New Tricyclic Ring Systems of Fused 1,4-Diazepines

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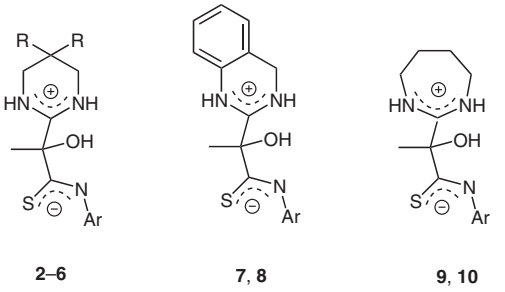
Abstract: New heterocyclic systems of pyrimido[1,2-*d*][1,4]diazepine, [1,4]diazepino[7,1-*b*]quinazoline, and [1,4]diazepino[1,7-*a*][1,3]diazepine were obtained in specific reactions of DMAD with zwitterionic compounds.

Key words: pyrimido[1,2-*d*][1,4]diazepine, [1,4]diazepino[7,1-*b*]quinazoline, [1,4]diazepino[1,7-*a*][1,3]diazepine, triazatricyclo[7.2.1.0^{3,8}]dodec-7-ene, DMAD

Biological activity of 1,4-diazepine derivatives[1] have already been explored for many years. Undoubtedly [1,4]benzodiazepines belong to the family of privileged structures.[2–5] When fused with pyrrole,[3,4] or benzimidazole[5] rings, [1,4]diazepines play a crucial role in a number of biologically active compounds. Pyrimido[4,5]-1,4-benzodiazepine derivatives show appreciable inhibitor activity against the KDR tyrosine kinase.[6] The diazepinoquinazoline system is present in naturally occurring alkaloids such as asperlicin, which is a cholecystokinin antagonist.[7] A rare O-bridged azepine skeleton is present in molecules of interesting zoanthamine alkaloids such as zoanthamine,[8] which have been isolated from the polyps of marine zoanthis. Our recent work has focused on synthetic applications of zwitterionic compounds **2**–**10**[9–12] (Figure 1), which we obtained as a result of an unusual rearrangement during reactions of 2-anilino-2-methoxy-3-oxothiobutanoic acid anilide derivatives **1** with various aliphatic 1,3- and 1,4-diamines. Scheme 1 shows an example of the reaction. The process involved cyclisation followed by a sigmatropic rearrangement of 3-oxoacid derivatives to 2-hydroxy acid derivatives in their zwitterionic forms **2**–**10**. This mechanism and complexity of the reactions is discussed more extensively in our previous work.[9]

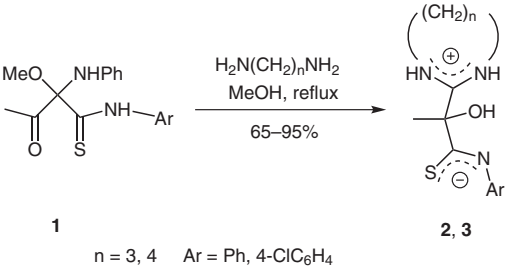
We have already found[10–12] that the compounds **2**–**10** are important synthetic precursors, capable of reacting both with electrophiles and nucleophiles. The reactions led to novel, highly functionalised, saturated, or partially saturated heterocyclic systems. Those heterocycles also could serve as ionic liquids,[12] after transformation into salts of various acids.

Continuing our research we investigated the reactivity of the zwitterionic compounds **2**–**10** towards DMAD. Acetylenedicarboxylates are known to undergo cycloaddition reactions easily, especially with ionic compounds; this made the zwitterions **2**–**10** interesting reactants for preparing polycyclic heterocycles. Reactions between DMAD and the zwitterions **2**–**10** were performed in 1:1 molar ratio of the reagents in refluxing methanol.



2 R = H, Ar = Ph
3 R = H, Ar = 4-ClC$_6$H$_4$
4 R = Me, Ar = Ph
5 R = Me, Ar = 4-ClC$_6$H$_4$
6 R = Me, Ar = 4-MeOC$_6$H$_4$
7 Ar = Ph
8 Ar = 4-ClC$_6$H$_4$
9 Ar = Ph
10 Ar = 4-ClC$_6$H$_4$

Figure 1 Zwitterionic compounds **2**–**10**



Scheme 1

The progress of the reactions was monitored by TLC, though the formation of products could be easily observed since they were generally yellow in contrast to the colourless substrates. In most cases products were formed within seconds even at room temperature, but we found out that heating to mild reflux for about 40 minutes gave the best results. As a result of the reactions, pyrimido[1,2-*d*][1,4]diazepine, [1,4]diazepino[7,1-*b*] quinazoline, and [1,4]diazepino[1,7-*a*][1,3]diazepine derivatives were formed. All the obtained compounds have O-bridges in their 1,4-diazepine rings (Scheme 2).

Structures of the products were determined from their spectra and confirmed by X-ray crystal structure of **11**.

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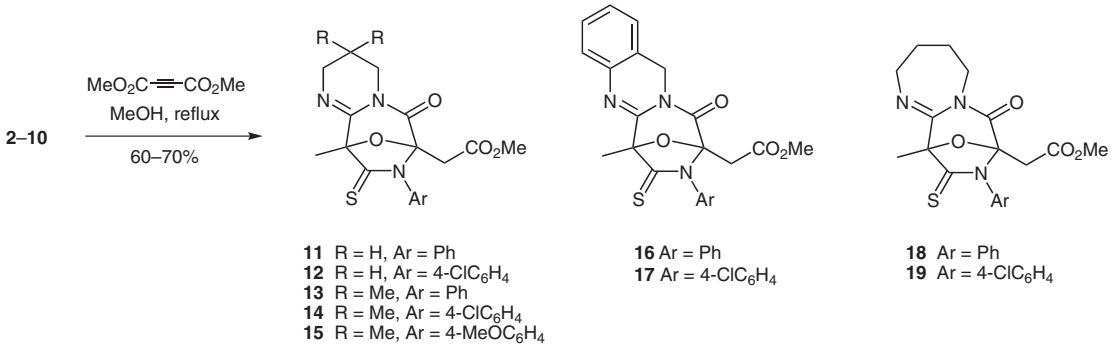


11 R = H, Ar = Ph
12 R = H, Ar = 4-ClC$_6$H$_4$
13 R = Me, Ar = Ph
14 R = Me, Ar = 4-ClC$_6$H$_4$
15 R = Me, Ar = 4-MeOC$_6$H$_4$

16 Ar = Ph
17 Ar = 4-ClC$_6$H$_4$

18 Ar = Ph
19 Ar = 4-ClC$_6$H$_4$

Scheme 2

There was a clear evidence for the formation of C=S bond in the ^{13}C NMR spectra: the thiocarbonyl carbon atom signals appeared at δ = 196–198 ppm; they were not present in the spectra of the substrates. Both ^{1}H and ^{13}C NMR spectra indicated that, contrary to the substrates, all methylene groups of the pyrimidine and 1,3-diazepine rings in the compounds **11**–**15**, **18**, and **19** were different. This suggested that in each case, reactions took place on two nitrogen atoms, one of the hetero ring and one of the SCNAr moieties (Figure 1). Based on our previous work[10] we expected the formation of C=N bond in the hetero rings. We could not reveal if the OH groups of **2**–**10** participated in the reactions, because corresponding signals were not visible in the ^{1}H NMR spectra of the substrates.

There were signals from two carbon atoms in ^{13}C NMR spectra of the products (at δ = 95 ppm and δ = 30–35 ppm, respectively) that must have originated from the triple bond of DMAD; as the atom absorption correspond to sp^3 carbon atoms, the bond must have been fully reduced during the reaction. The signals at δ = 30–35 were attributed to the CH_2 group at C7 of the obtained system. The corresponding signals of aliphatic hydrogen atoms appeared in the range from δ = 3.0 to 3.4 in the ^{1}H NMR spectra. This was confirmed with an HSQC experiment for the compound **11**.

The molecular structures of the products were finally confirmed by the X-ray analysis of **11**.[13] A perspective view of the molecule of **11** with the crystallographic atom numbering scheme is shown in Figure 2. The unsaturated six-membered pyrimidine hetero ring N7–C8–N12–C13–C14–C15 adopted a boat conformation with the C14 atom as the flap atom. There was one C=N bond (C8–N12, 1.261 Å) in the hetero ring. The C=S bond was rather short (1.636 Å). The terminal phenyl ring C21–C22–C23–C24–C25–C26 was disordered due to rotational freedom around the N3–C21 single bond. No specific model of this disorder could be found. As a result the atomic displacement parameters of the atoms forming the ring were rather high. The presence of the residual electron density peak of 0.61 e·Å^{-3} can also be attributed to this disorder. The conformation of the molecule was stabilised by a few intramolecular close contacts (Table 1), of which the strongest was C20–H120···O18. The crystal structure did not show typical intermolecular hydrogen bonds.

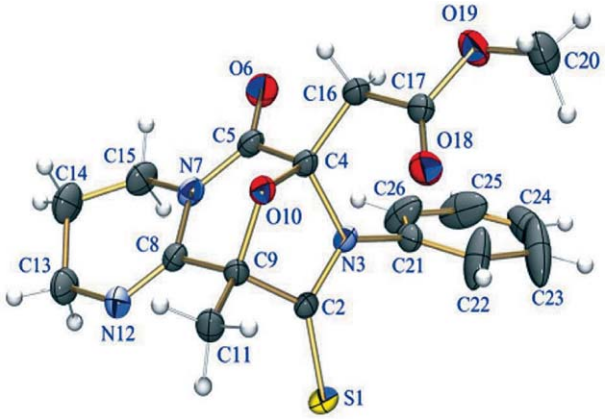


Figure 2 X-ray crystal structure of **11**

Table 1 Intramolecular Hydrogen Bonds in **11**

D–H···A	D–A [Å]	H···A [Å]	D–H [Å]	D–H···A [°]
C11–H111···N12	2.830(4)	2.75(3)	0.97(3)	85(2)
C16–H116···O6	2.802(4)	2.52(4)	0.95(3)	97(2)
C15–H215···O6	2.740(5)	2.52(4)	0.95(4)	106(3)
C20–H120···O18	2.650(7)	2.51(6)	1.02(4)	87(3)

Theoretically, there were two possible regioisomers **A** and **B** that could be formed in the case of the compounds **16** and **17** (Figure 3), but only one was isolated in each case. The positions of the benzene rings in these products were determined by HMBC spectra for compound **16**. The HMBC spectra showed a correlation between the carbon atom of the amide carbonyl group (δ = 162 ppm) and the protons of the CH_2 group (δ = 5.08 and 4.90 ppm) in the quinazoline ring, which would not have been possible in the case of the **B** regioisomer. This clearly indicated that the correct structures of **16** and **17** corresponded to **A** shown in Figure 3.

The probable mechanism of the reactions leading to tricyclic systems **11**–**19** starts with an electrophilic attack of the C2 carbon atom of a DMAD molecule on the nitrogen atom of the iminothiolate fragment of **2**–**10** with simultaneous oxygenation of the 1,3-diazahetero ring in zwitter-

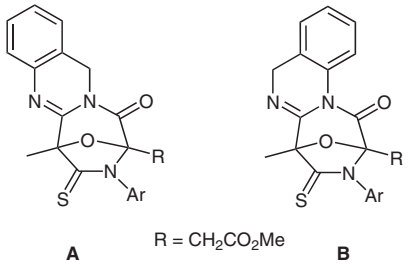
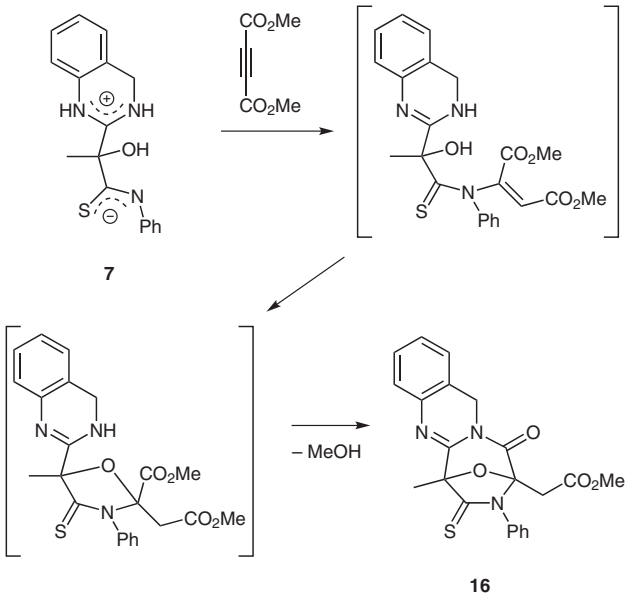


Figure 3 Possible regioisomers **A** and **B** for compounds **16** and **17**

ionic compounds **2**–**10**. The second step is a 5-*exo*-trig ring closure via addition of the same C2 carbon to the OH group and formation of the oxazolidine ring. A following intramolecular cyclocondensation process leads to the formation of the 1,4-diazepine ring of the unusual systems **11**–**19** (Scheme 3).



Scheme 3

In conclusion, we have used zwitterionic compounds **2**–**10** in the tandem addition–cyclocondensation reactions with dimethyl acetylenedicarboxylate. This clean and fast reactions, proceeding under moderately mild conditions, led to the hitherto unknown unusual triazatricyclo[7.2.1.0^{3,8}]dodec-7-ene and triazatricyclo[8.2.1.0^{3,9}]dodec-8-ene tricyclic systems.

Melting points were determined on an Electrothermal IA9000 digital melting point apparatus and are uncorrected. The IR spectra were obtained on a Bruker IFS 48 spectrometer at r.t.. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX 500 NMR spectrometer using TMS as an internal standard. Chemical shifts are reported in ppm downfield from TMS. Yields are given for pure products.

Reaction of DMAD with Zwitterionic Compounds 2–18; General Procedure

A mixture of the corresponding zwitterionic compound **2**–**10** (1.6 mmol) and DMAD (1.6 mmol, 0.21 mL) was stirred for 40 min in refluxing MeOH (30 mL). The solvent was removed under reduced pressure and the residue was dissolved in Et_2O (5 mL) and cooled to 10 °C until the product precipitated completely. The crude products were purified by crystallisation from EtOH or hexane–toluene mixture.

9-Methyl-12-oxa-2-oxo-11-phenyl-10-thioxo-3,7,11-triazatricyclo[7.2.1.0^{3,8}]dodec-7-en-1-ylacetic Acid Methyl Ester (11)

Yield: 0.41 g (68%); yellow crystals; mp 126–127 °C.

IR (KBr): 1746 (C=O, ester), 1706 (C=O), 1657 (C=N), 1494 (C=S), 1289 (S=C–N), 1209 (C–O, ester), 1082 cm^{-1} (C–O–C).

^{1}H NMR (DMSO-d_6): δ = 7.60–7.20 (m, 5 H_{arom}), 3.70 (m, 2 H, pyrimidine ring), 3.50 (t, *J* = 5.4 Hz, 2 H, pyrimidine ring), 3.59 (s, 3 H, OCH_3), 3.27 (d, *J* = 16.8 Hz, 1 H, CH_2C=O), 3.07 (d, *J* = 16.8 Hz, 1 H, CH_2C=O), 1.91–1.70 (m, 2 H, pyrimidine ring), 1.77 (s, 3 H, CH_3C–O).

^{13}C NMR (DMSOd_6): δ = 199.3 (C=S), 166.9 (C=O, ester), 162.2 (C=O), 145.8 (N=CN), 135.3–127.6 (arom), 95.2 (O*C*C=O), 91.2 (CH_3*C*–O), 51.8 (OCH_3), 44.0 (*C*H_2N=C), 38.6 (CH_2N), 35.0 (*C*H_2C=O), 19.8 (C*C*H_2C, pyrimidine ring), 19.6 (*C*H_3C–O).

MS (EI): *m*/*z* (%) = 373 (86.9, M^+), 342 (22.4, $M^+ - 2\ CH_3 + H^+$), 273 (100, $M^+ - COCH_2CO_2CH_3 + H^+$), 240 (50.2, M^+ – PhNCS + 2 H^+), 179 (68.4, M^+ – PhNCS – CO_2CH_3), 77 (26.3, Ph).

Anal. Calcd for $C_{18}H_{19}N_3O_4S$: C, 57.90; H, 5.13; N, 11.25. Found: C, 57.93; H, 5.16; N, 11.45.

11-(4′-Chlorophenyl)-9-methyl-12-oxa-2-oxo-10-thioxo-3,7,11-triazatricyclo[7.2.1.0^{3,8}]dodec-7-en-1-ylacetic Acid Methyl Ester (12)

Yield: 0.46 g (70%); yellow crystals; mp 147–148 °C.

IR (KBr): 1752 (C=O, ester), 1698 (C=O), 1657 (C=N), 1494 (C=S), 1293 (S=C–N), 1201 (C–O, ester), 1092 cm^{-1} (C–O–C).

^{1}H NMR (DMSO-d_6): δ = 7.62 (d, *J* = 9.0 Hz, 2 H_{arom}), 7.28 (d, *J* = 9.0 Hz, 2 H_{arom}), 3.84–3.54 (m, 2 H, pyrimidine ring), 3.60 (s, 3 H, OCH_3), 3.49 (t, *J* = 5.7 Hz, 2 H, pyrimidine ring), 3.29 (d, *J* = 17.0 Hz, 1 H, CH_2C=O), 3.12 (d, *J* = 17.0 Hz, 1 H, CH_2C=O), 1.93–1.69 (m, 2 H, pyrimidine ring), 1.76 (s, 3 H, CH_3C–O).

^{13}C NMR (DMSO-d_6): δ = 199.6 (C=S), 166.9 (C=O, ester), 162.2 (C=O), 145.7 (N=CN), 134.3–129.7 (arom), 95.4 (O*C*C=O), 91.3 (CH_3*C*–O), 51.9 (OCH_3), 44.1 (*C*H_2N=C), 35.0 (CH_2N), 30.6 (*C*H_2CO), 19.8 (C*C*H_2C, pyrimidine ring), 19.7 (*C*H_3C–O).

MS (EI): *m*/*z* (%) = 408 (88.2, M^+), 374 (27.6, M^+ – SH), 308 (100, $M^+ - OCCH_2CO_2CH_3$ – H), 181 (55.4, $M^+ - ClC_6H_4NH - OCCH_2CO_2CH_3$ – H), 137 (48.2, $M^+ - ClC_6H_4NHCS - OCCH_2CO_2CH_3$ – H), 110 (30.5, pyrimidine ring + C=O).

Anal. Calcd for $C_{18}H_{18}ClN_3O_4S$: C, 53.01; H, 4.42; N, 10.31. Found: C, 52.99; H, 4.41; N, 10.15.

5,5,9-Trimethyl-12-oxa-2-oxo-11-phenyl-10-thioxo-3,7,11-triazatricyclo[7.2.1.0^{3,8}]dodec-7-en-1-ylacetic Acid Methyl Ester (13)

Yield: 0.39 g (61%); yellow crystals; mp 164–166 °C.

IR (KBr): 1750 (C=O, ester), 1717 (C=O), 1663 (C=N), 1496 (S=C), 1168 (C–O, ester), 1076 cm^{-1} (C–O–C).

^{1}H NMR (DMSO-d_6): δ = 7.55 (d, *J* = 9.0 Hz, 2 H_{arom}), 7.18 (d, *J* = 9.0 Hz, 2 H_{arom}), 3.59 (s, 3 H, OCH_3), 3.59 (d, *J* = 12.5 Hz, 1 H, pyrimidine ring), 3.31 (d, *J* = 17 Hz, 1 H, CH_2C=O), 3.25 (s, 2 H, pyrimidine ring), 3.23 (d, *J* = 12.5 Hz, 1 H, pyrimidine ring), 3.08 (d, *J* = 17 Hz, 1 H, CH_2C=O), 1.82 (s, 3 H, CH_3C–O), 0.97 (s, 3 H, CH_3), 0.84 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6): δ = 199.4 (C=S), 166.8 (C=O, ester), 162.7 (C=O), 144.7 (N=CN), 135.2–127.5 (arom), 95.3 (O*C*C=O), 91.1

(CH_3C–O), 55.8 (CH_2N=C), 51.8 (OCH_3), 48.7 (CH_2N), 35.1 (CH_2CO), 27.1 [$C(CH_3)_2$], 23.9 (CH_3), 23.0 (CH_3).

MS (EI): *m*/*z* (%) = 401 (92.6, M^+), 301 (100.0, M^+ – $COCH_2CO_2CH_3$ + H), 268 (45.0, M^+ – $COCH_2CO_2CH_3$ – S), 209 (37.5, M^+ – $PhNCOCH_2CO_2CH_3$), 193 (22.5, M^+ – PhNCS – $CH_2CO_2CH_3$).

Anal. Calcd for $C_{20}H_{23}N_3O_4S$: C, 59.83; H, 5.77; N, 10.47. Found: C, 60.10; H, 5.78; N, 10.56.

11-(4′-Chlorophenyl)-5,5,9-trimethyl-12-oxa-2-oxo-10-thioxo-3,7,11-triazatricyclo[7.2.1.0^{3,8}]dodec-7-en-1-ylacetic Acid Methyl Ester (14)

Yield: 0.45 g (65%); yellow crystals; mp 175–176 °C.

IR (KBr): 1750 (C=O, ester), 1696 (C=O), 1660 (C=N), 1450 (C=S), 1295 (S=C–N), 1205 (C–O, ester), 1094 cm^{-1} (C–O–C).

^{1}H NMR (DMSO-d_6): δ = 7.64 (d, *J* = 9.0 Hz, 2 H_{arom}), 7.22 (d, *J* = 9.0 Hz, 2 H_{arom}), 3.60 (s, 3 H, OCH_3), 3.56 (d, *J* = 12.5 Hz, 1 H, pyrimidine ring), 3.33 (d, *J* = 17 Hz, 1 H, CH_2C=O), 3.24 (s, 2 H, pyrimidine ring), 3.23 (d, *J* = 12.5 Hz, 1 H pyrimidine ring), 3.13 (d, *J* = 17 Hz, 1 H, CH_2C=O), 1.79 (s, 3 H, CH_3C–O), 0.96 (s, 3 H, CH_3), 0.83 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6): δ = 199.6 (C=S), 166.8 (C=O, ester), 162.7 (C=O), 144.6 (N=CN), 134.3– 129.4 (arom), 95.3 (O*C*C=O), 91.1 (CH_3C–O), 55.8 (CH_2N=C), 51.8 (OCH_3), 48.7 (CH_2N), 34.9 (CH_2CO), 27.1 [$C(CH_3)_2$], 23.8 (CH_3), 23.1 (CH_3).

MS (EI): *m*/*z* (%) = 436 (89.2, M^+), 336 (100.0, M^+ – $COCH_2CO_2CH_3$ + H), 303 (37.8, M^+ – $COCH_2CO_2CH_3$ – S), 209 (39.2, M^+ – $C_6H_4ClNCOCH_2CO_2CH_3$), 194 (25.3, M^+ – C_6H_4ClNCS – $CH_2CO_2CH_3$).

Anal. Calcd for $C_{20}H_{22}ClN_3O_4S$: C, 55.10; H, 5.09; N, 9.64. Found: C, 55.41; H, 4.95; N, 9.70.

11-(4′-Methoxyphenyl)-5,5,9-trimethyl-12-oxa-2-oxo-10-thioxo-3,7,11-triazatricyclo[7.2.1.0^{3,8}]dodec-7-en-1-ylacetic Acid Methyl Ester (15)

Yield: 0.41 g (60%); yellow crystals; mp 168–169 °C.

IR (KBr): 1751 (C=O, ester), 1705 (C=O), 1664 (C=N), 1511 (S=C), 1163 (C–O, ester), 1073 cm^{-1} (C–O–C).

^{1}H NMR (DMSO-d_6): δ = 7.60 (d, *J* = 9.0 Hz, 2 H_{arom}), 7.23 (d, *J* = 9.0 Hz, 2 H_{arom}), 3.60 (d, *J* = 12.5 Hz, 1 H, pyrimidine ring), 3.27 (s, 2 H, pyrimidine ring), 3.25 (d, *J* = 12.5 Hz, 1 H, pyrimidine ring), 3.62 (s, 3 H, OCH_3), 3.50 (s, 3 H, CH_3–O), 3.32 (d, *J* = 17 Hz, 1 H, CH_2C=O), 3.11 (d, *J* = 17 Hz, 1 H, CH_2C=O), 1.90 (s, 3 H, CH_3C–O), 1.02 (s, 3 H, CH_3), 0.88 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6): δ = 199.6 (C=S), 167.0 (C=O, ester), 162.9 (C=O), 145.1 (N=CN), 127.0– 135.5 (arom), 95.7 (O*C*C=O), 91.5 (CH_3C–O), 55.9 (CH_2N=C), 52.0 (OCH_3), 50.2 (OCH_3), 48.8 (CH_2N), 35.2 (CH_2CO), 27.4 [$C(CH_3)_2$], 23.8 (CH_3), 23.1 (CH_3).

MS (EI): *m*/*z* (%) = 432 (90.1, M^+), 332 (100.0, M^+ – $COCH_2CO_2CH_3$ + H), 299 (40.0, M^+ – $COCH_2CO_2CH_3$ – S), 210 [32.7, M^+ – $C_6H_4(OCH_3)NCOCH_2CO_2CH_3$], 194 [28.7, M^+ – $C_6H_4(OCH_3)NCS$, – $CH_2CO_2CH_3$].

Anal. Calcd for $C_{21}H_{25}N_3O_5S$: C, 58.45; H, 5.84; N, 9.74. Found: C, 58.70; H, 5.89; N, 9.61.

9-Methyl-12-oxa-2-oxo-11-phenyl-10-thioxo-3,7,11-triazabenzo[*e*]tricyclo[7.2.1.0^{3,8}]dodec-7-en-1-ylacetic Acid Methyl Ester (16)

Yield: 0.38 g (57%); yellow crystals; mp 212–214 °C.

IR (KBr): 1751 (C=O, ester), 1707 (C=O), 1640 (C=N), 1492 (C=S), 1291 (S=C–N), 1175 (C–O, ester), 1073 cm^{-1} (C–O–C).

^{1}H NMR (DMSO-d_6): δ = 7.27–7.55 (m, 9 H_{arom}), 5.08 (d, *J* = 16.8 Hz, 1 H, CH_2N), 4.90 (d, *J* = 16.8 Hz, 1 H, CH_2N), 3.61 (s, 3 H, OCH_3), 3.35 (d, *J* = 16.8 Hz, 2 H, CH_2C=O,), 3.13 (d, CH_2C=O, *J* = 16.8 Hz, 1 H), 1.93 (s, 3 H, CH_3C–O).

^{13}C NMR (DMSO-d_6): δ = 198.1 (C=S), 167.0 (C=O, ester), 162.0 (C=O), 145.8 (N=CN), 122–138 (arom), 95.5 (O*C*C=O), 91.0 (CH_3C–O), 52.0 (OCH_3), 41.8 (CH_2N), 35.2 (CH_2CO), 19.6 (CH_3C–O).

MS (EI): *m*/*z* (%) = 335 (46.8, M^+ – $CCH_2CO_2CH_3$ – H), 284 (37.0, M^+ – PhNHCS – H), 256 (79.4, M^+ – $CH_2CO_2CH_3$ – NHPh), 169 (99.6, quinazoline + CC=O – H), 129 (100.0. quinazoline ring – H).

Anal. Calcd for $C_{22}H_{19}N_3O_4S$: C, 62.69; H, 4.54; N, 9.97. Found: C, 62.51; H, 4.56; N, 10.00.

11-(4′-Chlorophenyl)-9-methyl-12-oxa-2-oxo-10-thioxo-3,7,11-triazabenzo[*e*]tricyclo[7.2.1.0^{3,8}]dodec-7-en-1-ylacetic Acid Methyl Ester (17)

Yield: 0.45 g (62%); pale yellow crystals; mp 231–232 °C.

IR (KBr): 1752 (C=O, ester), 1707 (C=O), 1641 (C=N), 1492 (C=S), 1292 (S=C–N), 1175 (C–O, ester), 1073 cm^{-1} (C–O–C).

^{1}H NMR (DMSO-d_6): δ = 7.57–7.24 (m, 8 H_{arom}), 5.10 (d, *J* = 16.8 Hz, 1 H, CH_2N), 4.92 (d, *J* = 16.8 Hz, 1 H, CH_2N), 3.61 (s, 3 H, OCH_3), 3.37 (d, *J* = 16.8 Hz, 2 H, CH_2C=O), 3.12 (d, *J* = 16.8 Hz, 1 H, CH_2C=O), 1.93 (s, 3 H, CH_3C–O).

^{13}C NMR (DMSO-d_6): δ = 198.0 (C=S), 166.8 (C=O, ester), 161.9 (C=O), 145.7 (N=CN), 137.3–122.3 (arom), 95.4 (O*C*C=O), 90.9 (CH_3C–O), 51.9 (OCH_3), 41.7 (CH_2N), 35.0 (CH_2CO), 19.5 (CH_3C–O).

MS (EI): *m*/*z* (%) = 370 (50.5, M^+ – $CCH_2CO_2CH_3$ – H), 284 (40.6, M^+ – $C_6H_4ClNHCS$ – H), 256 (82.3, M^+ – $CH_2CO_2CH_3$ – NHC_6H_4Cl), 169 (84.4, quinazoline + CC=O – H), 129 (100.0, quinazoline ring – H).

Anal. Calcd for $C_{22}H_{18}ClN_3O_4S$: C, 57.96; H, 3.98; N, 9.22. Found: C, 58.07; H, 4.12; N, 9.03.

10-Methyl-13-oxa-2-oxo-12-phenyl-11-thioxo-3,8,12-triazatricyclo[8.2.1.0^{3,9}]tridec-8-en-1-ylacetic Acid Methyl Ester (18)

Yield: 0.44 g (65%); yellow crystals; mp 151–152 °C.

IR (KBr): 1743 (C=O, ester), 1710 (C=O), 1658 (C=N), 1498 (C=S), 1290 (S=C–N), 1209 (C–O, ester), 1085 cm^{-1} (C–O–C).

^{1}H NMR (DMSO-d_6): δ = 7.55–7.18 (m, 5 H_{arom}), 3.76 (m, 2 H, diazepine ring), 3.52 (m, 2 H, diazepine ring), 3.60 (s, 3 H, OCH_3), 3.25 (d, *J* = 16.8 Hz, 1 H, CH_2C=O), 3.05 (d, *J* = 16.8 Hz, 1 H, CH_2C=O), 1.96–1.80 (m, 4 H, diazepine ring), 1.76 (s, 3 H, CH_3C–O).

^{13}C NMR (DMSO-d_6): δ = 199.4 (C=S), 167.0 (C=O, ester), 162.4 (C=O), 145.6 (N=CN), 135.3–127.6 (arom), 95.1 (O*C*C=O), 91.0 (CH_3C–O), 51.7 (OCH_3), 44.2 (CH_2N=C), 38.5 (CH_2N), 35.0 (CH_2CO), 20.0 (CH_2, diazepine ring), 19.8 (CH_2, diazepine ring), 19.6 (CH_3C–O).

MS (EI): *m*/*z* (%) = 387 (78.2, M^+), 286 (100, M^+ – $COCH_2CO_2CH_3$ + H^+), 254 (45.6, M^+ – PhNCS + 2 H^+) 193 (52.8, M^+ – PhNCS – CO_2CH_3), 77 (20.1, Ph).

Anal. Calcd for $C_{19}H_{21}N_3O_4S$: C, 58.90; H, 5.46; N, 10.85. Found: C, 59.06; H, 5.55; N, 10.74.

12-(4′-Chlorophenyl)-13-oxa-2-oxo-10-methyl-11-thioxo-3,8,12-triazatricyclo[8.2.1.0^{3,9}]tridec-8-en-1-ylacetic Acid Methyl Ester (19)

Yield: 0.46 g (68%); yellow crystals; mp 174–175 °C.

IR (KBr): 1751 (C=O, ester), 1700 (C=O), 1658 (C=N), 1490 (C=S), 1294 (S=C–N), 1200 (C–O, ester), 1090 cm^{-1} (C–O–C).

^{1}H NMR (DMSO-d_6): δ = 7.60 (d, J = 9.0 Hz, 2 H_{arom}), 7.27 (d, J = 9.0 Hz, 2 H_{arom}), 3.76 (m, 2 H, diazepine ring), 3.52 (m, 2 H, diazepine ring), 3.60 (s, 3 H, OCH_3), 3.24 (d, J = 16.8 Hz, 1 H, CH_2C=O), 3.03 (d, J = 16.8 Hz, 1 H, CH_2C=O), 1.96–1.80 (m, 4 H, diazepine ring), 1.75 (s, 3 H, CH_3C–O).

^{13}C NMR (DMSO-d_6): δ = 199.6 (C=S), 166.9 (C=O, ester), 162.3 (C=O), 145.5 (N=CN), 135.8–129.2 (arom), 95.1 (OCC=O), 91.0 (CH_3C–O), 51.7 (OCH_3), 44.1 (CH_2N=C), 38.5 (CH_2N), 35.0 (CH_2CO), 20.0 (CH_2, diazepine ring), 19.8 (CH_2, diazepine ring), 19.6 (CH_3C–O).

MS (EI): m/z (%) = 421 (80.1, M^+), 319 (100, $M^+ - OCCH_2CO_2CH_3 - H$), 192 (43.8, $M^+ - ClC_6H_4NH - OCCH_2CO_2CH_3 - H$), 148 (47.8, $M^+ - ClC_6H_4NHCS - OCCH_2CO_2CH_3 - H$).

Anal. Calcd for $C_{19}H_{20}ClN_3O_4S$: C, 54.09; H, 4.78; N, 9.96. Found: C, 54.21; H, 4.65; N, 10.04.

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(13) Compound **11** with formula $C_{18}H_{19}N_3O_4S$ crystallises in the triclinic system, space group $P\bar{1}$, with unit cell parameters a = 8.8020 (2), b = 10.1138 (2), c = 11.1187 (2) Å, α = 74.932 (1), β = 75.122 (1), γ = 74.018 (1)°, V = 900.36 (3) Å^3, Z = 2. A total of 4115 independent reflections [R(int) = 0.0278] were collected on a sample (size 0.3 × 0.2 × 0.15 mm) using KappaCCD diffractometer and MoKα radiation. The structure was solved by direct methods with SHELXS97[14] and refined by the full-matrix least-squares method on F^2 using SHELXL97[15] program. Final discrepancy indices for $I > 2\sigma(I)$ were equal $R1$ = 0.0573, w$R2$ = 0.1048 and $R1$ = 0.091, w$R2$ = 0.1642 for all data. The final difference Fourier map of electron density had the largest peak and hole of 0.61 and –0.305 e·Å^{-3}, respectively. All calculations and molecular graphics were done using the WinGX package.[16] The structural data were deposited at the Cambridge Crystallographic Data Centre. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html, or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 (1223)336033; e-mail: deposit@ccdc.cam.ac.uk, under reference number CCDC 720638

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