An Efficient Synthesis of new Thiazolopyrimidinones under Microwave Irradiation

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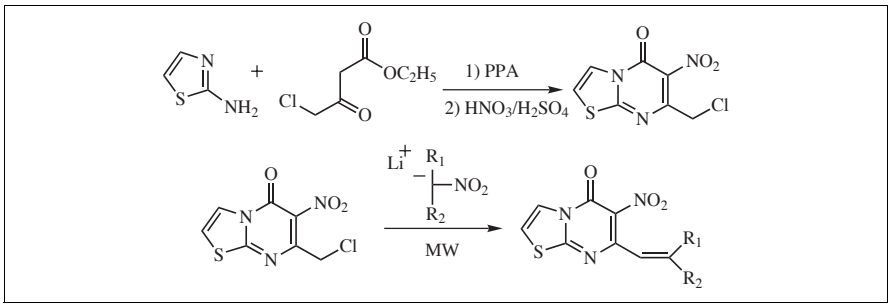

7-Chloromethyl-6-nitro-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**2**) is obtained by cyclocondensation of 2-aminothiazole with ethyl 4-chloroacetoacetate. This product was shown to react with various nitronate or malonate anions under microwave irradiation to give potentially bioactive 6-nitro-5*H*-thiazolo[3,2-*a*]pyrimidin-5-ones. Extension to other anions centered on *S* atom allows for the generalization this synthetic procedure.

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Introduction.

Fused pyrimidines represent an important class of heterocyclic compounds of chemotherapeutic importance. Their antifungal [1], antibacterial [2-5], antiviral [6] and cytotoxic [7] properties are well documented. Thiazolopyrimidines, in particular, are reported to possess various therapeutic properties such as analgesic [8], anti-inflammatory [9-12], anti-anxiety [13,14], antipsychotic [15-18], anti-HIV-1 [19], antidepressant [20], anti-bacterial [21,22] and antifungal [23] activities.

The application of microwaves, as an efficient heating source, in organic reactions, was recognized in the mid-1980s [24,25]. Since then, numerous successful reactions with dramatically enhanced reaction rates have been disclosed. Microwave-assisted reactions have received much interest because of their simple operation, non-inert atmosphere reaction conditions, the use of less toxic solvents, greater selectivity and the formation of higher yields in rather shorter time [26-29]. Microwave irradiation has become a powerful tool for the rapid synthesis of a variety of bioactive molecules under solvent-free conditions.

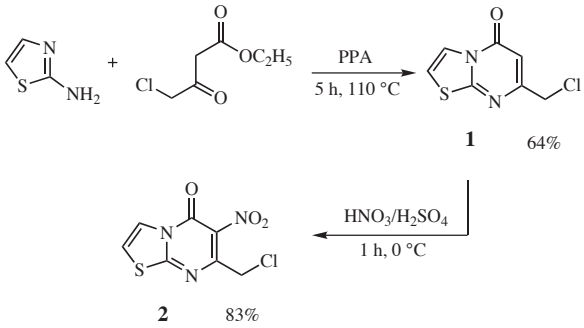
In continuation of our interest in the synthesis of fused pyrimidine heterocycles [30,31], as potential bioactive molecules, we report herein the preparation of new 6-nitro-5*H*-thiazolo[3,2-*a*]pyrimidin-5-ones, *via* a chain single electron transfer reaction under microwave irradiation.

Results and Discussion.

7-Chloromethyl-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**1**) was prepared by cyclocondensation of 2-aminothiazole with ethyl 4-chloroacetoacetate, in presence of polyphosphoric acid, in 64% yield [32] (Scheme 1). The intermediate derivative **1** was nitrated using HNO_3-H_2SO_4 mixture, to give 7-chloromethyl-6-nitro-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**2**) in 83% yield.

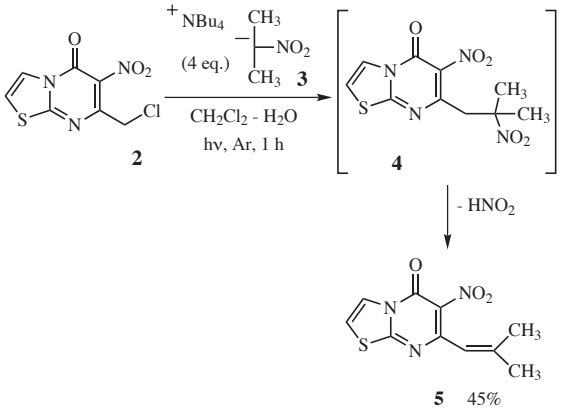
The compound **2** was treated with 2-nitropropane anion (**3**) under $S_{RN}1$ reaction conditions (inert atmosphere, photostimulation) to afford the ethylenic derivative **5** as shown in Scheme 2.

Scheme 1



The *C*-alkylated product **4** was not isolated because nitrous acid elimination is very rapid in basic medium due to the acidity of the methylene protons. The best yield of **5** was obtained when the reaction was carried out under phase transfer conditions for 1 h (40% tetrabutyl-ammonium hydroxide in water and dichloromethane) using 4 equivalents of 2-nitropropane anion (**3**). The electron transfer mechanism was confirmed by complete inhibition studies [33].

Scheme 2



On the other hand, the above reaction was also carried out under microwave conditions by varying power and reaction time (Table 1).

Scheme 3

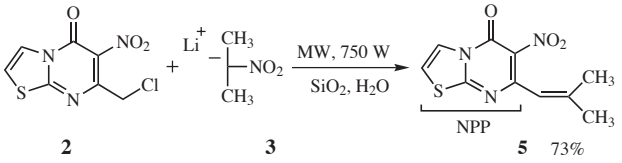


Table 1

Entry	Reaction time (mn)	Power (W)	Yields (%)	
			2	**5**
-	60	Standard conditions	10	45
1	4	350	98	-
2	4	750	95	-
3	4	900	-	55
4	6	350	94	-
5	6	750	30	40
6	6	900	25	58
7	8	350	90	-
8	8	750	-	73
9	8	900	-	50

All reactions were performed by using open Erlenmeyer flask Pyrex, using 4 eq. of nitronate anion (**3**), 3 mL of water, 1 g of silica gel. Irradiations were carried out in a domestic microwave oven (Whirlpool MO 111).

The alkene **5** was isolated in 73% yield (Scheme 3), against 45% using classical reaction conditions. When the microwave power increased, the *C*-alkylation yield decreased, and the formation of untractable tarry matters became more important (Entry 9).

From these interesting results, we sought to develop a general procedure of chain single electron transfer reaction in thiazolo[3,2-*a*]pyrimidin-5-one series and we have extended these experimental conditions to different anions **6-17** (Table 2).

The use of the optimal microwave experimental conditions (entry 8, Table 1) in the reaction of **2** with various nitronate anions (aliphatic, cyclic or heterocyclic) **6-14**, has afforded good yields of new thiazolo[3,2-*a*]pyrimidin-5-one derivatives **18-26** (Table 2). The obtained yields (42-70%) were generally higher than those observed under classical reaction conditions (35-40%). It is worthy to note that, when the ethylenic derivative is unsymmetrical, only the *E* isomer is obtained. On the other hand, under the same conditions, the reaction between *S*-centered anion, the benzenesulfinic acid **15** and derivative **2** gave the required product **27** in 46% yield (against 33% under classical conditions).

Moreover, we have shown that the reaction of **2** with 2-nitropropionic acid ethyl ester **16** and diethyl nitromalonate anion **17** led to the corresponding ethylenic compound **28**, **29** under microwave irradiation respectively in 39 and 71% yield.

Table 2

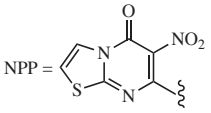
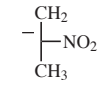
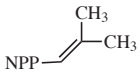
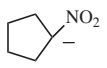
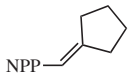
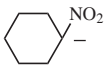
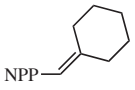
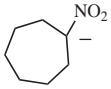
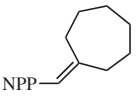
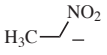
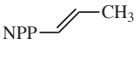
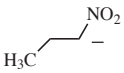
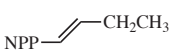
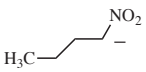
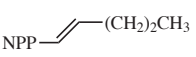
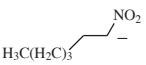
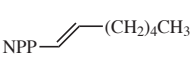
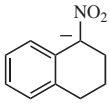
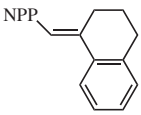
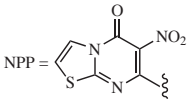
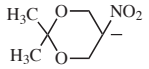
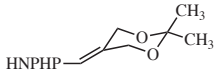
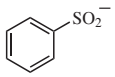
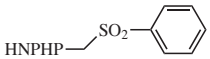
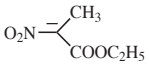
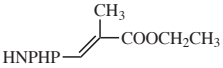
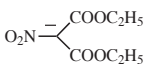
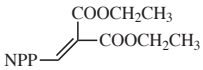
N°	Anion	N°	Compound NPP = 	Yield (%) SC	MW
3		**5**		45	73
6		**18**		40	70
7		**19**		37	68
8		**20**		35	65
9		**21**		37	48
10		**22**		39	46
11		**23**		37	45
12		**24**		35	42
13		**25**		35	48

Table 2 (continued)

N°	Anion	N°	Compound	Yield (%)	
				SC	MW
14		**26**		33	61
15		**27**		33	46
16		**28**		35	39
17		**29**		68	71

SC: standard conditions (hν, argon, r.t., 1 h). MW: microwave conditions (750 W, 8 min).

Conclusion.

We have described a highly efficient microwave-induced procedure for the synthesis of a series of different thiazolo[3,2-*a*]pyrimidin-5-one derivatives using a domestic microwave oven. The reactions were found to proceed remarkably faster and under milder conditions than those carried out under classical conditions. We have demonstrated that microwave irradiation can be effectively employed for electron transfer *C*-alkylation (followed by base-promoted nitrous acid elimination) or *S*-alkylation reactions. This procedure provides a practical, efficient, and environmentally friendly process for heterocyclic synthesis. Study of biological properties of the prepared compounds is under investigation.

Acknowledgements.

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EXPERIMENTAL

Melting points were determined on Büchi B-540 and are uncorrected. Elemental analyses were performed by the Centre de Microanalyses of the University of Aix-Marseille 3 and of the INP-ENSCT (Toulouse, France). Both ^{1}H and ^{13}C NMR spectra were determined on a Bruker ARX 200 spectrometer. The ^{1}H chemical shifts are reported as ppm downfield from tetramethylsilane (Me_4Si), and the ^{13}C chemical shifts were referenced to the solvent peak: $CDCl_3$ deuteriochloroform (76.9 ppm). Solvents were dried by conventional methods. Silica gel 60 (Merck, particle size 0.063-0.200 mm, 70-230 mesh ASTM) was used as a stationary phase in column chromatography. TLC were performed on 5 cm x 10 cm aluminum plates coated with silica gel 60F-254 (Merck) using the appropriate eluent. Reactions under microwave irradiation were performed in a domestic microwave oven, Whirlpool® MO 111.

The lithium salt of 2-nitropropane (**3**) [34], nitroalkanes **6-13** [35,36], 2,2-dimethyl-5-nitro-1,3-dioxane (**14**) [37] and ethyl 2-nitropropionate (**16**) [38] were prepared as previously described. The sodium salt of benzenesulfinic acid (**15**) and diethyl nitromalonate (**17**) were commercially available.

7-Chloromethyl-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**1**).

A mixture of polyphosphoric acid (7.5 g), 2-aminothiazole (1.25 g, 12.5 mmol) and ethyl 4-chloroacetoacetate (2.8 g, 17 mmol) was stirred at 110 °C for 5 h. After cooling, a 10% sodium hydroxide (50 mL) ice-cold solution was slowly added to adjust the pH to 7. The mixture was filtered and the thus collected precipitate was purified by column chromatography on silica gel, using dichloromethane-ethyl acetate (6:4) as an eluent. Recrystallization from ethanol gave yellow solid, mp 133 °C (Lit., 132 °C) [39], yield 1.6 g (64%). ^{1}H NMR (deuteriochloroform, 200 MHz) δ 4.45 (s, 2H), 6.47 (s, 1H), 7.06 (d, J = 4.9 Hz, 1H), 8.00 (d, J = 4.9 Hz, 1H).

7-Chloromethyl-6-nitro-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**2**)

To a solution of 7-chloromethyl-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**1**) (1 g, 4.5 mmol) in concentrated sulfuric acid (3 mL), fuming nitric acid (2 mL) was added dropwise at 0 °C. The reaction mixture was stirred at the same temperature for 1 h and then was poured into ice-cold water (50 mL). The solid precipitate was collected by filtration and the product was dissolved in dichloromethane (20 mL). This solution was washed with saturated sodium bicarbonate solution (3 x 20 mL) and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the residual solid was recrystallized from ethanol to give yellow crystals mp 166 °C, yield 0.92 g (83%). ^{1}H NMR (deuteriochloroform, 200 MHz) δ 4.68 (s, 2H), 7.30 (d, J = 4.9 Hz, 1H), 8.17 (d, J = 4.9 Hz, 1H). ^{13}C NMR (deuteriochloroform, 50 MHz) δ 42.6 (CH_2), 117.6 (CH), 123.4 (CH), 150.9 (C), 155.1 (C), 157.1 (C), 164.4 (C).

Anal. Calcd for $C_7H_4N_3O_3ClS$: C, 34.23; H, 1.64; N, 17.11. Found: C, 34.16; H, 1.69; N, 17.09.

General Procedures for the Reaction of **2** with Different Anions **3**, **6-17**.

Classical Conditions.

Under nitrogen atmosphere, an aqueous solution of 40% tetrabutylammonium hydroxide in water (2.11 g, 3.2 mmol) was added to the corresponding nitroalkane (3.2 mmol) or 2,2-dimethyl-5-nitro-1,3-dioxane (0.52 g, 3.2 mmol) or benzene sulfinic acid (0.46 g, 3.2 mmol) or ethyl 2-nitropropionate (0.47 g, 3.2 mmol) or diethyl nitromalonate (0.65 g, 3.2 mmol). The reaction mixture was stirred at r.t. for 1 h. Then a solution of **2** (0.20 g, 0.81 mmol) in dichloromethane (10 mL) was added. Stirring was maintained for 1 h under irradiation with two 60 W tungsten lamps from a distance of 10 cm. The organic layer was separated and the aqueous layer was extracted with dichloromethane (3 x 10 mL). The combined organic layers were dried over magnesium sulfate and evaporated under reduced pressure. Purification by column chromatography on silica gel using dichloromethane-ethyl acetate (6:4) as eluent and recrystallization from ethanol gave the required products **5**, **18-29**.

Microwave Irradiation Conditions.

7-Chloromethyl-6-nitro-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**2**) (0.20 g, 0.81 mmol) and the corresponding nitroalkane lithium salt **3**, **6-13** or the lithium salt of 2,2-dimethyl-5-nitro-1,3-dioxane (**14**) (0.54 g, 3.2 mmol) or the sodium salt of benzene sulfinic acid (**15**) (0.53 g, 3.2 mmol) or the lithium salt of ethyl 2-nitropropionate (**16**) (0.49 g, 3.2 mmol) or the sodium salt of diethyl nitromalonate (**17**) (0.73 g, 3.2 mmol), in H_2O (3 mL), was intimately mixed with 1 g of silica gel 60 (Merck, particle size 0.063-0.200 mm, 70-230 mesh ASTM). The mixture was placed in an open Erlenmeyer Pyrex flask and irradiated in a domestic microwave oven (Whirlpool MO 111) for 8 min at a power of 750 W. The crude product was dissolved in dichloromethane (20 mL). The organic layer was then dried over anhydrous magnesium sulfate, evaporated under reduced pressure. Purification by column chromatography on silica gel using dichloromethane-ethyl acetate (6:4) as eluent and recrystallization from ethanol gave the corresponding products **5**, **18-29**.

7-(2-Methylpropenyl)-6-nitro-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**5**).

Yellow solid, mp 218 °C, ^{1}H NMR (deuteriochloroform, 200 MHz) δ 2.37 (s, 3H), 2.46 (s, 3H), 6.63 (s, 1H), 6.93 (d, J = 4.9 Hz, 1H), 8.24 (d, J = 4.9 Hz, 1H). ^{13}C NMR (deuteriochloroform, 50 MHz) δ 19.9 (CH_3), 20.7 (CH_3), 117.6 (CH), 120.6 (CH), 123.4 (CH), 150.9 (C), 156.5 (C), 157.1 (C), 164.5 (C).

Anal. Calcd for $C_{10}H_9N_3O_3S$: C, 47.80; H, 3.61; N, 16.72. Found: C, 47.71; H, 3.58; N, 16.51.

7-Cyclopentylidenemethyl-6-nitro-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**18**).

Yellow solid, mp 140 °C, ^{1}H NMR (deuteriochloroform, 200 MHz) δ 1.50-1.56 (m, 4H), 2.28-2.33 (m, 2H), 2.74-2.80 (m, 2H), 6.15 (s, 1H), 7.13 (d, J = 4.9 Hz, 1H), 8.05 (d, J = 4.9 Hz; 1H). ^{13}C NMR (deuteriochloroform, 50 MHz) δ 25.7 (CH_2), 26.9 (CH_2), 32.9 (CH_2), 37.7 (CH_2), 117.6 (CH), 120.03 (CH), 123.5 (CH), 150.9 (C), 156.5 (C), 157.1 (C), 164.4 (C).

Anal. Calcd for $C_{12}H_{11}N_3O_3S$: C, 51.98; H, 4.00; N, 15.15. Found: C, 51.78; H, 3.98; N, 15.07.

7-Cyclohexylidenemethyl-6-nitro-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**19**).

Yellow solid, mp 178 °C, ^{1}H NMR (deuteriochloroform, 200 MHz) δ 1.69-1.72 (m, 6H), 2.56-2.60 (m, 2H), 2.93-2.95 (m, 2H), 6.42 (s, 1H), 7.11 (d, J = 4.9 Hz, 1H), 8.03 (d, J = 4.9 Hz; 1H). ^{13}C NMR (deuteriochloroform, 50 MHz) δ 25.7 (CH_2), 27.6 (CH_2), 28.9 (CH_2), 30.9 (CH_2), 38.4 (CH_2), 117.6 (CH), 121.5 (CH), 123.4 (CH), 150.9 (C), 156.5 (C), 157.1 (C), 164.4 (C).

Anal. Calcd for $C_{13}H_{13}N_3O_3S$: C, 53.60; H, 4.50; N, 14.42. Found: C, 53.42; H, 4.47; N, 14.35.

7-Cycloheptylidenemethyl-6-nitro-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**20**).

Yellow solid, mp 146 °C, ^{1}H NMR (deuteriochloroform, 200 MHz) δ 1.62-1.70 (m, 8H), 2.44-2.49 (m, 2H), 2.87-2.91 (m, 2H), 6.21 (s, 1H), 7.12 (d, J = 4.9 Hz, 1H), 8.05 (d, J = 4.9 Hz; 1H). ^{13}C NMR (deuterio-chloroform, 50 MHz) δ 25.5 (CH_2), 27.6 (CH_2), 28.9 (CH_2), 29.4 (CH_2), 31.2 (CH_2), 39.9 (CH_2), 117.6 (CH), 122.2 (CH), 123.4 (CH), 151.0 (C), 156.5 (C), 157.2 (C), 164.4 (C).

Anal. Calcd for $C_{14}H_{15}N_3O_3S$: C, 55.07; H, 4.95; N, 13.76. Found: C, 55.05; H, 4.88; N, 13.71.

6-Nitro-7-propenyl-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**21**).

Yellow solid, mp 199 °C, ^{1}H NMR (deuteriochloroform, 200 MHz) δ 2.02 (q, J = 1.5 Hz, 3H), 6.68 (d, J = 14.9 Hz, 1H), 7.13 (d, J = 4.9 Hz, 1H), 7.30 (d, J = 14.9 Hz, 1H), 8.03 (d, J = 4.9 Hz, 1H). ^{13}C NMR (deuteriochloroform, 50 MHz) δ 20.5 (CH_3), 117.6 (CH), 123.4 (CH), 125.5 (CH), 128.5 (CH), 150.8 (C), 156.5 (C), 157.1 (C), 164.4 (C).

Anal. Calcd for $C_9H_7N_3O_3S$: C, 45.57; H, 2.97; N, 17.71. Found: C, 45.53; H, 2.95; N, 17.70.

7-But-1-enyl-6-nitro-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**22**).

Yellow solid, mp 186 °C, ^{1}H NMR (deuteriochloroform, 200 MHz) δ 1.15 (t, J = 7.3 Hz, 3H), 2.35 (q, J = 7.3 Hz, 2H), 6.49 (d, J = 15.1 Hz, 1H), 7.09 (d, J = 15.1 Hz, 1H), 7.29 (d, J = 15.1Hz, 1H), 8.09 (d, J = 4.9 Hz, 1H). ^{13}C NMR (deuteriochloroform, 50 MHz) δ 12.9 (CH_3), 26.0 (CH_2), 117.5 (CH), 123.4 (CH), 125.8 (CH), 128.5 (CH), 150.8 (C), 156.4 (C), 157.2 (C), 164.4 (C).

Anal. Calcd for $C_{10}H_9N_3O_3S$: C, 47.80; H, 3.61; N, 16.72. Found: C, 47.66; H, 3.59; N, 16.65.

6-Nitro-7-pent-1-enyl-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**23**).

Yellow solid, mp 173 °C, ^{1}H NMR (deuteriochloroform, 200 MHz) δ 1.40 (t, J = 7.3 Hz, 3H), 1.50 (m, 2H), 2.20 (m, 2H), 6.54 (d, J = 14.9 Hz, 1H), 7.15 (d, J = 4.9 Hz, 1H), 7.43 (d, J = 14.9 Hz, 1H), 8.01 (d, J = 4.9 Hz, 1H). ^{13}C NMR (deuterio-chloroform, 50 MHz) δ 13.7 (CH_3), 22.5 (CH_2), 26.0 (CH_2), 117.6 (CH), 123.4 (CH), 125.8 (CH), 128.5 (CH), 150.9 (C), 156.5 (C), 157.2 (C), 164.5 (C).

Anal. Calcd for $C_{11}H_{11}N_3O_3S$: C, 49.80; H, 4.18; N, 15.84. Found: C, 49.67; H, 4.16; N, 15.79.

7-Hept-1-enyl-6-nitro-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**24**).

Yellow solid, mp 170 °C, ^{1}H NMR (deuteriochloroform, 200 MHz) δ 1.08 (m, 3H), 1.32 (m, 4H), 1.55 (m, 2H), 2.30 (m, 2H), 6.12 (d, J = 14.9 Hz, 1H), 7.10 (d, J = 4.9 Hz, 1H), 7.35 (d, J = 14.9 Hz, 1H), 8.09 (d, J = 4.9 Hz, 1H). ^{13}C NMR (deuterio-chloroform, 50 MHz) δ 13.8 (CH_3), 21.8 (CH_2), 22.8 (CH_2), 24.1 (CH_2), 26.9 (CH_2), 117.7 (CH), 123.5 (CH), 125.9 (CH), 128.5 (CH), 150.9 (C), 156.5 (C), 157.3 (C), 164.5 (C).

Anal. Calcd for $C_{13}H_{15}N_3O_3S$: C, 53.23; H, 5.15; N, 14.32. Found: C, 53.20; H, 5.13; N, 14.30.

7-(3,4-Dihydro-2*H*-naphthalen-1-ylidenemethyl)-6-nitro-5*H*-thiazolo[3,2-*a*] pyrimidin-5-one (**25**).

Yellow solid, mp 200 °C, ^{1}H NMR (deuteriochloroform, 200 MHz) δ 1.95 (m, 2H), 2.83 (m, 2H), 3.19 (t, J = 7.2 Hz, 2H), 6.91 (s, 1H), 7.16 (m, 4H), 7.62 (d, J = 4.9 Hz, 1H), 8.09 (d, J = 4.9 Hz, 1H). ^{13}C NMR (deuteriochloroform, 50 MHz) δ 31.7 (CH_2), 33.8 (CH_2), 37.0 (CH_2), 117.6 (CH), 123.5 (CH), 125.0 (CH), 125.6 (CH), 125.9 (CH), 126.4 (CH), 127.9 (CH), 128.5 (CH), 134.9 (C), 137.9 (C), 150.9 (C), 157.1 (C), 157.9 (C), 164.6 (C).

Anal. Calcd for $C_{17}H_{13}N_3O_3S$: C, 60.17; H, 3.86; N, 12.38. Found: C, 60.10; H, 3.80; N, 12.31.

7-(2,2-Dimethyl[1,3]dioxan-5-ylidenemethyl)-6-nitro-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**26**).

Yellow solid, mp 150 °C, ^{1}H NMR (deuteriochloroform, 200 MHz) δ 1.42 (s, 6H), 4.34 (s, 2H), 5.01 (s, 2H), 6.23 (s, 1H), 7.16 (d, J = 4.9 Hz, 1H), 8.06 (d, J = 4.9 Hz, 1H). ^{13}C NMR (deuteriochloroform, 50 MHz) δ 21.6 (CH_3), 22.9 (CH_3), 63.3 (CH_2), 65.2 (CH_2), 99.0 (C), 117.6 (CH), 123.5 (CH), 125.6 (CH), 135.8 (C), 150.8 (C), 156.5 (C), 157.1 (C), 164.5 (C).

Anal. Calcd for $C_{13}H_{13}N_3O_5S$: C, 48.29; H, 4.05; N, 13.00. Found: C, 48.05; H, 4.03; N, 12.93.

7-Benzenesulfonylmethyl-6-nitro-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**27**).

Yellow solid, mp 235 °C, ^{1}H NMR (deuteriochloroform, 200 MHz) δ 5.19 (s, 2H), 7.83 (d, J = 4.9 Hz, 1H), 8.094-8.07 (m, 5H), 8.48 (d, J = 4.9 Hz, 1H). ^{13}C NMR (deuteriochloroform, 50 MHz) δ 57.9 (CH_2), 117.7 (CH), 123.5 (CH), 127.9 (2xCH), 129.1 (2xCH), 134.2 (CH), 138.6 (C), 150.9 (C), 155.2 (C), 157.0 (C), 164.5 (C).

Anal. Calcd for $C_{13}H_9N_3O_5S_2$: C, 44.44; H, 2.58; N, 11.96. Found: C, 44.42; H, 2.57; N, 11.95.

Ethyl-2-methyl-3-(6-nitro-5-oxo-5*H*-thiazolo[3,2-*a*]pyrimidin-7-yl)acrylate (**28**).

Yellow solid, mp 157 °C, ^{1}H NMR (deuteriochloroform, 200 MHz) δ 1.33 (t, J = 7.1 Hz, 3H), 2.26 (s, 3H), 4.28 (q, J = 7.1 Hz, 2H), 7.17 (d, J = 4.9 Hz, 1H), 7.47 (s, 1H), 8.16 (d, J = 4.9 Hz, 1H). ^{13}C NMR (deuterio-chloroform, 50 MHz) δ 14.2 (CH_3), 14.9 (CH_3), 63.4 (CH_2), 117.6 (CH), 123.5 (CH), 137.1 (CH), 141.1 (C), 150.7 (C), 155.0 (C), 157.1 (C), 164.4 (C), 169.1 (C).

Anal. Calcd for $C_{12}H_{11}N_3O_5S$: C, 46.60; H, 3.58; N, 13.59. Found: C, 46.57; H, 3.56; N, 13.58.

Diethyl 2-[(6-nitro-5-oxo-5*H*-thiazolo[3,2-*a*]pyrimidin-7-yl)-methylene]malonate (**29**)

Yellow solid, mp 168 °C, ^{1}H NMR (deuteriochloroform, 200 MHz) δ 1.23 (t, J = 7.1 Hz, 6H), 4.25 (q, J = 7.1 Hz, 4H), 7.15 (d, J = 4.9 Hz, 1H), 7.54 (s, 1H), 8.04 (d, J = 4.9 Hz, 1H). ^{13}C NMR (deuteriochloroform, 50 MHz) δ 14.8 (CH_3), 15.4 (CH_3), 61.6 (CH_2), 62.8 (CH_2), 117.5 (CH), 123.5 (CH), 129.1 (CH), 144.0 (C), 150.9 (C), 155.2 (C), 157.1 (C), 162.4 (C), 164.5 (C), 165.1 (C).

Anal. Calcd for $C_{14}H_{13}N_3O_7S$: C, 45.78; H, 3.57; N, 11.44. Found: C, 45.75; H, 3.55; N, 11.43.

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