DICHOTOMY IN THE RING OPENING REACTION OF 5-[(2-FURYL)METHYLIDENE]-2,2-DIMETHYL-1,3-DIOXANE-4,6-DIONE WITH CYCLIC SECONDARY AMINES

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5-[(2-Furyl)methylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**1a**) treated with equimolar amount of pyrrolidine or hexahydroazepine afforded 5-(pyrrolidine)- (**2a**) or 5-[(hexahydroazepine-1-yl)-2-hydroxypenta-2,4-dien-1-ylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**2d**). Their treatment with hydrobromic acid led to cyclization and formation of stable 5-cyclopentenyl-4*H*-1,3-dioxine hydrobromides (**3a**, **3d**). Under the same conditions **1a** treated with morpholine or piperidine yielded a mixture of **2b**, **3b** and **2c**, **3c**, respectively. The corresponding 3-substituted furans **1b**–**1e** gave only substituted 5-cyclopentenyl-4*H*-1,3-dioxines (**3e**–**3i**). The use of an excess amine in reaction with **1a** yielded unexpectedly 5-(3,5-dihetaryl-cyclopent-2-en-1-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-diones (**9a–9c**) and 5-[5-hexahydroazepin-1-ium-1-ylidene-2-(hexahydroazepin-1-yl)cyclopent-1-en-1-yl]-2,2-dimethyl-4-oxo-4*H*-1,3-dioxin-6-olates (**10**).

Key words: Substituted Meldrum's acids; 4*H*-1,3-Dioxines; Cyclopentenones; Furans; Amides; Ring opening; Cyclizations; Crystal structure; Reaction mechanisms.

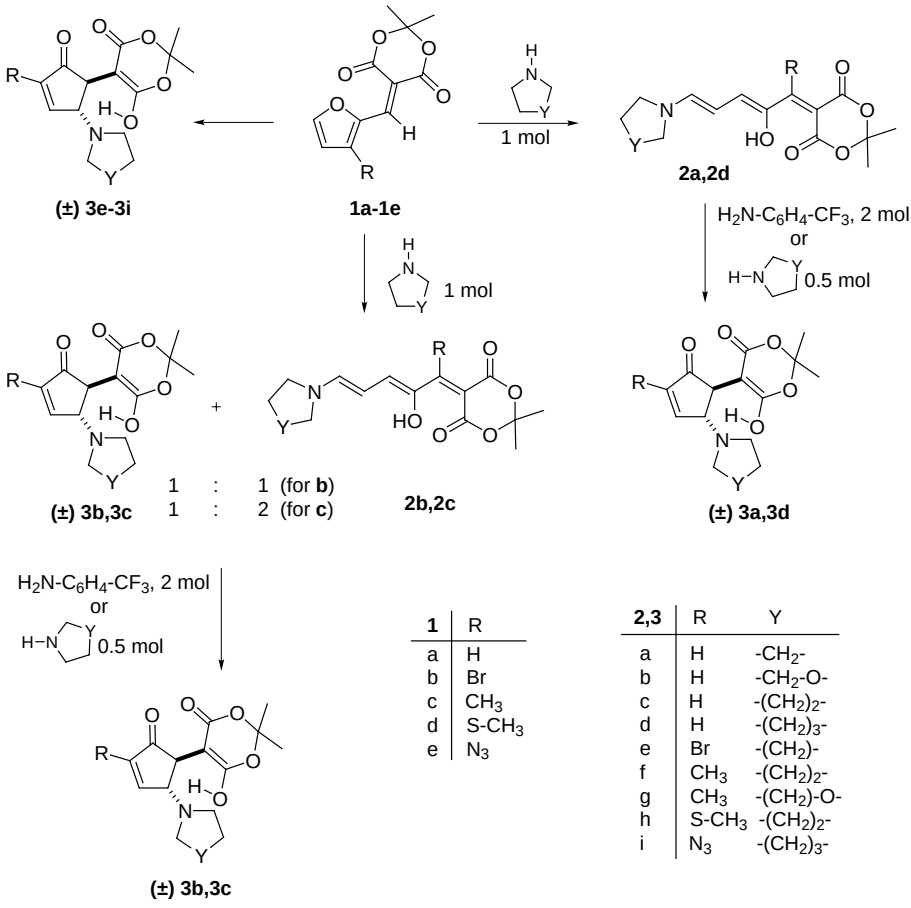
Furans have proved to be useful precursors for a wide variety of cyclopentenones, compounds present in numerous natural products[1,2]. The most promising aspects of furan chemistry concern cleavage reactions. The ring-opening reactions of furan derivatives with acids[3] and amines[4] have

been extensively investigated by a number of authors. The products of these reactions are usually 1,4-bifunctional alkenes. On the other hand, 2,4- or 4,5-disubstituted cyclopenten-1-one can be obtained as a product of the reaction of two molecules of a primary aromatic amine with one molecule of furan-2-carbaldehyde[5]. The reaction of furan-2-carbaldehyde with three or four molecules of aniline gives 1,6-dianilino-4-phenyl-7-(phenylimino)-3a,4,4a,7,7a,7b-hexahydro-1*H*-dicyclopenta[*b*,*d*]pyrrol-2(3*H*)-one. By contrast, in the ring-opening reactions with aromatic or secondary cyclic amines, only a few furylethylenes have yet been studied[6–8].

The aim of the present study was to investigate the reaction of activated furans with cyclic secondary amines. We report the synthesis of a new type of substituted cyclopentenes starting from easily accessible 5-[(2-furyl)-methylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**1a**). We have found that the composition of the products of the reaction of furan **1a** with secondary cyclic amines depends on the type and amounts of the amine used. For example, the reaction of furan **1a** with an equimolar amount of pyrrolidine and hexahydroazepine gave substituted 5-(aminopenta-2,4-dien-1-ylidene)-1,3-dioxane-4,6-diones **2a** and **2d**, respectively. In case of morpholine or piperidine, mixtures of **2b** and **3b** or **2c** and **3c**, respectively, were obtained. On the other hand, treatment of furan **1a** with 1.5 molar excess of amine afforded substituted 5-(cyclopent-3-en-1-yl)-4*H*-1,3-dioxin-4-ones (**3a**–**3d**). The use of high excess of amines gives a new type of substituted cyclopentenes **9a**–**9c** and **10**.

RESULTS AND DISCUSSION

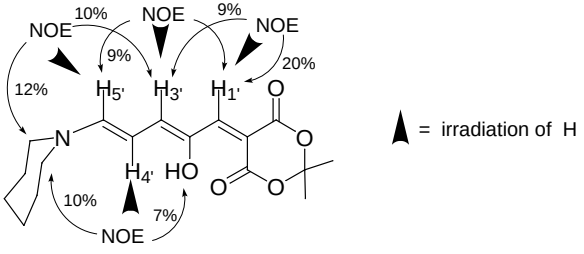
When the reaction between furan **1a** and pyrrolidine was carried out under the condition used by Lewis and Mulquiney[5b] in the 2 : 1 or 1 : 1 molar ratio, we were able to isolate from the reaction mixture high yields of a red crystalline compound. On the basis of ^{1}H and ^{13}C NMR spectra we assigned this product the structure of 5-[2-hydroxy-5-(pyrrolidin-1-yl)penta-2,4-dien-1-ylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**2a**). The presence of the CH=CH–CH=C system is supported by the fact, that the two –CH= protons and the methylidene proton constitute a three spin AMX pattern. A rather large coupling constant between the two –CH= protons suggests the *trans* configuration on the C=C bond. The *trans* configuration was also confirmed by a nuclear Overhauser effect experiment (Fig. 1). The same result was obtained by heating of **1a** with hexahydroazepine. Whereas the reaction of furan **1a** with pyrrolidine and hexahydroazepine afforded pure 5-aminopenta-2,4-dien-1-ylidenes (**2a** and **2d**, respectively), the use of



1	R
a	H
b	Br
c	CH_3
d	S-CH_3
e	N_3

2,3	R	Y
a	H	-CH_2-
b	H	-CH_2-O-
c	H	-$(CH_2)_2$-
d	H	-$(CH_2)_3$-
e	Br	-(CH_2)-
f	CH_3	-$(CH_2)_2$-
g	CH_3	-(CH_2)-O-
h	S-CH_3	-$(CH_2)_2$-
i	N_3	-$(CH_2)_3$-

SCHEME 1

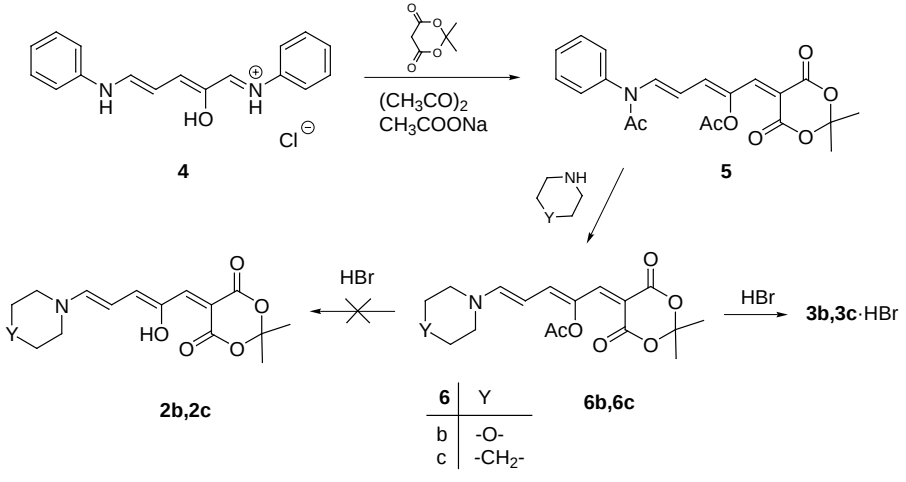


2d

FIG. 1
DIFNOE ^{1}H NMR experiment of compound **2d**

morpholine or piperidine in the 2 : 1 or 1 : 1 molar ratio resulted in formation of a mixture of two compounds; the product of ANRO (addition of nucleophile followed by a ring opening) **2b** and ANRORC (addition of nucleophile, ring opening and ring closure) **3b** (the **2b**/**3b** ratio 1 : 1, the **2c**/**3c** ratio 2 : 1; both from ^{1}H NMR) (Scheme 1). All attempts to separate this mixture were unsuccessful. While prolongation of the reaction time and higher temperature influenced the ratio of **2b**/**3b** only negligibly, the change of solvent gave higher yields of the mixture (acetone 78–87%, acetonitrile 77–86%, ethyl acetate 80–89%, toluene 90–95%). It seems possible that the reaction forming a compound of either structure of **2** and **3** might be a function of the basicity of the amine used; weaker bases forming a mixture of **2** and **3**, while stronger bases gave only open-chain structures **2**.

We assume that compounds **2b** and **2c** can be obtained by the reaction of *N*-(5-anilino-2-hydroxypenta-2,4-dien-1-ylidene) aniline hydrochloride (**4**, Stenhouse salt) with 2,2-dimethyl-1,3-dioxane-4,6-dione (Meldrum′s acid) in a mixture of sodium acetate and acetic anhydride, giving 5-[2-acetoxy-5-*N*-(phenylacetamido)penta-2,4-dien-1-ylidene]-2,2-dimethyl -1,3-dioxane-4,6-dione (**5**) and by its subsequent nucleophilic substitution with morpholine or piperidine. However, attempts to prepare **2b** and **2c** by hydrolysis of the respective *O*-acetyl derivatives (**6b** and **6c**) failed. Instead, the reaction gave hydrobromides of **3b** and **3c** in low to moderate yields (Scheme 2). When 3-substituted furan derivatives **1b**–**1e**, which can be easily prepared from the corresponding 3-substituted 2-furancarbaldehydes by treatment with Meldrum's acid, reacted with cyclic secondary amines in



SCHEME 2

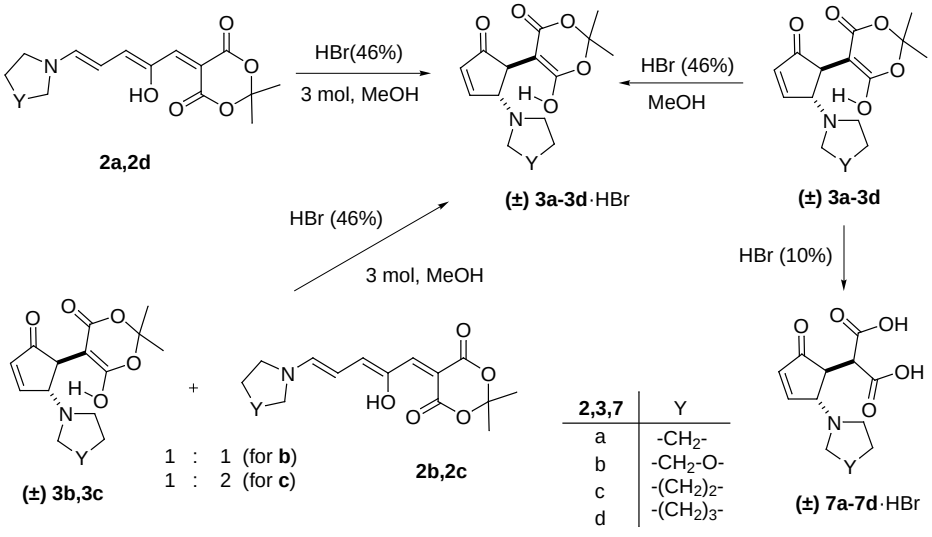
methanol solution, 1,2,3,4-tetrasubstituted cyclopentenes **3e**–**3i** were formed. However, no opened form of the furan ring could be isolated (Scheme 1).

It is apparent from Scheme 1, that 5-aminopenta-2,4-dien-1-ylidene compounds **2a** and **2d** can serve as stable, open-chain intermediates, the cyclization of which leads to cyclopentenes **3a** and **3d**, respectively. In an attempt to support this assumption or to find appropriate conditions for cyclization, a survey of reactions of various cyclic secondary and aromatic amines and mineral acids was carried out under various conditions. Initial attempts to convert **2a** and **2d** to **3a** and **3d**, respectively, in neutral condition (reflux in methanol for 2–48 h) led to the recovery of the starting material. The base-catalyzed cyclization using tertiary amines was also unsuccessful. On the other hand, reaction of **2a** with pyrrolidine in a 2 : 1 molar ratio gave a good yield of **3a**. Surprisingly, treatment of **2a** with piperidine or morpholine resulted in the formation of a mixture of the expected cyclopentene **3a**, together with a small amount of unexpected compound **3b** (using morpholine as a base) or **3c** (using piperidine as a base). We assume that the cyclopentene **3a** underwent a β-elimination of the pyrrolidine ring to form cyclopentadienone[5d] which, in turn, adds piperidine or morpholine to form **3b** or **3c**. Attempts to separate these mixtures were unsuccessful, due to the solubility problems with **3**. The same results were obtained in the reaction of **2d**. Out of aromatic amines used, the best results were obtained with 4-(trifluoromethyl)aniline, but the amine has to be used in the 1 : 2 molar ratio. The reaction between furan **1a** and 4-(trifluoromethyl)aniline afforded only pure **3a**–**3d**, no formation of the 5-[4-(trifluoromethyl)anilino]cyclopentene was observed.

When **2a** was refluxed in methanol containing one drop of a mineral acid for 15 min, a low yield of **3a** was obtained. On the other hand, addition of excess mineral acids to the refluxed mixture of **2a** caused an immediate precipitation of the insoluble cyclopentene hydrobromide **3a** (Scheme 3). The best results were obtained with 46% hydrobromic acid (hydrochloric or sulfuric acid gave a mixture of products, acetic acid did not react with **2a**). Similarly, reaction of **2d** with hydrobromic acid gave cyclopentene hydrobromide **3d**.

It was interesting to examine the cyclization reaction of the corresponding mixtures of **2b**, **3b** and **2c**, **3c** under similar conditions to those used with 5-aminopenta-2,4-dien-1-ylidene derivatives **2a** and **2d**. Thus, a mixture of **2b**, **3b** heated with morpholine in a 2 : 1 molar ratio in methanol afforded the corresponding cyclopentene **3b** in good yield. Under these conditions a mixture of **2c**, **3c** reacts similarly with piperidine to provide **3c**

(Scheme 1). In all cases, only one product was isolated from the reaction mixture. It was shown that a mixture of **2b**, **3b** and **2c**, **3c** can be used for the preparation of cyclopentene hydrobromide **3b**, **3c**, too. When a mixture of **2b**, **3b** or **2c**, **3c** was refluxed in methanol containing 3 moles of hydrobromic acid, after a few minutes solely the corresponding cyclopentene hydrobromide **3b** or **3c** was formed. In the presence of hydro-

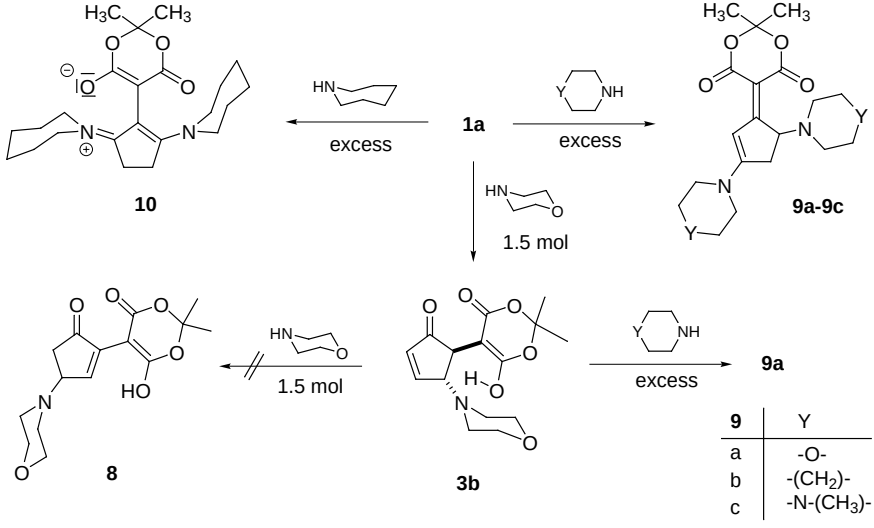


SCHEME 3

bromic acid, a methanolic solution of the cyclopentenes **3a**–**3d** gave the corresponding cyclopentene hydrobromides **3a**–**3d** in good yield, too (Scheme 3). On the other hand, it has been found that the results of the reaction of **3a**–**3d** with hydrobromic acid are strongly dependent on the nature of the solvent. While the reaction of **3a**–**3d** with hydrobromic acid in methanol resulted in the formation of cyclopentenone hydrobromides **3a**–**3d**, treatment with 10% hydrobromic acid afforded substituted malonic acid hydrobromides **7a**–**7d** (Scheme 3). The coupling constants (3.1–3.7 Hz) between H-1′and H-5′ in **3a**–**3d** or **7a**–**7d** clearly show the *trans* configuration and a significant nuclear Overhauser effect (0%) between H-1′and H-5′ indicates a trans relationship of these protons in space. The configuration of 1,3-dioxane-4,6-dione or 4*H*-1,3-dioxin-4-one ring in **3a**–**3d** was confirmed by ^{1}H and ^{13}C NMR (ref.[9]). In the ^{1}H NMR spectra of compounds **3a**–**3d**, the signals of H-5 protons are absent, whereas in the 1,3-dioxane ring the signal of H-5 at 3.5–3.8 ppm is present. Likewise in ^{13}C NMR spec-

trum of **3a**–**3d**, the signals of carbon C-5 at 65–75 ppm are present at a higher field as a quartet, whereas in the 1,3-dioxane ring the carbon C-5 at 45–50 ppm is represented by doublets. Therefore we assume that the 1,3-dioxane-4,6-dione ring exists in the enol form as 4*H*-1,3-dioxin-4-one due to interaction between the amine nitrogen lone pair and hydroxy group of the 4*H*-1,3-dioxine ring.

It is known that 2,4-diarylaminocyclopentenone derivatives are more stable structures than their 4,5-disubstituted isomers. Those 4,5-isomers can by converted to the more stable 2,4-isomers in a reaction with amines. On the contrary, in our reactions **1a** treated with cyclic secondary amines produced only compounds **3**. Therefore, we attempted to carry out the transformation of cyclopentene **3b** to his isomer **8** (Scheme 4). For this transformation, different temperatures and molar ratios of amines were used. In all cases, when **3b** was heated in methanol containing a small excess of morpholine, only the starting compound was obtained. On the



SCHEME 4

other hand, heating of **3b** in an excess of morpholine provided low yield of a new crystalline compound (Scheme 4). ^{1}H NMR spectrum of this compound revealed the presence of two morpholine rings, which were proved by a singlet at 6.93 ppm (1 H), by the presence of one doublet of doublet with chemical shifts 2.68 ppm (1 H) and by one sharp doublet with chemical shifts 2.96 ppm (1 H), respectively (both doublets showed a large cou-

pling typical of the protons of an ABX system). Spin decoupling experiments indicated that the X proton absorbs as a doublet (1 H) with chemical shifts 4.98 ppm. ^{13}C NMR spectrum confirmed the presence of the 1,3-dioxane-4,6-dione ring but not that of a conjugated C=O group (≈200 ppm). As a result, the structure of 5-[3,5-(dimorpholinocyclopent-2-en-1-ylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**9a**) was assigned to this product. The full molecular structure of compound **9a** was further confirmed by X-ray analysis (Table I, Fig. 2). Further experiments showed, that when an excess of morpholine acts on the starting compound **1a**, it reacts in the same way, forming **9a** in a 68% yield. Similar results were obtained in the reaction of furan **1a** with excess of piperidine or 1-methylpiperazine yielding compounds **9b** and **9c**, respectively (Scheme 4). Attempts to prepare a substituted cyclopentene compound by the reaction of furan **1a** with pyrrolidine failed. A considerable difference in reactivity of furan **1a** with hexahydroazepine was observed. Instead of the desired 5-[3,5-di(hexahydroazepin-1-yl)cyclopent-2-en-1-ylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione, we obtained a new type of 1,2,3-trisubstituted cyclopentene, which was identified as the 5-[5-hexahydroazepin-1-ium-1-ylidene-2-(hexahydroazepin-1-yl)cyclopent-1-en-1-yl]-2,2-dimethyl-4-oxo-4*H*-1,3-dioxin-6-olate (**10**), represented by a mesomeric structure (Scheme 5). The full molecular structure of compound **10** was confirmed by X-ray analysis (Table I, Figs 3, 4).

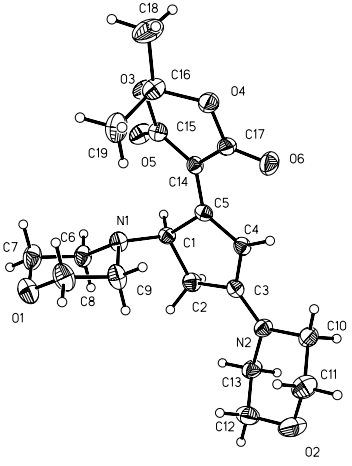
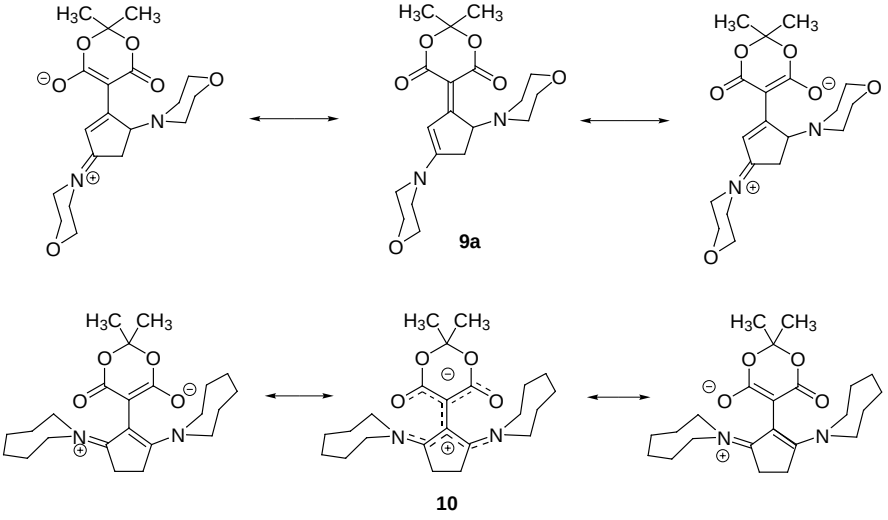


FIG. 2
The molecular structure of **9a** with the 50% probability displacement ellipsoids



SCHEME 5

TABLE I
Crystal data of compounds **9a** and **10**

	9a	**10**
Empirical formula	$C_{19}H_{30}N_2O_8$	$C_{46}H_{68}N_4O_8$
Color; habit	yellow needles	colorless needles
Crystal size, mm	0.35 × 0.48 × 0.55	0.20 × 0.05 × 0.05
Crystal system	tetragonal	monoclinic
Space group	$I4_1/a$ (No.88)	*Pc* (No.7)
Unit cell dimensions		
a, Å	27.033(5)	7.409(2)
b, Å	27.033(5)	27.403(6)
c, Å	11.492(4)	10.468(2)
β, °		90.87(3)
Volume, Å^3	8 398(3)	2 124.9(7)
Z	16	2
Formula weight, g mol^{-1}	414.51	805.07
Density (calculated), g cm^{-3}	1.311	1.258
Absorption coefficient, mm^{-1}	0.063	0.049
F(000)	3 552	872

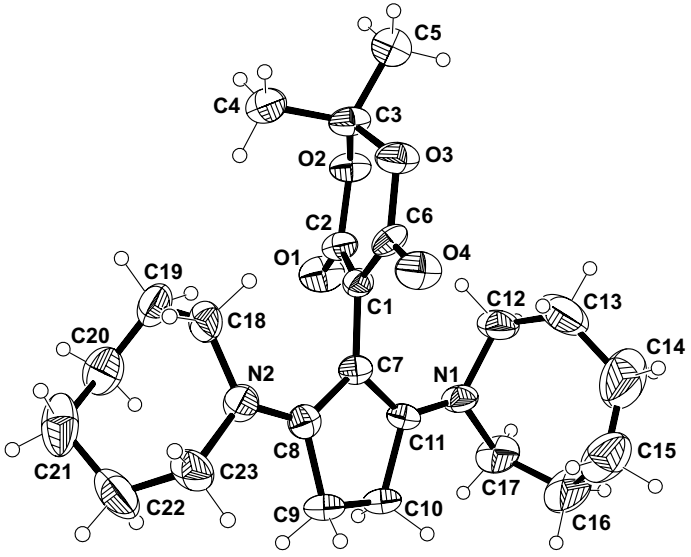


FIG. 3
The molecular structure of one molecule of **10** with the 50% probability ellipsoids

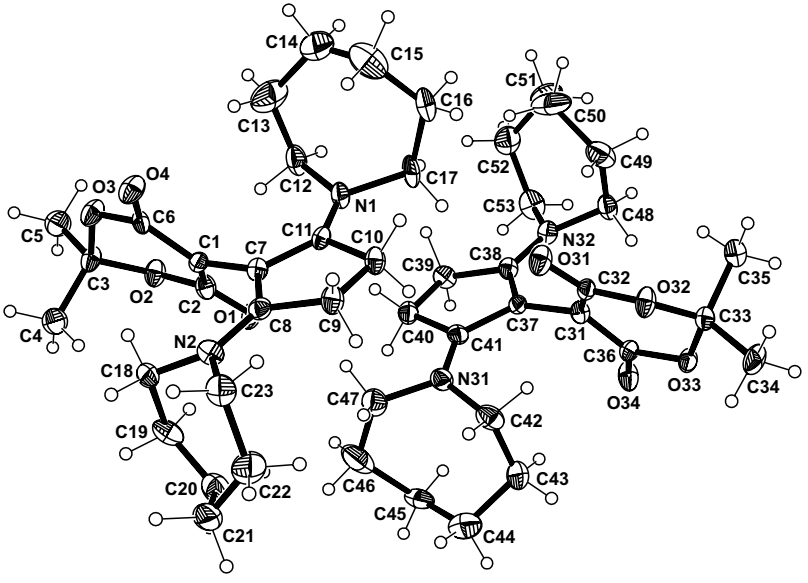
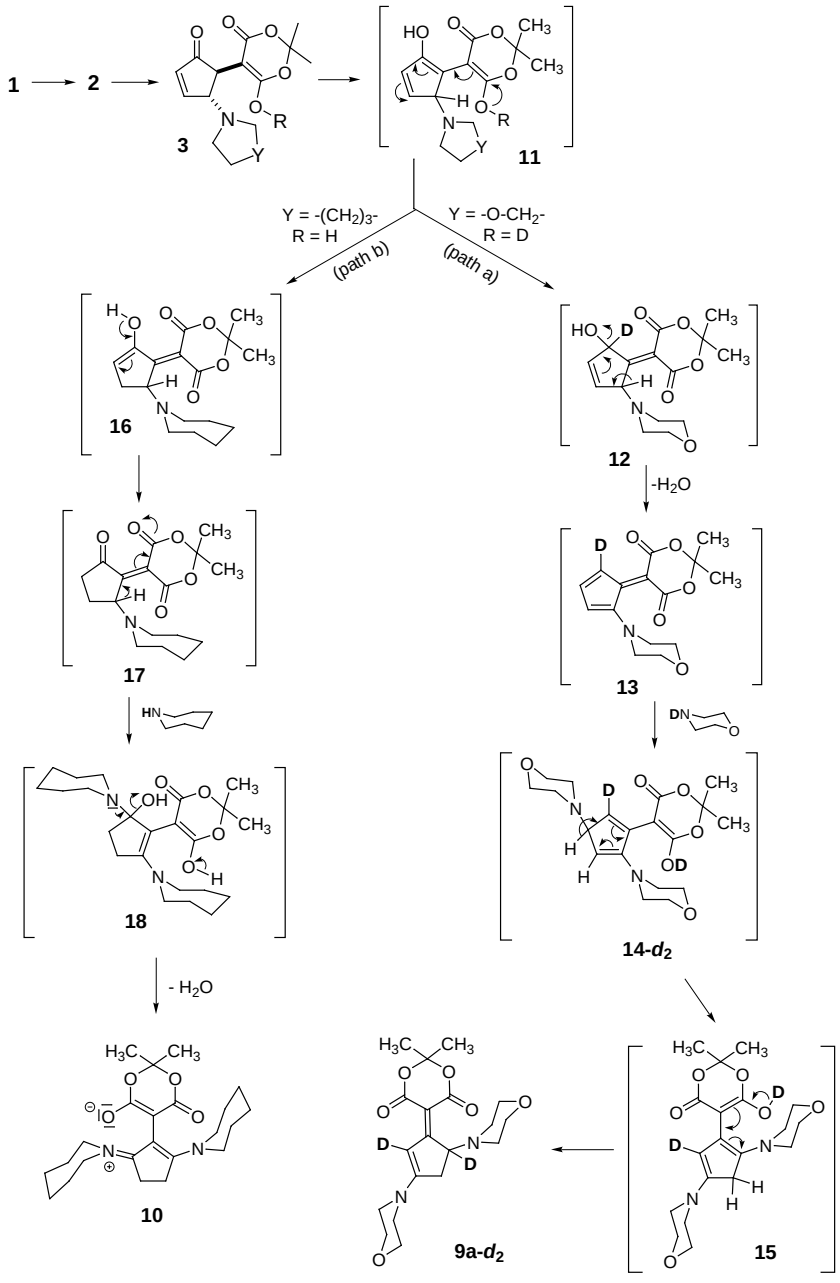
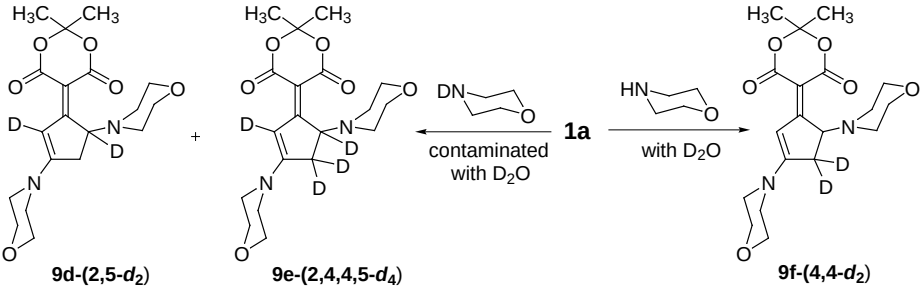


FIG. 4
The molecular structure of **10** with the 30% probability ellipsoids

The reaction between furan **1a** with excess of cyclic secondary amines is evidently a complex one and we can only speculate on its course. We presume that the first reaction step is the attack of the amine on position 5 of the furan ring, as has been suggested in related cases[8,10], followed by formation of the intermediate 5-morpholino-(**2b**) or 5-(hexahydroazepin-1-yl-2-hydroxypenta-2,4-dien-1-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (**2d**) – a compound which represents probably the first stable free base of a substituted Stenhouse salts described so far. Basic cyclization of the intermediate **2b** or **2d** to give the 5-substituted (cyclopent-3-en-1-yl)-4*H*-1,3-dioxin-4-one (**3b** or **3d**) follows (Scheme 1). The next step is the reaction of the formed enol **11**, which could be the starting intermediate for the formation of **9** (path a) or **10** (path b) (Scheme 6). The increase in bulkiness of the used cyclic amines causes the reaction to take different course, leading to the intermediate **12** and **16**, respectively. The relatively unhindered morpholine removes the α-proton from the carbon C-5, the molecule then loses one molecule of water, giving the cyclopentadienylidene derivative **13** (path a). Morpholine then adds to the conjugated system to form the double allylic system **14**; finally an intramolecular transfer of proton in **15** takes place to form **9a-d_2**. On the other hand, the bulky hexahydroazepine probably cannot remove the α-proton with the subsequent loss of water (path b). An intramolecular transfer of proton leads to the formation of cyclopentanone **17**. Addition of another molecule of hexahydroazepine to form enamine **18** and finally elimination of molecule of water leads to the formation of the stable mesomeric compound **10** (Scheme 6). This assumption was confirmed by independent reaction of **1a** with 4-deuteriomorpholine[13]. To our surprise, this reaction afforded in addition to the expected **9d-(2,5-d_2)** also the tetradeuterioproduct **9e-(2,4,4,5-d_4)**. This product might be formed by the reaction of **9d-(2,5-d_2)** with D_2O, present in the reaction mixture. Such reactions of substituted cyclopent-2-enones with D_2O leading to substituted cyclopent-2-enones-d_2 are common[5a]. Evidence supporting this formula was obtained by the reaction of **1a** with excess of morpholine containing D_2O (99.8%) (Scheme 7). The 5-(3,5-dimorpholinocyclopent-2-en-1-ylidene)(4,4-d_2)-2,2-dimethyl-1,3-dioxane-4,6-dione [**9f-(4,4-d_2)**] which was obtained in 46% yield was shown to have both deuterium atoms in position 4 of the cyclopentene ring. In the ^{1}H NMR spectrum of **9f-(4,4-d_2)** the doublet at 2.96 and doublet of doublet at 2.68 ppm were completely lacking while the remaining signal at 4.98 ppm showed the expected simplification to singlet. In the ^{1}H NMR spectrum of **9d-(2,5-d_2)** the singlet at 6.93 and doublet at 4.98 ppm were completely lacking while the remaining


1
2
3
11
Y = -(CH2)3-
R = H
(path b)
Y = -O-CH2-
R = D
(path a)
16
12
-H2O
17
13
18
14-d2
- H2O
10
9a-d2
15

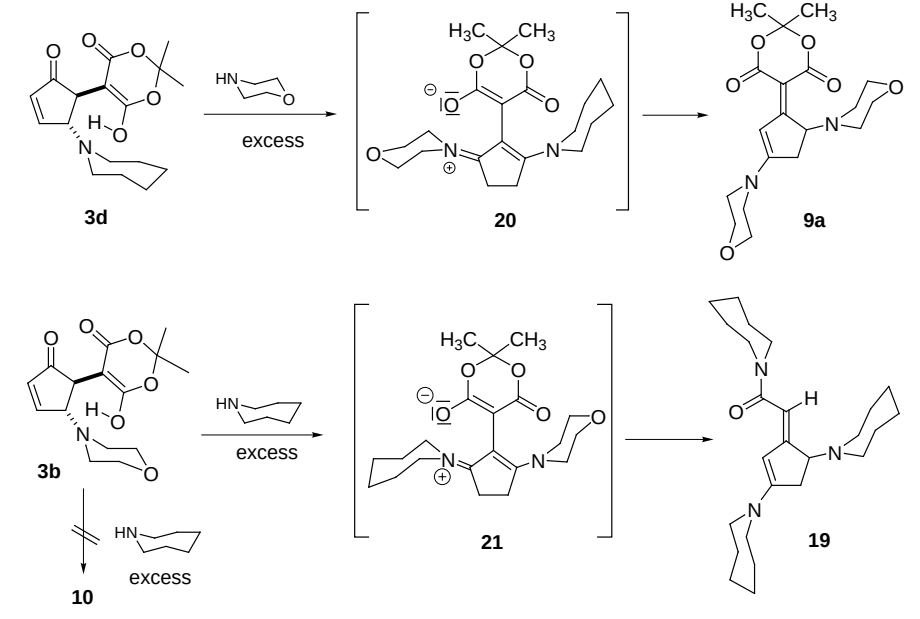
SCHEME 6



SCHEME 7

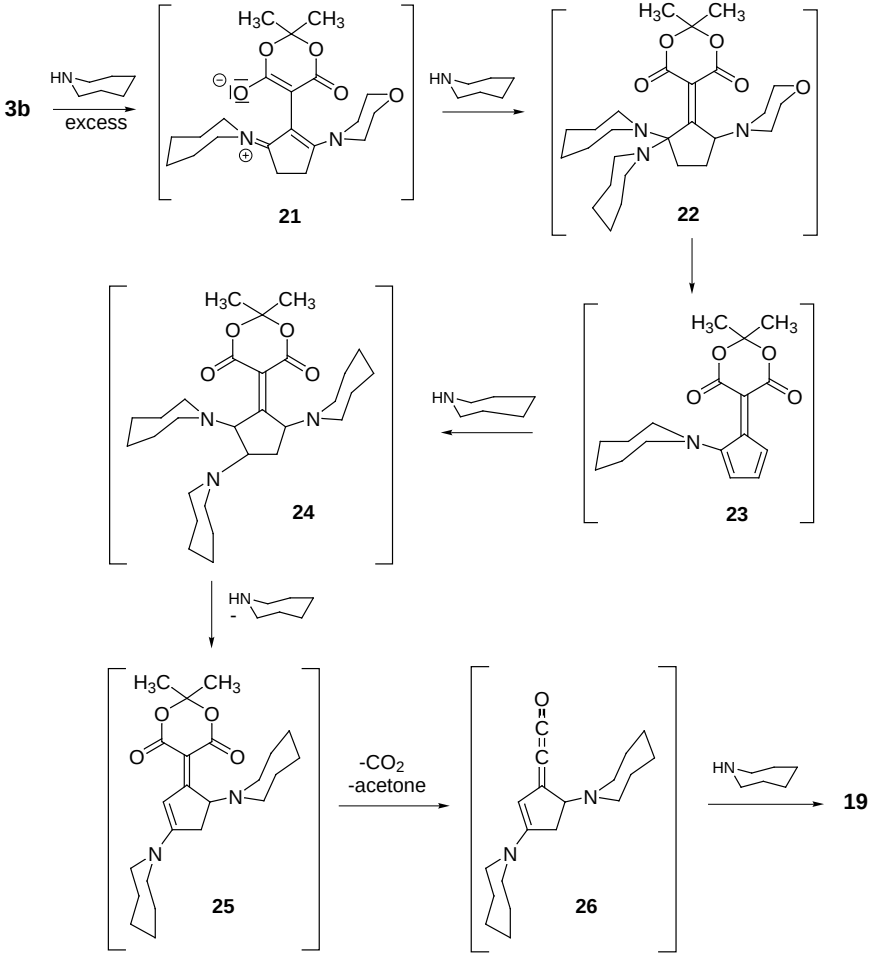
doublet of doublet and doublet at 2.68 ppm showed the expected simplification to two doublets.

We carried out a cross-experiment of isolated intermediates **3b** and **3d** with hexahydroazepine and morpholine, respectively. While cyclopentene **3d** in reaction with morpholine yielded **9a**, cyclopentene **3b** with hexahydroazepine afforded substituted amide **19**, instead of the expected mesomeric compound **10** (Scheme 8). The probable mechanism for the for-



SCHEME 8

mation of **19** is outlined in Scheme 9. We suppose, that cyclopentene **3b** would react with hexahydroazepine analogously to the Scheme 6 (path b), however under the formation of the mesomeric intermediate **21** (Scheme 9).



SCHEME 9

The next step involves the addition of hexahydroazepine to the iminium C=N double bond under formation of the aminal **22**. The subsequent loss of two molecules of amine results in the formation of the diene **23**. Reaction with another molecules of hexahydroazepine gives compound **25**. The final product, amide **19**, is formed by addition of an amine to substituted ketene **26**. This reaction has been already observed[9b]. It is possible, that the

compounds **10** carrying in positions 2 and 5 the corresponding amines represent intermediates in the reaction between **1a** and cyclic secondary amines. The solubility of the intermediate seems to be the discriminating factor, for piperidine and morpholine both give soluble, and hence reactive intermediates, whereas hexahydroazepine gives an insoluble intermediate, the precipitation of which stops any further reaction. In an attempt to prove this claim compound **10** was heated at 95 °C for 48 h with an excess of piperidine and morpholine, respectively. No reaction was observed, due to insolubility of the starting compound **10**.

The substituted cyclopentenes **9** and **10** were evidently formed from one molecule of furan **1a** and two molecules of the corresponding cyclic secondary amine. However, the 1 : 2 molar ratio of furan **1a** to the amines is not sufficient and further experiments showed that amines have to be used as solvents for this reaction to occur.

When 3-substituted furan derivatives **1b**–**1e** were treated in neat amines, no formation of substituted cyclopentenes **9** or **10** occurred, even after prolonged heating.

In conclusion, this study shows that 5-[(2-furyl)methylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**1a**) reacts with cyclic secondary amines in a multitude of ways. The products of these reactions depends on the type and amounts of the amines used. These reactions allowed us to prepare tri- or tetrasubstituted cyclopentene rings utilizing ring opening of the furan in a one-pot process.

EXPERIMENTAL

The melting points were determined on a Kofler block Boetius and are uncorrected. Infrared spectra (wavenumbers in cm^{-1}) were recorded on a PU 9800 FTIR Philips analytical spectrometer, calibrated with polystyrene foil, using KBr technique (0.3 mg of compound/300 mg KBr). Electron impact mass spectra were determined on an AEI Manchester MS 902S mass spectrometer with direct inlet at an ionization electron energy of 70 eV. Microanalyses were performed using a Carlo–Erba 1102 elemental analyser. ^{1}H NMR (300 MHz) and ^{13}C NMR (75.05 MHz) spectra were obtained with a Varian VXR-300 instrument at 25 °C in hexadeuteriodimethyl sulfoxide with tetramethylsilane as internal standard. Chemical shifts are given in ppm (δ-scale), coupling constants (*J*) in Hz. The purity of the products and the reaction course were monitored by TLC sheets F-254 (Merck), detection being made with iodine vapours and UV light. 5-[(2-Furyl)methylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**1a**) was prepared according to ref.[12], 3-bromofuran-2-carbaldehyde according to ref.[6b], 3-methylfuran-2-carbaldehyde according to ref.[14], 5-[(3-azido-2-furyl)methylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**1e**) according to ref.[15].

Preparation of 5-(2-Hydroxypenta-2,4-dien-1-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-diones (**2**). General Procedure

A solution of corresponding amine (10 mmol) in dry toluene (10 ml) was added in one portion to a vigorously stirred solution of 5-[(2-furyl)methylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**1a**; 2.22 g, 10 mmol) in dry toluene (10 ml). After 2 min, the mixture was cooled and stirred at 0 °C for 30 min. The deep-red precipitate was filtered off, washed with cold toluene (10 ml), cold diethyl ether (10 ml) and dried on air. The analytically pure compound was obtained by crystallization from dimethyl sulfoxide.

5-[2-Hydroxy-5-(pyrrolidin-1-yl)penta-2,4-dien-1-ylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**2a**). Yield 2.75 g (94%), m.p. 179–182 °C. ^{1}H NMR: 1.59 s, 6 H (2 × CH_3); 1.90–2.04 m, 4 H (2 × CH_2); 3.60–3.69 m, 2 H (CH_2-N); 3.80–3.84 m, 2 H (CH_2-N); 6.00 dd, 1 H, *J* = 13.1, *J* = 11.5 (H-4′); 6.56 s, 1 H (H-1′); 7.25 d, 1 H, *J* = 13.4 (H-3′); 8.16 d, 1 H, *J* = 11.3 (H-5′); 11.38 s, 1 H (OH). ^{13}C NMR: 24.26 (CH_2); 24.32 (CH_2); 25.97 (2 × CH_3); 49.94 (CH_2-N); 54.41 (CH_2-N); 85.02 (C-5); 102.07 (C-2); 106.20 (C-4′); 130.12 (C-1′); 143.10 (C-2′); 152.90 (C-3′); 159.13 (C-5′); 162.35 (C-6); 162.47 (C-4). MS, *m/z* (%): 293 ($M^{+\bullet}$, 8), 235 (34), 218 (14), 191 (47), 163 (60), 149 (14), 134 (44), 108 (23), 81 (35), 70 (53), 43 (100), 28 (45). For $C_{15}H_{19}NO_5$ (293.3) calculated: 61.42% C, 6.53% H, 4.78% N; found: 61.23% C, 6.49% H, 4.69% N.

5-[5-(Hexahydroazepin-1-yl)-2-hydroxypenta-2,4-dien-1-ylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**2d**). Yield 2.92 g (91%), m.p. 201–203 °C. ^{1}H NMR: 1.55–1.56 m, 4 H (2 × CH_2); 1.59 s, 6 H (2 × CH_3); 1.74–1.78 m, 4 H (2 × CH_2); 3.67–3.77 m, 4 H (2 × CH_2-N); 6.09 dd, 1 H, *J* = 12.9, *J* = 11.5 (H-4′); 6.60 s, 1 H (H-1′); 7.11 d, 1 H, *J* = 12.9 (H-3′); 8.03 d, 1 H, *J* = 11.5 (H-5′); 11.36 s, 1 H (OH). ^{13}C NMR: 25.28 (CH_2); 25.56 (CH_2); 25.96 (2 × CH_3); 26.92 (CH_2); 28.36 (CH_2); 49.78 (CH_2-N); 57.44 (CH_2-N); 85.46 (C-5); 102.13 (C-2); 104.54 (C-4′); 131.0 (C-1′); 143.18 (C-2′); 153.61 (C-3′); 162.71 (C-5′); 162.25 (C-6); 162.27 (C-4). For $C_{17}H_{23}NO_5$ (321.4) calculated: 63.54% C, 7.21% H, 4.36% N; found: 63.33% C, 7.09% H, 4.29% N.

Mixture of 5-[2-hydroxy-5-morpholinopenta-2,4-dien-1-ylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**2b**) *and 6-hydroxy-2,2-dimethyl-5-(5-morpholino-2-oxocyclopent-3-en-1-yl)-4H-1,3-dioxin-4-one* (**3b**). Yield 2.71 g (88%), m.p. 174–176 °C. ^{1}H NMR: 1.50 s, 6 H (CH_3); 1.59 s, 6 H (CH_3); 3.36 m, 8 H (2 × CH_2-N); 3.76 m, 8 H (2 × CH_2-O); 4.50 bs, 1 H (H-5_{cyclop}); 6.21 dd, 1 H, *J* = 12.61, *J* = 12.13 (H-4_{dien}); 6.55 dd, 1 H, *J* = 6.0, *J* = 1.9 (H-3_{cyclop}); 6.64 s, 1 H (H-1_{dien}); 7.15 d, 1 H, *J* = 13.02 (H-3_{dien}); 7.82 dd, 1 H, *J* = 6.0, *J* = 1.9 (H-4_{cyclop}); 8.02 d, 1 H, *J* = 11.64 (H-5_{dien}); 10.02 bs, 1 H (OH_{cyclop}); 11.36 s, 1 H (OH_{dien}).

Mixture of 5-[2-hydroxy-5-(piperidin-1-yl)penta-2,4-dien-1-ylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**2c**) *and 6-hydroxy-2,2-dimethyl-5-[2-oxo-5-(piperidin-1-yl)cyclopent-3-en-1-yl]-4H-1,3-dioxin-4-one* (**3c**). Yield 2.66 g (87%), m.p. 196–198 °C. ^{1}H NMR: 1.49 s, 6 H (CH_3); 1.57 m, 12 H (6 × CH_2); 1.67 s, 6 H (CH_3); 3.69 m, 8 H (CH_2-N); 4.42 bs, 1 H (H-5_{cyclop}); 6.20 dd, 1 H, *J* = 12.21, *J* = 12.45 (H-4_{dien}); 6.55 m, 1 H (H-3_{cyclop}); 6.53 s, 1 H (H-1_{dien}); 7.12 d, 1 H, *J* = 13.18 (H-3_{dien}); 7.81 dd, 1 H, *J* = 6.0, *J* = 1.8 (H-4_{cyclop}); 8.02 d, 1 H, *J* = 11.48 (H-5_{dien}); 10.08 bs, 1 H (OH_{cyclop}); 11.35 s, 1 H (OH_{dien}).

Preparation of 5-[2-Acetoxy-5-*N*-(phenylacetamido)penta-2,4-dien-1-ylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**5**)

2,2-Dimethyl-1,3-dioxane-4,6-dione (1.73 g, 0.012 mol) was dissolved in a mixture of CH_3COONa (1.2 g, 12 mmol) and acetic anhydride (23 ml). The salt **4** (3.0 g, 10 mmol) was rapidly added portionwise to the vigorously stirred mixture. After stirring at room temperature for 24 h, the precipitate was collected and the mother liquor was poured into ice-cold

water (150 ml). The solid was filtered off after 30 min, washed with water and dried in air. Crystallization from methanol afforded 2.24 g (56%) of **5**, m.p. 144–147 °C (methanol), R_F 0.59 (AcOEt). ^{1}H NMR (DMSO-d_6): 1.63 s, 6 H (2 × CH_3); 1.84 s, 3 H (CH_3-CON); 1.98 s, 3 H (CH_3-COO); 5.01 dd, 1 H, *J* = 12.6, *J* = 13.2 (H-4′); 7.48–7.71 m, 6 H (Ph, H-1′); 7.53 d, 1 H, *J* = 12.7 (H-3′); 8.28 d, 1 H, *J* = 13.4 (H-5′). ^{13}C NMR: 19.23 (CH_3COO); 23.21 (CH_3CON); 26.81 (2 × CH_3); 103.94 (C-5); 105.97 (C-4′); 108.45 (C-2); 128.45, 129.48 and 130.28 (Ph); 137.92 (C-2′); 140.35 (Ar-N); 145.11 (C-1′); 147.61 (C-3′); 156.13 (C-5′); 158.77 (C-4); 163.15 (C-6); 167.43 (O-C=O); 169.26 (N-C=O). MS, *m/z* (%): 399 (M^+, 10), 299 (40), 257 (50), 240 (26), 213 (28), 172 (30), 136 (31), 121 (20), 93 (60), 77 (38), 58 (88), 44 (100), 28 (68). For $C_{21}H_{21}NO_7$ (399.4) calculated: 63.15% C, 5.30% H, 3.51% N; found: 63.02% C, 5.21% H, 3.42% N .

Preparation of 5-(2-Acetoxypenta-2,4-dien-1-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (**6**). General Procedure

A solution of morpholine (0.48 g, 5.5 mmol) or piperidine (0.46 g, 5.5 mmol) in methanol (1 ml) was added to a vigorously stirred suspension of compound **5** (2.0 g, 5 mmol) in dry methanol (15 ml). After several minutes, the mixture became homogeneous and then a solid deposited. After stirring for 2 h, the solid was collected, washed with ice-cold methanol and purified by crystallization from methanol.

5-(2-Acetoxy-5-morpholinopenta-2,4-dien-1-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (**6b**). Yield 1.24 g (71%), m.p. 209–211 °C, R_F 0.47 (MeOH). ^{1}H NMR (DMSO-d_6): 1.53 s, 6 H (2 × CH_3); 2.16 s, 3 H (CH_3COO); 3.66 m, 4 H (2 × CH_2-N); 3.74 m, 4 H (2 × CH_2-O); 5.77 dd, 1 H, *J* = 12.2, *J* = 12.7 (H-4′); 7.38 s, 1 H (H-1′); 7.46 d, 1 H, *J* = 12.2 (H-3′); 7.76 d, 1 H, *J* = 12.2 (H-5′). ^{13}C NMR: 20.53 (CH_3COO); 26.11 (2 × CH_3); 48.21 (2 × CH_2-N); 65.59 (2 × CH_2-O); 92.58 (C-5); 99.08 (C-4′); 101.31 (C-2); 134.25 (C-2′); 142.93 (C-1′); 154.22 (C-3′); 155.88 (C-4); 156.23 (C-6); 159.42 (C-5′); 167.22 (O-C=O). For $C_{17}H_{21}NO_7$ (351.1) calculated: 58.11% C, 6.02% H, 3.99% N; found: 58.08% C, 5.87% H, 3.88% N.

5-[2-Acetoxy-5-(piperidin-1-yl)penta-2,4-dien-1-ylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**6c**). Yield 1.32 g (76%), m.p. 230–232 °C, R_F 0.48 (MeOH). ^{1}H NMR (DMSO-d_6): 1.57 s, 6 H (2 × CH_3); 1.67 m, 6 H (3 × CH_2); 2.16 s, 3 H (CH_3COO); 3.63 m, 4 H (2 × CH_2-N); 5.79 dd, 1 H, *J* = 12.5, *J* = 11.9 (H-4′); 7.31 s, 1 H (H-1′); 7.43 d, 1 H, *J* = 12.5 (H-3′); 7.76 d, 1 H, *J* = 11.9 (H-5′). ^{13}C NMR: 20.53 (CH_3COO); 22.62 (CH_2); 23.13 (CH_2); 26.07 (CH_2); 46.72 (2 × CH_2-N); 50.28 (CH_2-N); 90.85 (C-5); 99.58 (C-4′); 101.05 (C-2); 119.93 (C-1′); 133.88 (C-2′); 141.77 (C-3′); 154.64 (C-4); 154.79 (C-6); 159.85 (C-5′); 167.19 (O-C=O). For $C_{18}H_{23}NO_6$ (349.4) calculated: 61.88% C, 6.64% H, 4.01% N; found: 61.78% C, 6.57% H, 3.82% N.

Preparation of Substituted 5-Cyclopentenyl-6-hydroxy-4*H*-1,3-dioxin-4-ones **3a**–**3d**

A) A solution of amine (2.5 mmol) was added in one portion to a stirred solution of 1,3-dioxane-4,6-dione **2a**, **2d** or a mixture of **2b**, **3b** or **2c**, **3c** (5 mmol) in dry methanol (10 ml). The mixture was refluxed for 15 min, first becoming homogeneous and then subsequently depositing a solid. The mixture was cooled and stirred at 0 °C for 10 min, the formed precipitate was filtered off and crystallized.

B) 4-(Trifluoromethyl)aniline (1.61 g, 10 mmol) in methanol (5 ml) was added to a solution of corresponding 1,3-dioxane-4,6-dione **2a**, **2d** or a mixture of **2b**, **3b** or **2c**, **3c** (5 mmol) in dry methanol (5 ml) and the mixture was refluxed for 4 h. The solution was cooled to 0 °C

and the precipitate was filtered off. The analytically pure compounds were obtained by crystallization from a large amount of water.

6-Hydroxy-2,2-dimethyl-5-[2-oxo-5-(pyrrolidin-1-yl)cyclopent-3-en-1-yl]-4H-1,3-dioxin-4-one (**3a**). Yield 1.58 g (54%) method *A* and 1.34 g (46%) method *B*, m.p. 199–203 °C. ^{1}H NMR (CF_3COOD): 1.77 s, 3 H (CH_3); 1.90 s, 3 H (CH_3); 2.18–2.28 m, 4 H (2 × CH_2); 3.13 m, 1 H (CH_2-N); 3.60 m, 1 H (CH_2-N); 3.80–3.92 m, 3 H (CH_2-N, H-4′); 5.08 bs, 1 H (H-2′); 6.88 dd, 1 H, *J*(4′,3′) = 6.0, *J*(4′,2′) = 1.8 (H-4′); 7.84 dd, 1 H, *J*(3′,4′) = 5.9, *J*(3′,2′) = 1.8 (H-3′). ^{13}C NMR: 26.38 (CH_2); 26.88 (CH_2); 29.28 (CH_3); 31.83 (CH_3); 48.64 (C-1′); 53.27 (CH_2-N); 58.15 (CH_2-N); 69.38 (C-5′); 111.56 (C-2); 142.44 (C-3′); 155.70 (C-4′); 168.06 (C-4); 171.19 (C-6); 205.95 (C-2′). MS, *m/z* (%): 293 (M^+, 7), 235 (28), 218 (15), 189 (48), 163 (40), 149 (11), 134 (39), 120 (18), 108 (20), 95 (15), 81 (25), 70 (53), 43 (100), 28 (65). For $C_{15}H_{19}NO_5$ (293.3) calculated: 61.42% C, 6.53% H, 4.78% N; found: 61.56% C, 6.65% H, 4.89% N.

6-Hydroxy-2,2-dimethyl-5-(5-morpholino-2-oxocyclopent-3-en-1-yl)-4H-1,3-dioxin-4-one (**3b**). Yield 1.04 g (68%) method *A* and 0.8 g (52%) method *B*, m.p. 206–209 °C. ^{1}H NMR (CF_3COOD): 1.46–2.14 m, 12 H (2 × CH_3, 3 × CH_2); 2.73 m, 1 H (CH_2-N); 3.37 m, 1 H (CH_2-N); 3.48–3.54 m, 2 H (CH_2-N); 3.64 d, 1 H, *J* = 2.94 (H-1′); 4.75 bs, 1 H (H-5′); 6.62 d, 1 H, *J* = 5.9 (H-3′); 7.75 d, 1 H, *J* = 5.9 (H-4′). ^{13}C NMR (CF_3COOD): 22.98 (CH_2); 25.63 (CH_2); 25.93 (CH_2); 26.44 (CH_3); 28.79 (CH_3); 46.06 (C-1′); 52.35 (CH_2-N); 56.67 (CH_2-N); 71.37 (C-5′); 111.98 (C-2); 140.90 (C-3′); 155.50 (C-4′); 167.82 (C-4); 170.01 (C-6); 205.32 (C-2′). For $C_{16}H_{21}NO_5$ (307.3) calculated: 62.53% C, 6.89% H, 4.56% N; found: 62.41% C, 6.71% H, 4.47% N.

6-Hydroxy-2,2-dimethyl-5-[2-oxo-5-(piperidin-1-yl)cyclopent-3-en-1-yl]-4H-1,3-dioxin-4-one (**3c**). Yield 0.94 g (62%) method *A* and 0.85 g (55%) method *B*, m.p. 153–156 °C. ^{1}H NMR (CF_3COOD): 1.39 s, 3 H (CH_3); 1.47 s, 3 H (CH_3); 2.91–3.93 m, 9 H (2 × CH_2-N, 2 × CH_2-O, H-1′); 3.37 m, 1 H (CH_2-N); 4.68 m, 1 H (H-5′); 6.51 d, 1 H, *J* = 5.8 (H-3′); 7.64 d, 1 H, *J* = 5.9 (H-4′). ^{13}C NMR (CF_3COOD): 27.61 (CH_3); 29.72 (CH_3); 47.04 (C-1′); 51.68 (CH_2-N); 55.09 (CH_2-N); 67.39 (2 × CH_2-O); 72.58 (C-5′); 112.90 (C-2); 142.44 (C-3′); 155.52 (C-4′); 168.83 (C-4); 170.88 (C-6); 205.84 (C-2′). For $C_{15}H_{19}NO_6$ (309.3) calculated: 58.25% C, 6.19% H, 4.53% N; found: 58.06% C, 6.01% H, 4.77% N.

5-[5-(Hexahydroazepin-1-yl)-2-oxocyclopent-3-en-1-yl]-6-hydroxy-2,2-dimethyl-4H-1,3-dioxin-4-one (**3d**). Yield 0.82 g (51%) method *A* and 0.67 g (42%) method *B*, m.p. 192–195 °C. ^{1}H NMR (CF_3COOD): 1.82–2.17 m, 14 H (2 × CH_3, 4 × CH_2); 3.12 m, 1 H (CH_2-N); 4.27 m, 1 H (CH_2-N); 3.49–3.89 m, 3 H (2 × CH_2-N, H-1′); 4.86 m, 1 H (H-5′); 6.59 d, 1 H, *J* = 5.7 (H-3′); 7.74 d, 1 H, *J* = 5.7 (H-4′). ^{13}C NMR (CF_3COOD): 26.87 (CH_3); 26.91 (CH_2); 28.06 (CH_2); 28.52 (CH_2); 29.13 (CH_2); 29.64 (CH_3); 47.41 (C-1′); 53.79 (CH_2-N); 59.97 (CH_2-N); 73.01 (C-5′); 112.98 (C-2); 142.61 (C-3′); 155.98 (C-4′); 168.21 (C-4); 171.28 (C-6); 205.62 (C-2′). For $C_{17}H_{23}NO_5$ (321.4) calculated: 63.54% C, 7.21% H, 4.36% N; found: 63.41% C, 6.98% H, 4.47% N.

Preparation of Substituted 5-Cyclopentenyl-6-hydroxy-4*H*-1,3-dioxin-4-one Hydrobromides **3a**–**3d**

A) To a refluxed solution of furan **1a** (2.22 g, 10 mmol) in methanol (10 ml), the corresponding amine (15 mmol) in methanol (2 ml) was added. The mixture was stirred under reflux for 5 min and 46% hydrobromic acid (3.5 ml, 30 mmol) was added in one portion to the clear mixture. The mixture was stirred at 0 °C for 15 min and the formed solid was filtered off.

B) The corresponding 5-aminopenta-2,4-dien-1-ylidenes **2a**, **2d** or a mixture of **2b**, **3b** and **2c**, **3c** (10 mmol) in methanol (5 ml) was heated to 45 °C. Hydrobromic acid (46%; 3.6 ml, 30 mmol) in methanol (4 ml) was added in one portion and the mixture was refluxed. After a few minutes, the red colored solution became colorless. Cooling of the solution at 0 °C for 1 h resulted in the precipitation of colorless needles.

C) A solution of 46% hydrobromic acid (1.75 ml, 15 mmol) in methanol (1 ml) was added to a vigorously stirred suspension of compound **3a**–**3d** (10 mmol) in methanol (10 ml) at 50 °C. After short exothermic reaction, the mixture became homogeneous and then a solid deposited. The mixture was cooled and stirred at 0 °C for 30 min. The precipitate was filtered off, washed with cold dry acetone and dried on air. The analytically pure compounds were obtained by crystallization from a mixture acetonitrile–water.

6-Hydroxy-2,2-dimethyl-5-[2-oxo-5-(pyrrolidin-1-yl)cyclopent-3-en-1-yl]-4H-1,3-dioxin-4-one hydrobromide (**3a**). Yield 2.62 g (67%) method *A*, 2.10 g (56%) method *B* and 2.58 g (69%) method *C*, m.p. 172–175 °C. IR (KBr): 1 771 (C=O), 1 742 (C=O), 1 721 (C=O), 1 591 (C=C). ^{1}H NMR (CF_3COOD): 1.82 s, 3 H (CH_3); 1.92 s, 3 H (CH_3); 2.19–2.23 m, 4 H (2 × CH_2); 3.12 m, 1 H (CH_2-N); 3.55 m, 1 H (CH_2-N); 3.82–3.89 m, 3 H (CH_2-N, H-4′); 5.34 bs, 1 H (H-2′); 6.88 d, 1 H, J(4′,3′) = 5.8 (H-4′); 7.88 d, 1 H, J(3′,4′) = 5.8 (H-3′). ^{13}C NMR (CF_3COOD): 26.06 (CH_2); 27.61 (CH_2); 29.01 (CH_3); 49.37 (C-1′); 52.16 (CH_2-N); 57.19 (CH_2-N); 68.62 (C-2′); 112.19 (C-2); 141.93 (C-4′); 155.96 (C-3′); 170.30 (C-4); 173.93 (C-6); 206.93 (C-5′). MS, *m/z* (%): 293 ($M^{+\bullet}$, 7, – HBr), 235 (28), 218 (15), 189 (48), 163 (40), 149 (11), 134 (39), 120 (18), 108 (20), 95 (15), 81 (25), 70 (53), 43 (100), 28 (65). For $C_{15}H_{20}BrNO_5$ (374.2) calculated: 48.14% C, 5.39% H, 21.35% Br, 3.74% N; found: 47.96% C, 5.21% H, 21.21% Br, 3.68% N.

6-Hydroxy-2,2-dimethyl-5-(5-morpholino-2-oxocyclopent-3-en-1-yl)-4H-1,3-dioxin-4-one hydrobromide (**3b**). Yield 2.74 g (70%) method *A*, 2.46 g (63%) method *B* and 2.77 g (71%) method *C*, m.p. 164–168 °C (dec.). ^{1}H NMR (CF_3COOD): 1.88 s, 3 H (CH_3); 1.99 s, 3 H (CH_3); 3.37 m, 1 H (CH_2); 3.92 m, 4 H (2 × CH_2-N); 4.18 d, 1 H, J = 3.7 (H-1′); 4.42 m, 4 H (2 × CH_2-O); 3.37 m, 1 H (CH_2-N); 5.53 m, 1 H (H-5′); 6.89 d, 1 H, J = 5.8 (H-3′); 8.03 d, 1 H, J = 5.9 (H-4′). ^{13}C NMR (CF_3COOD): 27.54 (CH_3); 28.81 (CH_3); 46.73 (C-1′); 50.23 (CH_2-N); 54.38 (CH_2-N); 68.89 (2 × CH_2-O); 71.71 (C-5′); 111.81 (C-2); 141.66 (C-3′); 154.99 (C-4′); 168.84 (C-4); 169.78 (C-6); 206.12 (C-2′). For $C_{15}H_{20}BrNO_6$ (390.2) calculated: 46.17% C, 5.17% H, 20.48% Br, 3.59% N; found: 46.01% C, 5.05% H, 20.38% Br, 3.49% N.

6-Hydroxy-2,2-dimethyl-5-[2-oxo-5-(piperidin-1-yl)cyclopent-3-en-1-yl]-4H-1,3-dioxin-4-one hydrobromide (**3c**). Yield 2.89 g (71%) method *A*, 2.06 g (53%) method *B* and 2.83 g (73%) method *C*, m.p.188–190 °C. ^{1}H NMR (CF_3COOD): 2.12–2.31 m, 6 H (3 × CH_2); 3.05 m, 1 H (CH_2-N); 3.57 m, 1 H (CH_2-N); 3.73–3.89 m, 3 H (2 × CH_2-N, H-1′); 5.01 bs, 1 H (H-5′); 6.99 d, 1 H, J = 5.7 (H-3′); 8.18 d, 1 H, J = 5.9 (H-4′). ^{13}C NMR (CF_3COOD): 24.09 (CH_2); 26.24 (CH_2); 27.08 (CH_2); 25.58 (CH_3); 26.05 (CH_3); 47.70 (C-1′); 52.87 (CH_2-N); 58.93 (CH_2-N); 68.73 (C-5); 72.47 (C-5′); 112.49 (C-2); 141.92 (C-3′); 156.99 (C-4′); 169.72 (C-4); 170.63 (C-6); 207.56 (C-2′). For $C_{16}H_{22}BrNO_5$ (388.3) calculated: 49.50% C, 5.71% H, 20.58% Br, 3.61% N; found: 49.36% C, 5.58% H, 20.49% Br, 3.52% N.

5-[5-(Hexahydroazepin-1-yl)-2-oxocyclopent-3-en-1-yl]-6-hydroxy-2,2-dimethyl-4H-1,3-dioxin-4-one hydrobromide (**3d**). Yield 2.84 g (71%) method *A*, 2.32 g (58%) method *B* and 2.81 g (70%) method *C*, m.p. 184–187 °C. ^{1}H NMR (CF_3COOD): 1.79 s, 3 H (CH_3); 1.93 s, 3 H (CH_3); 1.99–2.31 m, 8 H (4 × CH_2); 3.14 m, 1 H (CH_2-N); 3.62 m, 1 H (CH_2-N); 3.71–3.92 m, 2 H (CH_2-N, H-1′); 5.12 m, 1 H (H-5′); 6.82 d, 1 H, J = 5.8 (H-3′); 7.93 d, 1 H, J = 5.8 (H-4′); 8.74 bs, 1 H (OH). ^{13}C NMR (CF_3COOD): 26.97 (CH_2); 27.27 (CH_2); 27.31 (CH_3); 27.97 (CH_2); 28.05 (CH_2); 28.84 (CH_3); 47.67 (C-1′); 53.03 (CH_2-N); 59.41 (CH_2-N); 69.12 (C-5);

72.64 (C-5′); 118.80 (C-2); 141.71 (C-3′); 156.30 (C-4′); 168.63 (C-4); 170.09 (C-6); 206.56 (C-2′). For $C_{17}H_{24}BrNO_5$ (401.1) calculated: 50.76% C, 6.01% H, 19.86% Br, 3.48% N; found: 50.59% C, 5.89% H, 19.75% Br, 3.39% N.

Preparation of Substituted Malonic Acid Hydrobromides **7**. General Procedure

The corresponding substituted cyclopentene **3a**–**3d** (1 mmol) was dissolved in 10% hydrobromic acid (5 ml) at 40 °C and the solution was then stirred for 10 min. After cooling to room temperature, the mixture was evaporated *in vacuo* to one quarter of its volume and the residue was poured into dry acetone (25 ml). The precipitate was collected, washed with dry acetone (2 ml) and dried at 50 °C. The analytically pure compounds were obtained by crystallization from a mixture methanol–acetone.

2-[2-Oxo-5-(pyrrolidin-1-yl)cyclopent-3-en-1-yl]malonic acid hydrobromide (**7a**). Yield 0.51 g (61%), m.p. 172–175 °C (dec.). ^{1}H NMR (DMSO-d_6): 1.96–2.08 m, 4 H (2 × CH_2); 3.14 m, 1 H (H-1′); 3.25–3.68 m, 4 H (2 × CH_2-N); 4.09 d, 1 H, *J* = 3.8 (H-2); 4.64 m, 1 H (H-5′); 6.64 dd, 1 H, *J* = 6.0, *J* = 1.8 (H-3′); 7.92 dd, 1 H, *J* = 6.0, *J* = 1.8 (H-4′); 10.47 bs, 1 H (OH). ^{13}C NMR: 22.81 (CH_2); 46.80 (C-2); 50.50 (CH_2-N); 51.08 (C-1′); 52.09 (CH_2-N); 66.13 (C-5′); 138.13 (C-3′); 154.43 (C-4′); 168.77 (COOH); 169.12 (COOH); 202.42 (C-2′). For $C_{12}H_{16}BrNO_5$ (334.2) calculated: 43.13% C, 4.83% H, 23.91% Br, 4.19% N; found: 43.01% C, 4.70% H, 23.78% Br, 4.09% N.

2-[5-Morpholino-2-oxocyclopent-3-en-1-yl]malonic acid hydrobromide (**7b**). Yield 0.49 g (56%), m.p. 140-143 °C (dec.). ^{1}H NMR (DMSO-d_6): 3.22–3.38 m, 3 H (CH_2-N, H-1′); 3.48–3.61 m, 2 H (CH_2-N); 3.82–3.94 m, 4 H (CH_2-O); 4.06 d, 1 H, *J* = 3.6 (H-2); 4.58 m, 1 H (H-5′); 6.63 dd, 1 H, *J* = 6.0, *J* = 1.8 (H-3′); 8.01 dd, 1 H, *J* = 6.0, *J* = 1.8 (H-4′). ^{13}C NMR: 44.79 (C-2); 49.48 (CH_2-N); 51.48 (C-1′); 63.60 (CH_2-O); 68.61 (C-5′); 138.25 (C-3′); 153.28 (C-4′); 168.93 (COOH); 169.21 (COOH); 202.28 (C-2′). For $C_{12}H_{16}BrNO_6$ (350.2) calculated: 41.16% C, 4.61% H, 22.82% Br, 4.00% N; found: 40.92% C, 4.69% H, 22.71% Br, 4.12% N.

2-[2-Oxo-5-(piperidin-1-yl)cyclopent-3-en-1-yl]malonic acid hydrobromide (**7c**). Yield 0.56 g (64%), m.p. 149–152 °C (dec.). ^{1}H NMR (DMSO-d_6): 1.47–1.53 m, 1 H (CH_2); 1.75–1.92 m, 5 H (CH_2); 2.83–2.89 m, 1 H (CH_2-N); 3.29 m, 1 H (H-1′); 3.34–3.58 m, 3 H (CH_2-N); 4.15 d, 1 H, *J* = 3.6 (H-2); 4.52 m, 1 H (H-5′); 6.34 dd, 1 H, *J* = 5.9, *J* = 1.9 (H-3′); 8.04 dd, 1 H, *J* = 5.9, *J* = 1.8 (H-4′); 9.93 bs, 1 H (OH). ^{13}C NMR: 21.15 (2 × CH_2); 22.91 (CH_2); 44.72 (C-2); 49.21 (CH_2-N); 51.20 (CH_2-N); 51.57 (C-1′); 68.65 (C-5′); 138.02 (C-3′); 153.64 (C-4′); 168.96 (COOH); 169.29 (COOH); 202.36 (C-2′). For $C_{13}H_{18}BrNO_5$ (348.2) calculated: 44.84% C, 5.21% H, 22.95% Br, 4.02% N; found: 44.71% C, 5.29% H, 22.79% Br, 4.09% N.

2-[5-(Hexahydroazepin-1-yl)-2-oxocyclopent-3-en-1-yl]malonic acid hydrobromide (**7d**). Yield 0.53 g (59%), m.p. 139–142 °C (dec.). ^{1}H NMR (DMSO-d_6): 1.62–1.66 m, 4 H (CH_2); 1.69–1.75 m, 4 H (CH_2); 3.16 m, 1 H (H-1′); 3.21–3.54 m, 4 H (CH_2-N); 4.21 d, 1 H, *J* = 3.9 (H-2); 4.63 m, 1 H (H-5′); 6.67 dd, 1 H, *J* = 6.0, *J* = 1.8 (H-3′); 8.01 dd, 1 H, *J* = 6.0, *J* = 1.8 (H-4′); 9.91 bs, 1 H (OH). ^{13}C NMR: 24.01 (CH_2); 24.03 (CH_2); 25.44 (CH_2); 45.36 (C-2); 51.47 (C-1′); 52.03 (CH_2-N); 69.75 (C-5′); 138.66 (C-3′); 153.58 (C-4′); 169.05 (COOH); 169.53 (COOH); 202.11 (C-2′). For $C_{14}H_{20}BrNO_5$ (362.2) calculated: 46.42% C, 5.57% H, 22.06% Br, 3.87% N; found: 46.30% C, 5.43% H, 22.09% Br, 3.98% N.

Preparation of 5-[Cyclopent-2-en-1-ylidene]-2,2-dimethyl-1,3-dioxane-4,6-diones **9a**–**9c**. General Procedure

A solution of furan **1a** (2.22 g, 10 mmol) in the corresponding amine (0.15 mol) was heated at 90 °C for 5 min and then slowly cooled to room temperature. After stirring at room temperature for 16 h, the solid was filtered off and washed with cold methanol (–20 °C). The resulting precipitate was crystallized from methanol and then dried at 80 °C for 4 h.

5-[3,5-Bis(morpholino)cyclopent-2-en-1-ylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**9a**). Yield 2.53 g (67%), m.p. 143–146 °C. IR (KBr): 1 687 (C=O), 1 682 (C=O), 1 610 (C=C). ^{1}H NMR ($CDCl_3$): 1.58 s, 3 H (CH_3); 1.59 s, 3 H (CH_3); 2.27–2.29 m, 2 H (CH_2-N); 2.37–2.39 m, 2 H (CH_2-N); 2.68 dd, 1 H, J = 17.9, J = 6.6 ($H_{4'\alpha}$); 2.96 d, 1 H, J = 17.8 ($H_{4'\beta}$); 3.47–3.50 m, 4 H (CH_2-N); 3.64–3.68 m, 4 H (CH_2O); 3.70–3.74 m, 4 H (CH_2O); 4.98 d, 1 H, J = 6.6 (H-5′); 6.93 s, 1 H (H-2′). ^{13}C NMR ($CDCl_3$): 25.46 (2-CH_3); 27.82 (2-CH_3); 28.25 (C-4′); 48.39 (CH_2-N); 49.06 (CH_2-N); 49.08 (CH_2-N); 49.64 (CH_2-N); 65.02 (C-5′); 66.11 (CH_2-O); 66.47 (CH_2-O); 67.12 (2 × CH_2-O); 67.13 (2 × CH_2-O); 91.96 (C-5); 101.99 (C-2); 107.58 (C-2′); 163.46 (C-4); 164.62 (C-6); 175.83 (C-3′); 179.82 (C-1′). MS, *m/z* (%): 378 ($M^{+\bullet}$ – CH_3COCH_3, 8), 293 (9), 235 (11), 207 (9), 191 (45), 163 (14), 149 (14), 105 (13), 87 (25), 68 (19), 58 (100), 43 (85), 28 (95). For $C_{19}H_{26}N_2O_6$ (378.2) calculated: 60.34% C, 6.93% H, 7.41% N; found: 60.41% C, 7.02% H, 7.37% N.

5-[3,5-Bis(piperidin-1-yl)cyclopent-2-en-1-ylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**9b**). Yield 2.28 g (61%), m.p. 207–208 °C. IR (KBr): 1 714 (C=O), 1 680 (C=O), 1 597 (C=C). ^{1}H NMR ($CDCl_3$): 1.35–1.53 m, 4 H (2 × CH_2); 1.56–1.63 m, 2 H (CH_2); 1.68–1.74 m, 12 H (2 × CH_3, 3 × CH_2); 2.31–2.42 m, 4 H (2 × CH_2-N); 2.48 dd, 1 H, J = 17.9, J = 6.1 ($H_{4'\alpha}$); 2.75 d, 1 H, J = 17.8 ($H_{4'\beta}$); 3.56 m, 2 H (CH_2-N); 3.64 m, 2 H (CH_2-N); 5.14 d, 1 H, J = 6.1 (H-5′); 7.18 s, 1 H (H-2′). ^{13}C NMR ($CDCl_3$): 23.73 (CH_2); 24.76 (CH_2); 25.13 (CH_3); 25.77 (CH_2); 26.19 (2 × CH_2); 26.56 (CH_2); 28.20 (C-4′); 49.29 (CH_2-N); 50.34 (CH_2-N); 51.05 (2 × CH_2-N); 65.68 (C-5′); 90.39 (C-5); 101.66 (C-2); 107.76 (C-2′); 163.70 (C-4); 165.01 (C-6); 176.00 (C-3′); 180.63 (C-1′). For $C_{21}H_{30}N_2O_4$ (374.5) calculated: 67.35% C, 8.07% H, 7.48% N; found: 67.26% C, 7.98% H, 7.37% N.

5-[3,5-Bis(4-methylpiperazin-1-yl)cyclopent-2-en-1-ylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**9c**). Yield 2.34 g (58%), m.p.143–146 °C. IR (KBr): 1 714 (C=O), 1 681 (C=O), 1 597 (C=C). ^{1}H NMR ($CDCl_3$): 1.66 s, 3 H (CH_3); 1.71 s, 3 H (CH_3); 2.22 s, 3 H (N-CH_3); 2.33 s, 3 H (N-CH_3); 2.37–2.59 m, 13 H (6 × CH_2-N, $H_{4'\alpha}$); 2.77 d, 1 H, J = 17.8 ($H_{4'\beta}$); 3.52–3.59 m, 2 H (CH_2-N); 3.62–3.71 m, 2 H (CH_2-N); 5.21 d, 1 H, J = 6.1 (H-5′); 7.06 s, 1 H (H-2′). ^{13}C NMR ($CDCl_3$): 25.43 (CH_3); 27.84 (CH_3); 28.20 (C-4′); 45.75 (CH_2-N); 46.06 (CH_2-N); 48.83 (CH_2-N); 49.45 (CH_2-N); 54.15 (CH_2-N); 54.67 (CH_2-N); 55.14 (2 × CH_2-N); 64.60 (C-5′); 91.34 (C-5); 101.81 (C-2); 107.53 (C-2′); 163.46 (C-4); 164.79 (C-6); 175.88 (C-3′); 180.12 (C-1′). For $C_{21}H_{32}N_4O_4$ (404.5) calculated: 62.35% C, 7.97% H, 13.85% N; found: 62.21% C, 7.88% H, 13.78% N.

5-[5-(Hexahydroazepin-1-ium-1-ylidene)-2-(hexahydroazepin-1-yl)cyclopent-1-en-1-yl]-2,2-dimethyl-4-oxo-4H-1,3-dioxin-6-olate (**10**). Yield 2.86 g (71%), m.p. 243–245 °C. IR (KBr): 1 611 (C=C), 1 526 (C=C). ^{1}H NMR ($CDCl_3$): 1.58–1.69 m, 14 H (2 × CH_3, 4 × CH_2); 1.76–1.84 m, 8 H (4 × CH_2); 2.81 s, 4 H (H-3′, H-4′); 3.53 t, 4 H, J = 11.4, J = 5.8 (2 × CH_2); 4.02 t, 4 H, J = 11.3, J = 5.7 (2 × CH_2). ^{13}C NMR ($CDCl_3$): 26.41 (CH_2); 26.70 (CH_2); 27.62 (2 × CH_3); 28.10 (CH_2); 28.38 (CH_2); 29.36 (CH_2); 51.09 (2 × CH_2-N); 53.76 (2 × CH_2-N); 101.12 (C-2); 104.86, 165.88, 179.40. For $C_{23}H_{34}N_2O_4$ (402.5) calculated: 68.63% C, 8.51% H, 6.96% N: found: 68.51% C, 8.40% H, 6.79% N.

Reaction of **3d** with Morpholine.
5-[3,5-Bis(morpholino)cyclopent-2-en-1-ylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**9a**)

A solution of cyclopentene **3d** (0.97 g, 30 mmol) in morpholine (0.45 mol) was heated at 90 °C for 5 min and then slowly cooled to room temperature. After stiring at room temperature for 16 h, the solid was filtered off and washed with cold methanol (–20 °C). The solid was recrystallized from methanol to give 0.48 g (43%) of **9a**. The product was in all respects identical with the substance obtained from the reaction of **1a** with morpholine.

Reaction of **3b** with Hexahydroazepine.
1-{[3,5-Bis(hexahydroazepin-1-yl)cyclopent-2-en-1-ylidene]acetyl}hexahydroazepine (**19**)

The title compound was prepared from **3b** (0.92 g, 30 mmol) and hexahydroazepine (4.5 g, 0.45 mol) in the same manner as described in the preceding experiment. Yield 0.71 g (59%), m.p. 245–249 °C (CH_2Cl_2–hexane). ^{1}H NMR ($CDCl_3$): 1.35–1.43 m, 4 H (2 × CH_2); 1.68–1.79 m, 20 H (10 × CH_2); 2.87 dd, 1 H, *J* = 17.6, *J* = 1.8 ($H_{4'\alpha}$); 3.17 dd, 1 H, *J* = 17.6, *J* = 7.2 ($H_{4'\beta}$); 3.51 m, 8 H (4 × CH_2-N); 3.77 m, 4 H (2 × CH_2-N); 4.36 dd, 1 H, *J* = 7.2, *J* = 1.8 (H-5′); 5.15 s, 1 H (H_{ol}); 7.28 s, 1 H (H-2′). ^{13}C NMR ($CDCl_3$): 25.90 (CH_2); 25.99 (CH_2); 26.25 (CH_2); 26.48 (CH_2); 26.85 (CH_2); 27.15 (2 × CH_2); 28.01 (2 × CH_2); 28.64 (CH_2); 28.75 (CH_2); 38.77 (C-4′); 51.14 (CH_2-N); 51.35 (CH_2-N); 51.81 (CH_2-N); 52.57 (CH_2-N); 72.66 (C-5′); 92.98 (C-2′); 101.18 (C_{ol}); 166.72 (C=O); 177.21 (C-3′); 183.83 (C-1′). MS, *m/z* (%): 399 ($M^{+\bullet}$, 12), 273 (82), 204 (41), 177 (52), 99 (48), 84 (20), 70 (62), 56 (52), 44 (100), 28 (48). For $C_{25}H_{41}N_3O$ (399.6) calculated: 75.14% C, 10.34% H, 10.52% N; found: 74.98% C, 10.49% H, 10.42% N.

Reaction of **1a** with 4-Deuteriomorpholine

A solution of furan **1a** (0.11 g, 0.5 mmol) and 4-deuteriomorpholine (0.65 g, 7.5 mmol) was heated at 90 °C for 5 min and then slowly cooled to room temperature. After stiring at room temperature for 16 h, the solid was filtered off and recrystallized from methanol-d_4 to give a mixture of **9d-(2,5-*d*$_2$)** and **9e-(2,4,4,5-*d*$_4$)**. Yield 80 mg (43%), m.p. 250–255 °C. ^{1}H NMR ($CDCl_3$): 1.58 s, 3 H (CH_3); 1.59 s, 3 H (CH_3); 2.27–2.29 m, 2 H (CH_2-N); 2.37–2.39 m, 2 H (CH_2-N); 2.68 dd, 1 H, *J* = 17.9, *J* = 6.6 ($H_{4'\alpha}$); 2.96 d, 1 H, *J* = 17.8 ($H_{4'\beta}$); 3.47–3.50 m, 4 H (CH_2-N); 3.64–3.68 m, 4 H (CH_2O); 3.70–3.74 m, 4 H (CH_2O); 4.98 d, 1 H, *J* = 6.6 (H-5′); 6.93 s, 1 H (H-2′). ^{13}C NMR: 25.46 (2-CH_3); 27.82 (2-CH_3); 28.25 (C-4′); 48.39 (CH_2-N); 49.06 (CH_2-N); 49.08 (CH_2-N); 49.64 (CH_2-N); 65.02 (C-5′); 66.11 (CH_2-O); 66.47 (CH_2-O); 67.12 (2 × CH_2-O); 67.13 (2 × CH_2-O); 91.96 (C-5); 101.99 (C-2); 107.58 (C-2′); 163.46 (C-4); 164.62 (C-6); 175.83 (C-3′); 179.82 (C-1′).

Reaction of **1a** with Morpholine and D_2O.
5-(3,5-Dimorpholinocyclopent-2-en-1-ylidene)(4,4-d_2)-2,2-dimethyl-1,3-dioxane-4,6-dione [**9f-(4,4-*d*$_2$)**]

The title compound was prepared from **1a** (1.1 g, 5 mmol), morpholine (6.5 g, 75 mmol) and D_2O (0.2 g, 20 mmol) in the same manner as described in the preceding experiment. Yield 0.98 g (52%), m.p. 252–256 °C (from methanol-d_4). ^{1}H NMR ($CDCl_3$): 1.67 s, 3 H (CH_3); 1.71 s, 3 H (CH_3); 2.34–2.37 m, 2 H (CH_2-N); 2.42–2.48 m, 2 H (CH_2-N); 3.55–3.71 m, 8 H (CH_2-N, CH_2O); 3.80–3.84 m, 4 H (CH_2O); 5.17 s, 1 H (H-5′); 7.06 s, 1 H (H-2′). ^{13}C NMR: 25.44 (CH_3); 27.73 (CH_3); 48.19 (CH_2-N); 48.37 (CH_2-N); 49.66 (CH_2-N); 50.62

(CH_2-N); 64.91 (C-5′); 66.10 (CH_2-O); 66.47 (CH_2-O); 67.14 (CH_2-O); 67.19 (CH_2-O); 91.89 (C-5); 102.02 (C-2); 107.65 (C-2′); 163.53 (C-4); 164.64 (C-6); 175.61 (C-3′); 179.83 (C-1′).

3-Methylsulfanylfuran-2-carbaldehyde

A solution of 2-(3-bromo-2-furyl)-1,3-dioxolane (7.3 g, 33 mmol) in anhydrous ether (20 ml) was added during 5 min to 19 ml of 1.6 M butyllithium at –70 °C. The resulting mixture was pressed with nitrogen into a solution of dimethyl disulfide (3.6 g, 37 mmol) in anhydrous ether (20 ml). After standing at room temperature for 3 h, the reaction mixture was poured into water. The ether layer was then hydrolyzed by careful addition of cold 5% hydrochloric acid (38 ml) followed by stirring for 1 h. The layers were separated and the aqueous layer was extracted several times with ether. The ether solution was sequentially washed with a solution of sodium hydroxide and water, and then dried over $MgSO_4$. Evaporation of the solvents *in vacuo* gave a dark oil which was purified by distillation yielding 3.2 g (68%) of crude aldehyde, b.p. 103–115 °C/1.8 kPa. Redistillation yielded 2.4 g (51%) of pure aldehyde, b.p. 108–110 °C/1.9 kPa. ^{1}H NMR ($CDCl_3$): 2.51 s, 1 H (CH_3-S); 6.61 d, 1 H, J = 1.8 (H-4′); 7.65 d, 1 H, J = 1.8 (H-5′); 9.75 s, 1 H (CH=O). ^{13}C NMR ($CDCl_3$): 15.53 (CH_3-S); 111.72 (C-4); 134.22 (C-3); 147.10 (C-2); 147.62 (C-5); 176.53 (CH=O).

Preparation of 5-[(3-Substituted-2-furyl)methylidene]-2,2-dimethyl-1,3-dioxane-4,6-diones (**1b**–**1d**). General Procedure

A solution of corresponding aldehyde (25 mmol) in EtOH (1 ml) was added in one portion to a well stirred solution containing Meldrum's acid (3.6 g, 25 mmol) and 1,2-diaminoethane diacetate (90 mg, 1 mmol) in EtOH (15 ml). The reaction mixture was refluxed for 3 min and then stirred at room temperature for 3 h. The formed solid of **1b** and **1c** was separated by filtration, **1d** was purified by chromatography (silica, AcOEt–hexane 1 : 5 to 1 : 1), washed with water (3 × 15 ml), dried and crystallized from AcOEt–hexane (1 : 4).

5-[(3-Bromo-2-furyl)methylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**1b**). Yield 6.02 g (80%), m.p. 162–163 °C. ^{1}H NMR (DMSO-d_6): 1.65 s, 6 H (2 × CH_3); 7.13 dd, 1 H, J = 1.8, J = 0.2 (H-4′); 7.79 s, 1 H (H-6′); 8.29 dd, 1 H, J = 1.8, J = 0.8 (H-5′); s-trans. ^{13}C NMR (DMSO-d_6): 26.9 q (2 × CH_3); 104.5 s (C-2); 110.3 s (C-5); 117.6 d (C-4′); 119.5 s (C-3′); 132.9 d (C-6′); 145.6 s (C-2′); 151.7 d (C-5′); 158.1 s (C-4, C-6); 162.8 s (C-6, C-4). MS, *m/z* (%): 301 ($M^{+\bullet}$, 19). For $C_{11}H_9BrO_5$ (301.1) calculated: 43.88% C, 3.01% H, 26.54% Br; found: 43.81% C, 2.90% H, 26.40% Br.

2,2-Dimethyl-5-[(3-methyl-2-furyl)methylidene]-1,3-dioxane-4,6-dione (**1c**). Yield 4.1 g (71%), m.p. 144–145 °C. ^{1}H NMR (DMSO-d_6): 1.71 s, 6 H (2 × CH_3); 2.31 s, 3 H (CH_3); 6.78 d, 1 H, J = 1.96 (H-4′); 7.89 s, 1 H (H-6′); 8.15 d, 1 H, J = 1.96 (H-5′). ^{13}C NMR: 11.27 q (CH_3); 27.8 q (2 × CH_3); 103.8 s (C-2′); 106.7 s (C-5); 116.7 d (C-4′); 134.4 d (C-6′); 141.6 s (C-3′); 145.3 s (C-2′); 151.1 d (C-5′); 158.5 s (C-4, C-6); 163.3 s (C-6, C-4). For $C_{12}H_{12}O_5$ (236.2) calculated: 61.82% C, 5.12% H; found: 61.78% C, 5.05% H.

2,2-Dimethyl-5-{[3-(methylsulfanyl)-2-furyl]methylidene}-1,3-dioxane-4,6-dione (**1d**). Yield 2.46 g (54%), m.p. 183–186 °C, R_F 0.21 (AcOEt). ^{1}H NMR ($CDCl_3$): 1.78 s, 6 H (2 × CH_3); 2.55 s, 3 H (CH_3-S); 6.66 d, 1 H, J = 1.83 (H-4′); 7.82 d, 1 H, J = 1.81 (H-5′); 8.12 s, 1 H (H-6′). ^{13}C NMR ($CDCl_3$): 16.92 q (CH_3-S); 27.45 q (CH_3); 27.55 q (CH_3); 104.09 s (C-2); 106.81 s (C-5); 113.42 d (C-4′); 133.73 d (C-6′); 143.45 s (C-3′); 145.03 s (C-2′); 150.42 d (C-5′); 159.35 s (C-4, C-6); 163.78 s (C-6, C-4). For $C_{12}H_{12}O_5S$ (268.3) calculated: 53.72% C, 4.51% H, 11.95% S; found: 53.62% C, 4.45% H, 11.85% S.

Preparation of Cyclopent-3-en-1-yl-4*H*-1,3-dioxin-4-ones **3e**–**3i**

The title compounds were prepared from **1b**–**1e** (5 mmol) and the corresponding amine (5 mmol) in the same manner as described in the preceding experiment.

6-Hydroxy-2,2-dimethyl-5-[3-bromo-2-oxo-5-(pyrrolidin-1-yl)cyclopent-3-en-1-yl]-4H-1,3-dioxin-4-one (**3e**). Yield 1.28 g (69%), m.p. 169–173 °C. ^{1}H NMR (CF_3COOD): 1.70 s, 3 H (CH_3); 1.84 s, 3 H (CH_3); 2.08–2.22 m, 4 H (CH_2); 3.14 m, 1 H (CH_2-N); 3.34 m, 1 H (CH_2-N); 3.65 d, 1 H, *J* = 3.4 (H-1′); 3.72–3.88 m, 2 H (CH_2-N); 4.93 m, 1 H (H-5′); 7.82 d, 1 H, *J* = 2.1 (H-4′). ^{13}C NMR (CF_3COOD): 24.03 (CH_2); 24.64 (CH_3); 26.98 (CH_3); 45.16 (C-1′); 51.09 (CH_2-N); 55.85 (CH_2-N); 69.98 (C-5′); 110.59 (C-2); 130.41 (C-3′); 149.92 (C-4′); 165.52 (C-4); 168.40 (C-6); 196.39 (C-2′). For $C_{15}H_{18}BrNO_5$ (372.2) calculated: 48.40% C, 4.87% H, 21.47% Br, 3.76% N; found: 48.21% C, 4.74% H, 21.41% Br, 3.69% N.

6-Hydroxy-2,2-dimethyl-5-[3-methyl-2-oxo-5-(piperidin-1-yl)cyclopent-3-en-1-yl]-4H-1,3-dioxin-4-one (**3f**). Yield 1.14 g (71%), m.p. 202–204 °C. ^{1}H NMR (CF_3COOD): 1.62–1.67 m, 1 H (CH_2); 1.91 s, 3 H (CH_3); 2.03 s, 3 H (CH_3); 2.07 s, 3 H (CH_3); 2.16–2.43 m, 5 H (CH_2); 3.07 t, 1 H, *J* = 10.6 (CH_2-N); 3.50 t, 1 H, *J* = 11.4 (CH_2-N); 3.62 m, 2 H (CH_2-N); 3.89 m, 1 H (H-1′); 4.87 m, 1 H (H-5′); 7.61 bs, 1 H (H-4′). ^{13}C NMR (CF_3COOD): 23.61 (CH_3); 26.18 (CH_2); 26.51 (CH_2); 26.82 (CH_2); 26.97 (CH_3); 29.34 (CH_3); 46.59 (C-1′); 52.52 (CH_2-N); 57.14 (CH_2-N); 70.74 (C-5′); 112.54 (C-2); 148.92 (C-4′); 152.28 (C-3′); 168.48 (C-4); 170.72 (C-6); 205.75 (C-2′). For $C_{17}H_{23}NO_5$ (321.4) calculated: 63.54% C, 7.21% H, 4.36% N; found: 63.38% C, 7.35% H, 4.26% N.

6-Hydroxy-2,2-dimethyl-5-[3-methyl-5-morpholino-2-oxo-cyclopent-3-en-1-yl]-4H-1,3-dioxin-4-one (**3g**). Yield 1.07 g (66%), m.p. 193–195 °C. ^{1}H NMR (CF_3COOD): 1.97 s, 3 H (CH_3); 2.06 s, 3 H (CH_3); 2.13 s, 3 H (CH_3); 3.52 t, 1 H (CH_2-N); 3.86–3.97 m, 3 H (CH_2-N); 4.09 d, 1 H, *J* = 2.1 (H-1′); 4.22–4.52 m, 4 H (CH_2O); 5.14 m, 1 H (H-5′); 7.71 bs, 1 H (H-4′). ^{13}C NMR (CF_3COOD): 11.75 (CH_3); 27.24 (CH_3); 29.26 (CH_3); 46.70 (C-1′); 51.02 (CH_2-N); 54.44 (CH_2-N); 67.03 (CH_2O); 71.08 (C-5′); 112.52 (C-2); 148.19 (C-4′); 152.96 (C-3′); 168.75 (C-4); 170.54 (C-6); 205.61 (C-2′). For $C_{16}H_{21}NO_6$ (323.3) calculated: 59.43% C, 6.55% H, 4.33% N; found: 59.21% C, 6.36% H, 4.28% N.

6-Hydroxy-2,2-dimethyl-5-[3-methylsulfanyl-2-oxo-5-(piperidin-1-yl)cyclopent-3-en-1-yl]-4H-1,3-dioxin-4-one (**3h**). Yield 1.22 g (69%), m.p. 200–206 °C. ^{1}H NMR (CF_3COOD): 1.67–1.71 m, 1 H (CH_2); 1.99 s, 3 H (CH_3); 2.07 s, 3 H (CH_3); 2.16–2.38 m, 5 H (CH_2); 2.61 s, 3 H (CH_3-S); 3.18 t, 1 H, *J* = 10.6 (CH_2-N); 3.62 t, 1 H, *J* = 11.4 (CH_2-N); 3.81–3.92 m, 2 H (CH_2-N); 4.07 m, 1 H (H-1′); 4.99 m, 1 H (H-5′); 7.21 bs, 1 H (H-4′). ^{13}C NMR (CF_3COOD): 14.98 (CH_3-S); 23.75 (CH_2); 26.29 (CH_2); 26.64 (CH_2); 27.04 (CH_3); 29.40 (CH_3); 47.12 (C-1′); 52.54 (CH_2-N); 57.07 (CH_2-N); 71.46 (C-5′); 112.76 (C-2); 137.30 (C-4′); 155.73 (C-3′); 168.43 (C-4); 170.66 (C-6); 201.30 (C-2′). For $C_{17}H_{23}NO_5S$ (353.4) calculated: 57.77% C, 6.56% H, 3.96% N; found: 57.62% C, 6.42% H, 3.88% N.

6-Hydroxy-2,2-dimethyl-5-[3-azido-5-(hexahydroazepin-1-yl)-2-oxocyclopent-3-en-1-yl]-4H-1,3-dioxin-4-one (**7i**). Yield 1.33 g (74%), m.p. 148–149 °C. ^{1}H NMR (CF_3COOD): 1.31–1.86 m, 8 H (CH_2); 1.94 s, 3 H (CH_3); 2.11 s, 3 H (CH_3); 3.31 m, 1 H (CH_2-N); 3.65–3.75 m, 4 H (CH_2-N, H-1′); 4.93 m, 1 H (H-5′); 7.77 d, 1 H, *J* = 2.1 (H-4′). ^{13}C NMR (CF_3COOD): 26.33 (CH_3); 26.71 (CH_2); 27.91 (CH_2); 29.44 (CH_3); 46.57 (C-1′); 53.04 (CH_2-N); 59.64 (CH_2-N); 67.12 (C-5); 69.98 (C-5′); 112.96 (C-2); 129.52 (C-3′); 149.78 (C-4′); 167.92 (C-4); 170.89 (C-6); 197.39 (C-2′). For $C_{17}H_{22}N_4O_5$ (362.4) calculated: 56.34% C, 6.12% H, 15.46% N; found: 56.19% C, 6.04% H, 15.36% N.

Crystal Structure Determination of **9a**

Single crystals of **9a** were prepared by slow crystallization from water. A suitable crystal of compound **9a** was mounted on a Stoe–Siemens AED diffractometer. Intensity data were collected at 293 K using graphite-monochromated MoKα (λ = 0.71069 Å) radiation. Accurate cell parameters were obtained by least-squares analysis of the setting angles of 44 automatically centered reflections ($20.7 < 2\theta > 28.9°$). The ω/2θ scan mode was used and three standard reflections (004, 460 and 600) were remeasured every 90 min; no significant systematic fluctuation was found. Intensities were corrected for Lorentz and polarization effects. Empirical absorption correction was considered unnecessary. The structure was solved by direct methods using SHELXS86 (ref.[16]) and refined by the full-matrix least-squares methods on F^2 values. All non-H atoms were refined anisotropically and H atoms isotropically. All hydrogen atoms were located from the difference Fourier map and those bonded to carbon atoms were constrained on geometrical grounds (C–H distance 0.96 Å). All calculations were carried out using the SHELXL93 (ref.[17]) program for refinement, PARST (ref.[18]) for geometrical calculations and ORTEP (ref.[19]) for structure drawing. As scattering factor data were used those in SHELXL93. Crystal data and structure refinement parameters are given in Table I.

Molecule of **9a**, which was shown to crystallize with two molecules of water (for detail see Table II), consists of two morpholine and one 2,2-dimethyl-1,3-dioxane-4,6-dione rings linked to an unsaturated five-membered carbon ring. Both morpholine rings possess a chair conformation. They are not equivalently bonded to the cyclopentene ring, because one of them takes part in the delocalized π-bonding system [N(morpholine)–C(cyclopentene)] = 1.316(7) Å and 1.469(6) Å, respectively. The 2,2-dimethyl-1,3-dioxane-4,6-dione ring possesses a half-chair conformation. Inspection of the interatomic distances shows a large delocalized π-system encompassing [O(6)(sp)–C(17)(sp^2)– or O(5)(sp^2)–C(15)(sp^2)]–C(14)(sp^2)–C(5)(sp^2)–C(4)(sp^2)–C(3)(sp^2)–N(2)(sp^2). This conjugation causes that primary single bond C(4)–C(5) has interatomic distance of 1.384(7) Å which is less than the lengths of double bonds C(5)–C(14) and C(3)–C(4) of 1.411(7) Å and 1.406(7) Å, respectively. These facts were also confirmed by quantum-chemical studies.

TABLE II
Possible hydrogen bonds (in Å) in **9a**

(D)onor	(H)ydrogen	(A)ccept or	D–H	D···A	H···A	D–H···A
O1W	H1WA	O1[a]	0.84(9)	2.82(1)	2.00(9)	164(9)
O2WB	H2BA	O6[b]	0.69(1)	2.83(1)	2.15(0)	167.9(8)
C2	H10A	O5[c]	0.97(1)[e]	3.38(1)	2.61(1)	136.3(5)
O2WA	H2AA	O5[d]	0.65(1)	2.88(1)	2.28(0)	154.3(8)
C10	H13A	O1W	0.97(1)[e]	3.39(1)	2.54(1)	146.4(5)

[a] Transformed by $-y + 5/4$, $x - 3/4$, $-z + 1/4$. [b] Transformed by $y + 1/4$, $-x + 5/4$, $z + 1/4$. [c] Transformed by $-y + 7/4$, $x - 3/4$, $z + 1/4$. [d] Transformed by $-x + 2$, $-y + 1$, $-z + 1$. [e] These lengths were constrained during the refinement.

Quantum-Chemical Calculations

The standard semiempirical AM1 (Austin Model) method of quantum chemistry (AMPAC program package)[20,21] was used to calculate the electronic structure of **9a**. The model systems are based on experimental solid-state (models A1–A4) and well optimized (model B1) geometries. The results are evaluated in terms of Mulliken-population-analysis bond orders (BO) and atomic charges[22] (Q).

TABLE III
Relevant bond lengths (in Å) and bond orders in X-ray geometries of $C_5H_4(C_4O_2Me_2)(NC_4OH_8)_2$ (model A1), with H_2O molecule located at O(6) position (model A2), at O(5) position (model A3) and in both positions (model A4) as well as isolated optimized $C_5H_4(C_4O_2Me_2)(NC_4OH_8)_2$ geometry (model B1). Standard deviations for experimental data are in parentheses

Model	Bond lengths		Bond orders				
	A1–A4	B1	A1	A2	A3	A4	B1
O4–C16	1.434(6)	1.427	0.92	0.92	0.92	0.92	0.92
O4–C17	1.376(6)	1.380	0.97	0.97	0.98	0.97	0.98
C16–O3	1.434(6)	1.426	0.93	0.93	0.93	0.93	0.93
O3–C15	1.381(6)	1.381	0.96	0.97	0.96	0.96	0.98
C14–C15	1.442(7)	1.461	0.98	0.98	0.98	0.98	0.96
C15–O5	1.203(5)	1.233	1.83	1.18	1.84	1.81	1.82
C14–C17	1.450(7)	1.462	0.97	0.97	0.98	0.98	0.96
C5–C14	1.411(6)	1.361	1.52	1.51	1.51	1.49	1.60
C17–O6	1.206(5)	1.233	1.82	1.82	1.80	1.80	1.81
C4–C5	1.384(6)	1.433	1.23	1.24	1.24	1.25	1.15
C1–C5	1.524(6)	1.529	0.96	0.96	0.96	0.96	0.96
C3–C4	1.406(6)	1.388	1.46	1.44	1.44	1.43	1.55
C4–H(C4)	0.93	1.094	0.95	0.95	0.95	0.95	0.93
C2–C3	1.497(6)	1.519	0.98	0.98	0.98	0.98	0.97
C3–N2	1.316(6)	1.360	1.26	1.26	1.27	1.27	1.18
C1–C2	1.544(6)	1.558	0.95	0.95	0.95	0.95	0.94
C2–H(C2)	0.97	1.118	0.96	0.96	0.96	0.96	0.95
		1.119					
C1–N1	1.469(6)	1.454	0.97	0.97	0.97	0.97	0.97
C1–H(C1)	0.98	1.133	0.95	0.94	0.95	0.94	0.93

The main aim of the quantum-chemical studies of **9a** was to explain the bonding properties of O=C(15,17)–C(14)–C(5)–C(4)–C(3)–N(morpholine) chain within dioxane, cyclopentene and planar morpholine rings (two related mesomeric structures, Scheme 5). For this purpose, the experimental (solid state) geometry of isolated $C_5H_4(C_4O_2Me_2)$ $(NC_4OH_8)_2$ (model A1) as well as that with H_2O molecule located at the O(6) position (model A2), at the O(5) position (model A3) and in both positions (model A4) were used. The fixed geometry of these models, however, reflects the solid-state influences. For comparison with experimental data obtained from solution, the geometry of isolated $C_5H_4(C_4O_2Me_2)$ $(NC_4OH_8)_2$ (model B1) was optimized. Our results confirm significant environmental dependence of the degree of bond conjugation under study (see bond lengths and bond order values in Table III).

Crystal Structure Determination of **10**

Diffraction data were collected at 293 K on a Siemens SMART CCD area detector diffractometer using 0.3° ω-scans. The crystal-to-detector distance was 3.85 cm. Graphite-monochromated MoKα radiation, λ = 0.71093 Å, was used. The structure was solved by direct methods and subsequent Fourier difference techniques, and refined anisotropically by common least-squares methods[17]. The hydrogen atoms were positioned geometrically and refined riding on the coordinates of the parent carbon atoms. The weighting scheme was $\Sigma w(|F_o|^2 - |F_c|^2)^2$, where $w^{-1} = \sigma^2(F_o^2) + (0.0329P)^2 + 0.8612P$, with $3P = F_o^2 + 2F_c^2$. The absolute structure could not been determined reliably (Flack parameter, x = –1.18(230)). Crystal data and structure refinement parameters are given in Table I.

The crystal structure of **10** contains two independent molecules which differ slightly in bond distances and angles (Fig. 4). The main difference is an disorder of the carbon atom C45 which is disordered through two positions allowing to hexahydroazepine ring to possess two different conformations, chair/boat (40/60). Other three seven-member hexahydroazepine rings accept the chair conformation. Shorter C–C bonding distances in cyclopentene ring as well as in 2,2-dimethyl-1,3-dioxane-4,6-dione ring give the evidence of the electron density delocalization through the fragments N1–C11–C7–C8–N2 (N31–C41–C37–C38–N32, respectively) and O1–C2–C1–C6–O4 (O31–C32–C31–C36–O34, respectively). Atoms of the mentioned fragments lie in the planes with deviations less than 0.06 Å. Cyclopentene ring and 2,2-dimethyl-1,3-dioxane-4,6-dione ring form dihedral angles of 70° in both independent molecules.

Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC-144314 (**9a**) and CCDC-144315 (**10**). Copies of the data can be obtained free of charge on application to CCDC, e-mail: deposit@ccdc.cam.ac.uk.

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