Pyrimidine Derivatives. X.[1] Synthesis of New Tricyclic Hetero Compounds Possessing a Pyrimidine Ring: 8,1,3,10-Thiatriazatricyclo[4.3.0.0^{6,10}]-dodecanes and 8,1,3,10-Thiatriazatricyclo[4.4.0.0^{6,10}]tridecanes

Toshio KINOSHITA,* Yukihiro WATANABE, Yumiko TAKAISHI, Tomoko OKUNAKA, Setsuko NAKAO, and Sunao FURUKAWA

School of Pharmaceutical Sciences, Nagasaki University, 1–14 Bunkyo-machi, Nagasaki 852, Japan.
Received November 24, 1992

Several new tricyclic hetero compounds possessing a pyrimidine ring were formed by reaction of 5-bromo- (and 5-nitro)-1-(2-bromoethyl, 3-bromopropyl, and 2-bromopropyl)-6-bromomethyl-3-methyl-2,4(1*H*,3*H*)-pyrimidinediones (1a—c and 7a, b) with thiourea derivatives: namely, 5-bromo-(and 5-nitro)-9-imino-3-methyl-(and 3,11-dimethyl)-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.3.0.0^{6,10}]dodecanes (2a—4a, 2c, and 8a—10a) and 5-bromo-(and 5-nitro)-9-imino-3-methyl-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.4.0.0^{6,10}]tridecanes (2b—4b and 8b—10b). A new ring transformation reaction was found: compound 8b was converted to 7-acetylimino-3-methyl-2,4-dioxo-6,1,3,8-thiatriazatricyclo-[4.4.0.1^{5,8}]dodec-5(12)-ene (11) by reaction with acetic anhydride.

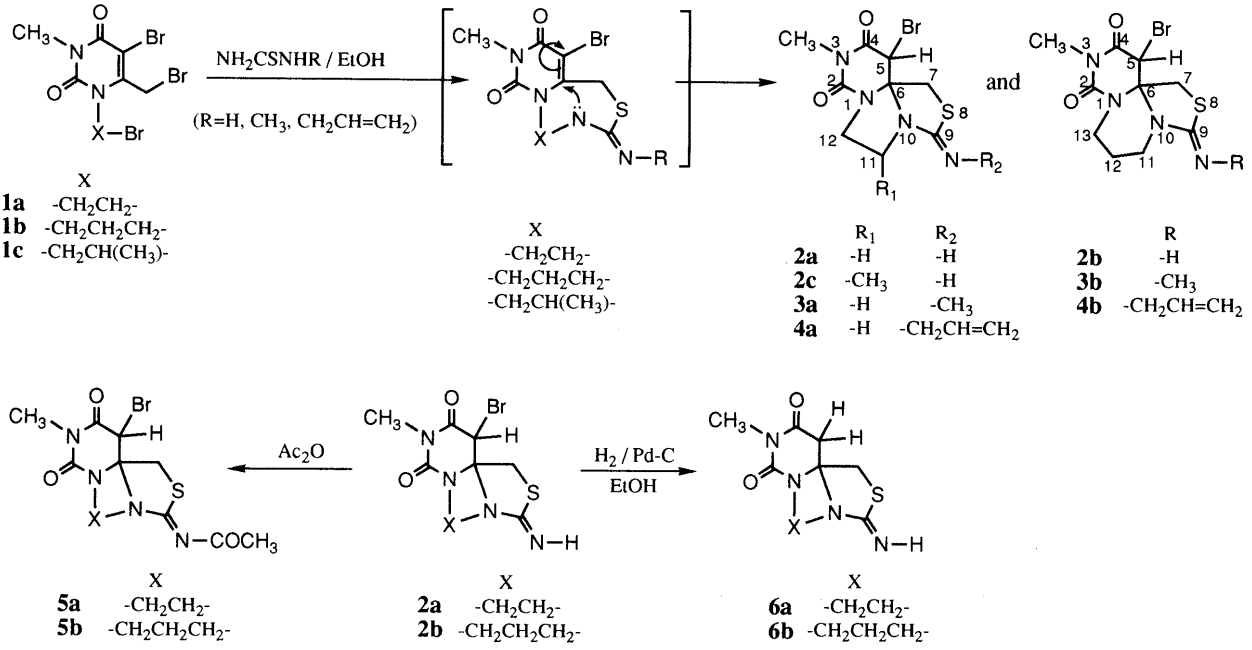
Keywords 8,1,3,10-thiatriazatricyclo[4.3.0.0^{6,10}]dodecane; 1-bromoalkyl-6-bromomethylpyrimidinedione; thiourea; intramolecular Michael-type addition

Previously, we have described the preparation[2,3] of several bromo-substituted pyrimidine derivatives, such as **1a**, **1b**, and **1c** possessing a bromo substituent at the 5-position and side chains at the 1- and 6-positions by various means, and the reaction[2,4] of the bromo-substituted pyrimidines with several nucleophiles. Thus, 5-bromo-1-(2-bromoethyl, 3-bromopropyl, and 2-bromopropyl)-6-bromomethyl-3-methyl-2,4(1*H*,3*H*)-pyrimidinediones (**1a**, **1b**, and **1c**) were easily converted to disulfur-substituted products by treatment with sodium *N*,*N*-dimethyldithiocarbamate or potassium thioacetate.

It is well-known that a halogen atom is converted to a mercapto group by reaction with thiourea followed by alkaline hydrolysis. During the investigation of the reaction of bromo-substituted pyrimidines having bromo-substituted side chains at the 1- and 6-positions on the ring with thiourea in the usual manner, the resulting products were found to have a novel hetero-tricyclic ring system. In this paper, we wish to report the structural determination of the reaction products and the extension of this reaction to various bromo-substituted pyrimidines and thiourea derivatives.

Reaction of 1a with Thiourea and Structural Determination of the Reaction Product (2a) Compound **1a** was heated with 2 eq of thiourea in EtOH under reflux for 1 h, then the separated crystalline mass collected. It was established to have the molecular formula of $C_9H_{12}Br_2N_4O_2S$ by elemental analysis. The FAB-MS of **2a**·**HBr** showed maximal ion peaks at *m/z* 321 and 319 with almost the same intensities and the molecular formula $C_9H_{11}BrN_4O_2S$ (corresponding to M-HBr), so this compound must be the hydrobromide. Then **2a**·**HBr** was treated with 5% sodium hydrogen carbonate to give **2a**, which was established to be $C_9H_{11}BrN_4O_2S$ by elemental analysis and FAB-MS. The structure of **2a** was confirmed to be 5-bromo-9-imino-3-methyl-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.3.0.0^{6,10}]-dodecane, based on the following spectral experiments. The UV spectrum of **2a** showed no absorption band at near 300 nm, corresponding to the starting material (**1a**).[2] This observation suggested that the carbon–carbon double bond on the pyrimidine ring had been converted to a single bond. The IR spectrum of **2a** showed the characteristic N–H absorption of an imino group at 3290 cm^{-1}, and this absorption band disappeared in the spectrum of **5a**, which was obtained on treatment **2a** with acetic anhydride. The ^{1}H–^{13}C correlated spectroscopy (COSY) experiment on **2a** indicated the presence of N–CH_3, CH_2, CH_2CH_2, CH, two C=O, and two quaternary carbons. The partial structures C(2)O–N(3)C$\underline{H}_3$, C(4)O–N(3)C$\underline{H}_3$, NH=C(9)–S–C(7)$\underline{H}_2$, C(6)–C(7)$\underline{H}_2$, and C(5)–C(6)–C(7)H_2 were identified by the ^{1}H–^{13}C COSY long-range coupling experiment (the carbon–hydrogen intersections are indicated by underlining). The proton signals of –CH_2CH_2– were separated into four parts and split into a more complex pattern, as measured at 400 MHz; therefore, this moiety must be part of a rigid ring structure. In order to determine the position of the bromine atom, **2a** was hydrogenated on 10% palladium–carbon to give **6a**. The ^{1}H–^{13}C COSY experiment with **6a** showed no carbon or proton signal due to –CHBr–, while new –CH_2– signals were observed at δ 41.42 (^{13}C) and at δ 2.71 (^{1}H, J=2.0 and 15.8 Hz) and 3.40 (^{1}H, J=15.8 Hz). The ^{1}H–^{13}C COSY (long-range coupling) showed intersections due to carbon–hydrogen coupling (underlined) of C(4)O–C(5)$\underline{H}_2$ and C(6)–C(5)$\underline{H}_2$. The above NMR data indicated that the bromine atom must be joined to the 5-position of **2a**. The carbon–nitrogen bond across the 6- and 10-positions must be formed by a Michael-type addition of the NH moiety to the 6-position of the pyrimidine ring. The stereochemistry of the Michael-type addition was presumed to be *trans* on the basis of the nuclear Overhauser effect (NOE)-difference spectrum (NOEDS) experiment. Namely, the NOEDS of **2a** was observed as a 4% enhancement between one of C(7)–H_2 (δ 3.23) and C(5)–H (δ 4.97). Almost the same enhancement (4%) was observed between one of C(7)-H_2 (δ 3.30) and one of C(5)–H_2 (δ 2.71) in the case of **6a**.

Reactions of 1b, 1c, 7a, and 7b with Thiourea Derivatives Similarly, 5-bromo-6-bromomethyl-1-(3-bromopropyl and 2-bromopropyl)-3-methyl-2,4(1*H*,3*H*)-pyrimidinediones (**1b** and **1c**) were treated with thiourea derivatives to give



1a X = $-CH_2CH_2-$
1b X = $-CH_2CH_2CH_2-$
1c X = $-CH_2CH(CH_3)-$

	X
	$-CH_2CH_2-$
	$-CH_2CH_2CH_2-$
	$-CH_2CH(CH_3)-$

	R_1	R_2
2a	-H	-H
2c	$-CH_3$	-H
3a	-H	$-CH_3$
4a	-H	$-CH_2CH=CH_2$

	R
2b	-H
3b	$-CH_3$
4b	$-CH_2CH=CH_2$

	X
5a	$-CH_2CH_2-$
5b	$-CH_2CH_2CH_2-$

	X
2a	$-CH_2CH_2-$
2b	$-CH_2CH_2CH_2-$

	X
6a	$-CH_2CH_2-$
6b	$-CH_2CH_2CH_2-$

Chart 1

TABLE I. ^{1}H-NMR Data for 8,1,3,10-Thiatriazatricyclo[4.3.0.0^{6,10}]dodecanes (**2a**, **2c**, **5a**, and **6a**)

Compd. No.	Positions						
	5	7	11 or 12	12 or 11	N–CH_3	=N–H	Other
2a	4.97 s	3.23 d J=11.7 3.51 d J=11.7	3.73 ddd J=7.0, 10.3, 10.6 4.06 ddd J=1.1, 7.2, 10.6	3.61 ddd J=7.2, 10.3, 10.6 4.26 ddd J=1.1, 7.0, 10.6	3.23 s	7.2 br s	
2c	5.04 s	3.15 d J=11.4 3.40 d J=11.4	4.26 m (1H)	3.33 dd J=8.8, 11.0 4.41 dd J=6.6, 11.0	3.22 s	7.1 br s	C–CH_3 1.59 d J=6.2
5a	4.93 s	3.21 d J=12.1 3.40 d J=12.1	3.70 ddd J=7.3, 10.3, 11.4 4.28 ddd J=1.1, 7.3, 11.4	3.92 ddd J=7.3, 10.3, 11.0 4.32 ddd J=1.1, 7.3, 11.0	3.24 s		CO–CH_3 2.27 s
6a	2.71 dd J=2.0, 15.8 3.40 d J=15.8	3.19 d J=11.0 3.30 dd J=2.0, 11.0	3.38 dd J=6.0, 11.1 4.10 dd J=6.4, 11.1	3.50 dd J=6.4, 11.8 4.19 dd J=6.9, 11.8	3.19 s	7.1 br s	

TABLE II. ^{1}H-NMR Data for 8,1,3,10-Thiatriazatricyclo[4.4.0.0^{6,10}]tridecanes (**2b**, **5b**, and **6b**)

Compd. No.	Positions							
	5	7	11 or 13	12	13 or 11	N–CH_3	=N–H	Other
2b	5.03 s	3.15 d J=11.8 3.46 d J=11.8	3.06 dt J=3.7, 13.4 4.52 ddd J=2.6, 5.5, 13.4	2.06 m 2.22 m	3.77 ddd J=3.3, 5.5, 13.2 4.04 dt J=9.9, 13.2	3.24 s	6.8 br s	
5b	5.04 s	3.12 d J=12.2 3.37 d J=12.2	3.08 m 4.56 ddd J=2.5, 5.7, 13.7	2.09 m 2.26 m	3.88 ddd J=7.7, 10.3, 14.0 4.41 ddd J=3.8, 8.8, 14.0	3.25 s		CO–CH_3 2.25 s
6b	2.95 dd J=1.8, 16.1 3.10 d J=16.1	3.15 d J=11.0 3.34 dd J=1.8, 11.0	2.98 m 4.32 ddd J=3.6, 10.6, 13.9	1.95 m 2.05 m	3.05 m 4.44 ddd J=1.1, 7.7, 13.9	3.21 s	6.6 br s	

TABLE III. ^{13}C-NMR Data for 8,1,3,10-Thiatriazatricyclo[4.3.0.0^{6,10}]dodecanes (**2a**, **2c**, **5a**, and **6a**)

Compd. No	Positions										
	2	4	5	6	7	9	11 or 12	12 or 11	N–CH_3	CH_3	CO
2a	149.27	165.00	47.17	83.49	38.90	161.90	45.44	47.69	28.44		
2c	149.35	165.16	47.11	84.34	38.47	165.16	55.77	54.17	28.43	16.01	(C–CH_3)
5a	149.81	167.57	45.50	81.95	38.08	164.58	46.08	48.61	28.68	27.07	183.20
6a	150.58	166.92	41.42	81.23	40.49	162.51	45.41	46.43	27.82		

TABLE IV. ^{13}C-NMR Data for 8,1,3,10-Thiatriazatricyclo[4.4.0.0^{6,10}]tridecanes (**2b**, **5b**, and **6b**)

Compd. No.	Positions											
	2	4	5	6	7	9	11 or 13	12	13 or 11	N–CH_3	CH_3	CO
2b	150.28	164.70	46.77	78.59	36.44	158.98	36.67	20.42	41.02	28.71		
5b	150.58	167.20	44.75	78.16	35.73	164.47	36.43	20.43	42.94	28.59	27.05	183.58
6b	151.66	166.86	37.75	77.19	35.83	159.23	34.53	21.35	35.79	28.07		

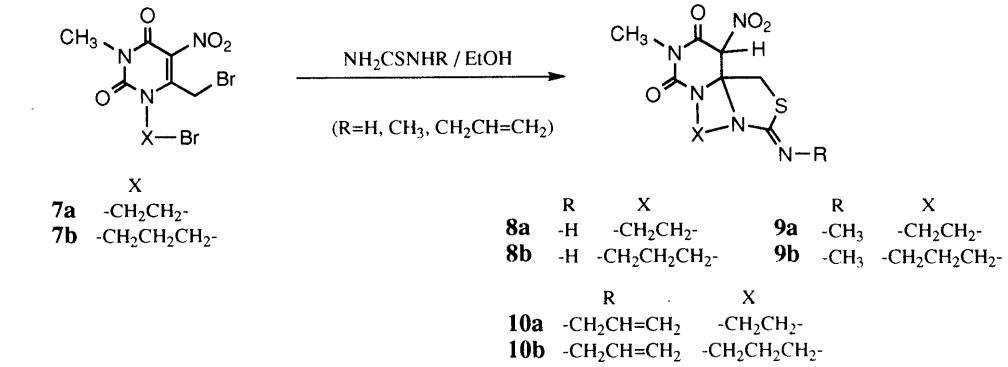


Chart 2

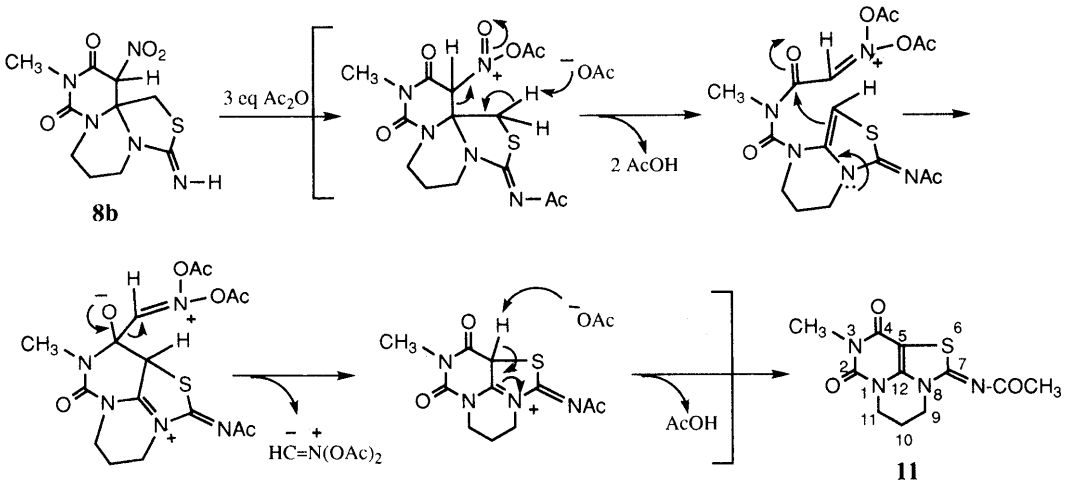


Chart 3

the corresponding tricyclic compounds: 5-bromo-9-imino-3-methyl (and 3,11-dimethyl)-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.3.0.0^{6,10}]dodecanes (**2c**·**HBr**, **2c**, **3a**, and **4a**) and 5-bromo-9-imino-3-methyl-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.4.0.0^{6,10}]tridecanes (**2b**·**HBr**, **3b**·**HBr**, **4b**·**HBr**, **4b**·**HBr**, and **2b**). The structures of the products were established in the same manner as above (Chart 1).

A number of groups have subjected nitro-olefins to Michael-type addition reactions.[5] Previously, we have prepared 5-nitropyrimidine derivatives[1] which possessed a nitro-olefin as a partial structure; the compounds appear to be more reactive than 5-bromopyrimidines in Michael-type addition.

6-Bromomethyl-1-(2-bromoethyl and 3-bromopropyl)-3-methyl-5-nitro-2,4(1*H*,3*H*)-pyrimidinediones[1] (**7a** and **7b**) were treated with thiourea derivatives to give the corres-

ponding tricyclic compounds: 9-imino-3-methyl-5-nitro-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.3.0.$0^{6,10}$]dodecanes (**8a·HBr**, **9a·HBr**, **10a·HBr**, **8a**, and **10a**) and 9-imino-3-methyl-5-nitro-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.4.0.$0^{6,10}$]tridecanes (**8b·HBr**, **9b·HBr**, **10b·HBr**, and **10b**), respectively. The structures of the reaction products were established by elemental and spectral analyses. In the ^{1}H-NMR spectra of **8a·HBr**, the signals of N–CH_3 and the 5-position are split into two peaks, namely δ 3.15 and 3.17 (N–CH_3), δ 6.41 and 6.78 (C(5)-H), and the latter peaks disappeared on addition of deuterium oxide. These phenomena were observed in all of the hydrobromides of the nitro-tricyclic compounds obtained above. Based on the above evidence, the hydrobromides appear to exist as a mixture of stereoisomers (epimers at C(5)) in solution, and these isomers would be interconvertible *via* pseudo-nitronic acid intermediates.

In order to prepare the *N*-acetyl derivatives, compounds **8a·HBr** and **8b·HBr** were treated with acetic anhydride. In the case of **8a·HBr**, pure products could not be obtained. On the other hand, **8b·HBr** was converted to 7-acetylimino-3-methyl-2,4-dioxo-6,1,3,8-thiatriazatricyclo[4.4.0.1^{5,8}]-dodec-5(12)-ene (**11**). The ring transformation presumably proceeded with nitromethane extrusion, and a plausible reaction pathway is shown in Chart 3.

Conclusion

We found that the reactions of bromomethyl-1-(2-bromoethyl, 3-bromopropyl, and 2-bromopropyl)-3-methyl-5-bromo-(and nitro-)2,4(1*H*,3*H*)-pyrimidinediones with thiourea derivatives afforded new tricyclic hetero compounds (5-bromo-(and nitro-)9-imino-3-methyl-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.3.0.$0^{6,10}$]dodecanes and -[4.4.0.$0^{6,10}$]tridecanes) in one step, presumably *via* intramolecular Michael-type addition. A new ring transformation, from 5-nitro-8,1,3,10-thiatriazatricyclo[4.4.0.$0^{6,10}$]-tridecane to 6,1,3,8-thiatriazatricyclo[4.4.0.1^{5,8}]dodec-5(12)-ene, was found.

Experimental

General Melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. The IR spectra were taken with a JASCO IR-810 spectrophotometer. The UV spectra were measured on a Hitachi 323 or a Shimadzu UV-300 spectrophotometer in EtOH solution. The NMR spectra were taken on a Hitachi R-600 (60 MHz for ^{1}H), a JEOL JNM FX-90Q (90 MHz for ^{1}H, 22.5 MHz for ^{13}C), or a JEOL JNM GX-400 (400 MHz for ^{1}H, 100 MHz for ^{13}C) Fourier-transform spectrometer, and were measured in $CDCl_3$ solution unless otherwise mensioned. Chemical shifts are expressed in ppm (δ) relative to tetramethylsilane as an internal standard. Mass spectra (MS) were obtained on a JEOL JMS-DX-303 equipped with a JMA-DA-5000 data processor.

General Procedures for the Reaction of 5-Bromo-(or Nitro-)1-(bromoalkyl)-6-bromomethyl-2,4(1*H*,3*H*)-pyrimidinedione with Thiourea Derivatives A solution of a 5-bromopyrimidine (1.0 eq) and a thiourea (2.0 eq) [or a 5-nitropyrimidine (1.0 eq) and a thiourea (1 eq)] in EtOH (5 ml/1 mmol) was refluxed for 1 h. After cooling with ice-water, the separated crystalline mass was collected and recrystallized from a suitable solvent to give the corresponding hydrobromide. The hydrobromide was stirred with 5% $NaHCO_3$ solution for 1.5 h, and the mixture was extracted with $CHCl_3$ (3 times). The combined extract was dried over $MgSO_4$ and filtered. The filtrate was concentrated to dryness and the resulting crystalline product was recrystallized from a suitable solvent to give the free base. If necessary, the product was purified by silica gel column chromatography.

5-Bromo-9-imino-3-methyl-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.3.0.$0^{6,10}$]dodecane Hydrobromide (2a·HBr) Yield 52%, mp 284—285 °C. Colorless needles (MeOH). IR (KBr): 1721, 1675, 1658 (C=O) cm^{-1}. UV: end absorption. Electron impact (EI)-MS *m/z*: 320 [(M−HBr)$^+$ for ^{81}Br], 318 [(M−HBr)$^+$ for ^{79}Br]. FAB-MS *m/z*: 321 [((M−HBr)+1)$^+$ for ^{81}Br], 319 [((M−HBr)+1)$^+$ for ^{79}Br]. *Anal.* Calcd for $C_9H_{12}Br_2N_4O_2S$: C, 27.02; H, 3.02; Br, 39.95; N, 14.00; S, 8.01. Found: C, 27.06; H, 3.05; Br, 39.76; N, 13.88; S, 7.83.

5-Bromo-9-imino-3-methyl-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.3.0.$0^{6,10}$]dodecane (2a) Yield 39% (from **1a**), mp 157—159 °C. Colorless needles (acetone). IR (KBr): 3290 (br, =N–H), 1718, 1679 (C=O) cm^{-1}. UV: end absorption. EI-MS *m/z*: 320 (M$^+$ for ^{81}Br), 318 (M$^+$ for ^{79}Br). *Anal.* Calcd for $C_9H_{11}BrN_4O_2S$: C, 33.87; H, 3.47; Br, 25.04; N, 17.55; S, 10.05. Found: C, 34.05; H, 3.46; Br, 25.10; N, 17.36; S, 10.04.

5-Bromo-9-imino-3-methyl-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.4.0.$0^{6,10}$]tridecane Hydrobromide (2b·HBr) Yield 34%, mp >250 °C. Colorless cubes (MeOH). IR (KBr): 3100—2800 (N$^+$–H), 1720, 1682, 1652 (C=O) cm^{-1}. UV: end absorption. EI-MS *m/z*: 334 [(M−HBr)$^+$ for ^{81}Br], 332 [(M−HBr)$^+$ for ^{79}Br], 255 [(334 and 332−Br)$^+$]. *Anal.* Calcd for $C_{10}H_{14}Br_2N_4O_2S$: C, 29.00; H, 3.41; Br, 38.59; N, 13.53; S, 7.74. Found: C, 29.04; H, 3.36; Br, 38.32; N, 13.43; S, 7.87.

5-Bromo-9-imino-3-methyl-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.4.0.$0^{6,10}$]tridecane (2b) Yield 90% (from hydrobromide), mp 185—187 °C. Colorless needles (acetone, EtOH). IR (KBr): 3300 (NH), 1708, 1678 (C=O) cm^{-1}. UV: end absorption. EI-MS *m/z*: 334 (M$^+$ for ^{81}Br), 332 (M$^+$ for ^{79}Br). *Anal.* Calcd for $C_{10}H_{13}BrN_4O_2S$: C, 36.05; H, 3.93; Br, 23.98; N, 16.81; S, 9.62. Found: C, 36.17; H, 3.90; Br, 23.72; N, 16.78; S, 9.87.

5-Bromo-3,11-dimethyl-9-imino-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.3.0.$0^{6,10}$]dodecane Hydrobromide (2c·HBr) Yield 30%, mp >270 °C. Colorless needles (MeOH). IR (KBr): 3090—2970 (N$^+$–H), 1709, 1671 (C=O) cm^{-1}. UV: end absorption. EI-MS *m/z*: 334 [(M−HBr)$^+$ for ^{81}Br], 332 [(M−HBr)$^+$ for ^{79}Br], 253 (334 and 332−Br)$^+$. *Anal.* Calcd for $C_{10}H_{14}Br_2N_4O_2S$: C, 29.00; H, 3.41; Br, 38.59; N, 13.53; S, 7.74. Found: C, 29.06; H, 3.40; Br, 38.59; N, 13.39; S, 7.81.

5-Bromo-3,11-dimethyl-9-imino-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.3.0.$0^{6,10}$]dodecane (2c) Yield 65% (from hydrobromide), mp 195—196 °C. Colorless plates (AcOEt). IR (KBr): 3295 (br, N$^+$–H), 1719, 1680 (C=O) cm^{-1}. UV: end absorption. EI-MS *m/z*: 334 (M$^+$ for ^{81}Br), 332 (M$^+$ for ^{79}Br), 253 [(334 and 332−Br)$^+$]. *Anal.* Calcd for $C_{10}H_{13}BrN_4O_2S$: C, 36.05; H, 3.93; Br, 23.98; N, 16.81; S, 9.62. Found: C, 36.08; H, 3.87; Br, 24.22; N, 16.79; S, 9.57.

5-Bromo-3-methyl-9-methylimino-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.3.0.$0^{6,10}$]dodecane (3a) Yield 29%, mp 200–201 °C. White fine crystals (MeOH). IR (KBr): 1720, 1680 (C=O) cm^{-1}. UV λ_{max} nm (log ε): 207 (4.19). ^{1}H-NMR (90 MHz) δ: 3.11 (3H, s, =N–CH_3), 3.22 (3H, s, N–CH_3), 3.30 and 3.31 (2H, AB type and coupling constants could not be read, C(7)-H_2), 3.4—4.5 (4H, m, CH_2CH_2), 4.88 (1H, s, C(5)-H). EI-MS *m/z*: 334 (M$^+$ for ^{81}Br) and 332 (M$^+$ for ^{79}Br). *Anal.* Calcd for $C_{10}H_{13}BrN_4O_2S$: C, 36.04; H, 3.93; Br, 23.98; N, 16.81; S, 9.62. Found: C, 36.25; 3.84; Br, 23.70; N, 16.85; S, 9.67.

5-Bromo-3-methyl-9-methylimino-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.4.0.$0^{6,10}$]tridecane Hydrobromide (3b·HBr) Yield 39%, mp >260 °C. White fine crystals (MeOH). IR (KBr): 1720, 1680 (C=O) cm^{-1}. UV: end absorption. ^{1}H-NMR (90 MHz, DMSO-d_6) δ: 2.1 (2H, m, C(12)-H_2), 3.06 (3H, s, =N–CH_3), 3.09 (3H, s, N–CH_3), 3.2–4.5 (4H, m, 2×N–CH_2), 3.74 and 4.02 (2H, each d, J=12.5 Hz, C(7)-H_2), 5.36 (1H, s, C(5)-H). EI-MS *m/z*: 348 [(M−HBr)$^+$ for ^{81}Br], 346 [(M−HBr)$^+$ for ^{79}Br]. *Anal.* Calcd for $C_{11}H_{16}Br_2N_4O_2S$: C, 30.86; H, 3.77; Br, 37.33; N, 13.09; S, 7.49. Found: C, 30.81; H, 3.57; Br, 37.56; N, 13.04; S, 7.59.

9-Allylimino-5-bromo-3-methyl-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.3.0.$0^{6,10}$]dodecane (4a) Yield 32%, mp 168—171 °C. White fine crystals (MeOH–AcOEt). IR (KBr): 1720, 1680 (C=O) cm^{-1}. UV λ_{max} nm (log ε): 213 (4.21). ^{1}H-NMR (90 MHz) δ: 3.22 (3H, s, N–CH_3), 3.30 and 3.31 (2H, AB type and coupling constants could not be read, C(7)-H_2), 3.4–4.3 (4H, m, –CH_2CH_2–), 3.89 (2H, ddd, J=1.3, 1.5, 5.4 Hz, N–C$\underline{H}_2$–CH=), 4.89 (1H, s, C(5)-H), 5.09 (1H, tdd, J=1.3, 1.8, 9.9 Hz, CH=C$\underline{H}_2$ (*cis*)), 5.18 (1H, tdd, J=1.5, 1.8, 17.1 Hz, CH=C$\underline{H}_2$ (*trans*)), 5.91 (1H, tdd, J=5.4, 9.1, 17.1 Hz, CH_2–C$\underline{H}$=CH_2). EI-MS *m/z*: 360 (M$^+$ for ^{81}Br), 358 (M$^+$ for ^{79}Br). *Anal.* Calcd for $C_{12}H_{15}BrN_4O_2S$: C, 40.11; H, 4.21; Br, 22.24; N, 15.60; S, 8.93. Found: C, 40.18; H, 4.13; Br, 21.89; N, 15.47; S, 8.89.

9-Allylimino-5-bromo-3-methyl-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.4.0.$0^{6,10}$]tridecane Hydrobromide (4b·HBr) Yield 34%, mp >260 °C. White fine crystals (MeOH–AcOEt). IR (KBr): 1718, 1675 (C=O) cm^{-1}.

UV λ_{max} nm (log ε): 220 (4.18). ^{1}H-NMR (90 MHz, DMSO-d_6) δ: 2.1 (2H, m, C(12)-H_2), 3.09 (3H, s, N–CH_3), 3.2–4.5 (4H, m, 2 × N–CH_2), 3.80 and 4.01 (2H, each d, J = 12.5 Hz, C(7)-H_2), 4.04 (2H, ddd, J = 1.5, 1.8, 5.1 Hz, N–C$\underline{H}_2$–CH=), 5.29 (1H, tdd, J = 1.5, 1.8, 9.9 Hz, CH=C$\underline{H}_2$ (*cis*)), 5.33 (1H, tdd, J = 1.5, 1.8, 17.1 Hz, CH=C$\underline{H}_2$ (*trans*)), 5.73 (1H, s, C(5)-H), 5.81 (1H, tdd, J = 5.1, 9.9, 17.1 Hz, CH_2–C$\underline{H}$=CH_2). EI-MS m/z: 374 [(M − HBr)$^+$ for ^{81}Br], 372 [(M − HBr)$^+$ for ^{79}Br]. *Anal.* Calcd for $C_{13}H_{18}Br_2N_4O_2S$: C, 34.38; H, 3.99; Br, 35.19; N, 12.34; S, 7.06. Found: C, 34.38; H, 3.82; Br, 35.15; N, 12.33; S, 6.99.

9-Acetylimino-5-bromo-3-methyl-2,4-dioxo-8,1,3,10-thiatriazatricyclo-[4.3.0.0^{6,10}]dodecane (5a) A mixture of **2a**·**HBr** (3.0 g, 7.5 mmol) in acetic anhydride (6 ml) and pyridine (60 ml) was heated at 90—95 °C for 3 h. After removal of the solvent, the residue was extracted with $CHCl_3$ (3 times) and the combined extract was washed with 10% HCl, then with 5% $NaHCO_3$. The organic layer was dried over $MgSO_4$ and filtered. The filtrate was concentrated to dryness, and the residue was crystallized from acetone (or AcOEt) to give 1.5 g (54%) of colorless cubes, mp 194—195 °C. IR (KBr): 1718, 1680 (C=O) cm^{-1}. UV λ_{max} nm (log ε): 258 (4.22). EI-MS m/z: 362 (M$^+$ for ^{81}Br), 360 (M$^+$ for ^{79}Br). *Anal.* Calcd for $C_{11}H_{13}BrN_4O_3S$: C, 36.58; H, 3.63; Br, 22.12; N, 15.51; S, 8.88. Found: C, 36.72; H, 3.59; Br, 22.10; N, 15.52; S, 8.64.

9-Acetylimino-5-bromo-3-methyl-2,4-dioxo-8,1,3,10-thiatriazatricyclo-[4.4.0.0^{6,10}]tridecane (5b) A solution of **2b** (0.58 g, 1.75 mmol) in acetic anhydride (6 ml) and pyridine (5 drops) was heated at 90—95 °C for 3 h. The reaction mixture was worked up as described above. The filtrate was concentated to dryness, and the residue was crystallized from acetone to give 0.48% (73%) of white fine crystals, mp 236—238 °C. IR (KBr): 1795, 1675 (C=O) cm^{-1}. UV λ_{max} nm (log ε): 259 (4.28). EI-MS m/z: 376 (M$^+$ for ^{81}Br), 374 (M$^+$ for ^{79}Br). *Anal.* Calcd for $C_{12}H_{15}BrN_4O_3S$: C, 38.41; H, 4.03; Br, 21.30; N, 14.93; S, 8.54. Found: C, 38.69; H, 4.08; Br, 21.38; N, 14.85; S, 8.48.

9-Imino-3-methyl-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.3.0.0^{6,10}]-dodecane (6a) A mixture of **2a**·**HBr** (540 mg, 1.35 mmol) and 10% Pd–C (210 mg) in EtOH–H_2O mixture (1 : 1, 50 ml) was stirred overnight under an H_2 atmosphere. After removal of the catalyst, the solvent was evaporated to dryness. The residue was dissolved in H_2O, made alkaline with 5% $NaHCO_3$, and extracted with $CHCl_3$. The combined extract was dried over $MgSO_4$ and filtered. The filtrate was concentrated to dryness, and the residue was crystallized from MeOH–AcOEt to give 240 mg (74%) of colorless needles, mp 170—171 °C. IR (KBr): 3320 (NH), 1718, 1670 (C=O) cm^{-1}. UV: end absorption. EI-MS m/z: 240 (M$^+$). *Anal.* Calcd for $C_9H_{12}N_4O_2S$: C, 44.99; H, 5.03; N, 23.32; S, 13.34. Found: C, 45.05; H, 4.97; N, 23.20; S, 13.31.

9-Imino-3-methyl-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.4.0.0^{6,10}]-tridecane (6b) A mixture of **2b** (1.0 g, 3.0 mmol) and 10% Pd–C (300 mg) in EtOH (30 ml) was stirred for 2 h under an H_2 atmosphere. The reaction mixture was worked up as described above. The filtrate was concentrated to dryness, and the residue was crystallized from MeOH to give 490 mg (64%) of colorless needles, mp 214—215 °C. IR (KBr): 3300 (NH), 1710, 1655 (C=O) cm^{-1}. UV: end absorption. EI-MS m/z: 254 (M$^+$). *Anal.* Calcd for $C_{10}H_{14}N_4O_2S$: C, 47.22; H, 5.55; N, 22.03; S, 12.60. Found: C, 47.22; H, 5.46; N, 21.98; S, 12.39.

9-Imino-3-methyl-5-nitro-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.3.-0.0^{6,10}]dodecane Hydrobromide (8a·HBr) Yield 46%, mp > 260 °C. Colorless needles (MeOH). IR (KBr): 3130—2700 (N$^+$ − H), 1740, 1700, 1658 (C=O), 1570, 1365 (C-NO_2) cm^{-1}. ^{1}H-NMR (90 MHz, DMSO-d_6) δ: 3.15 and 3.17 (total 3H, each signal s, N–CH_3), 3.6—4.3 (6H, m, C(7)-H_2 and –CH_2CH_2–), 6.41 and 6.78 (total 1H, each signal s, C(5)-H), 10.7 (1H, br s, =N–H). EI-MS m/z: 285 [(M − HBr)$^+$]. *Anal.* Calcd for $C_9H_{12}BrN_5O_4S$: C, 29.52; H, 3.30; Br, 21.82; N, 19.12; S, 8.76. Found: C, 29.77; H, 3.51; Br, 21.58; N, 18.91; S, 8.51.

9-Imino-3-methyl-5-nitro-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.3.-0.0^{6,10}]dodecane (8a) Yield 21% (from hydrobromide). Colorless paste. IR (KBr): 3400—2800 (N–H), 1730, 1690 (C=O), 1560, 1395 (C–NO_2) cm^{-1}. UV λ_{max} nm (log ε): 333 (3.43). ^{1}H-NMR (90 MHz) δ 3.11 and 3.38 (each 1H, d, J = 11.8 Hz, C(7)-H_2), 3.0—4.8 (4H, m, C(11)-H_2 and C(12)-H_2), 3.31 (3H, s, N–CH_3), 5.67 (1H, s, C(5)-H), 7.2 (1H, br, s, =N–H). High resolution (HR)-MS: Calcd for $C_9H_{11}N_5O_4S$: 285.0484. Found: 285.0508.

9-Imino-3-methyl-5-nitro-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.4.-0.0^{6,10}]tridecane Hydrobromide (8b·HBr) Yield 40%, mp 230 °C. Colorless prisms (MeOH). IR (KBr): 3150—2900 (N$^+$–H), 1740, 1697, 1665 (C=O), 1565, 1390 (C–NO_2) cm^{-1}. UV λ_{max} nm (log ε): 326 (3.92). ^{1}H-NMR (90 MHz, DMSO-d_6) δ: 2.0 (2H, br s, C(12)-H_2), 3.11 and 3.17 (total 3H, each signal s, N–CH_3), 3.3—4.6 (6H, m, C(7)-H_2 and 2 × N–CH_2), 6.39 and 7.07 (total 1H, each signal s, C(5)-H), 10.4 (1H, br s, =N–H). EI-MS m/z: 299 [(M − HBr)$^+$]. *Anal.* Calcd for $C_{10}H_{14}BrN_5O_4S$: C, 31.59; H, 3.71; Br, 21.02; N, 18.42; S, 8.43. Found: C, 31.77; H, 3.81; Br, 20.78; N, 18.21; S, 8.18.

3-Methyl-9-methylimino-5-nitro-2,4-dioxo-8,1,3,10-thiatriazatricyclo-[4.3.0.0^{6,10}]dodecane Hydrobromide (9a·HBr) Yield 40%, mp > 240 °C. White fine crystals (MeOH–CH_2Cl_2). IR (KBr): 2750 (br, N$^+$–H), 1740, 1690 (C=O), 1560, 1385 (C–NO_2) cm^{-1}. UV λ_{max} nm (log ε): 325 (2.82). ^{1}H-NMR (90 MHz, DMSO-d_6) δ: 3.06, 3.08, 3.13, and 3.15 (total 6H, each signal s, 2 × N–CH_3), 3.2—4.4 (6H, m, C(7)-H_2 and –CH_2CH_2–), 6.31 and 6.78 (total 1H, each signal s, C(5)-H). EI-MS m/z: 299 [(M − HBr)$^+$]. *Anal.* Calcd for $C_{10}H_{14}BrN_5O_4S$: C, 31.59; H, 3.71; Br, 21.02; N, 18.42, S, 8.43. Found: C, 31.69; H, 3.64; Br, 20.77; N, 18.39; S, 8.42.

3-Methyl-9-methylimino-5-nitro-2,4-dioxo-8,1,3,10-thiatriazatricyclo-[4.4.0.0^{6,10}]tridecane Hydrobromide (9b·HBr) Yield 37%, mp > 260 °C. Colorless prisms (MeOH). IR (KBr): 3150—2900 (N$^+$–H), 1735, 1700 (C=O), 1560, 1340 (C–NO_2) cm^{-1}. UV λ_{max} nm (log ε): 323 (3.97). ^{1}H-NMR (90 MHz, DMSO-d_6) δ: 2.0 (2H, br s, C(12)-H_2), 3.03, 3.11, 3.18, and 3.22 (total 6H, each signal s, 2 × N–CH_3), 3.2—4.6 (6H, m, C(7)-H_2 and 2 × N–CH_2), 6.33 and 7.08 (total 1H, each signal s, C(5)-H). EI-MS m/z: 313 [(M − HBr)$^+$]. *Anal.* Calcd for $C_{11}H_{16}BrN_5O_4S$: C, 33.51; H, 4.09; Br, 20.27; N, 17.76; S, 8.13. Found: C, 33.69; H, 3.94; Br, 20.08; N, 17.75; S, 8.00.

9-Allylimino-3-methyl-5-nitro-2,4-dioxo-8,1,3,10-thiatriazatricyclo[4.3.-0.0^{6,10}]dodecane Hydrobromide (10a·HBr) Yield 62%, mp > 250 °C. White fine crystals (MeOH–$CHCl_3$). IR (KBr): 2750 (br, N$^+$–H), 1740, 1693 (C=O), 1560, 1385 (C–NO_2) cm^{-1}. UV: end absorption. ^{1}H-NMR (90 MHz, DMSO-d_6) δ: 3.08 and 3.15 (total 3H, each signal s, N–CH_3), 3.7—4.4 (8H, m, C(7)-H_2, –CH_2CH_2– and N–C$\underline{H}_2$–CH=), 5.1—5.4 (2H, m, CH_2–CH=C$\underline{H}_2$), 5.6—6.1 (1H, m, CH_2–C$\underline{H}$=CH_2), 6.34 and 6.80 (total 1H, each signal s, C(5)-H). EI-MS m/z: 325 [(M − HBr)$^+$]. *Anal.* Calcd for $C_{12}H_{16}BrN_5O_4S$: C, 35.48; H, 3.97; Br, 19.67; N, 17.24; S, 7.89. Found: C, 35.28; H, 3.84; Br, 19.89; N, 17.17; S, 7.49.

9-Allylimino-3-methyl-5-nitro-2,4-dioxo-8,1,3,10-thiatriazatricyclo-[4.3.0.0^{6,10}]dodecane (10a) Yield 39% (from hydrobromide). Colorless paste. IR (KBr): 1738, 1690 (C=O), 1560, 1320 (C–NO_2) cm^{-1}. UV λ_{max} nm (log ε): 330 (3.66). ^{1}H-NMR (90 MHz) δ: 3.23 and 3.25 (2H, AB type and coupling constants could not be read, C(7)-H_2), 3.28 (3H, s, N–CH_3), 3.4—4.4 (4H, m, –CH_2CH_2–), 3.90 (2H, ddd, J = 1.3, 1.5, 5.3 Hz, N–C$\underline{H}_2$–CH=), 5.06 (1H, tdd, J = 1.3, 1.8, 9.9 Hz, CH=C$\underline{H}_2$ (*cis*)), 5.20 (1H, tdd, J = 1.5, 1.8, 17.1 Hz, CH=C$\underline{H}_2$ (*trans*)), 5.65 (1H, s, C(5)-H), 5.89 (1H, tdd, J = 5.3, 9.9, 17.1 Hz, CH_2–C$\underline{H}$=CH_2). EI-MS m/z: 325 (M$^+$). HR-MS: Calcd for $C_{12}H_{15}I_4N_5S$: 325.0844. Found: 325.0844.

9-Allylimino-3-methyl-5-nitro-2,4-dioxo-8,1,3,10-thiatriazatricyclo-[4.4.0.0^{6,10}]tridecane Hydrobromide (10b·HBr) Yield 45%, mp 207—210 °C. Colorless prisms (MeOH). IR (KBr): 3150—2900 (N$^+$–H), 1737, 1697, 1650 (C=O), 1570, 1340 (C–NO_2) cm^{-1}. UV λ_{max} nm (log ε): 323 (3.92). ^{1}H-NMR (90 MHz, DMSO-d_6) δ: 2.0 (2H, br s, C(12)-H_2), 3.11 and 3.18 (total 3H, each signal s, N–CH_3), 3.3—4.6 (8H, m, C(7)-H_2, 2 × N–CH_2, and N–C$\underline{H}_2$–CH=), 5.0—5.4 (2H, m, CH_2–CH=C$\underline{H}_2$), 5.6—6.1 (1H, m, CH_2–C$\underline{H}$=CH_2), 6.32 and 7.07 (total 1H, each signal s, C(5)-H). EI-MS m/z: 339 [(M − HBr)$^+$]. *Anal.* Calcd for $C_{13}H_{18}BrN_5O_4S$: C, 37.15; H, 4.32; Br, 19.01; N, 16.66; S, 7.63. Found: C, 37.17; H, 4.15; Br, 19.01; N, 16.69; S, 7.71.

9-Allylimino-3-methyl-5-nitro-2,4-dioxo-8,1,3,10-thiatriazatricyclo-[4.4.0.0^{6,10}]tridecane (10b) Yield 34% (from hydrobromide), mp 144—145 °C. Pale yellow prisms (MeOH). IR (KBr): 1737, 1697 (C=O), 1570, 1335 (C–NO_2) cm^{-1}. UV λ_{max} nm (log ε): 330 (3.69). ^{1}H-NMR (90 MHz, DMSO-d_6) δ: 1.9 (2H, m, C(7)-H_2), 3.09 and 3.17 (total 3H, each signal s, N–CH_3), 3.5—4.5 (8H, m, C(7)-H_2, 2 × N–CH_2, and N–C$\underline{H}_2$–CH=), 4.9—5.3 (2H, m, CH_2–CH=C$\underline{H}_2$), 5.8 (1H, tdd, J = 4.9, 9.9, 17.1 Hz, CH_2–C$\underline{H}$=CH_2), 7.00 (1H, s, C(5)-H). EI-MS m/z: 339 (M$^+$). *Anal.* Calcd for $C_{13}H_{17}N_5O_4S + 0.5\,CH_3OH$: C, 45.62; H, 5.39; N, 19.71; S, 9.02. Found: C, 45.70; H, 5.29; N, 19.78; S, 9.10.

7-Acetylimino-3-methyl-2,4-dioxo-6,1,3,8-thiatriazatricyclo[4.4.0.1^{5,8}]-dodec-5(12)-ene (11) A solution of **8b**·**HBr** (5.05 g, 13.3 mmol) in acetic anhydride (50 ml) was heated at 90—95 °C for 2 h. After removal of the solvent *in vacuo*, the residue was treated with 5% $NaHCO_3$ and extracted with $CHCl_3$ (3 times). The combined extract was dried over $MgSO_4$ and filtered. The filtrate was concentrated to a small volume and chromatographed on a silica gel column with $CHCl_3$–CH_3CN (19 : 1). The resulting crystalline mass was recrystallized from AcOEt–MeOH to give 2.2 g (59%) of colorless needles, mp > 300 °C. IR (KBr): 1702, 1660 (C=O) cm^{-1}. UV λ_{max} nm (relative intensities): 229 (75), 269 (27); molar absorptivity could not be calculated because of insolubility in EtOH.

^{1}H-NMR (400 MHz) δ: 2.32 (3H, s, $COCH_3$), 2.34 (2H, m, C(10)-H_2), 3.39 (3H, s, N–CH_3), 4.08 (2H, t, J=5.9 Hz, C(11 or 9)-H_2), 4.21 (2H, t, J=5.9 Hz, C(9 or 11)-H_2). ^{13}C-NMR (100 MHz, C–H COSY) δ: 20.35 (CO–$\underline{C}H_3$), 27.01 (C(10)), 28.22 (N–CH_3), 40.63 (C(9 or 11)), 43.09 (C(11 or 9)), 91.31 (C(5)), 140.08 (C(12)), 150.27 (C=O (2)), 156.85 (C(7)), 165.84 (C=O (4)), 181.64 ($\underline{C}O$–CH_3). EI-MS m/z: 280 (M^+). *Anal.* Calcd for $C_{11}H_{12}N_4O_3S$: C, 47.13; H, 4.31; N, 19.99; S, 11.44. Found: C, 47.25; H, 4.30; N, 19.93; S, 11.18.

References and Notes

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