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Solid-Phase Synthesis of 4(1*H*)-Quinolone and Pyrimidine Derivatives Based on a New Scaffold—Polymer-Bound Cyclic Malonic Acid Ester

Xian Huang* and Zhanxiang Liu

Department of Chemistry, Zhejiang University (Campus Xixi), Hangzhou 310028, Zhejiang, P. R. China, and State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, P. R. China.

huangx@mail.hz.zj.cn

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An efficient method for the preparation of polymer-bound cyclic malonic acid ester starting from Merrifield resin has been developed. Reaction of the resin-bound cyclic malonic acid ester with triethyl orthoformate and subsequent double substitution with nucleophilic reagents, such as arylamine, urea, thiourea, 2-aminobenzothiazoles, or isothiosemicarbazones, afforded the corresponding polymer-bound substituted aminomethylene cyclic malonic acid esters, which upon thermal treament led to 4(1*H*)-quinolones, 3-substituted uracils and thiouracils, 4*H*-pyrimido[2,1-*b*]-benzothiazol-4-ones, and 1-(*N*-alkylidene or benzylideneamino)-1,6-dihydro-2-methylthio-6-oxo-pyrimidines, depending on the structures of the nucleophilic reagents.

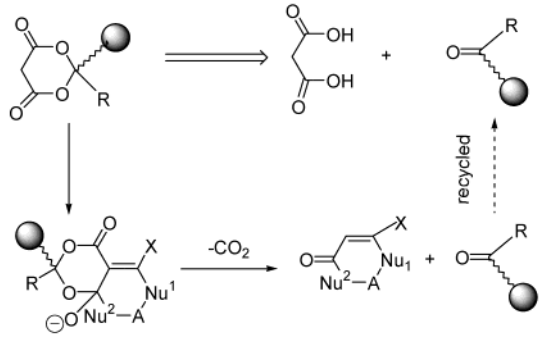
Introduction

Recently, the preparation and screening of combinatorial libraries have become an attractive method for the discovery of pharmaceutical lead compounds. Heterocyclic molecules are of biological interest due to their potential physical and chemical properties.[1] Solid-phase organic synthesis (SPOS) enjoys several advantages over the traditional solution-phase synthesis, such as use of excess reagents for a complete reaction, simple separation (filtration), and the potential of being automated.

Meldrum's acid (2,2-dimethyl-1,3-dioxane-4,6-dione) is a versatile intermediate in organic synthesis,[2] which is mainly caused by electrophilic attack (via the anion) at C-5 and nucleophilic attack at C-4 and C-6 along with the unique ring-opening reaction. A number of substituted 5-methylene derivatives of Meldrum's acid are readily available by condensing Meldrum's acid with triethylorthoformate,[3a] dimethylformamide dimethylacetal,[3b] imidates,[3c] or CS_2.[3d]

Our group has reported the novel synthesis of quinolones,[4a] pyrazolones,[4b] pyrimidines,[4c] and oxazinones[4d] starting from 5,5-(bismethylthiomethylene)-2,2-dimethyl-1,3-dioxane-4,6-dione. In this paper we wish to report our recent results on the solid-phase synthesis of heterocyclic compounds, 4(1*H*)-quinolones, 3-substituted uracils and thiouracils, 4*H*-pyrimido[2,1-*b*]benzothiazol-4-ones, and 1-(*N*-alkylidene or benzylideneamino)-1,6-dihydro-2-methylthio-6-oxo-pyrimidines. Here, the challages are the following: (1) preparation of a resin-bound cyclic malonic acid ester; (2) its solid-phase reaction with binucleophiles; and (3) the cleavage of the resin and the release of the heterocyclic products (Scheme 1).

SCHEME 1



Results and Discussion

Preparation of the Resin-Bound Cyclic Malonic acid Ester. In solution-phase synthesis, Meldrum's acid

* Address correspondence to this author at Zhejiang University. Fax: 86-571-88807077.

(1) For recent reviews on SPOS, see: (a) Brown, R. C. D. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3293−3320. (b) Booth, S.; Hermkens, P. H. H.; Ottenheijm, H. C. J.; Rees, D. C. *Tetrahedron* **1998**, *54*, 15385−15443. (c) James, I. W. *Tetrahedron* **1999**, *55*, 4855−4946. (d) Corbett, J. W. *Org. Prep. Proced. Int*. **1998**, *30*, 491−550. (e) Lorsbach, B. A.; Kurth, M. J. *Chem. Rev*. **1999**, *99*, 1549−1581. (f) Guillier, F.; Orain, D.; Bradley, M. *Chem. Rev*. **2000**, *100*, 2091−2157. (g) Sammelson, R. E.; Kurth, M. J. *Chem. Rev*. **2001**, *101*, 137−202.

(2) For reviews about Meldrum's acid, see: (a) McNab, H. *Chem. Soc. Rev*. **1978**, *7*, 345−358. (b) Chen, B. C. *Heterocycles* **1991**, *32*, 529−597. (c) Gaberm, A. M.; McNab, H. *Synthesis* **2001**, 2059−2074.

(3) (a) Bihlmayer, G. A.; Derflinger, G.; Derkosch, J.; Polansky, O. E. *Monatsh. Chem*. **1967**, *98*, 564−578. (b) Ziegler, F. E.; Guenther, T.; Nelson, R. V. *Synth. Commun*. **1980**, *10*, 661−665. (c) Celerier, J. P.; Richaud, M. G.; Lehommet, G. *Synthesis* **1983**, 195−197. (d) Huang, X.; Chen, B. C. *Synthesis* **1986**, 967−968.

(4) (a) Chen, B. C.; Huang, X.; Wang J. *Synthesis* **1987**, 482−483. (b) Chen, B. C.; Huang, X.; Ma, S. M. *Synth. Commun*. **1987**, *17*, 1519−1522. (c) Ye, F. C.; Chen, B. C.; Huang, X. *Synthesis* **1989**, *4*, 317−320. (d) Huang, X.; Chen, B. C.; Wu, G. Y.; Chen, H. B. *Synth. Commun*. **1991**, *21*, 1213−1221.

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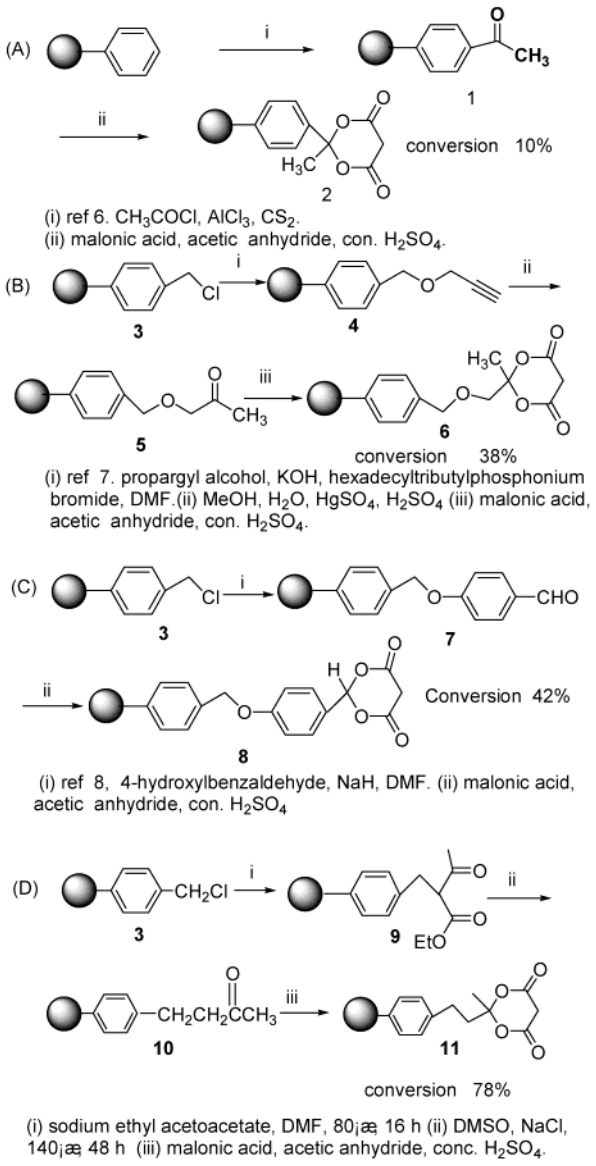
SCHEME 2 [a]



[a] Conditionsa: (A) (i) Reference 6. CH_3COCl, $AlCl_3$, CS_2. (ii) Malonic acid, acetic anhydride, concentrated H_2SO_4. (B) (i) Reference 7. Propargyl alcohol, KOH, hexadecyltributylphosphonium bromide, DMF. (ii) MeOH, H_2O, $HgSO_4$, H_2SO_4. (iii) Malonic acid, acetic anhydride, concentrated H_2SO_4. (C) (i) Reference 8, 4-hydroxylbenzaldehyde, NaH, DMF. (ii) Malonic acid, acetic anhydride, concentrated H_2SO_4. (D) (i) Sodium ethyl acetoacetate, DMF, 80 °C, 16 h. (ii) DMSO, NaCl, 140 °C, 48 h. (iii) Malonic acid, acetic anhydride, concentrated H_2SO_4.

and its derivatives were prepared by the condensation of malonic acid with ketone in acetic anhydride containing a catalytic amount of concetrated H_2SO_4.[5] Therefore we must preload the carbonyl compound to a polymer chain (Scheme 2). The advantage of this strategy is that the resin-bound ketone can be reused after each synthesis. Our initial approach to polymer-supported cyclic malonic acid ester was to draw upon polymer-bound acetophenone **1**.[6] Unfortunately, we obtained the cyclic malonic acid ester resin **2** with a poor conversion of 10% (Scheme 2A). Then we decided to synthesize and evaluate alternative resins. Thus, resins **5** and **7** became our targets. We prepared the polymer-bound benzyloxyacetone **5** from Merrifield resin **3**.[7] From this resin, the resin-bound cyclic malonic acid ester **6** was obtained with 38% conversion (Scheme 2B). We also tried to prepare 4-benzyloxybenzaldehyde resin **7**.[8] After reacting with malonic acid, resin **8** was formed in a conversion of 42% (Scheme 2C). Finally, we noted that the conversion of polymer-bound ketone **10** with the two carbon-atom chain between the carbonyl group and the phenyl group to the polymer-bound cyclic malonic acid ester by Ott's method[9] was 78% (Scheme 2D). The main reason for the better conversion is probably the improved swelling properties of **10** and the higher reactivity of the carbonyl group due to the decrease of the steric hindrance. Our solid-phase synthetic route to **10** (Scheme 2D) started with the commercially available Merrifield resin. Its reaction with sodium ethyl acetoacetate in DMF gave the β-keto ester resin **9**, which afforded the ketone resin **10** by decarboxylation in DMSO.

Solid-Phase Synthesis of 4(1*H*)-Quinolone. 4(1*H*)-Quinolone and its derivatives have attracted the attention of synthetic organic chemists for many years because these structural features are found in a wide variety of naturally occurring alkaloids.[10a] On the other hand, 4(1*H*)-quinolones are effective building blocks in the syntheses of some compounds with interesting pharmacological properties. For example, 4-alkylaminoquinoline derivatives are used for treatment of malaria.[10b] Recently, *Arnoamines A* was prepared through 4(1*H*)-quinolones.[11]

In a preliminary communication, we have reported the solid-phase synthesis of 4(1*H*)-quinolones from the resin **11** (Scheme 3).[12] Resin **11** was treated with triethyl orthoformate and various arylamines to give the resin-bound arylaminomethylene cyclic malonic acid ester **12**.[13] Excess reagents were removed by filtration before the resin was heated for thermal cyclization. The newly formed resin was washed with EtOH and acetone after thermal cleavage to give the products **13**. Products **13** generally do not require further purification and show good purity (>90%) as determined by the ^{1}H NMR spectra (400 MHz) (Table 1).

The multistep synthesis from Merrifield resin to final products was monitored by the FT-IR spectra. In the IR spectrum of resin **9**, there were two strong bands at 1740 and 1716 cm^{-1}, typical for the C═O groups of β-keto esters. The peak at 1260 cm^{-1} (CH_2−Cl) of Merrifield resin disappeared. The formation of resin **10** was shown by the existence of a strong single carbonyl peak at 1716

(5) (a) Meldrum, A. N. *J. Chem. Soc.* **1908**, *93*, 598−600. (b) Davidson, D.; Berhardt, S. A. *J. Am. Chem. Soc.* **1948**, *70*, 3426−3428.

(6) Frechet, J. M. J.; Nuyens, L. J. *Can. J. Chem.* **1976**, *54*, 926−934.

(7) .Manzocchi, A.; Fiecchi, A.; Santaniello, E. *Synthesis* **1987**, 1007−1009.

(8) .Routledge, A.; Stock, H. T.; Filtsch, S. L.; Turner, N. J. *Tetrahedron Lett.* **1997**, *38*, 8287−8290.

(9) (a) Ott, E. *Ann.* **1913**, *401*, 159−177. (b) Michael, A.; Weiner, N. *J. Am. Chem. Soc.* **1936**, *58*, 680−685.

(10) (a) Reitsema, R. H. *Chem. Rev.* **1948**, *43*, 43−68. (b) Andersag, H.; Breitner, S.; Jung, H. U.S. Patent 2,233,970; *Chem. Abstr.* **1941**, *35*, 3771.[7]

(11) Delfourne, E.; Roubin, C.; Bastide, J. *J. Org. Chem.* **2000**, *65*, 5476−5479.

(12) Huang, X.; Liu, Z. X. *Tetrahedron Lett.* **2001**, *42*, 7655−7657.

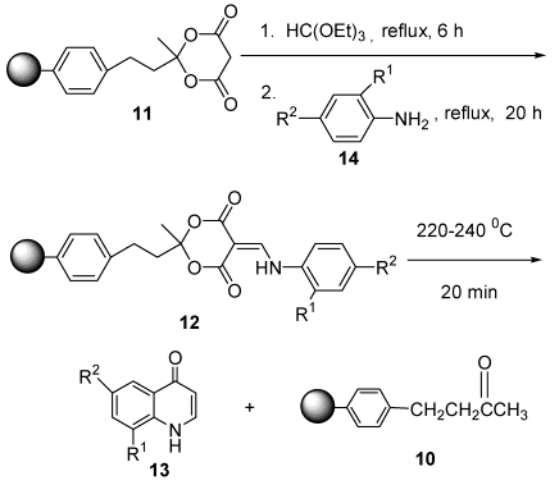
(13) (a) Cassis, R.; Tapia, R.; Valderrama, J. A. *Synth. Commun.* **1985**, *15*, 125−133. (b) Gordon, H. J.; Martin, J. C.; McNab, H. *J. Chem. Soc., Chem. Commun.* **1983**, 957−958.

TABLE 1. Yields and Purities of 4(1*H*)-Quinolones

entry	product	R^1	R^2	yield (%)[a]	purity (%)[b]
1	**13a**	H	H	62	95
2	**13b**	CH_3	H	59	90
3	**13c**	H	$COCH_3$	59	92
4	**13d**	H	NO_2	62	90
5	**13e**	NO_2	H	47	94
6	**13f**	H	OCH_3	57	91
7	**13g**	H	CH_3	49	90
8	**13h**	H	Br	58	93
9	**13i**	Cl	Cl	61	93

[a] The crude yields are based on the loading of the cyclic malonic acid ester resin **11**. [b] The purity was determined by ^{1}H NMR (400 MHz).

SCHEME 3



cm^{-1} of the carbonyl group. The cyclic malonic acid ester **11** was monitored by IR spectra which showed carbonyl peaks at 1767 and 1794 cm^{-1}. There was also a weak peak at 1710 cm^{-1} because resin **10** was not completely converted into **11**. When the cyclic malonic acid ester resin was converted to resin **12**, the IR carbonyl peak shifted to 1738 and 1684 cm^{-1} (**12a**, R^1 = H, R^2 = H) with a new peak appearing at 1625 cm^{-1} (C=C). Rresin **12** was cleaved by thermal cyclization. It was noted that resin **12** underwent a smooth and clean cyclization at 220−240 °C to afford **13** and resin **10,** which can be reused.[14] This is a novel traceless cleavage strategy based on the electrocyclization of an aminoketene intermediate.[13]

Solid-Phase Synthesis of 4*H*-Pyrimido[2,1-*b*]benzothiazol-4-ones and 5*H*-Thiazolo[3,2-*a*]pyrimidin-5-ones (Scheme 4). These compounds were successfully prepared via solution-phase synthesis by our group[4c] and others.[13a] We used 2-aminobenzothiazole or 2-amino-4-methylthiazole as binucleophiles. When the cyclic malonic acid ester resin **11** was converted to resin **16**, the IR carbonyl peak shifted to 1730 and 1670 cm^{-1} with a new peak appearing at 1615 cm^{-1} (C=C) (**16**a, R^1 = H, R^2 = CH_3O). Resin **16** was cleaved by thermal cyclization to form the heterocyclic compounds **17** (Table 2).

When 2-amino-4-methylthiazole (**15g**) was used, 3-methyl-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**17g**) was obtained.

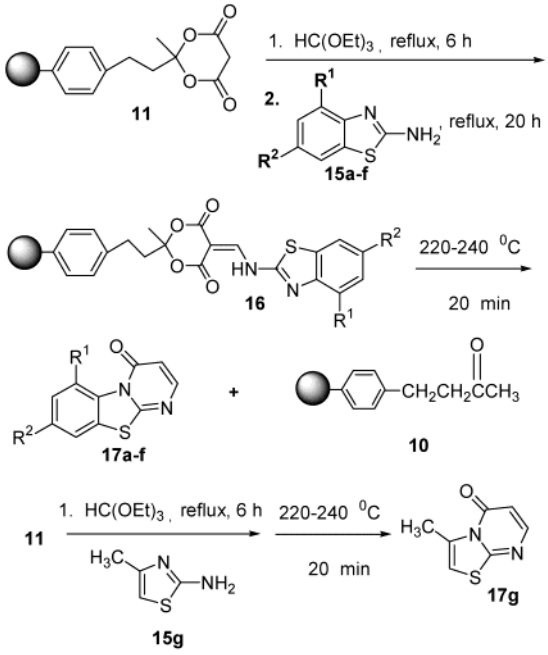
(14) The IR spectroscopy of the recovered resin shows a single strong carbonyl peak at 1716 cm^{-1}. The loading of this resin is 1.80 mmol/g (based on the C=O group).

TABLE 2. Yields and Purities of 4*H*-Pyrimido[2,1-*b*]benzothiazol-4-ones and 5*H*-Thiazolo[3,2-*a*]pyrimidin-5-ones

entry	product	R^1	R^2	yield (%)[a]	purity (%)[b]
1	**17a**	H	CH_3O	72	>95
2	**17b**	H	CH_3	82	>95
3	**17c**	CH_3	H	77	>95
4	**17d**	H	H	86	>95
5	**17e**	H	Cl	81	>95
6	**17f**	H	Br	77	>95
7	**17g**			80	>95

[a] The crude yields were based on the loading of the cyclic malonic acid ester resin **11**. [b] Determined by ^{1}H NMR.

SCHEME 4



Isothiosemicarbazones (**18**) are a polyfunctional nucleophile for the formation of nitrogen-containing heterocycles.[15] When the cyclic malonic acid ester resin **11** was converted to resin **19** by its reaction with **18**, the IR carbonyl peak shifted to 1735 and 1690 cm^{-1} (**19a**, R^1 = R^2 = CH_3) with new peaks appearing at 1585 (C=C) and 1276 cm^{-1} (C−S). Thermal cyclization afforded the heterocyclic compounds **20** in good yield and high purity (Table 3).

Solid-Phase Synthesis of Uracils and Thiouracils. Uracils and thiouracils are important compounds in organic synthesis[16a] and are involved in a large number of biological processes.[16b] Valderrama and co-workers prepared the uracil and 2-thiouracil from Meldrum's acid in a solution-phase synthesis.[16c] Starting from resin **11,** its reaction with $HC(OEt)_3$ afforded the resin-bound

(15) (a) Yamazaki, C. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 3289−3294 (b) Yamazaki, C. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 1846−1855 (c) Yamazaki, C. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1767−1772.

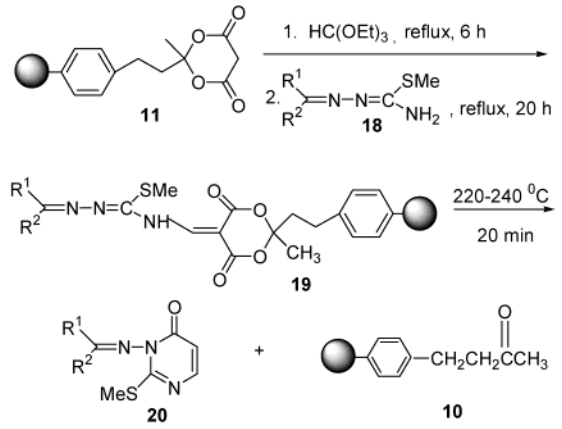
(16) (a) Brown, D. J. *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon Press: Oxford, New York, 1984; Vol. 3, Part 2B, pp 57−155. (b) Manuelidis, L.; Langer-Safer, P. R.; Ward, D. C. *J. Cell Biol.* **1982**, *95*, 619−625. (c) Cassis, R.; Tapia, R.; Valderrama, J. A. *Synth. Commun.* **1984**, *14*, 961−965. (d) Whitehead, C. W. *J. Am. Chem. Soc.* **1952**, *74*, 4267−4271.

TABLE 3. Yields and Purities of 1-(*N*-Alkylidene or benzylideneamino)-1,6-dihydro-2-methylthio-6-oxo-pyrimidine

entry	product	R_1	R_2	yield (%)[a]	purity (%)[b]
1	**20a**	CH_3	CH_3	86	>92
2	**20b**	Ph	H	80	>95
3	**20c**	4-ClC_6H_4	H	81	>95
4	**20d**	4-ClC_6H_4	CH_3	79	>95
5	**20e**	Ph	Et	78	>90
6	**20f**	Ph	Ph	72	>95
7	**20g**	Ph	CH_3	80	>92

[a] The crude yields were based on the loading of the cyclic malonic acid ester resin **11**. [b] Determined by ^{1}H NMR.

SCHEME 5



5-ethoxymethylene Meldrum's acid, followed by substitution with ureas or thioureas **21** to form resin **22** (Scheme 6).

When the cyclic malonic acid ester resin was converted to resin **22**, the carbonyl IR peak shifted to 1730 and 1680 cm^{-1} (**22a**). Also a new peak appeared at 3300 cm^{-1} (NH). The resin **22** was cleaved by thermal cyclization to afford **23**.

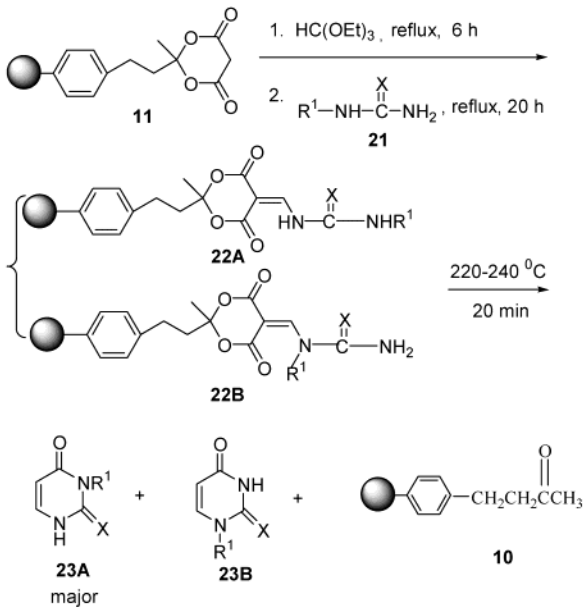
In the condensation of monosubstituted ureas or thioureas with 5-ethoxymethylene Meldrum's acid two isomers **23A** and **23B** could be formed due to the regioselectivity of the nucleophilic substitution. The condensation of monosubstituted ureas with diethyl ethoxymethylenemalonate occurred exclusively between the unsubstituted nitrogen of the urea and the ethoxymethylene group of the ester.[16c] In most cases, **23A** were always formed as the major product when monosubstituted ureas or thioureas were used. The compounds were identified by comparison of their ^{1}H NMR (6-H, 5-H) spectra with the reported data. For example, the ^{1}H NMR spectra of product **23e** showed 5-H proton signals at δ_H 6.03−6.05 (5-H, J = 7.56 Hz, 1H) and δ_H 6.49−6.51 (0.3 H). Compared with the reported data,[29] the 5-H of 3-phenyl-2-thiouracil shows a proton signal at 5.95 ppm (J = 7.5 Hz), which is similar to the 5-H proton signal of the major product (**23eA**). So the major product (**23eA**) is 3-phenyl-2-thiouracil. The isomeric ratio was 77:23 (**23eA**:**23eB**). The results are listed in Table 4.

TABLE 4. Yields and Purities of 3-Substituted Uracils and Thiouracils

entry	product	R^1	X	**23A**/**23B**[a]	yield (%)[b]	purity (%)
1	**23a**	H	O		80	>90
2	**23b**	H	S		72	>95
3	**23c**	4-$CH_3C_6H_4$	O	100/0	76	90
4	**23d**	4-$CH_3C_6H_4$	S	77/23	65	90
5	**23e**	C_6H_5	S	77/23	82	92
6	**23f**	C_6H_5	O	88/12	68	88
7	**23g**	$PhCH_2$	O	100/0	78	92
8	**23h**	$PhCH_2$	S	95/5	74	90
9	**23i**	4-ClC_6H_4	S	77/23	80	>95
10	**23j**	CH_3	O	100/0	82	>95

[a] The isomeric ratios (**23A** and **23B**) obtained from ^{1}H NMR. [b] The yields were based on the loading of the cyclic malonic acid ester resin **11**.

SCHEME 6



Conclusions

In summary, we have developed a method for the preparation of polymer-bound cyclic malonic acid ester. A series of 4(1*H*)-quinolones, 3-substituted uracils and thiouracils, 4*H*-pyrimido[2,1-*b*]benzothiazol-4-ones, and 1-(*N*-alkylidene or benzylideneamino)-1,6-dihydro-2-methylthio-6-oxo-pyrimidines were synthesized by thermal cyclization cleavage. Moreover, the present strategy

(17) Yamazaki, C. *Can. J. Chem.* **1975**, *53*, 610−615.
(18) (a) Li, D. F.; Jiang, G. J.; Li, J. S. *Chem. J. Chin. Univ.* **1990**, *11*, 205−207. (b) Gupta, P. R.; Ojha, K. G.; Kumar, M. *J. Heterocycl. Chem.* **1980**, *17*, 1325−1327.
(19) Heindel, N. D.; Kennewell, P. D.; Fisch, V. B. *J. Heterocycl. Chem.* **1969**, *6*, 77−81.
(20) *Beilsteins Handbuch Der Organischen Chemie*; Springer-Verlag, Berlin, 1953; 21II, p 67.
(21) Riegel, B.; Lappin, G. R.; Adelson, B. H.; Jackson, R. I.; Albisett, C. J., Jr.; Dodson, R. M.; Baker, R. H. *J. Am. Chem. Soc.* **1946**, *68*, 1264−1266.
(22) Sterling Drug Inc. British Patent 1147760, 1969; *Chem. Abstr.* **1969**, *71*, 49967a.
(23) Schofield, K.; Swain, T. *J. Chem. Soc.* **1950**, 384−392.
(24) Surrey, A. R.; Hammer, H. F. *J. Am. Chem. Soc.* **1946**, *68*, 1244−1246.
(25) Dunwell, D. W.; Evans, D. *J. Chem. Soc.(C)* **1971**, 2094−2098.
(26) Wade, J. J.; Hegel, R. F.; Toso, C. B. *J. Org. Chem.* **1979**, *11*, 1811−1816.
(27) Andrew, H. F.; Bradsher, C. K. *J. Heterocycl. Chem.* **1967**, 577−581.
(28) Bernath, G.; Stajer, G.; Szabo, A. E.; Szoke-Molnar Z.; Sohar, P.; Argay, G.; Kalman, A. *Tetrahedron* **1987**, *43*, 1921−1930.
(29) Stajer, G.; Szabo, A. E.; Pintye, J.; Bernath, G. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2483−2487.

described a traceless cleavage SPOS route. The resin-bound cyclic malonic acid ester can be considered to be an appropriate scaffold for solid-phase synthesis of heterocyclic compounds for potential use in combinatorial chemistry. Application toward the synthesis of more biologically interesting heterocycles using this strategy will be reported in due course. Here, due to the high temperature used for thermal cyclization, the methodology may be limited to thermally stable heterocycles. However, with the liable ketal structure in **11**, it is obvious that other cleavage protocol with milder conditions can be developed for the solid-phase synthesis of other libraries of heterocyclic compounds. In addition, it should be noted that the polymer-bound ketone could easily be regenerated for reuse after cleavage. Thus, the protocol developed here will be a starting point for the solid-phase synthesis of heterocyclic compounds.

Experimental Section

Melting points were uncorrected. The compounds 2-aminobenzothioazole **15**[17] and isothiosemicarbazones **18**[18] were prepared according to the literature method.

Procedure for the Preparation of the Resin-Bound Cyclic Malonic Acid Ester. To the solution of sodium ethyl acetoacetate (39.2 mmol, 5.96 g) in 30 mL of DMF was added Merrifield resin **3** (2 g, 1% cross-linked, 200−400 mesh, loading = 1.96 mequiv Cl/g) and the mixture was stirred at 80 °C for 16 h. After the mixture was washed with DMF, EtOH, and CH_2Cl_2, the β-keto ester resin **9** was obtained. The β-keto ester resin **9** (2 g) was suspended in a mixture of DMSO (30 mL), NaCl (40 mmol), and H_2O (120 mmol) and the mixture was refluxed for 48 h. After the solution was washed with water, DMF, EtOH, and CH_2Cl_2, ketone resin **10** (loading = 1.88 mmol/g, based on C=O) was obtained. A solution of malonic acid (38 mmol), concentrated sulfuric acid (0.1 mL), and acetic anhydride (117 mmol) was allowed to stand for 24 h at room temperature and was then concentrated at 40 °C under reduced pressure. Resin **10** (2 g, preswelled in dry CH_2Cl_2) was added to the residue at 0 °C. Then 2 mL of dry CH_2Cl_2 was added to the mixture and the mixture was stirred at 15 °C for 24 h. The resin was then washed with water, EtOH, and CH_2Cl_2. The cyclic malonic acid ester resin **11** (loading = 1.20 mmol/g) was obtained. The loading of resin **11** was determined by reversed titration with hydrochloride acid after saponification with excess NaOH in EtOH.

General Procedure for the Solid-Phase Synthesis of 4(1*H*)-Quinolones. A suspension of resin **11** (500 mg, 1.20 mmol/g) in triethyl orthoformate (50 equiv, 5 mL) was refluxed for 6 h. Then arylamine (10 equiv) was added and the mixture was refluxed for 24 h. The resin was filtered, washed with 3 × 5 mL of EtOH, 3 × 5 mL with CH_2Cl_2, and thermally cyclized with an oil bath at 240 °C for 20 min under N_2 atmosphere. The mixture was washed with EtOH/acetone completely in the sintered glass funnel, and the filtrates were combined to afford the product by evaporation.

4(1*H*)-Quinolinone (13a): Mp 208−210 °C (lit.[19] mp 209−211 °C). ^{1}H NMR (DMSO-d_6) δ 6.02 (d, J = 7.4 Hz, 1H), 7.27−7.31 (m, 1H, ArH), 7.52 (d, J = 8.3 Hz, 1H, ArH), 7.59 (m, 1H, ArH), 7.87 (d, J = 7.4 Hz, 1H), 8.04 (dd, J = 8.1, 1.5 Hz, 1H, ArH). MS *m*/*z* (rel intensity) 145 (M^+, 100), 117(76), 90(43). IR ν 3070, 1641, 1611, 1547 cm^{-1}.

8-Methyl-4(1*H*)-quinolinone (13b): Mp 203−205 °C (lit.[20] mp 206 °C). ^{1}H NMR (DMSO-d_6) δ 2.48 (s, 3H, CH_3), 6.05 (d, J = 7.6 Hz, 1H), 7.19 (m, 1H, ArH), 7.48 (d, J = 7 Hz, 1H, ArH), 7.81−7.84 (m, 1H, ArH), 7.95 (d, J = 7.6 Hz, 1H), 11.09 (br s, 1H, NH). MS *m*/*z* (rel intensity) 159 (M^+, 100), 130 (77). IR ν 3163, 3091, 1643, 1622, 1557 cm^{-1}.

6-Acetyl-4(1*H*)-quinolinone (13c): Mp 284−286 °C (lit.[21] mp 285−286 °C). ^{1}H NMR (DMSO-d_6) δ 2.66 (s, 3H, CH_3), 6.34 (d, J = 7.3 Hz, 1H), 7.72 (d, J = 8.76 Hz, 1H, ArH), 8.05 (d, J = 7.3 Hz, 1H, ArH), 8.17 (dd, J = 8.7 and 2 Hz, 1H, ArH), 8.75 (d, J = 2 Hz, 1H, ArH), 12.57 (s, 1H, NH). MS *m*/*z* (rel intensity) 187 (M^+, 66), 172 (100), 144 (65), 116 (42), 89 (39). IR ν 3055, 3149, 2783, 1670, 1649, 1558, 1276 cm^{-1}.

6-Nitro-4(1*H*)-quinolinone (13d): Mp 324−327 °C (lit.[19] mp 325−330 °C).^{1}H NMR (DMSO-d_6) δ 6.18 (d, J = 7.56 Hz, 1H), 7.72 (d, J = 9 Hz, 1H, ArH), 8.04 (d, J = 7.56 Hz, 1H), 8.41−8.44 (dd, J = 9, 3 Hz, 1H, ArH), 8.84 (d, J = 2.68 Hz, 1H, ArH), 12.31 (br s, 1H, NH). *MS m*/*z* (rel intensity): 190 (M^+, 100), 144 (39), 116 (64), 89 (71). IR ν 3327, 3244, 1690, 1642, 1602, 1496, 1312, 1248 cm^{-1}.

8-Nitro-4 (1*H*)-quinolinone (13e): Mp 196−198 °C (lit.[21] mp 198−199 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.43 (dd, J = 7.64, 1.36 Hz, 1H), 7.44 (t, J = 8 Hz, 1H, ArH), 7.75 (dd, J = 7.6, 6 Hz, 1H), 8.66 (dd, J = 8.1, 6, 1.6 Hz, 1H, ArH), 8.80 (dd, J = 8.1, 1.24 Hz, 1H, ArH), 11.2 (br s, 1H, NH). MS *m*/*z* (rel intensity) 190 (M^+, 100), 162 (14), 144 (29), 116 (36). IR ν 3328, 3244, 1642, 1602, 1497, 1312, 1248 cm^{-1}.

6-Methoxy-4(1*H*)-quinolinone (13f): Mp 248−250 °C (lit.[19] mp 250−252 °C). ^{1}H NMR (DMSO-d_6) δ 3.82 (s, 3H, CH_3), 6.00 (d, J = 7.24 Hz, 1H), 7.27 (dd, J = 9, 3 Hz, 1H), 7.48 (d, J = 3 Hz, 1H), 7.52 (d, J = 9 Hz, 1H), 7.84 (d, J = 7.32 Hz, 1H), 11.8 (br s, 1H). MS *m*/*z* (rel intensity) 175 (M^+, 100), 160 (24), 145 (27), 132 (39), 104 (36). IR ν 3241, 3156, 2994, 1640, 1595, 1521, 1387 cm^{-1}.

6-Methyl-4(1*H*)-quinolinone (13g): Mp 238−240 °C (lit.[22] mp 237−239 °C). ^{1}H NMR (DMSO-d_6) δ 2.40 (s, 3H, CH_3), 5.99 (d, J = 7 Hz, 1H), 7.46 (m, 2H), 7.85−7.88 (m, 2H), 11.75 (s, 1H). MS *m*/*z* (rel intensity) 159 (M^+, 100). 130 (54). IR ν 3168, 3092, 1643, 1622 cm^{-1}.

6-Bromo-4(1*H*)-quinolinone (13h): Mp 282−284 °C (lit.[23] mp 282−284 °C). ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.07 (d, J = 7.4 Hz, 1H), 7.51 (d, J = 8.8 Hz, 1H), 7.78 (dd, J = 8.8, 2 Hz, 1H), 7.94 (d, J = 7.4 Hz, 1H), 8.15 (d, J = 2 Hz, 1H), 11.9 (br s, 1H). MS *m*/*z* (rel intensity) 223 (M^+, ^{79}Br, 100), 225 (M^+, ^{81}Br, 98), 195 (22), 144 (27), 116 (97), 89 (48). IR ν 3051, 2887, 1645, 1624, 1606, 1551, 1510 cm^{-1}.

6,8-Dichloro-4(1*H*)-quinolinone (13i): Mp 309−311 °C (lit.[24] mp 309−311 °C). ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.16 (d, J = 7.3 Hz, 1H), 7.89 (d, J = 7.6 Hz, 1H), 8.01 (d, J = 2.4 Hz, 1H), 8.03 (d, J = 2.36 Hz, 1H), 11.6 (br s, 1H). MS *m*/*z* (rel intensity) 213 (M^+, ^{35}Cl, 100), 215 (M^+, ^{37}Cl, 60). IR ν 3051, 1641, 1623, 1606, 1553, 1508 cm^{-1}.

General Procedure for the Solid-Phase Synthesis of 4*H*-Pyrimido[2,1*b*]benzothiazol-4-ones and 5*H*-Thiazolo-[3,2-*a*]pyrimidin-5-ones. A suspension of resin **11** (500 mg, 1.20 mmol/g) in triethyl orthoformate (50 equiv, 5 mL) was refluxed for 6 h. The 2-aminobenzothiazole or 2-amino-4-methylthiazole (5 equiv) was added. The mixture continued to reflux for 6 h. The resin was filtered and washed with 3 × 5 mL of EtOH, 3 × 5 mL with CH_2Cl_2. Then the resin was heated with an oil bath at 240 °C for 20 min under N_2 atmosphere. The resin was washed with EtOH/acetone completely in the sintered glass funnel. The filtrates were combined and the solvents removed in vacuo to afford the product.

8-Methoxyl-4*H*-pyrimido[2,1-*b*]benzothiazol-4-one (17a): Light yellow needles. Mp 198−199 °C (lit.[25] mp 198−199 °C). ^{1}H NMR (DMSO-d_6) δ 3.84 (s, 3H), 6.40 (d, 1H, J = 6.52 Hz), 7.14−7.17 (dd, 2H, J = 9.2, 2.4 Hz), 7.70 (d, 1H, J = 2.4 Hz), 8.01 (d, 1H, J = 6.52 Hz), 8.81 (d, 1H, J = 9.2 Hz). IR ν_{max} 3446, 3119, 2925, 1673,1600, 1560, 1495, 1290, 1259, 1169, 1044, 991, 815, 756 cm^{-1}. MS *m*/*z* (rel intensity) 232 (M^+, 100), 204 (38), 189 (52), 161 (13), 134 (13), 53 (29).

8-Methyl-4*H*-pyrimido[2,1-*b*]benzothiazol-4-one (17b): Light yellow solid. Mp 176−178 °C. ^{1}H NMR ($CDCl_3$) δ 2.49 (s, 3H), 6.41 (d, 1H, J = 6.52 Hz), 7.32−7.34 (dd, 1H, J = 8.6, 1 Hz), 7.49 (s, 1H), 7.93 (d, 1H, J = 6.52 Hz), 8.97 (d, 1H, J = 8.6 Hz). ^{13}C NMR ($CDCl_3$) δ 21.468, 109.288, 119.930, 121.792, 124.228, 128.063, 133.926, 137.732, 151.753, 160.992, 162.385. IR (KBr) ν_{max} 2917, 1697, 1566, 1498, 1467, 1319, 1293, 1259, 991, 884, 751 cm^{-1}. MS *m*/*z* (rel intensity) 216 (M^+, 100), 188

(79), 187 (24), 121 (17), 77 (31). Elemental Anal. Calcd for $C_{11}H_8N_2OS$: C 61.09; H 3.73; N 12.95. Found: C 61.38; H 3.92; N 12.86.

6-Methyl-4*H*-pyrimido[2,1-*b*]benzothiazol-4-one (17c): Light yellow solid. Mp 106−108 °C. ^{1}H NMR ($CDCl_3$) δ 2.62 (s, 3H), 6.33 (d, 1H, J = 6.52 Hz), 7.31−7.39 (m, 2H), 7.45−7.47 (m, 1H), 7.85 (d, 1H, J = 6.52 Hz). ^{13}C NMR ($CDCl_3$) δ 24.259, 109.217, 119.269, 125.413, 127.250, 130.964, 131.169, 134.382, 151.255, 160.819, 163.111. IR ν_{max} 2930, 1694, 1573, 1497, 1470, 1381, 1280, 1243, 987, 813, 755 cm^{-1}. MS *m*/*z* (rel intensity) 216 (M^+, 97), 188 (100), 161 (14), 146 (12), 121 (21), 103 (17), 77 (41). Elemental Anal. Calcd for $C_{11}H_8N_2OS$: C 61.09; H 3.73; N 12.95. Found: C 61.38; H 3.92; N 12.86.

4*H*-Pyrimido[2,1-*b*]benzothiazol-4-one (17d): Light yellow solid. Mp 166−168 °C (lit.[26] mp 168 °C) ^{1}H NMR ($CDCl_3$) δ 6.43 (d, 1H, J = 6.52 Hz), 7.49−7.57 (m, 2H), 7.69−7.71 (m, 1H), 7.94 (d, 1H, J = 6.52 Hz), 9.10−9.12 (m, 1H). IR ν_{max} 1682, 1577, 1499, 1256, 994, 827, 759 cm^{-1}. MS *m*/*z* (rel intensity) 202 (M^+, 100), 174 (98), 146 (12), 134 (11), 120 (10), 108 (9), 90 (11), 69 (15).

8-Chloro-4*H*-pyrimido[2,1-*b*]benzothiazol-4-one (17e): Light yellow solid. Mp 198−200 °C. ^{1}H NMR ($CDCl_3$) δ 6.42 (d, 1H, J = 6.52 Hz), 7.48−7.52 (dd, 1H, J = 9, 2.1 Hz), 7.68 (d, 1H, J = 2.1 Hz), 7.94 (d, 1H, J = 6.52 Hz), 9.02 (d, 1H, J = 9 Hz). ^{13}C NMR ($CDCl_3$) δ 109.656, 121.084, 121.579, 125.809, 127.446, 133.122, 134.544, 151.976, 160.731, 161.898. IR ν_{max} 3068, 1680, 1575, 1494, 1406, 1284, 1247, 989, 812, 739 cm^{-1}. MS *m*/*z* (rel intensity) 236 (M^+, 100), 238 ($M^+ + 2$, 37), 208 (95), 210 (36), 173 (20), 133 (27), 107 (14). Elemental Anal. Calcd for $C_{10}H_5ClN_2OS$: C 50.75; H 2.13; N 11.84. Found: C 50.61, H 2.38, N 11.79.

8-Bromo-4*H*-pyrimido[2,1-*b*]benzothiazol-4-one (17f): Light yellow solid. Mp 200−202 °C. ^{1}H NMR ($CDCl_3$) δ 6.41 (d, 1H, J = 6.52 Hz), 7.63−7.65 (dd, 1H, J = 9, 2 Hz), 7.83 (d, 1H, J = 2 Hz), 7.94 (d, 1H, J = 6.52 Hz), 8.98 (d, 1H, J = 9 Hz). ^{13}C NMR ($CDCl_3$) δ 108.854, 119.801, 120.510, 123.610, 125.259, 129.445, 134.145, 151.191, 159.920, 160.953. IR ν_{max} 3103, 1681, 1577, 1493, 1402, 1284, 1248, 990, 826, 811, 790, 732 cm^{-1}. MS *m*/*z* (rel intensity) 280 (M^+, 100), 282 ($M^+ + 2$, 100), 254 (78), 252 (78), 173 (40), 133 (37), 69 (29). Elemental Anal. Calcd for $C_{10}H_5N_2OS$: C 42.72; H 1.79; N 9.96. Found: C 42.95; H 1.83; N 9.78.

3-Methyl-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (17g): Light yellow solid. Mp 126−128 °C (lit.[27] mp 128−129 °C). ^{1}H NMR ($CDCl_3$) δ 2.82 (d, 3H, J = 1.32 Hz), 6.19 (d, 1H, J = 6.52 Hz), 6.44 (t, 1H, J = 1.32 Hz), 7.85 (d, 1H, J = 6.52 Hz). ^{13}C NMR ($CDCl_3$) δ 18.664, 105.835, 107.420, 136.876, 152.466, 161.524, 165.234. IR ν_{max} 3113, 1670, 1617, 1595, 1481, 1417, 1284, 1235, 1147, 968, 812, 761 cm^{-1}. MS *m*/*z* (rel intensity) 166 (M^+, 100), 138 (72), 93 (18), 71 (29), 72 (21), 67 (15), 52 (13), 45 (32).

General Procedure for the Solid-Phase Synthesis of 1-(*N*-Alkylidene or benzylideneamino)-1,6-dihydro-2-methylthio-6-oxo-pyrimidine. A suspension of resin **11** (500 mg, 1.20 mmol/g) in triethyl orthoformate (50 equiv, 5 mL) was refluxed for 6 h. The isothiosemicarbazone (3 equiv) was added and the mixture was refluxed for 12 h. The resin was filtered and washed with 3 × 5 mL of EtOH, 3 × 5 mL with CH_2Cl_2, and thermally cyclized with an oil bath at 240 °C for 20 min under N_2 atmosphere. The mixture was washed with EtOH and acetone completely in the sintered glass funnel and the filtrates were combined to afford the product by evaporation.

1-(*N*-Isopropylideneamino)-1,6-dihydro-2-methylthio-6-oxo-pyrimidine (20a): Light yellow needles. Mp 158−160 °C. ^{1}H NMR ($CDCl_3$) δ 1.86 (s, 3H), 2.30 (s, 3H), 2.48 (s, 3H), 6.24 (d, 1H, J = 6.4 Hz), 7.78 (d, 1H, J = 6.4 Hz). IR ν_{max} 3300, 3198, 2926, 1698, 1634, 1482, 1360, 1184 cm^{-1}. ^{13}C NMR ($CDCl_3$) δ 14.337, 14.414, 20.226, 110.199, 151.460, 157.064, 160.294, 182.797. MS *m*/*z* (rel intensity) 197 (M^+, 16), 182 (100), 112 (28), 95 (10), 56 (83). Elemental Anal. Calcd for $C_8H_{11}N_3OS$: C 48.71; H 5.62; N 21.30. Found: C 48.68; H 5.72; N 21.28.

1-(*N*-Benzylideneamino)-1,6-dihydro-2-methylthio-6-oxo-pyrimidine (20b): White solid. Mp 118−120 °C. ^{1}H NMR ($CDCl_3$) δ 2.50 (s, 3H), 6.28 (d, 1H, J = 6.4 Hz), 7.48−7.55 (m, 3H), 7.72 (d, 1H, J = 6.4 Hz), 7.87−7.90 (m, 2H), 9.26 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 14.761, 110.903, 128.956, 129.138, 129.733, 132.706, 150.859, 157.252, 159.418, 165.353. IR ν_{max} 3052, 2928, 1679, 1610, 1597, 1574, 1471, 1301, 1287, 1224 cm^{-1}. MS *m*/*z* (rel intensity) 246 (M^+, 18), 245 (3), 230 (6), 171 (0.60), 142 (100), 112 (35), 95 (24), 77 (24), 51 (25). Elemental Anal. Calcd for $C_{12}H_{11}N_3OS$: C 58.76; H 4.52; N 17.13. Found: C 58.79; H 4.67; N 17.05.

1-(*N*-4-Chlorophenylmethylideneamino)-1,6-dihydro-2-methylthio-6-oxo-pyrimidine (20c): Light yellow needles. Mp 146−148 °C. ^{1}H NMR ($CDCl_3$) δ 2.49 (s, 3H), 6.27 (d, 1H, J = 6.42 Hz), 7.45 (dd, 2H, J = 6.76, 1.72 Hz), 7.73 (d, 1H, J = 6.42 Hz), 7.80−7.83 (dd, 2H, J = 6.76, 1.72 Hz), 9.32 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 14.792, 110.937, 129.345, 130.213, 131.323, 138.869, 150.884, 159.540, 163.346, 164.035. IR ν_{max} 3300, 3198, 2927, 1676, 1607, 1593, 1568, 1478, 1405, 1314, 1292, 1092, 823 cm^{-1}. MS *m*/*z* (rel intensity) 279 (M^+, 1.53), 281 ($M^+ + 2$, 0.55), 264 (5), 142 (100), 112 (45), 95 (35), 75 (29). Elemental Anal. Calcd for $C_{12}H_{10}N_3OSCl$: C 51.52; H 3.60; N 15.02. Found: C 51.64; H 3.49; N 15.22.

1-[*N*(4-Chlorophenyl)ethylideneamino]-1,6-dihydro-2-methylthio-6-oxo- pyrimidine (20d): Light yellow needles. Mp 134−136 °C. ^{1}H NMR ($CDCl_3$) δ 2.23 (s, 3H), 2.52 (s, 3H), 6.28 (d, 1H, J = 6.4 Hz), 7.44 (d, 2H, J = 8.6 Hz), 7.80 (d, 1H, J = 6.4 Hz), 7.95 (d, 2H, J = 8.6 Hz).^{13}C NMR ($CDCl_3$) δ 14.426, 17.146, 110.156, 128.941, 129.223, 133.954, 138.506, 151.444, 156.812, 161.516, 176.558. IR ν_{max} 3062, 2922, 1681, 1487, 1368, 1334, 1287, 1141, 1092 cm^{-1}. MS *m*/*z* (rel intensity) 293 (M^+, 11), 295 ($M^+ + 2$, 3.88), 278 (100), 280 (37), 183 (14), 152 (51), 154 (17), 112 (67), 75 (40). Elemental Anal. Calcd for $C_{13}H_{12}N_3OSCl$: C 53.15; H 4.12; N 14.30. Found: C 53.51; H 3.94; N 14.30.

1-(*N*-Phenylpropylideneamino)-1,6-dihydro-2-methylthio-6-oxo-pyrimidine (20e): White solid. Mp 160−162 °C. ^{1}H NMR ($CDCl_3$) δ 1.05 (t, 3H, J = 7.6 Hz), 2.51(s, 3H), 2.60 (m, 2H), 6.28 (d, 1H, J = 6.43 Hz), 7.46−7.55 (m, 3H), 7.80 (d, 1H, J = 6.43 Hz), 7.93(m, 2H). ^{13}C NMR ($CDCl_3$) δ 11.558, 14.386, 23.736, 110.118, 128.243, 128.718, 131.851, 134.346, 151.424, 157.181, 161.478, 183.579. IR ν_{max} 3054, 2928, 1686, 1586, 1567, 1480, 1444, 1368, 1336, 1316 cm^{-1}. MS *m*/*z* (rel intensity) 321 (M^+, 13), 292 (27), 244 (58), 180 (42), 165 (31), 112 (64), 91 (23), 77 (100). Elemental Anal. Calcd for $C_{18}H_{15}N_3OS$: C 67.27; H 4.70; N 13.07. Found: C 67.45; H 4.54; N 12.96.

1-(*N*-Diphenylmethylideneamino)-1,6-dihydro-2-methylthio-6-oxo-pyrimidine (20f): White solid. Mp 96−98 °C. ^{1}H NMR ($CDCl_3$) δ 2.55 (s, 3H), 5.98 (d, 1H, J = 6.4 Hz), 7.32−7.39 (m, 4H), 7.40−7.44 (m, 3H), 7.53−7.55 (m, 1H), 7,59 (d, 1H, J = 6.4 Hz), 7.77−7.79 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 14.441, 110.106, 127.486, 128.003, 128.447, 130.134, 130.228, 132.596, 133.780, 135.565, 150.980, 156.415, 161.404, 180.175. IR ν_{max} 3049, 2925, 1681, 1593, 1569, 1481, 1336, 1301, 1134, 958 cm^{-1}. MS *m*/*z* (rel intensity) 274 (M^+, 16), 244 (100), 230 (14), 141 (7.6), 132 (26), 112 (23), 77 (19). Elemental Anal. Calcd for $C_{14}H_{15}N_3OS$: C 61.51; H 5.53; N 15.37. Found: C 61.46; H 5.68; N 15.30.

1-(*N*-Phenylethylideneamino)-1,6-dihydro-2-methylthio-6-oxo-pyrimidine (20g): White solid. Mp 76−78 °C. ^{1}H NMR ($CDCl_3$) δ 2.25 (s, 3H), 2.52 (s, 3H), 6.30 (d, 1H, J = 6.4 Hz), 7.46 (t, 2H, J = 7.6 Hz), 7.53 (d, 1H, J = 7.28 Hz), 7.80 (d, 1H, J = 6.4 Hz), 8.01 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 14.411, 17.185, 110.169, 127.911, 128.660, 132.129, 135.602, 151.408, 156.946, 161.583, 177.847. IR ν_{max} 3057, 2927, 1681, 1609, 1570, 1482, 1371, 1330, 1292, 1143 cm^{-1}. MS *m*/*z* (rel intensity) 259 (M^+, 10), 244 (100), 182 (13), 118 (48), 112 (44), 104 (20), 77 (67). Elemental Anal. Calcd for $C_{13}H_{13}N_3OS$:, C 60.21; H 5.05; N 16.20. Found: C 59.95; H 4.94; N 16.46.

General Procedure for the Solid-Phase Synthesis of 3-Substituted Uracils and Thiouracils 23. A suspension of resin **11** (500 mg, 1.20 mmol/g) in triethyl orthoformate (50 equiv, 5 mL) was refluxed for 6 h. Then urea **21** (5 equiv) was added and the mixture was refluxed for 12 h. The resin was filtered and washed with 3 × 5 mL of EtOH, 3 × 5 mL with CH_2Cl_2, and thermally cyclized with an oil bath at 240 °C for 20 min under N_2 atmosphere. The mixture was washed with EtOH/acetone completely in the sintered glass funnel, and the filtrates were combined to afford the product by evaporation.

Uracil (23a): Mp 309−312 °C (lit.[27] mp >300 °C). ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.44 (d, 1H, J = 7.08 Hz,), 7.38 (d, J = 7.0 Hz, 1H), 10.84 (br s, 1H), 11.03 (s, 1H). MS *m*/*z* (rel intensity) 112 (M^+, 100). 69 (91). IR ν 3112, 2926, 1768, 1716, 1668, 1417, 1233, 993, 823 cm^{-1}.

2-Thiouracil (23b): Mp 309−311 °C (lit.[27] mp 309−311 °C). ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.80 (d, 1H, J = 7.6 Hz), 7.40 (d, J = 7.6 Hz, 1H), 12.30 (br s, 2H). MS *m*/*z* (rel intensity) 128 (M^+, 100), 69 (31). IR ν 3092, 2930, 1707, 1685, 1637, 1569, 1385, 1224, 1178, 1164, 809, 561 cm^{-1}.

3-(4-Methylphenyl)uracil or 3-(4-methylphenyl)-2,3-dihydro-pyrimidin-4(1H)-one (23c): Mp 254−256 °C (lit.[28] mp 256−258 °C). ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.34 (s, 3H), 5.65 (d, 1H, J = 7.6 Hz), 7.06 (d, 2H, J = 8.4 Hz), 7.25 (d, 2H, J = 8.4 Hz), 7.51 (d, 1H, J = 7.6 Hz). MS *m*/*z* (rel intensity) 202 (M^+, 35), 133 (100), 105 (22), 91 (12), 77 (20). IR ν 3240, 2924, 1741, 1718, 1646, 1513, 1419, 818 cm^{-1}.

3-(4-Methylphenyl)-2-thiouracil or 3-(4-methylphenyl)-2,3-dihydro-2-thioxo-pyrimidin-4(1*H*)-one (23d): Mp 223 °C (lit.[29] mp 231−232 °C). ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.34 (s, 3H), 6.01 (d, 1H, J = 7.6 Hz), 6.47 (d, 0.3H, 1-substituted isomer, J = 7.08 Hz), 7.02 (m, 2.3H), 7.23 (m, 3H), 7.39 (d, 0.3H, 1-substituted isomer, J = 7.08 Hz), 7.50 (d, 1H, J = 7.6 Hz), 12.42 (br, 1.3H). MS *m*/*z* (rel intensity) 202 (M^+, 35), 133 (100), 105 (22), 91 (12), 77 (20). IR ν 3240, 2924, 1741, 1718, 1646, 1513, 1419, 818 cm^{-1}.

3-Phenyl-2-thiouracil or 3-phenyl-2,3-dihydro-2-thioxo-pyrimidin-4(1*H*)-one (23e): Mp 220−224 °C (lit.[29] mp 247−249 °C). ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.03 (d, 1H, J = 7.56 Hz), 6.49 (d, 0.3H, 1-substituted isomer, J = 7.2 Hz), 7.17 (m, 2.6H), 7.39 (m, 3.9H), 7.51−7.54 (m, 1H), 11.9 (br s, 0.3H), 12.66 (br s, 1H). MS *m*/*z* (rel intensity) 204 (M^+, 90), 203 (100), 135 (72), 77 (75), 51 (57). IR ν 3114, 2973, 1711, 1619, 1538, 1259, 1244, 805 cm^{-1}.

3-Phenyluracil or 3-phenyl-2,3-dihydropyrimidin-4(1*H*)-one (23f): Mp 238−242 °C (lit.[28] mp 246−247 °C). ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.67 (d, 1H, J = 7.52 Hz), 7.20 (m, 2H), 7.36−7.40 (m, 1H), 7.43−7.46 (m, 2H), 7.50−7.54 (m, 1H), 11.29 (br s, 1H). MS *m*/*z* (rel intensity) 188 (M^+, 82), 119 (100), 91 (34). IR ν 3112, 2924, 1717, 1673, 1645, 1489, 1233 cm^{-1}.

3-Benzyluracil or 3-benzyl-2,3-dihydropyrimidin-4(1*H*)-one (23g): Mp 180−182 °C (lit.[28] mp 182−183 °C). ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.936 (s, 2H), 5.60 (d, 1H, J = 7.52 Hz), 7.23−7.46 (m, 5H), 7.46 (d, 1H, J = 7.52 Hz). MS *m*/*z* (rel intensity) 202 (M^+, 99), 132 (51), 104 (19), 91 (76), 77 (48), 70 (100). IR ν 3088, 2965, 2924, 1737, 1709, 1652, 1436, 1232, 820, 760, 699 cm^{-1}.

3-benzyl-2-thiouracil or 3-benzyl-2,3-dihydro-2-thioxo-pyrimidin-4(1*H*)-one (23h): Mp 184−186 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.51 (s, 2H), 5.98 (d, 1H, J = 7.6 Hz), 7.29 (m, 5H), 7.48 (m, 1H), 12.652 (s, 1H). ^{13}C NMR (DMSO-d_6) δ 48.835, 104.741, 127.438, 127.635, 128.660, 136.680, 141.473, 160.809, 177.560. MS *m*/*z* (rel intensity) 218 (M^+, 100), 185 (34). 148 (16), 91 (63), 70 (39), 65 (32). IR ν 3123, 2979, 1714, 1732, 1646, 1533, 1385, 1356, 1224, 1192, 1167, 817, 754 cm^{-1}. Elemental Anal. Calcd for $C_{11}H_{10}N_2OS$: C 60.53; H 4.62; N 12.83. Found: C 60.58; H 4.56; N 12.77.

3-(4-Chlorophenyl)-2-thiouracil or 3-(4-chlorophenyl)-2,3-dihydro-2-thioxo-pyrimidin-4(1*H*)-one (23i): Mp 212−216 °C (lit.[29] mp 218−220 °C). ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.04 (d, 1H, J = 7.6 Hz), 6.51 (d, 0.3H, J = 6.8 Hz), 7.24 (m, 2.6H), 7.42 (d, 0.3H, J = 6.8 Hz), 7.51−7.54 (m, 3.6H), 12.0 (s, 0.3H), 12.71 (s, 1H). MS *m*/*z* (rel intensity) 238 (M^+, 100), 240 (M^+ + 2, 35), 185 (34). 169 (90), 171 (32), 111 (36), 113 (12), 75 (47). IR ν 3122, 2991, 1718, 1667, 1621, 1513, 1489, 1378, 1233, 1197 cm^{-1}.

3-Methyluracil or 3-methyl-2,3-dihydropyrimidin-4(1*H*)-one (23j): Mp 172−174 °C (lit.[28] mp 174−175 °C). ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.11 (s, 3H), 5.58 (d, 1H, J = 7.56 Hz), 7.41−7.45 (m, 1H), 11.12 (s, 1H). MS *m*/*z* (rel intensity) 126 (M^+, 100), 112 (5), 69 (88), 42 (71). IR ν 3231, 2960, 1708, 1659, 1644, 1444, 1232 cm^{-1}.

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Supporting Information Available: ^{1}H NMR spectra of **13a**−**i**, **17a**−**g**, **20a**−**g**, and **23a**−**j** and ^{13}C NMR spectra of **17b**, **17c**, **17e**, **17f**, **17g**, **20a**−**g, and 23h**. This material is available free of charge via the Internet at http://pubs.acs.org..

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