), 6.65 (q, J = 1.8 Hz, 1 H); m/e 180 (M^+, 100), 80 (18), 72 (58), 71 (49). Anal. Calcd for $C_8H_8N_2OS$: C, 53.32; H, 4.48; N, 15.55; S, 17.79. Found: C, 53.21; H, 4.41; N, 15.59; S, 17.49.

9e: mp 174-176 °C (dec. n-hexane - acetone); IR 1660s, 1560m, 1535m, 885m; ^{1}H NMR ($CDCl_3$) δ 2.42 (s, 3 H), 4.04 (t, J = 1.8 Hz, 2 H), 5.05 (q, J = 1.8 Hz, 1 H), 6.51 (q, J = 1.8 Hz, 1 H); m/e 260 (M^+, 88), 258 (M^+, 88), 179 (46), 72 (69), 71 (100), 45 (63). Anal. Calcd for $C_8H_7N_2OSBr$: C, 37.08; H, 2.72; N, 10.81; S, 12.38. Found: C, 37.29; H, 2.65; N, 10.78; S, 12.22.

9f: mp 91.0 °C (n-hexane - EtOH); IR 1640s, 1480m, 1330m, 1050m; ^{1}H NMR ($CDCl_3$) δ 1.63 (d, J = 7.2 Hz, 3 H), 4.44 (dq, J = 1.5, 7.2 Hz, 1 H), 5.21 (t, J = 1.5 Hz, 1 H), 6.31 (d, J = 4.8 Hz, 1 H), 6.72 (t, J = 1.5 Hz, 1 H), 8.24 (d, J = 4.8 Hz, 1 H); m/e 180 (M^+, 72), 165 (28), 86 (41), 71 (100), 45 (33). Anal. Calcd for $C_8H_8N_2OS$: C, 53.32; H, 4.48; N, 15.55; S, 17.79. Found: C, 53.33; H, 4.49; N, 15.44; S, 17.80.

9g: mp 101-103 °C (n-hexane - acetone); IR 1640s, 1480m, 1050m; ^{1}H NMR ($CDCl_3$) δ 1.62 (d, J = 7.2 Hz, 3 H), 2.01 (s, 3 H), 4.35 (dq, J = 1.5, 7.2 Hz, 1 H), 5.06 (t, J = 1.5 Hz, 1 H), 6.61 (t, J = 1.5 Hz, 1 H), 7.98 (s, 1 H); m/e 194 (M^+, 80), 179 (30), 86 (38), 71 (100), 45 (36). Anal. Calcd for $C_9H_{10}N_2OS$: C, 55.66; H, 5.19; N, 14.43; S, 16.51. Found: C, 55.73; H, 5.25; N, 14.29; S, 16.49.

9h and 9h': ^{1}H NMR ($CDCl_3$) δ 1.75 (d, J = 7.2 Hz, 1.5 H), 2.24 (s, 1.5 H), 3.25 (d, J = 6.6 Hz, 1 H), 3.95 (d, J = 1.8 Hz, 1 H), 5.45 - 5.87 (m, 1 H), 6.30 (d, J = 4.2 Hz, 1 H), 8.16 (d, J = 4.2 Hz, 0.5 H), 8.26 (d, J = 4.2 Hz, 0.5 H).

Cyclization Reaction of 10 to Thiazolo-1,2,4-triazinones 11 and 12

(A) Pd(II)-Catalyzed Cyclization of 10: General Procedure: A solution of 10 and $PdCl_2(PhCN)_2$ (indicated amounts in Table II) in indicated solvent (10 ml) was refluxed for indicated period of time under nitrogen atmosphere. After removal of the solvent, the residue was directly subjected to a column purification (silica gel, $CHCl_3$ - MeOH gradient) to afford 11, 12 and 13 (13 was eluded first, and 11 was the second). Analytically pure materials were obtained by recrystallization.

(B) Thermal Cyclization: Treatment of 10b (1 mmol) in refluxing MeOH for 20 h under nitrogen atmosphere resulted in a recovery of the starting material as judged from ^{1}H NMR and TLC monitoring.

(C) Base-Induced Cyclization of 10: General Procedure: A MeOH (10 ml) solution of 10 (1 mmol) and 1 N NaOH (indicated amounts in Table II) was refluxed for indicated period of time under nitrogen atmosphere. After cooling, the reaction mixture was neutralized by 1 N HCl, and then the solvent was removed under reduced pressure. The residue was subjected to column chromatography to provide 12 (and 11 in entry 8 in Table II). In the case of entry 10 in Table II, the product was a mixture of 12d and 14 (52 : 48 from their isolated yields). In entry 11 in Table II, 10d was treated with 0.1 equiv of NaH in DMF at 80 °C for 3 h. Usual extractive workup with $CHCl_3$ and a column purification furnished a mixture of 12d and 14 (78 : 22). Analytically pure samples were obtained by recrystallization.

11a: mp 134.1 °C (dec. EtOH); IR 1690s, 1525m, 1330m, 1210m; ^{1}H NMR ($CDCl_3$) δ 4.07 (t, J = 1.8 Hz, 2 H), 5.32 (q, J = 1.8 Hz, 1 H), 6.57 (q, J = 1.8 Hz, 1 H), 8.19 (s, 1 H); m/e 167 (M^+, 100), 139 (67), 72 (26), 69 (24). Anal. Calcd for $C_6H_5N_3OS$: C, 43.10; H, 3.01; N, 25.13; S, 19.18. Found: C, 43.21; H, 3.02; N, 25.22; S, 19.04.

12a: mp 160-163 °C (n-hexane - acetone); IR 1645s, 1560m, 1305m; ^{1}H NMR ($CDCl_3$) δ 4.19 (t, J = 2.1 Hz, 2 H), 4.89 (q, J = 2.1 Hz, 1 H), 5.52 (q, J = 2.1 Hz, 1 H), 7.61 (s, 1 H); m/e 167 (M^+, 37), 140 (88), 72 (100), 71 (48), 39 (41). Anal. Calcd for $C_6H_5N_3OS$: C, 43.10; H, 3.01; N, 25.13; S, 19.18. Found: C, 43.07; H, 3.07; N, 25.00; S, 19.00.

11b: mp 146.3 °C (n-hexane - acetone); IR 1675s, 1540m, 1495m, 1330m; ^{1}H NMR ($CDCl_3$) δ 2.41 (s, 3 H), 3.89 (t, J = 1.8 Hz, 2 H), 5.20 (q, J = 1.8 Hz, 1 H), 6.46 (q, J = 1.8 Hz, 1 H); m/e 181 (M^+, 43), 66 (100), 58 (63), 46 (82), 39 (100); UV [λ_{max}^{EtOH} nm (ε)] 305 (2,100), 231 (2,400). Anal. Calcd for $C_7H_7N_3OS$: C, 46.40; H, 3.89; N, 23.19; S, 17.70. Found: C, 46.31; H, 3.96; N, 23.57; S, 17.32.

12b: mp 187-189 °C (n-hexane - acetone); IR 1645s, 1575m, 1310m; ^{1}H NMR (MeOH-d_4) δ 2.27 (s, 3 H), 4.32 (t, J = 2.1 Hz, 2 H), 4.92 (q, J = 2.1 Hz, 1 H), 5.48 (q, J = 2.1 Hz, 1 H); m/e 181 (M^+, 22), 140 (85), 72 (100), 71 (40), 39 (28); UV [λ_{max}^{EtOH} nm (ε)] 257 (18,500). Anal. Calcd for $C_7H_7N_3OS$: C, 46.40; H, 3.89; N, 23.19; S, 17.70. Found: C, 46.25; H, 3.93; N, 23.06; S, 17.79.

11c: mp 90.6 °C (n-hexane - acetone); IR (neat) 1680s, 1505m, 1455m, 1330s; ^{1}H NMR ($CDCl_3$) δ 4.01 (t, J = 1.8 Hz, 2 H), 5.24 (q, J = 1.8 Hz, 1 H), 6.58 (q, J = 1.8 Hz, 1 H), 7.34 - 7.58 (m, 3 H), 8.03 - 8.25 (m, 2 H); m/e 243 (M^+, 100), 215 (39), 214 (29), 112 (23), 103((23). Anal. Calcd for $C_{12}H_9N_3OS$: C, 59.23; H, 3.73; N, 17.27. Found: C, 59.12; H, 3.89; N, 17.36.

12c: mp 184-185 °C (EtOH); IR 1640s, 1515m, 1080m; ^{1}H NMR (DMSO-d_6) δ 4.43 (t, J = 2.1 Hz, 2 H), 5.03 (q, J = 2.1 Hz, 1 H), 5.51 (q, J = 2.1 Hz, 1 H), 7.43 - 7.67 (m, 3 H), 8.04 - 8.24 (m, 2 H); m/e 243 (M^+, 9), 140 (100), 72 (71), 71 (24), 39 (22). Anal. Calcd for $C_{12}H_9N_3OS$: C, 59.23; H, 3.73; N, 17.27; S, 13.18. Found: C, 59.27; H, 3.68; N, 17.25; S, 13.27.

11d: mp 73-75 °C (n-hexane - acetone); IR 1675s, 1530m, 1310m; ^{1}H NMR ($CDCl_3$) δ 1.66 (d, J = 6.6 Hz, 3 H), 2.46 (s, 3 H), 4.44 (dq, J = 1.8, 6.6 Hz, 1 H), 5.27 (t, J = 1.8 Hz, 1 H), 6.56 (t, J = 1.8 Hz, 1 H); m/e 195 (M^+, 100), 167 (59), 85 (29), 59 (39), 53 (62). Anal. Calcd for $C_8H_9N_3OS$: C, 49.22; H, 4.65; N, 21.53. Found: C, 49.54; H, 4.76; N, 21.09.

12d: mp 129.9 °C (n-hexane - EtOH); IR 1640s, 1575m, 1485m; ^{1}H NMR ($CDCl_3$) δ 1.67 (d, J = 6.6 Hz, 3 H), 2.28 (s, 3 H), 4.44 (dq, J = 2.1, 6.6 Hz, 1 H), 4.71 (t, J = 2.1 Hz, 1 H), 5.43 (t, J = 2.1 Hz, 1 H); m/e 195 (M^+, 36), 154 (100), 139 (92), 86 (94), 71 (38). Anal. Calcd for $C_8H_9N_3OS$: C, 49.22; H, 4.65; N, 21.53; S, 16.43. Found: C, 49.31; H, 4.70; N, 21.45; S, 16.48.

14: mp 216-217 °C (n-hexane - EtOH); IR 1630s, 1480m; ^{1}H NMR ($CDCl_3$) δ 2.36 (s, 6 H), 2.46 (s, 3 H); m/e 195 (M^+, 34), 154 (100), 86 (54), 71 (38), 59 (58). Anal. Calcd for $C_8H_9N_3OS$: C, 49.22; H, 4.65; N, 21.53. Found: C, 49.33; H, 4.67; N, 21.40

11e: colorless oil; IR (neat) 1680s, 1505m, 1460m, 1340s; ^{1}H NMR ($CDCl_3$) δ 1.67 (d, J = 7.2 Hz, 3 H), 4.35 (dq, J = 1.8, 7.2 Hz, 1 H), 5.18 (t, J = 1.8 Hz, 1 H), 6.55 (t, J = 1.8 Hz, 1 H), 7.25 - 7.43 (m, 3 H), 7.91 - 8.12 (m, 2 H); m/e 257 (M^+, 100), 229 (32), 228 (31), 103 (33), 53 (45).

12e: mp 137.6 °C (n-hexane - acetone); IR 1650s, 1540s, 1330m, 1260m; ^{1}H NMR ($CDCl_3$) δ 1.68 (d, J = 7.2 Hz, 3 H), 4.50 (dq, J = 2.1, 7.2 Hz, 1 H), 4.77 (t, J = 2.1 Hz, 1 H), 5.51 (t, J = 2.1 Hz, 1 H), 7.27 - 7.42 (m, 3 H), 7.94 - 8.13 (m, 2 H); m/e 257 (M^+, 12), 154 (100), 139 (64), 86 (74), 71 (33). Anal. Calcd for $C_{13}H_{11}N_3OS$: C, 60.68; H, 4.31; N, 16.33; S, 12.46. Found: C, 60.42; H, 4.35; N,

16.10; S, 12.49.

Isomerization of 12d to 14: A MeOH solution of 12d (195 mg, 1 mmol) and 0.1 equiv of 1 N NaOH was refluxed for 1 h under nitrogen atmosphere. After cooling, the mixture was neutralized by 1 N HCl, and usual extractive workup with $CHCl_3$ and evaporation of the solvent provided spectroscopically pure material 14 (175 mg, 90% yield).

4-Allylthio-5-methylpyrimidin-2(1H)-one-1-d (6i): A solution of 6b in refluxing MeOH-d_4 (99.5% D) was treated for 1 h under nitrogen atmosphere. Removal of the solvent in vacuo provided 6i which isotopic purity was determind by ^1H NMR to be 76%.

Pd(II)-Catalyzed Cyclization of 6i to 9i: A solution of 6i (101 mg, 0.557 mmol) and $PdCl_2(PhCN)_2$ (11 mg, 0.028 mmol) in MeCN (10 ml) was refluxed for 3 h. The similar workup and purification to those in the case of Pd(II)-catalyzed cyclization of 6b gave 9i (62 mg, 61% yield) which isotopic purity was calculated to be 72% on the basis of ^1H NMR area intensities: ^1H NMR ($CDCl_3$) δ 2.02 (s, 3 H), 4.10 (d, J = 1.8 Hz, 2 H), 6.69 (t, J = 1.8 Hz, 1 H), 8.09 (s, 1 H).

Thermal Cyclization of 6b to 9i: A MeOH-d_4 (5 ml) solution of 6b (104 mg, 0.577 mmol) was refluxed for 26 h under nitrogen atmosphere. The similar workup and purification to those in the case of thermal cyclization of 6b afforded 9i (10 mg, 100% yield based on 9% conversion) and the starting material 6b (95 mg). The isotopic purity of the product (9i) was deduced by ^1H NMR to be greater than 90%.

NaOH-Induced Cyclization of 10d to 12g: A mixture of 10d (98 mg, 0.5 mmol) and a solution of NaOH in D_2O (0.906 M sol., 102 mg, 0.1 mmol) was treated in refluxing MeOH-d_4 (5 ml) for 4 h under nitrogen atmosphere. The similar workup and purification to those in the case of the preparation of 12d provided 12g (79 mg, 95% yield based on 85% conversion) and the starting compound 10d (15 mg). The isotopic purity of 12g was determined to be greater than 95% on the basis of ^1H NMR area intensities: ^1H NMR ($CDCl_3$) δ 1.67 (d, J = 6.6 Hz, 3 H), 2.28 (s, 3 H), 4.44 (dq, J = 2.1, 6.6 Hz, 1 H), 5.43 (d, J = 2.1 Hz, 1 H).

References and Notes

1 Hegedus, L. S.; Winton, P. M.; Varaprath, S. J. Org. Chem. 1981, 46, 2215. Some other examples are listed therein.
2 Utimoto, K.; Miwa, H.; Nozaki, H. Tetrahedron Lett. 1981, 22, 4277.
3 (a) Norton, J. R.; Shenton, K. E.; Schwartz, J. Tetrahedron Lett. 1975, 51. (b) Murray, T. F.; Norton, J. R. J. Am. Chem. Soc. 1979, 101, 4107. (c) Murray, T. F.; Samsel, E. G.; Varma, V.; Norton, J. R. Ibid. 1981, 103, 7520.
4 Mizutani, M.; Sanemitsu, Y.; Tamaru, Y.; Yoshida, Z. J. Org. Chem. 1983, 48,4585
5 Mizutani, M.; Sanemitsu, Y.; Tamaru, Y.; Yoshida, Z. Tetrahedron in press.
6 Viehe, H. G. "Chemistry of Acetylenes" ; Marcel Dekker : New York, 1969.
7 (a) Balasubramanian, K. K.; Venugopalan, B. Tetrahedron Lett. 1974, 2643. (b) Idem. Ibid. 1974, 2645.
8 Preliminary communication of this article: Mizutani, M.; Sanemitsu, Y.; Tamaru, Y.; Yoshida, Z. Tetrahedron Lett. 1985, 26, 1237.
9 Empirically the palladium catalyst seems to be poisoned by some decomposition impurities, especially for the cases where 5-10 mol% of Pd(II) are required.
10 Alkylation of 3-methylthio-6-alkyl-1,2,4-triazin-5(2H)-ones with CH_3I in the presence of base provided only N-2 alkylation product, and in the case of 6-phenyl derivative a mixture of the N-2 alkylation product and the N-4 alkylation product in a 4 : 1 ratio was obtained. (a) Gut, J.; Prystaš, M.; Jonáš, J. Collect. Czech. Chem. Commun. 1961, 26, 986. (b) Daunis, J.; Guindo, Y.; Jacquier, R.; Viallefont, P. Bull. Soc. Chim. Fr. 1972, 1511.
11 Johnson, B. F, G.; Lewis, J.; Jones, J. D.; Taylor, K. A. J. Chem. Soc. Dalton Trans. 1974, 34.
12 (a) Jonáš, J.; Gut, J. Collect. Czech. Chem. Commun. 1962, 27, 1886. (b) Uchytilová, V.; Fiedler, P.; Prystaš, M.; Gut, J. Ibid. 1971, 36, 1955. (c) Pitha, J.; Fiedler, P.; Gut, J. Ibid. 1966, 31, 1864. (d) Lee, J.; Paudler, W. W. J. Heterocycl. Chem. 1972, 9, 995. (e) Brown, D. J.; Jones, R. L. Aust. J. Chem. 1972, 25, 2711.
13 Daunis, J.; Jacquier, R.; Viallefont, P. Bull. Soc. Chim. Fr. 1971, 3658.
14 Brown, G. R. J. Chem. Soc. Perkin Trans. I 1973, 2022.
15 (a) Krzyzosiak, W. J.; Biernat, J.; Ciesiolka, J.; Gornicki, P.; Wiewiorowski, M. Tetrahedron Lett. 1979, 2647. (b) Krzyzosiak, W. J.; Biernat, J.; Ciesiolka, J.; Gornicki, P.; Wiewiorowski, M. Nucleic Acids Res. 1980, 8, 861.
16 (a) Ibrahim, E. S.; Shamseldine, S. A.; Soliman, F. S. G.; Labouta, I. M. Pharmazie 1979, 34, 7. (b) Doleschall, G.; Hornyak, G.; Hornyak-Hamori, M.; Lempert, k.; Wolfer, A. Acta Chim. Acad. Sci. Hung. 1967, 53, 385. (c) Doleschall, G.; Hornyak, G.; Lang, L.; Lempert, K.; Zauer, K. Acta Chim.(Budapest) 1968, 57, 191.
17 For the synthesis of the type of compound 11, to our knowledge, there is only two methods, which consists of an acid-catalyzed cyclization of 3-thio-4-allyl-1,2,4-triazine-3,5(2H,4H)-dione and a condensation of 2-hydrazinothiazoles with α-ketoacids. (a) See Ref. 4. (b) Doleschall, G.; Lempert, K. Acta Chim. Acad.Sci. Hung. 1967, 53, 397. (c) Le Count, D. J.; Taylor, P. J. Tetrahedron 1975, 31, 433.
18 Nyitrai, J.; Bekassy, S.; Lempert, K. Acta Chim. Acad. Sci. Hung. 1967, 53, 309. 3-Methyl-6,7-dihydro-4H-thiazolo[2,3-c][1,2,4]triazin-4-one and 6-methyl-2,3-dihydro-7H-thiazolo[3,2-b][1,2,4]triazin-7-one are obtained in a ratio 4:6 by the reaction of 3-thio-6-methyl-1,2,4-triazine-3,5(2H,4H)-dione and $1,2\text{-}BrCH_2CH_2Br$.
19 Sondheimer, F.; Ben-Efraim, D. A. J. Am. Chem. Soc. 1963, 85, 52.