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Palladium(0)-Catalysed Allylation of Uracils and Thiouracils. Influence of the Solvent on the Regioselectivity of the Allylation

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Abstract: Uracil and 5-substituted uracils are monoallylated at N-1 in H_2O-CH_3CN with the catalytic system$Pd(OAc)_2/P(C_6H_4$-*m*-$SO_3Na)_3$ (or tppts) although performing the reaction in H_2O/THF with the system $Pd_2(dba)_3$/dppb leads to diallylations at N-1 + N-3. 2-Thiouracil, 5-methyl-2-thiouracil (2-thiothymine) and 6-methyl-2-thiouracil are monoallylated at sulfur in H_2O/CH_3CN with the catalytic system $Pd(OAc)_2/P(C_6H_4$-*m*-$SO_3Na)_3$ (or tppts). Performing the reactions in H_2O/THF with the system $Pd_2(dba)_3$/dppb leads to diallylations at N-1 + N-3 of 2-thiouracil and 2-thiothymine whereas 6-methyl-2-thiouracil is diallylated at S + N-3. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

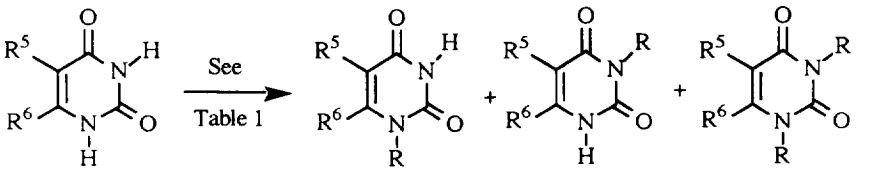
Palladium(0)-catalysed allylation of nucleophiles (the Tsuji-Trost reaction) is a versatile synthetic method and control of the selectivity is a topic of great interest.[1] Since 1991, this reaction has been extensively used in the allylation of heterocyclic systems bearing ambident nucleophiles, leading for example to carbanucleosides and nucleosides.[2] However some regioselectivity problems arise when two amide groups are present in the molecule, such as in the uracil family. Uracil has been reported to react at N-1[3a,e] and at N-1 + N-3.[3f,h] A similar behaviour was described for 5-methyluracil (thymine): reaction at N-1[3g] and at N-1 + N-3,[3b,c,d,f] indicating that the difference in reactivity between N-1 and N-3 is not high. Under similar conditions, 6-methyluracil reacts only at N-3.[3f] The use of sulfur nucleophiles in palladium(0)-catalyzed allylation chemistry is not so popular and this is probably due to the belief that the pronounced thiophilicity of palladium could poison the catalytic systems. However, Bosnich *et al.*[4a] obtained allyl alkyl sulfides in quite good yields starting from *O*-allyl *S*-alkyl dithiocarbonates in the presence of palladium(0). Trost *et al.* [4b] also obtained the corresponding allyl alkyl sulfides by reacting silylated thiols with allylic carbonates. More recently we have shown that allylation of thiols ocurred under very mild conditions in the presence of palladium(0) as the catalyst using carbonates as allylic substrates.[3f, 4c-f]

We have recently shown in a preliminary communication that using an organic-aqueous medium as the solvent and palladium acetate associated with the trisodium salt of the tri(*m*-sulfophenylphosphine) $P(C_6H_4$-*m*-$SO_3Na)_3$ (or tppts) as the catalyst gave very good selectivities at N-1 in the allylation of uracils and at sulfur in

the allylation of thiouracils.[5] In the present paper we report more details and an extension on the allylation in the uracil and thiouracil families catalysed by palladium(0) complexes using various solvents.

RESULTS AND DISCUSSION

We have studied the palladium(0)-catalysed allylation of uracil (**1a**), 5-methyluracil (**1b**) and 6-methyluracil (**1c**) under two sets of well defined experimental conditions: 1) Cinnamyl acetate/DBU (1/1) in H_2O/CH_3CN (17/2) at 60 °C with $Pd(OAc)_2$/tppts as the catalyst (conditions A); 2) Cinnamyl ethyl carbonate or cinnamyl methyl carbonate in H_2O/THF (3/1) at 60 °C with $Pd_2(dba)_3$/dppb as the catalyst (conditions B). The results are summarised in Table 1 and in Scheme 1 and for comparison the results obtained by one of us in DMSO[3f] were added.



1 **2** **3** **4**

a : $R^5 = R^6 = H$; **b** : $R^5 = CH_3$, $R^6 = H$; **c** : $R^5 = H$, $R^6 = CH_3$

Allylating reagents: *(E)*-PhCH=CHCH$_2$OCOX, X = OCH_3, OC_2H_5 and CH_3

R = *(E)*-PhCH=CHCH$_2$- in **2-4**

Scheme 1

Allylation of **1a-c** with cinnamyl ethyl carbonate in DMSO in the presence of $Pd(PPh_3)_4$ was shown previously to lead to a mixture of N-allylation products **2a-4a**, **2b-4b** and **3c-4c** respectively (entries 1, 5 and 8).[3f] Performing the reaction with cinnamyl acetate in water/acetonitrile in the presence of diazabicycloundecene (DBU) and $Pd(OAc)_2$/tppts as the catalyst afforded regioselectively 1-cinnamyluracil (**2a**) and 1-cinnamylthymine (**2b**) in quite good yields (entries 2, 3 and 6). We noticed that a large excess of allylating reagent results only in an improvement of the yield in monoallylated products, without formation of diallylated compounds. The use of cinnamyl ethyl carbonate under these conditions gave a very low yield due probably to the hydrolysis of the carbonate. Performing the reaction in H_2O/THF as the solvent and using cinnamyl methyl carbonate as the allylating reagent, the catalyst being $Pd_2(dba)_3$ and dppb, led to the exclusive formation of the diallylation products **4a** and **4b** in 71 % and 26 % chemical yields respectively (entries 4 and 7).

If allylation of 6-methyluracil (**1c**) in DMSO led predominantly to the allylated product at N-3 **3c** (entry 8),[3d,f] no allylation was observed in H_2O/CH_3CN or H_2O/THF using $Pd(OAc)_2$ /tppts as the catalyst. However performing the allylation of compound **1c** in H_2O/THF as the solvent and using cinnamyl ethyl carbonate as the allylating reagent, the catalyst being $Pd(dba)_2$ and dppb, led to the formation of the product of diallylation **4c** only (entries 9-11); working with an excess of carbonate gave a quite good yield with total consumption of the starting 6-methyluracil (**1c**), although the use of a limited amount of carbonate gave lower chemical yields with part of the starting material being recovered.

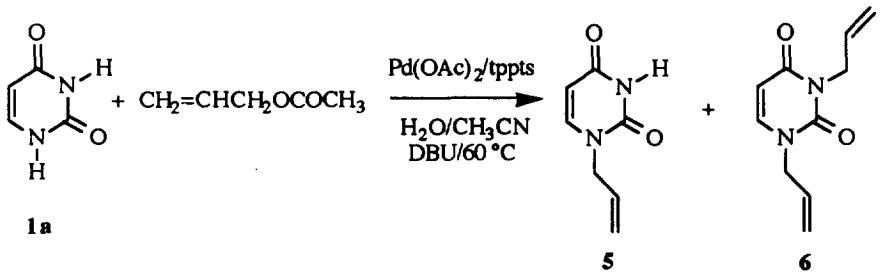
These results show clearly that conditions A [H_2O/CH_3CN and $Pd(OAc)_2$/tppts] allow the controlled monoallylation of uracil (**1a**) and thymine (**1b**) at N-1. A hypothesis explaining the formation of only **2a-b** is

Table 1. Reactions of Uracils **1a-c** with Cinnamyl Derivatives under Palladium(0) Catalysis

Entry	1 (mmol)	X (mmol)	Pd (mmol)	Phosphine (mmol)	Solvent (mL)	T °C/h	Products Yields (%)		
1[a]	**1a** (9.0)	OC_2H_5 (9.0)	$Pd(PPh_3)_4$ (0.4)	---	DMSO (20)	105/5.5	**2a** 38	**3a** 7	**4a** 9
2	**1a** (2.2)	CH_3 (2.4)[b]	$Pd(OAc)_2$ (0.08)	tppts (0.8)	H_2O/CH_3CN (17/2)	60/24	**2a** 40	---	---
3	**1a** (2.2)	CH_3 (8.9)[b]	$Pd(OAc)_2$ (0.08)	tppts (0.8)	H_2O/CH_3CN (17/2)	60/24	**2a** 80	---	---
4	**1a** (2.2)	OCH_3 (8.9)	$Pd_2(dba)_3$ (0.05)	dppb (0.2)	H_2O/THF (15/5)	60/24	---	---	**4a** 71
5[a]	**1b** (4.0)	OC_2H_5 (4.0)	$Pd(PPh_3)_4$ (0.2)	---	DMSO (20)	105/45	**2b** 30	**3b** 14	**4b** 7
6	**1b** (2.0)	CH_3 (7.9)[b]	$Pd(OAc)_2$ (0.08)	tppts (0.8)	H_2O/CH_3CN (17/2)	60/24	**2b** 53	---	---
7	**1b** (2.2)	OCH_3 (5.5)	$Pd_2(dba)_3$ (0.05)	dppb (0.2)	H_2O/THF (15/5)	60/24	---	---	**4b** 26
8[a]	**1c** (8.0)	OC_2H_5 (8.0)	$Pd(PPh_3)_4$ (0.4)	---	DMSO (25)	105/14	---	**3c** 49	**4c** 5
9	**1c** (2.0)	OC_2H_5 (2.0)	$Pd_2(dba)_3$ (0.04)	dppb (0.16)	H_2O/THF (15/5)	60/7	---	---	**4c** 11[c]
10	**1c** (2.0)	OC_2H_5 (2.0)	$Pd_2(dba)_3$ (0.08)	dppb (0.16)	H_2O/THF (15/5)	60/25	---	---	**4c** 60[d]
11	**1c** (2.0)	OC_2H_5 (6.0)	$Pd_2(dba)_3$ (0.08)	dppb (0.16)	H_2O/THF (15/5)	60/27	---	---	**4c** 83

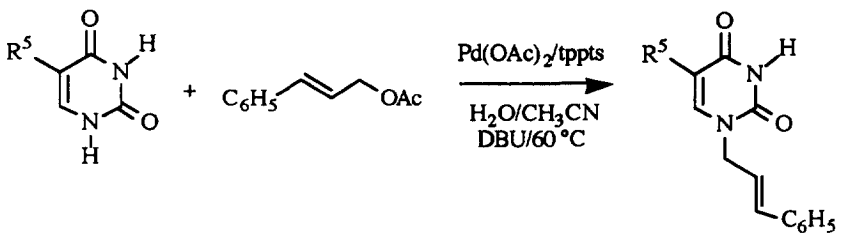
[a] Ref. 3f. [b] One equivalent of DBU with respect to cinnamyl acetate was introduced. [c] 75% of the starting 6-methyluracil was recovered. [d] 39% of the starting 6-methyluracil was recovered.

that the monoallylated compound is insoluble in the aqueous media and precipitates as an oil, and so diallylation cannot occur. To confirm this hypothesis, we performed two experiments with uracil (**1a**) under conditions A using allyl acetate, a less hydrophobic substrate, as the allylating reagent. We observed in this case the formation of the product of monoallylation at N-1 **5** and also of diallylation at N-1 + N-3 **6** (Scheme 2). In this particular case, the monoallylated product **5** is more soluble in the solvent used than **2a** and so the second



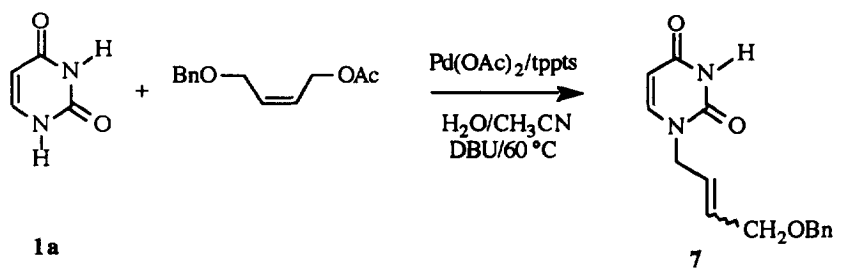
H_2O/CH_3CN 18/2 yield 52 % 11 %
H_2O/CH_3CN 10/10 yield 49 % 16 %

Scheme 2



d: R^5 = Br; **e**: R^5 = Cl; **f**: R^5 = F

Scheme 3



Scheme 4

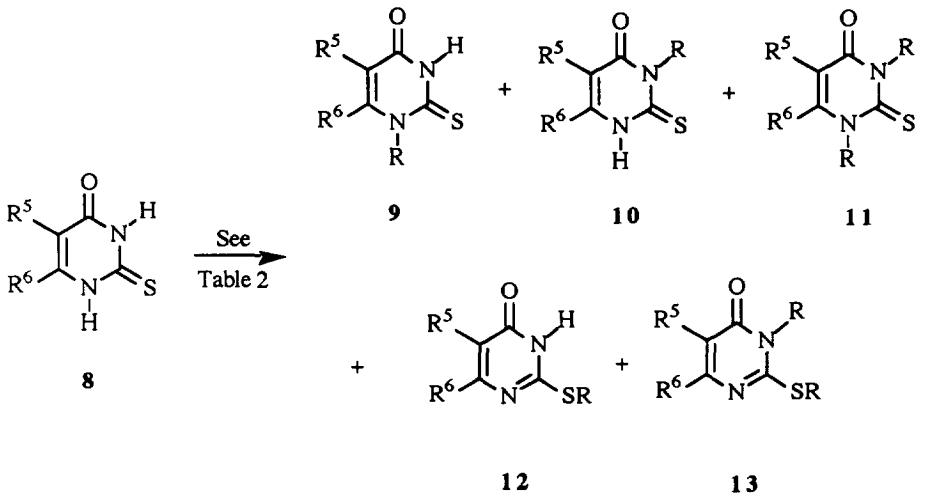
allylation occurs.

We used the conditions A for the allylation of uracils **1d-f** bearing a halogen atom at position 5 (Scheme 3). As expected only monoallylated products at N-1 **2d-f** were also obtained with chemical yields (non optimized) of 66 %, 32 % and 14 % respectively for R^5 = Br, R^5 = Cl and R^5 = F.

Uracil (**1a**) reacted with *(Z)*-4-benzyloxy-2-buten-1-ol acetate under conditions A to give also the monoallylated product **7** in 48 % chemical yield as a *E/Z* mixture (75/25) (Scheme 4). The *E/Z* stereochemistry at the double bond was assigned from the ^{13}C NMR data; we observed the signals for the allylic carbons NCH_2 and OCH_2 at δ 48.1 and 69.1 ppm for the *E* isomer and δ 44.5 and 65.3 ppm for the *Z* isomer.

We then studied the palladium(0)-catalysed allylation of thiouracil (**8a**), 5-methylthiouracil (**8b**) and 6-methylthiouracil (**8c**) under the same experimental conditions.The results are summarised in Table 2 and in

Scheme 5. Allylation of **8a-c** with cinnamyl ethyl carbonate in dioxane in the presence of $Pd(PPh_3)_4$ (entries 1, 5 and 8) led to a mixture of *N*-allylation and *S*-allylation products, respectively **9a-11a, 9b-12b** and **9c-13c**; however allylation at N-3 predominates in the case of 6-methyl-2-thiouracil (**8c**), indicating that the methyl group at C-6 decreases the reactivity of N-1 probably by steric reasons.



8 **9** **10** **11** **12** **13**

a : $R^5 = R^6 = H$; **b** : $R^5 = CH_3$, $R^6 = H$; **c** : $R^5 = H$, $R^6 = CH_3$
Allylating agents: *(E)*-PhCH=CHCH$_2$OCOX, X = OCH_3, OC_2H_5 and CH_3
R = *(E)*-PhCH=CHCH$_2$- in **9-13**

Scheme 5

When the allylation was performed under conditions A (entries 2, 6, 9 and 10) the sulfides **12a**, **12b** and **12c** were the products isolated in quite good yields even in the presence of a large excess of the allylating reagent. The reaction could also be run in pure water (entry 11), giving again only compound **12c**.

The use of conditions B led to very different results. Thus, compound **8a** reacted with two equivalents of the allylic carbonate to give only product **11a** (allylation at N-1/N-3, entry 4) although the use of only 1.5 equivalent of the allylation reagent allowed the isolation of **9a** (allylation at N-1) together with the diallylated compound **11a** (allylation at N-1 and N-3) (entry 3). From entry 7 it can be seen that also only compound of diallylation **11b** was obtained in the case of 2-thiothymine (**8b**). In the case of 6-methylthiouracil (**8c**), compound **13c** was isolated in very good yield if enough allylic carbonate was introduced, i.e. a three-fold excess (entry 13). This compound **13c** comes from a double allylation at sulfur and at N-3. Conversely, the introduction of limited amounts of allylating agent permitted to find out that allylation at N-3 occurred first to give product **10c**, allylation at sulfur on **10c** giving finally **13c** (entry 12). It is to be noticed that the use of tppts as the ligand in this solvent allowed the formation of compound **12c** only (entry 14).

The structures of compounds **9-13** were assigned by NMR studies. Sulfides **12** exhibit carbon and proton resonances at δ ca. 32.2 and at 3.9-4.0 ppm respectively, very far away from the corresponding N-CH_2 signals of related compounds. Of course, assignment of structure to diallylated products **11** and **13** is straightforward. However, a closer examination was required to decide between compounds **9** and **10**. We used the SDEPT-1D technique[6] which consists in selective transfer of magnetization from chosen protons to carbons placed two and three bonds away, which are the only ones observed under a well defined set of

Table 2. Reactions of 2-Thiouracils **8a-c** with Cinnamyl Derivatives under Palladium(0) Catalysis

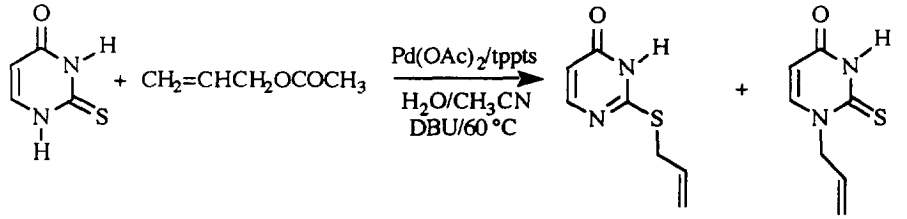
Entry	**8** (mmol)	X (mmol)	Pd (mmol)	Phosphine (mmol)	Solvent (mL)	T °C/h	Products Yields (%)				
1	**8a** (6.0)	OC_2H_5 (12.0)	$Pd(PPh_3)_4$ (0.3)	-	Dioxane (20)	Reflux/20	**9a** 20	**10a** 23	**11a** 40	-	-
2	**8a** (1.6)	CH_3 (8.0)[b]	$Pd(OAc)_2$ (0.05)	tppts (0.5)	H_2O/CH_3CN (17/2)	60/24	-	-	-	**12a** 53	-
3	**8a** (2.0)	OCH_3 (3.0)	$Pd_2(dba)_3$ (0.04)	dppb (0.16)	H_2O/THF (21/7)	60/24	**9a** 20	-	**11a** 43	-	-
4	**8a** (2.0)	OCH_3 (4.0)	$Pd_2(dba)_3$ (0.04)	dppb (0.16)	H_2O/THF (21/7)	60/24	-	-	**11a** 87	-	-
5	**8b** (5.0)	OC_2H_5 (5.0)	$Pd(PPh_3)_4$ (0.25)	-	Dioxane (20)	Reflux/48	**9b** 23	**10b** 17	**11b** 4	**12b** 6	-
6	**8b** (0.9)	Me (4.4)[b]	$Pd(OAc)_2$ (0.03)	tppts (0.3)	H_2O/CH_3CN (17/2)	60/24	-	-	-	**12b** 55	-
7	**8b** (1.0)	OC_2H_5 (1.6)	$Pd_2(dba)_3$ (0.025)	dppb (0.1)	H_2O/THF (9/3)	60/24	-	-	**11b** 46	-	-
8	**8c** (8.0)	OC_2H_5 (16.0)	$Pd(PPh_3)_4$ (0.56)	-	Dioxane (20)	Reflux/20	**9c** 8	**10c** 56	**11c** 4	-	**13c** 7
9	**8c** (1.8)	CH_3 (7.0)[a]	$Pd(OAc)_2$ (0.07)	tppts (0.7)	H_2O/CH_3CN (18/2)	60/24	-	-	-	**12c** 92	**13c** 4
10	**8c** (1.0)	CH_3 (4.0)[a]	$Pd_2(dba)_3$ (0.02)	tppts (0.2)	H_2O/CH_3CN (18/2)	60/20	-	-	-	**12c** 94	-
11	**8c** (1.0)	CH_3 (4.0)[a]	$Pd(OAc)_2$ (0.04)	tppts (0.4)	H_2O (20)	60/20	-	-	-	**12c** 98	-
12	**8c** (2.0)	OC_2H_5 (3.0)	$Pd_2(dba)_3$ (0.04)	dppb (0.16)	H_2O/THF (15/5)	60/17	-	**10c** 66	**11c** 5	**12c** 6	**13c** 17
13	**8c** (2.0)	OC_2H_5 (6.0)	$Pd_2(dba)_3$ (0.04)	dppb (0.16)	H_2O/THF (15/5)	60/17	-	-	-	-	**13c** 92
14	**8c** (1.0)	CH_3 (4.0)[a]	$Pd(OAc)_2$ (0.04)	tppts (0.4)	H_2O/THF (15/1)	60/20	-	-	-	**12c** 85	-

[a] One equivalent of DBU with respect to cinnamyl acetate was introduced.

experimental conditions. In the case of the pair **9a** and **10a** the SDEPT-1D details have been published.[4] For the pair **9b** and **10b**, the transfer of magnetisation from the protons at δ 4.94 ppm in **9b** results in enhanced signals at δ 141.8 ppm (C-6) and 175.2 ppm (C=S). However, a similar operation in **10b** enhances the signals at δ 175.5 ppm (C=S) and at δ 161.5 ppm (C=O). In addition, the signals of the olefinic carbon atoms at the cinnamyl chain are increased. Finally, in the case of pair **9c** and **10c**, homonuclear nOe was observed only for the olefinic protons upon irradiation of the methylene protons of **10c**; the same operation on the methylene group of **9c** (δ 4.64 ppm) produced a positive nOe on the C-6 methyl group signal.

These results show clearly that practical experimental conditions have been found to prepare selectively the products of allylation at sulfur (conditions A) and of diallylation at N-1/N-3 for 2-thiouracil (**8a**) and 2-thiothymine (**8b**), and at N-3/S for 6-methyl-2-thiouracil (**8c**) (conditions B).

A hypothesis explaining the regioselective allylation at sulfur under conditions A (H_2O/CH_3CN and $Pd(OAc)_2$/tppts) is that the S-allylated compound **12** is insoluble in the aqueous media (the formation of an oil was observed) and so it cannot react further. To confirm this hypothesis we performed some more experiments. We used allyl acetate in a large excess (4 moles of allyl acetate) as the allylating reagent with thiouracil (**8a**) (1 mole) under conditions A (Scheme 6). We observed the formation of the products of monoallylation at sulfur **14a** and also of monoallylation at N-1 **15a** in 23 and 28 % chemical yield respectively. Increasing the amount of acetonitrile changed the ratio **14a**/**15a** to 14 %/41 %. The monoallylated product **14a** is more soluble in water-acetonitrile than **12a** and so the rearrangement leading to the N-allylated product **15a** could occur. The structures of compounds **14** and **15** were again assigned by NMR studies. A positive nOe enhancement (10 %) was observed for the olefinic proton of **15a** at δ 7.75 ppm upon irradiation of the methylene protons at δ 4.81 ppm although the same operation on the methylene group of **14a** (δ 3.79 ppm) showed no nOe effect on the same olefinic proton.



8a **14a** **15a**

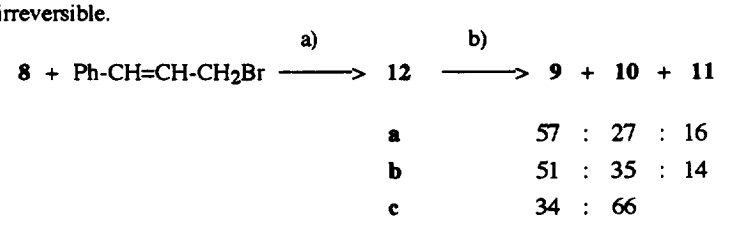
H_2O/CH_3CN	18/2	yield	23 %	28 %
H_2O/CH_3CN	10/10	yield	14 %	41 %

Scheme 6

We prepared also independently the sulfides **12a-c** by treatment of **8a-c** with cinnamyl bromide in basic medium as indicated in Scheme 7. Refluxing these sulfides in dioxane in the presence of a catalytic amount of palladium tetrakis(triphenylphosphine) resulted in the rearrangement to the N-allylated products **9a-11a**, **9b-11b**, and **9c-10c**, the ratio being measured by NMR on the crude product. It is worth-mentioning that the ratios of N-1:N-3:N-1/N-3 cinnamyl derivatives from the isomerizations of **12a** and **12b** are very similar to the ratios obtained in dioxane (entries 1 and 5 of Table 2).

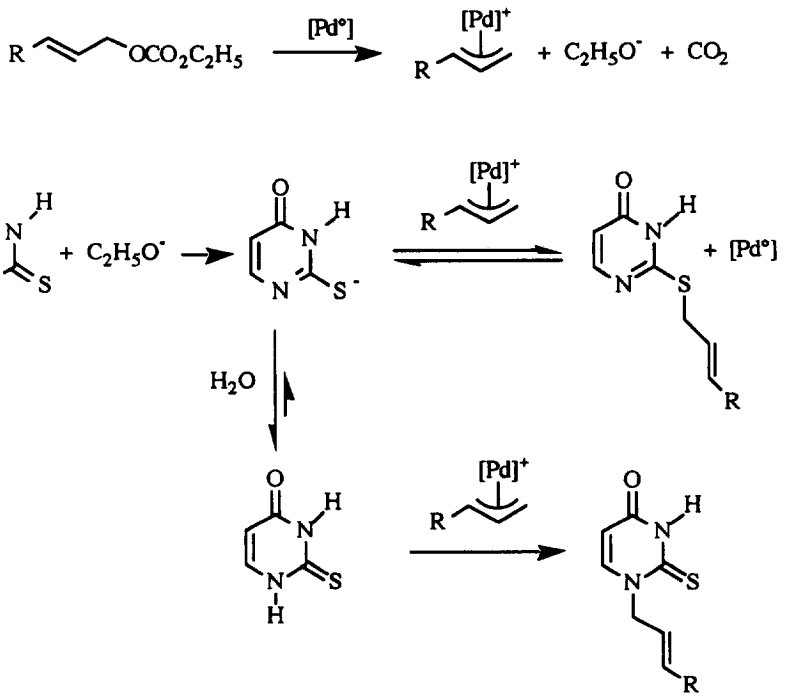
These results show clearly that allylation at sulfur atom is always faster than allylation at any nitrogen. However, the reaction of allylation at sulfur is reversible since 2-thiolate-4(3H)-pyrimidinone is a good leaving

group. In a mixture water-THF, the anion is protonated and so the allylation could occur only at nitrogen (Scheme 8).[4d] 2-Thiouracil group being not a good leaving group in π-allyl chemistry, the reaction of N-allylation is now irreversible.



Conditions: a) K_2CO_3, Bu_4NBr, butanone, reflux for **8a** or K_2CO_3, acetone, reflux, then K_2CO_3, H_2O, EtOAc for **8b** and **8c**; b) $Pd(PPh_3)_4$, dioxane, reflux.

Scheme 7



Scheme 8

CONCLUSION

In summary we have found very mild experimental conditions allowing the selective palladium(0)-catalysed selective monoallylation or diallylation of uracil derivatives. Unsubstituted uracil or uracils substituted at position 5 are monoallylated at N-1 in H_2O/CH_3CN using $Pd(OAc)_2$/tppts as the catalyst, whereas uracil substituted at position 6 is monoallylated at position N-3 in DMSO. Performing the reaction in H_2O/THF in the presence of $Pd_2(dba)_3$/dppb led to the diallylated product. In the case of thiouracil derivatives, whereas

thiouracil or thiothymine gave a mixture of allylated products in dioxane in the presence of $Pd(PPh_3)_4$, 6-methyl thiouracil is allylated predominantly at N-3 under the same conditions. Using H_2O/CH_3CN as the solvent and $Pd(OAc)_2$/tppts as the catalyst led the S-allylated product only, although performing the reaction in a mixture H_2O/THF in the presence of $Pd_2(dba)_3$/dppb gave the diallylated product at N-1 and N-3 for thiouracil and thiothymine, and the diallylated product at N-3 and S for 6-methylthiouracil.

EXPERIMENTAL SECTION

All reactions were carried out under nitrogen using Schlenk techniques. The solvents were distilled and stored under nitrogen. ^1H NMR (^{13}C NMR) spectra were registered at 200 or 250 MHz (50 or 62.5 MHz) using Me_4Si as internal standard. Chromatography was carried out on silica gel , Merck, grade 60 (230-400 mesh, 60 Å). Compounds **1a-f**, **8a-c**, allyl acetate, cinnamyl acetate, cinnamyl bromide, *(Z)*-4-benzyloxy-2-buten-1-ol, dppb or 1,4-bis (diphenylphosphino)butane and 1,8-diazabicyclo[5,4,0]undec-7-ene or DBU were from a commercial source. The carbonates were prepared using known procedures. The sulfonated phosphine tppts was a gift of Rhône-Poulenc. Products **2a-b**, **3a-c**, **4a-c** and **10c** were characterized by comparing their spectra with literature data.[3f]

Reaction of uracil (1a) and analogs with cinnamyl acetate under conditions A (Table 1, entry 3). A solution of $Pd(OAc)_2$ (18 mg, 0.08 mmol) and tppts (497 mg, 0.8 mmol) in 2 mL of H_2O was added to a solution of uracil (**1a**) (247 mg, 2.2 mmol) in 15 mL of H_2O contained in a Schlenk tube. To this solution was added cinnamyl acetate (1570 mg, 8.9 mmol) and DBU (1354 mg, 8.9 mmol) in 2 mL of acetonitrile. After stirring at 60 °C for 24 h, the aqueous solution was extracted with CH_2Cl_2 (6 x 60 mL). Evaporation of the solvent followed by column chromatography on silica gel with ethyl acetate-hexane or ethyl acetate-dichloromethane as the eluent gave the pure compound (401 mg, 80 % yield).

1-*(E)*-Cinnamyl-5-bromouracil (2d). Yield 66%; R_f 0.52 (ethyl acetate:hexane 2:1); mp 95-100 °C; ^1H NMR (DMSO-d_6, 200 MHz) δ 4.46 (d, 2H, J = 5.8 Hz, NCH_2), 6.40 (dt, 1H, J = 15.9 and 5.8 Hz, =C*H*-CH_2-), 6.60 (d, 1H, J = 15.9 Hz, =C*H*-C_6H_5), 7.20-7.50 (m, 5H, C_6H_5), 8.24 (s, 1H, NCH=), 11.82 (bs, 1H, NH); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 49.2 (NCH_2), 94.8 (=CBr), 123.8 (=*C*HC_6H_5), 126.4, 127.8, 128.5 and 135.8 (C_6H_5), 132.6 (CH_2-*C*H=), 144.9 (=CHN), 150.1 (CO), 159.6 (CO). Anal. Calcd for $C_{13}H_{11}N_2O_2Br$: C, 50.84; H, 3.61. Found: C, 50.98; H, 4.09.

1-*(E)*-Cinnamyl-5-chlorouracil (2e). Yield 32%; R_f 0.50 (ethyl acetate:hexane 1:1); mp 139 °C; ^1H NMR (DMSO-d_6, 200 MHz) δ 4.48 (d, 2H, J = 6.7 Hz, NCH_2), 6.14 (dt, 1H, J = 15.8 and 6.7 Hz, =C*H*-CH_2-), 6.63 (d, 1H, J = 15.8 Hz, =C*H*-C_6H_5), 7.20-7.40 (m, 5H, C_6H_5), 8.20 (s, 1H, NCH=), 11.60 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 49.2 (NCH_2), 106.4 (=CCl-), 123.8 (=*C*HC_6H_5), 126.4, 127.8, 128.6 and 135.9 (C_6H_5), 132.7 (CH_2-*C*H=), 142.5 (=CHN), 149.9 (CO), 159.5 (CO). Anal. Calcd for $C_{13}H_{11}N_2O_2Cl$: C, 59.44; H, 4.22. Found: C, 59.84; H, 4.17.

1-*(E)*-Cinnamyl-5-fluorouracil (2f). Yield 14%; R_f 0.13 (ethyl acetate:hexane 2:1); mp 120 °C; ^1H NMR (DMSO-d_6, 200 MHz) δ 4.41 (d, 2H, J = 5.7 Hz, NCH_2), 6.34 (dt, 1H, J = 15.9 and 5.7 Hz, =C*H*-CH_2-), 6.59 (d, 1H, J = 15.9 Hz, =C*H*-C_6H_5), 7.20-7.50 (m, 5H, C_6H_5), 8.10 (s, 1H, NCH=), 11.80 (bs, 1H, NH); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 48.9 (NCH_2), 123.8 (=*C*HC_6H_5), 126.4, 127.8, 128.5 and 135.9 (C_6H_5), 129.3 (=CHN), 139.8 (=CF-, J = 228 Hz), 132.4 (CH_2-*C*H=), 149.4 (CO), 159.2 (CO). Anal. Calcd for $C_{13}H_{11}N_2O_2F$: C, 63.41; H, 4.50. Found: C, 62.95; H, 4.97.

Reaction of uracil (1a) with allyl acetate or *(Z)* 4-benzyloxy-2-buten-1-ol acetate under conditions A.

1-Allyluracil (5). R_f 0.32 (ethyl acetate:dichloromethane 2:1); mp 100-101 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 4.25 (d, 2H, J = 5.3 Hz, NCH_2), 5.10 (bd, 1H, J = 16.9 Hz, -CH=CH_2), 5.16 (bd, 1H, J = 10.4 Hz, -CH=CH_2), 5.54 (d, 1H, J = 7.8 Hz, =CH-CO), 5.86 (ddt, 1H, J = 16.9, 10.4 and 5.3 Hz, CH=CH_2), 7.54 (d, 1H, J = 7.8 Hz, NCH=), 11.25 (bs, 1H, NH); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 49.0 (NCH_2), 101.0 (=*C*H-CO), 117.3 (CH=*C*H_2), 132.9 (*C*H=CH_2), 145.3 (=CHN), 150.6 (CO), 163.7 (CO). Anal. Calcd for $C_7H_8N_2O_2$: C, 55.26; H, 5.30. Found: C, 55.15; H, 5.53.

1,3-Diallyluracil (6). R_f 0.67 (ethyl acetate:dichloromethane 2:1); oil; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 4.35 (ddd, 2H, J = 5.4, 1.4 and 1.4 Hz, NCH_2), 4.40 (ddd, 2H, J = 5.4, 1.4 and 1.4 Hz, NCH_2), 5.03 (ddd, 1H, J = 17.8, 1.4 and 1.4 Hz, -CH=CH_2), 5.08 (ddd, 1H, J = 10.2, 1.4 and 1.4 Hz, -CH=CH_2), 5.74 (d, 1H, J = 7.8 Hz, =CH-CO), 5.75-6.00 (m, 2H, CH=CH_2), 7.65 (d, 1H,J = 7.8 Hz, NCH=); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 42.1 (NCH_2), 50.2 (NCH_2), 100.3 (=*C*H-CO), 116.3 (CH=*C*H_2), 117.4 (CH=*C*H_2), 132.4 (*C*H=CH_2), 132.9 (*C*H=CH_2), 144.0 (=CHN), 150.5 (CO), 162.0 (CO).

1-(4-Benzyloxy-2-butenyl)uracil (7) (as a *E*/*Z* mixture 75/25). Yield 48%; R_f 0.30 (ethyl acetate:dichloromethane 2:1); mp 107 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 3.90-4.05 (m, 2H, OCH_2), 4.18 (bd, 0.25 x 2H, J = 5.9 Hz, NCH_2 of *Z* isomer), 4.10-4.30 (m, 0.75x2H, NCH_2 of *E* isomer), 4.45 (s, 0.75 x 2H, O*C*$H_2C_6H_5$ of *E* isomer), 4.49 (s, 0.25 x 2H, O*C*$H_2C_6H_5$ of *Z* isomer), 5.50-5.80 (m, 3H, =CHCO- and -C*H*=C*H*CH_2-), 7.20-7.40 (m, 5H, C_6H_5), 7.59 (d, 1H, J = 7.8 Hz, NCH= of *E* isomer), 7.59 (d, 1H, J = 7.8 Hz, NCH= of *Z* isomer), 11.30 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 44.5 (NCH_2 of *Z* isomer), 48.1 (NCH_2 of *E* isomer), 65.3 (=CH*C*H_2O of *Z* isomer), 69.1 (=CH*C*H_2O of *E* isomer), 71.4 (O*C*$H_2C_6H_5$), 100.4 (=*C*H-CO of *E* isomer), 101.2 (=*C*H-CO of *Z* isomer), 126.2-138.3 (CH_2*C*H= and C_6H_5), 145.1 (=CHN of *Z* isomer), 145.2 (=CHN of *E* isomer), 150.6 (CO of *Z* isomer), 150.7 (CO of *E* isomer), 163.2 (CO of *Z* isomer), 163.7 (CO of *E* isomer). Anal. Calcd for $C_{15}H_{16}N_2O_3$: C, 66.14; H, 5.93. Found: C, 66.10; H, 5.80.

Reaction of 6-methyluracil (1c) with cinnamyl ethyl carbonate under conditions B (Table 1, entry 11). A solution of cinnamyl ethyl carbonate (1.237 g, 6.0 mmol) in THF (5 mL) was transferred from a Schlenk flask to a second Schlenk flask containing bis(dibenzylideneacetone)palladium (46 mg, 0.08 mmol) and 1,4-bis(diphenylphosphino)butane (136 mg, 0.32 mmol). This solution was added to a mixture of 6-methyluracil **1c** (252 mg, 2.0 mmol) in water (15 mL). After being heated at 60°C for 27 hours, till black palladium was precipitated, the mixture was partitioned between dichloromethane and water; the organic layer was dried and then evaporated. The residue was digested with diethyl ether, the ethereal filtrate was evaporated and the residue was chromatographed through a silica gel column with hexane-ethyl acetate mixtures of increasing polarity to afford 1,3-di-*(E)*-cinnamyl-6-methyluracil (**4c**) (596 mg, 83% yield) identical with an authentical sample.[3f]

Reaction of 2-thiouracil (8a) with cinnamyl ethyl carbonate in refluxing dioxane. (Table 2, entry 1). A solution of tetrakis(triphenylphosphine)palladium (347 g, 0.30 mmol) in anhydrous dioxane (5 mL) was added to a solution of cinnamyl ethyl carbonate (2.475 g, 12.0 mmol) in anhydrous dioxane (5 mL). The solution of precatalyst and allylating agent was added to a solution of **8a** (769 g, 6.0 mmol) in anhydrous

dioxane (10 mL) and the reaction mixture was refluxed for 20 h, until no starting materials remained (NMR monitoring). The solvent was evaporated and the residue was digested with diethyl ether to give a solid which was filtered off and characterized as compound **9a**. The filtrate (diethyl ether solution) was evaporated and the residue was chromatographed through a silica gel column with hexane:ethyl acetate (60:40) as eluent to afford compounds **11a** and **10a**.

1-*(E)*-Cinnamyl-2-thiouracil (9a): mp 225-226 °C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 4.97 (d, 2H, *J* = 5.9 Hz, NCH_2), 5.99 (d, 1H, *J* = 8.1 Hz, =CH-CO), 6.37 (dt, 1H, *J* = 16.2 and 5.9 Hz, =C*H*-CH_2-), 6.60 (d, 1H, *J* = 16.2 Hz, =*C*HC_6H_5), 7.25-7.45 (m, 5H, C_6H_5), 7.84 (d, 1H, *J* = 8.1 Hz, NCH=), 12.68 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 62.5 MHz) δ 54.6 (NCH_2), 107.0 (=*C*HCO), 123.3 (=*C*HC_6H_5), 126.6, 128.0, 128.2 and 136.0 (C_6H_5), 133.4 (CH_2-*C*H=), 145.8 (=CHN), 160.4 (CO), 176.5 (CS). Anal. Calcd for $C_{13}H_{12}N_2OS$: C, 63.91; H, 4.95; N, 11.47; S, 13.12. Found: C, 63.82; H, 4.96; N, 11.38; S, 13.21.

1,3-Di-*(E)*-cinnamyl-2-thiouracil (11a): mp 91-92 °C (ethanol); ^{1}H NMR (DMSO-d_6, 250 MHz) δ 5.08 (d, 2H, *J* = 5.8 Hz, NCH_2), 5.18 (d, 2H, *J* = 5.8 Hz, NCH_2), 6.15 (d, 1H, *J* = 7.7 Hz, =CH-CO), 6.33 (dt, 1H, *J* = 16.1 and 5.8 Hz, =C*H*-CH_2-), 6.41 (dt, 1H, *J* = 16.1 and 5.8 Hz, =C*H*-CH_2-), 6.59 (d, 1H, *J* = 16.1 Hz, =*C*HC_6H_5), 6.66 (d, 1H, *J* = 16.1 Hz, =*C*HC_6H_5), 7.18-7.43 (m, 10H, C_6H_5), 7.96 (d, 1H, *J* = 7.7 Hz, NCH=); ^{13}C NMR (DMSO-d_6, 62.5 MHz) δ 48.5 (NCH_2), 57.1 (NCH_2), 105.2 (=*C*HCO), 122.8 (=*C*HC_6H_5), 123.0 (=*C*HC_6H_5), 126.3, 126.5, 127.7, 128.1, 128.6, 128.7, 135.9 and 136.3 (C_6H_5), 132.8 (CH_2-*C*H=), 133.5 (CH_2-*C*H=), 144.6 (=CHN), 159.4 (CO), 176.8 (CS). Anal. Calcd for $C_{22}H_{20}N_2OS$: C, 73.30; H, 5.59; N, 7.77; S, 8.89. Found: C, 73.26; H, 5.58; N, 7.82; S, 8.88.

3-*(E)*-Cinnamyl-2-thiouracil (10a): mp 180-181 °C (ethanol); ^{1}H NMR (DMSO-d_6, 400 MHz) δ 5.05 (d, 2H, *J* = 5.9 Hz, NCH_2), 5.96 (d, 1H, *J* = 7.3 Hz, =CH-CO), 6.30 (dt, 1H, *J* = 16.2 and 5.9, =C*H*-CH_2-), 6.55 (d, 1H, *J* = 16.2 Hz, =C*H*C_6H_5), 7.18-7.48 (m, 6H, C_6H_5 and NCH=), 12.59 (d, 1H, *J* = 5.1 Hz, NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 47.1 (NCH_2), 104.5 (=*C*HCO), 122.9 (=*C*HC_6H_5), 126.4, 127.8, 128.8 and 136.3 (C_6H_5), 132.7 (CH_2-*C*H=), 141.0 (=CHN), 160.3 (CO), 176.7 (CS).

Other compounds obtained are indicated in Table 2.

1,3-Di-*(E)*-cinnamyl-5-methyl-2-thiouracil (11b): mp 161-162 °C (ethanol); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.95 (s, 3H, CH_3), 5.10 (d, 2H, *J* = 6.6 Hz, NCH_2), 5.33 (d, 2H, *J* = 6.6 Hz, NCH_2), 6.24 (dt, 1H, *J* = 15.9 and 6.6 Hz, =C*H*-CH_2-), 6.35 (dt, 1H, *J* = 15.9 and 6.6 Hz, =C*H*-CH_2-), 6.66 (d, 1H, *J* = 15.9 Hz, =C*H*C_6H_5), 6.82 (d, 1H, *J* = 15.9 Hz, =C*H*C_6H_5), 7.20-7.40 (m, 11H, C_6H_5 and =CHN); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 13.4 (CH_3), 49.5 (NCH_2), 57.9 (NCH_2), 114.9 (=CCO), 121.9 (=*C*HC_6H_5), 126.5, 126.6, 127.6, 128.4, 128.5, 128.6 and 136.6 (C_6H_5), 135.0 (CH_2-*C*H=), 135.6 (CH_2-*C*H=), 138.7 (=CHN), 161.0 (CO), 176.2 (CS). Anal. Calcd for $C_{23}H_{22}N_2OS$: C, 73.76; H, 5.92; N, 7.48; S, 8.56. Found: C, 73.64; H, 5.96; N, 7.48; S, 8.35.

3-*(E)*-Cinnamyl-5-methyl-2-thiouracil (10b): mp 159-160 °C (ethanol); ^{1}H NMR (DMSO-d_6, 250 MHz) δ 1.83 (s, 3H, CH_3), 5.07 (d, 2H, *J* = 6.2 Hz, NCH_2), 6.30 (dt, 1H, *J* = 16.0 and 6.2 Hz, =C*H*-CH_2-), 6.56 (d, 1H, *J* = 16.0 Hz, =C*H*C_6H_5), 7.15-7.45 (m, 6H, C_6H_5 and =CHN), 12.43 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 62.5 MHz) δ 12.9 (CH_3), 47.4 (NCH_2), 113.0 (=CCO), 123.0 (=*C*HC_6H_5), 126.4, 127.8, 128.7 and 136.3 (C_6H_5), 132.8 (CH_2-*C*H=), 137.2 (=CHN), 161.3 (CO), 175.3 (CS). Anal. Calcd for $C_{14}H_{14}N_2OS$: C, 65.09; H, 5.46; N, 10.84; S, 12.41. Found: C, 65.08; H, 5.40; N, 10.83; S, 12.38.

1-*(E)*-Cinnamyl-5-methyl-2-thiouracil (9b): mp 166-167 °C (ethanol); ^{1}H NMR (DMSO-d_6, 250 MHz) δ 1.80 (s, 3H, CH_3), 4.94 (d, *J* = 5.9 Hz, NCH_2), 6.36 (dt, *J* = 16.2 and 5.9 Hz, -CH=C*H*-CH_2-), 6.61 (d, *J*

= 16.2 Hz, CHC_6H_5), 7.20-7.45 (m, 5H, C_6H_5), 7.75 (s, 1H, =CHN), 12.59 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 62.5 MHz) δ 12.3 (CH_3), 54.7 (NCH_2), 115.6 (=CCO), 123.2 (=CHC_6H_5), 126.6, 128.1, 128.8 and 136.1 (C_6H_5), 133.3 (CH_2-CH=), 141.7 (=CHN), 161.3 (CO), 175.1 (CS).

1,3-Di-*(E)*-cinnamyl-6-methyl-2-thiouracil (11c): oil; ^1H NMR ($CDCl_3$, 250 MHz) δ 2.33 (s, 3H, CH_3), 5.28 (two overlapping d, 4H, J = 6.4 and 6.7 Hz, NCH_2), 5.85 (s, 1H, =CHCO), 6.29 (dt, J = 15.9 and 5.5 Hz, =C*H*-CH_2-), 6.30 (dt, 1H, J = 15.9 and 6.4 Hz, =C*H*-CH_2-), 6.48 (d, 1H, J = 15.9 Hz, =C*H*C_6H_5), 6.77 (d, 1H, J = 15.9 Hz, =C*H*C_6H_5), 7.10-7.40 (m, 10H, C_6H_5); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 20.8 (CH_3), 49.5 (NCH_2), 53.3 (NCH_2), 106.0 (=CCO), 121.8 (=CHC_6H_5), 122.0 (=CHC_6H_5), 126.3, 127.4, 127.9, 128.2, 128.4, 133.0 and 136.5 (C_6H_5), 134.6 (=$CHCH_2$-), 135.6 (=$CHCH_2$-), 152.3 (=CN), 159.2 (CO), 178.1 (CS).

1-*(E)*-Cinnamyl-6-methyl-2-thiouracil (9c): mp 95-97 °C; ^1H NMR ($CDCl_3$, 250 MHz) δ 2.26 (d, 3H, J = 0.7 Hz, CH_3), 4.64 (dd, 2H, J = 6.6 and 1.5 Hz, NCH_2), 6.25 (dt, 1H, J = 16.1 and 6.6 Hz, =C*H*-CH_2-), 6.28 (s, 1H, =CHCO), 6.59 (d, 1H, J = 16.1 Hz, =C*H*C_6H_5), 7.10-7.70 (m, 5H, C_6H_5); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 23.4 (CH_3), 47.9 (NCH_2), 113.0 (=CHCO), 122.4 (=CHC_6H_5), 126.5, 128.2, 128.5 and 134.6 (C_6H_5), 132.0 (=CHC_6H_5), 149.6 (=CN), 160.9 (CO), 163.9 (CS).

2-[*(E)*-Cinnamylthio]-4(3*H*)pyrimidinone (12a): *Rf* 0.64 (ethyl acetate: dichloromethane 2:1); mp 201-202 °C (ethanol): ^1H NMR (DMSO-d_6, 250 MHz) δ 3.98 (d, 2H, J = 7.3 Hz, SCH_2), 6.12 (d, 1H, J = 6.6 Hz, =CH-CO), 6.35 (dt, 1H, J = 16.2 and 7.3 Hz, =C*H*-CH_2-), 6.66 (d, 1H, J = 16.2 Hz, =C*H*C_6H_5), 7.20-7.44 (m, 5H, C_6H_5), 7.90 (d, 1H, J = 6.6 Hz, =CHN), 12.71 (bs, 1H, NH); ^{13}C NMR (DMSO-d_6, 62.5 MHz) δ 32.3 (SCH_2), 109.9 (=CHCO), 124.6 (=CHC_6H_5), 126.4, 127.9, 128.8 and 136.5 (C_6H_5), 133.1 (=CH-CH_2-), 154.0 (=CHN), 162.6 and 163.3 (CO, CS). Anal. Calcd for $C_{13}H_{12}N_2OS$: C, 63.91; H, 4.95; N, 11.47; S, 13.12. Found: C, 63.93; H, 4.96; N, 11.47; S, 13.12.

2-[*(E)*-Cinnamylthio)]-5-methyl-4(3*H*)-pyrimidinone (12b): mp 211-212 °C; *Rf* 0.43 (ethyl acetate:acetone 1:1); ^1H NMR (DMSO-d_6, 250 MHz) δ 1.85 (s, 3H, CH_3), 3.94 (d, 2H, J = 7.1 Hz, SCH_2), 6.34 (dt, 1H, J = 15.8 and 7.1 Hz, =C*H*-CH_2-), 6.65 (d, 1H, J = 15.8 Hz, =C*H*C_6H_5), 7.20-7.40 (m, 5H, C_6H_5), 7.77 (s, 1H, =CHN), 12.50 (bs, 1H, NH); ^{13}C NMR (DMSO-d_6, 62.5 MHz) δ 12.6 (CH_3), 32.2 (SCH_2), 119.1 (=CCO), 124.7 (=CHC_6H_5), 126.4, 127.9, 128.9 and 136.4 (C_6H_5), 133.0 (=CH-CH_2-), 150.7 (=CHN), 158.6 (CO), 163.5 (CS). Anal. Calcd for $C_{13}H_{12}N_2OS$: C, 65.09; H, 5.46; N, 10.84; S, 12.41. Found: C, 65.37; H, 5.60; N, 10.70; S, 11.96.

2-[*(E)*-Cinnamylthio]-6-methyl-4(3*H*)-pyrimidinone (12c). mp 169-170 °C; ^1H NMR (DMSO-d_6, 250 MHz) δ 2.14 (s, 3H, CH_3), 3.96 (d, 2H, J = 7.3 Hz, SCH_2), 5.97 (s, 1H, =CHCO), 6.34 (dt, 1H, J = 15.7 and 7.3 Hz, =C*H*-CH_2-), 6.67 (d, 1H, J = 15.7 Hz, CHC_6H_5), 7.20-7.40 (m, 5H, C_6H_5), 12.60 (bs, 1H, NH); ^{13}C NMR (DMSO-d_6, 62.5 MHz) δ 23.4 (CH_3), 32.3 (SCH_2), 106.9 (=CHCO), 124.7 (=CHC_6H_5), 126.3, 127.8, 128.7 and 136.4 (C_6H_5), 133.1 (=CH-CH_2-), 161.7 (CO), 164.1 (CS); MS (*m/z*, %): 258 ($M^{+\cdot}$, 23), 167 (100), 115 (32). Anal. Calcd for $C_{14}H_{14}N_2OS$: C, 65.09; H, 5.46; N, 10.84; S, 12.41. Found: C, 65.17; H, 5.58; N, 10.84; S, 12.11.

2-[*(E)*-Cinnamylthio]-3-[*(E)*-cinnamyl]-6-methylpyrimidin-4-one (13c): mp 87-88 °C (diethyl ether); ^1H NMR ($CDCl_3$, 250 MHz) δ 2.31 (s, 3H, CH_3), 4.04 (d, 2H, J = 7.7 Hz, NCH_2), 4.81 (d, 2H, J = 6.2 Hz, NCH_2), 6.09 (s, 1H, =CHCO), 6.23 (dt, 1H, J = 15.7 and 6.2 Hz, =C*H*-CH_2-), 6.28 (dt, 1H, J = 15.7 and 7.7 Hz, =C*H*-CH_2-), 6.65 (d, 1H, J = 15.7 Hz, =C*H*C_6H_5), 6.67 (d, 1H, J = 15.7 Hz, =C*H*C_6H_5), 7.30-7.40 (m, 10H, C_6H_5); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 23.7 (CH_3), 34.9 (NCH_2), 45.6 (NCH_2), 107.9

(=CCO), 121.5 (=CHC$_6$H$_5$), 123.3 (=CHC$_6$H$_5$), 126.4, 126.5, 127.8, 127.9, 128.5, 128.6, 134.2, 134.6, 136.1, 136.4, 162.3 (CO). MS (*m/z*, %) 374 ($M^{+\cdot}$, 9), 257 (15), 117 (45), 115 (100), 91 (29). Anal. Calcd for $C_{23}H_{22}N_2OS$: C, 73.76; H, 5.92; N, 7.48. Found: C, 72.69; H, 5.72; N, 7.37.

Reaction of allyl acetate with thiouracil (8a) under conditions A. The procedure as for entry 3 of Table 2 was used and the products were separated by column chromatography.

1-Allyl-2-thiouracil (15a): *Rf* 0.65 (ethyl acetate:dichloromethane 2:1); mp 114-116 °C; ^{1}H NMR (DMSO-d$_6$, 200 MHz) δ 4.81 (d, 2H, *J* = 5.4 Hz, NCH$_2$), 5.18 (bd, 1H, *J* = 15.8 Hz, -CH=C*H*$_2$), 5.24 (bd, 1H, *J* = 8.9 Hz, -CH=C*H*$_2$), 5.86 (ddt, 1H, *J* = 15.8, 8.9 and 5.4 Hz, C*H*=CH$_2$), 5.97 (d, 1H, *J* = 7.8 Hz, =CH-CO), 7.75 (d, 1H, *J* = 7.8 Hz, NCH=), 12.61 (bs, 1H, NH); ^{13}C NMR (DMSO-d$_6$, 50 MHz) δ 58.7 (NCH$_2$), 110.6 (=*C*H-CO), 122.2 (CH=*C*H$_2$), 137.1 (*C*H=CH$_2$), 149.5 (=CHN), 164.1 (CO), 180.2 (CS). Anal. Calcd for $C_7H_8N_2OS$: C, 49.98; H, 4.79. Found: C, 49.52; H, 4.82.

2-Allylthio-4(3H)-pyrimidone (14a): *Rf* 0.65 (ethyl acetate:dichloromethane 2:1); oil; ^{1}H NMR (DMSO-d$_6$, 200 MHz) δ 3.79 (d, 2H, *J* = 6.8 Hz, SCH$_2$), 5.12 (bd, 1H, *J* = 9.9 Hz, -CH=C*H*$_2$), 5.30 (bd, 1H, *J* = 16.5 Hz, -CH=C*H*$_2$), 5.91 (ddt, 1H, *J* = 16.5, 9.9 and 6.8 Hz), 6.10 (d, 1H, *J* = 6.2 Hz, =CH-CO), 7.87 (d, 1H, *J* = 6.2 Hz, NCH=), 12.64 (bs, 1H, NH); ^{13}C NMR (DMSO-d$_6$, 50 MHz) δ 36.2 (SCH$_2$), 113.7 (=*C*H-CO), 122.2 (CH=*C*H$_2$), 135.7 (*C*H=CH$_2$), 157.8 (=CHN), 166.3 (CO), 167.1 (CS). Anal. Calcd for $C_7H_8N_2OS$: C, 49.98; H, 4.79. Found: C, 49.52; H, 4.82.

Preparation of 2-[*(E)*-Cinnamylthio]-4(3*H*)pyrimidinone (12a). Solutions of tetrabutylammonium bromide (0.322 g, 1.0 mmol) in butanone (10 mL) and of cinnamyl bromide (1.971 g, 10.0 mmol) in butanone (10 mL) were sequentially added to a mixture of 2-thiouracil (**8a**) (1.281 g, 10.0 mmol), potassium carbonate (1.382 g, 10.0 mmol) and butanone (20 mL). After refluxing the mixture for 2.5 h, dichloromethane (25 mL) was added and the remaining solid was filtered and partitioned between water and ethyl acetate. The combined organic layers (ethyl acetate and dichloromethane) were dried and evaporated to afford sulfide **12a** (1.150 g, 47% yield).

Preparation of 2-[*(E)*-Cinnamylthio]-5-methyl-4(3*H*)-pyrimidinone (12b). A solution of cinnamyl bromide (1.183 g, 6.0 mmol) in acetone (10 mL) was added to a suspension of 2-thiothymine (**8b**), (0.853 g, 6.0 mmol), potassium carbonate (0.829 g, 6.0 mmol) and acetone (10 mL). After refluxing the mixture for 4 h, the solution was filtered and the remaining solid extracted with ethanol. The evaporation of ethanol affords a white solid (0.959 g). The acetone filtrate was evaporated to afford also a white solid (0.808 g) identical with the precedent . They were identified as the hydrobromide of **12b**: 88% overall yield; mp 200-210 °C; ^{1}H NMR (DMSO-d$_6$, 250 MHz) δ 1.77 (d, J = 1.1 Hz, 3H), 3.81 (d, J = 7.3 Hz, 2H), 6.33 (dt, J = 15.7 and 7.3 Hz, 1H), 6.55 (d, J = 15.7 Hz, 1H), 7.14-7.38 (m, 5H), 7.52 (bs, 1H); ^{13}C NMR(DMSO-d$_6$, 62.5 MHz): δ 13.9, 32.3, 116.0, 126.2, 126.8, 127.5, 128.8, 131.5, 136.8, 150.8, 164.1, 171.0. This hydrobromide was treated with aqueous potassium carbonate and ethyl acetate. The organic layer was dried and evaporated to afford quantitatively compound **12b**.

Preparation of 2-[*(E)*-Cinnamylthio]-6-methyl-4(3*H*)-pyrimidinone (12c). It was prepared by the same method as for **12b** to give the hydrobromide of **12c**: 79% yield; mp 163-165 °C; ^{1}H NMR (DMSO-d$_6$, 250 MHz): δ 1.95 (s, 3H), 3.77 (d, J = 6.9 Hz, 2H), 5.41 (s, 1H), 6.33 (dt, J = 15.7 and 6.9 Hz, 1H), 6.54 (d, J = 15.7 Hz, 1H), 7.15-7.40 (m, 5H); ^{13}C NMR (DMSO-d$_6$, 62.5 MHz): δ 23.2, 32.1, 105.8, 126.2,

127.4, 127.5, 128.7, 130.9, 137.0, 161.5, 167.3, 173.4. Anal. Calcd for $C_{14}H_{15}BrN_2OS$: C, 49.56; H, 4.46; N, 8.26. Found: C, 49.27; H, 4.51; N, 7.98. Compound **12c** was obtained in 92% yield.

Isomerisation of 12a-c. Typical experiment. A mixture of **12a** (200 mg, 0.80 mmol), tetrakis (triphenylphosphine)palladium (47 mg, 0.041 mmol) and anhydrous dioxane (15 mL) was refluxed for 20 h. After the conventional working up, the crude mixture was analyzed by ^1H NMR and the ratio of isomers indicated in Scheme 7 was observed.

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