Synthesis and Some Reactions of Functionalized Benzo[*b*]azonines and Bi(benzo[*b*]azonines)

Elsayed M. Afsah, Ahmed A. Fadda, Samir Bondock, and Mohamed M. Hammouda

Chemistry Department, Faculty of Science, Mansoura University, ET-35516, Mansoura, Egypt

Reprint requests to Prof. Dr. E. M. Afsah. E-mail: emafsah@yahoo.com

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Tetrahydro-1*H*-benzo[*b*]azonin-2,7-dione (**2a**) has been used as a precursor in the synthesis of dibenzo[*b,f*][1,5]diazacyclododecene and dibenzo[*b,g*][1,6]diazacyclododecene ring systems **4** and **5**, respectively, *via* periodate oxidation of the appropriate indolo-benzo[*b*]azonines **3** and **7**. The synthesis of hexahydro-benzo[*b*][1,4]diazecin-2,7-dione (**10**) has been achieved by the Schmidt reaction of **2a**.

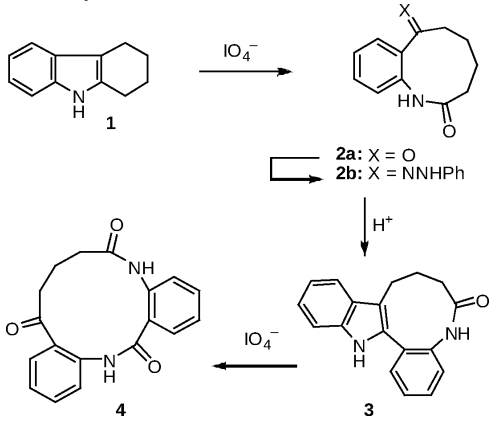
The periodate oxidation of 9,9′-methylenebis(2,3,4,9-tetrahydro-1*H*-carbazole) (**11**) afforded 1,1′-methylenebis(3,4,5,6-tetrahydro-1*H*-benzo[*b*]azonin-2,7-dione) (**12**). Its 6,6′-methylenebis isomer **13** was obtained by treating **2a** with formaldehyde. Oxidation of **16** gave the unsymmetrical bi(benzo [*b*]azonine) **17**.

The Mannich reaction of **2a** led to a mixture of its 6-methylene derivative **19** and the spirocyclic system **20**. The reactions of **2a** with aldimines and aromatic aldehydes were also investigated.

Key words: Benzo[*b*]azonines, Bi(benzo[*b*]azonines), Bis-(Mannich Bases), Periodate Oxidation

Introduction

Nine-membered *N*-heterocycles (heteronins) are significant classes of heterocyclic systems and constituents of various important naturally occurring and synthetic compounds. The azonine ring system has been the object of considerable synthetic efforts [1 – 6], because this system is present in various alkaloids. A number of azonines and benzo-annulated azonines have been studied with interest centered on their potential pharmaceutical activity as antimalarials [7] and analgesics [8], and on their antihypertensive [9] and CNS activity [10].



Scheme 1.

The dibenz[*d*,*f*]azonine ring system is the main part in laurifonine, laurifine and laurifinine alkaloids [11]. The azonine core is present in vinblastine and vincristine alkaloids [12, 13] which possess significant antitumor activity and have been widely used clinically.

However, the literature of benzoazonines, dibenzoazonines, azoninoindoles and related compounds is relatively limited [14 – 19], and there is no report on the synthesis of bi(benzoazonines) and related compounds. We report here on the synthesis and functionalization of the title compounds which possess considerable synthetic and pharmaceutical interest.

Results and Discussion

The periodate oxidation of 1,2,3,4-tetrahydrocarbazole (**1**) afforded 3,4,5,6-tetrahydro-1*H*-benzo[*b*]azonin-2,7-dione (**2a**) according to an earlier report [20]. The present work is concerned with attempts to extend the scope of the periodate oxidation of indoles to include the indolo-benzo[*b*]azonines of the type **3**, as a route to higher heterocyclic systems. This has been realized *via* a reaction sequence which involves the Fischer indolization of the phenylhydrazone **2b** to give 5,6,7,8- tetrahydro-9*H*-indolo[2,3-*d*]benzo[*b*] azonin-6-one (**3**) (Scheme 1). The periodate oxidation of **3** took place quite smoothly and indicated the

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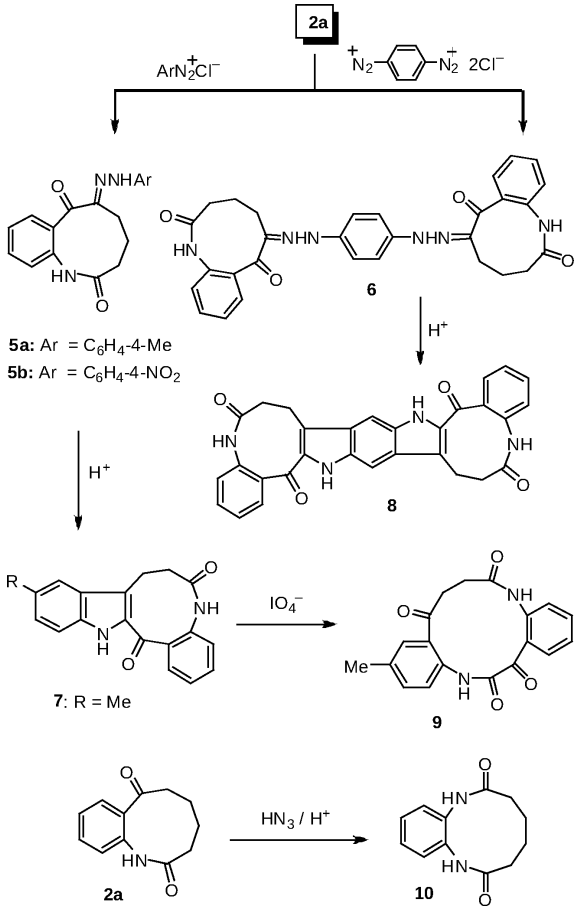
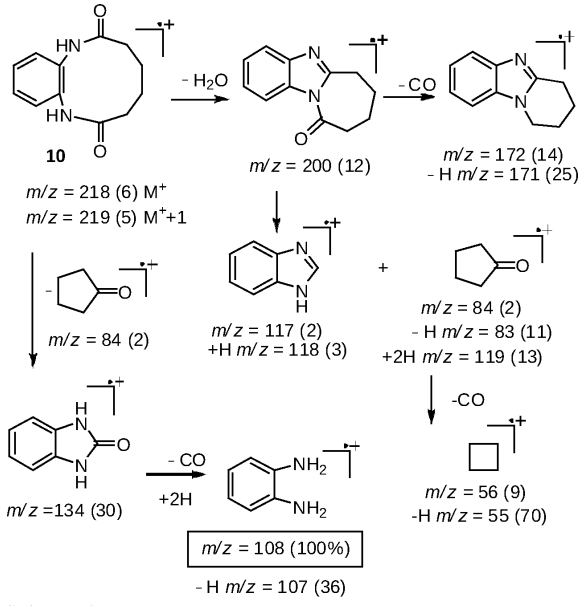


Scheme 2.



Scheme 3.

preparative value of this route to the 12-membered macrocyclic system **4**. The identity of **4** was demonstrated by the formation of a phenylhydrazone and by its spectral data.

In an alternative route to the dibenzo-diazacyclododecene ring system starting from **2a**, *via* the Fischer indolization periodate oxidation sequence, compound **2a** was treated with diazotized *p*-toluidine or *p*-nitroaniline to give 6-arylhydrazono-3,4,5,6-tetrahydro-1*H*-benzo[*b*]azonin-2,7-diones **5a**, **b**. A similar reaction of **2a** with bis(diazotized) *p*-phenylenediamine gave 6,6′-(1,4-phenylenedihydrazono)-bis (3,4,5,6-tetrahydro-1*H*-benzo[*b*]azonin-2,7-dione) (**6**) (Scheme 2).

Fischer indolization of **5a** and **6** afforded the indolobenzoazonines **7** and **8**, respectively. The periodate oxidation of **7** generated the macrocyclic system **9**. On the contrary, oxidation of **8** was not feasible due to its insolubility in commonly used solvents.

In the course of our investigation, compound **2a** was subjected to a Schmidt rearrangement to afford 1,3,4,5,6,8-hexahydro-benzo[*b*][1,4]diazecin-2,7-dione (**10**), as the sole product (Scheme 2). The assignment of the (NH) group between the (CO) group and the aryl moiety of **10** is based on previous studies on the Schmidt rearrangement [21 – 23], and also by analogy with the formation of tetrahydro-benzo[*b*]azepin-2-one [24] and tetrahydro-1*H*-benzo[*b*]azocin-2-one [25] from α-tetralone and 1-benzosuberone, respectively. In addition, there is much evidence that bulky substituents at the α-position exert stereocontrol on the reaction [24 – 28]. The mass spectrum of **10** showed the molecular ion at $m/z = 218$ $[M]^+$ and a fragmentation pattern which is in line with the proposed structure (Scheme 3).

The *o*-phenylenediamine moiety could be identified by two peaks at $m/z = 108$ (100 %, base peak) and 107 (36 %). The main fragmentation pathways encountered for **10** are indicated in Scheme 3. Its ^{1}H NMR spectrum revealed two triplets at $\delta = 1.83$ (4-H_2 and 5-H_2) and 2.12 (3-H_2 and 6-H_2), and a singlet at 9.22 (2 × CON*H*).

The potential importance of the periodate oxidation of indoles of the type **1** was established by its application to the synthesis of bi(benzoazonines) and related compounds (Scheme 4). This has been realized by treating **1** with formaldehyde to give 9,9′-methylenebis(2,3,4,9-tetrahydro-

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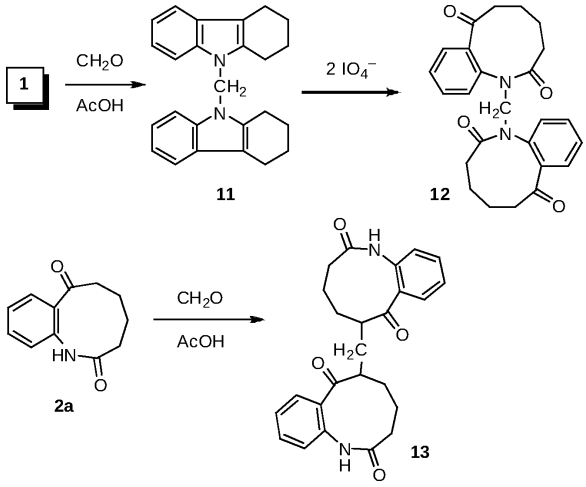
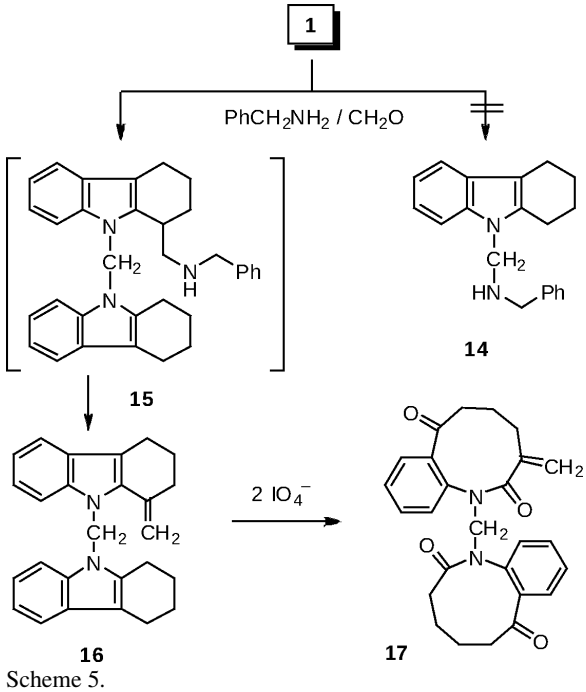
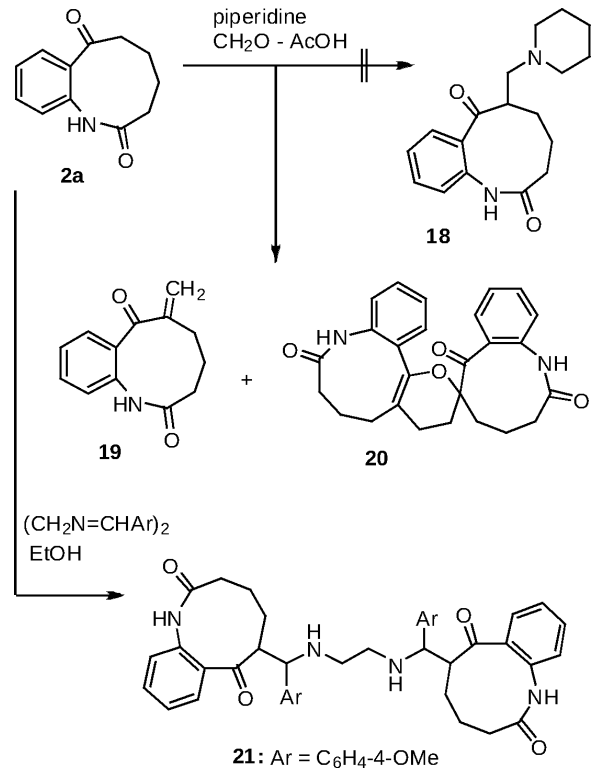


Scheme 4.



Scheme 5.

1*H*-carbazole) (**11**), the periodate oxidation of which afforded 1,1′-methylenebis(3,4,5,6-tetrahydro-1*H*-benzo[*b*]azonin-2,7-dione) (**12**). Its mass spectrum indicated the molecular ion peak at *m/z* = 416 $[M-2]^+$. Its isomer 6,6′-methylenebis(3,4,5,6-tetrahydro-1*H*-benzo[*b*]azonin-2,7-dione) (**13**) was obtained by treating **2a** with formaldehyde. The IR spectrum of **13** displayed strong bands at 3347 (NH), 1720 (CONH) and 1680 cm^{-1} (CO).



Scheme 6.

On the other hand, an attempt to prepare the Mannich base **14** by treating **1** with benzylamine and formaldehyde led to the formation of 1-methylene-9-(1,2,3,4-tetrahydro-9*H*-carbazol-9-ylmethyl)-2,3,4,9-tetrahydro-1*H*-carbazole (**16**), which was subjected to the periodate oxidation to afford the unsymmetrical bi(benzoazonine) **17** (Scheme 5). The structures of compounds **16** and **17** were supported by analytical and spectral data.

In view of the pharmacological activity and the synthetic potential of ketonic Mannich bases [26, 29 – 34], we investigated the Mannich reaction of **2a** with piperidine and formaldehyde anticipating the formation of the Mannich base **18**. Unexpectedly, however, it gave a mixture of 6-methylene-3,4,5,6-tetrahydro-1*H*-benzo[*b*]azonin-2,7-dione (**19**) (8 %) and the spirocyclic system **20** (53 %). The mass spectra of **19** and **20** showed the molecular ions at *m/z* = 215 and 430 $[M]^+$, respectively. The spontaneous deamination of **18** to give **19**, which undergoes Diels-Alder dimerization to afford **20**, is in line with the reported results of the Mannich reaction with thiochromanone [35] and [1]benzazepin-2,5-(3*H*,4*H*)-dione [36] (Scheme 6).

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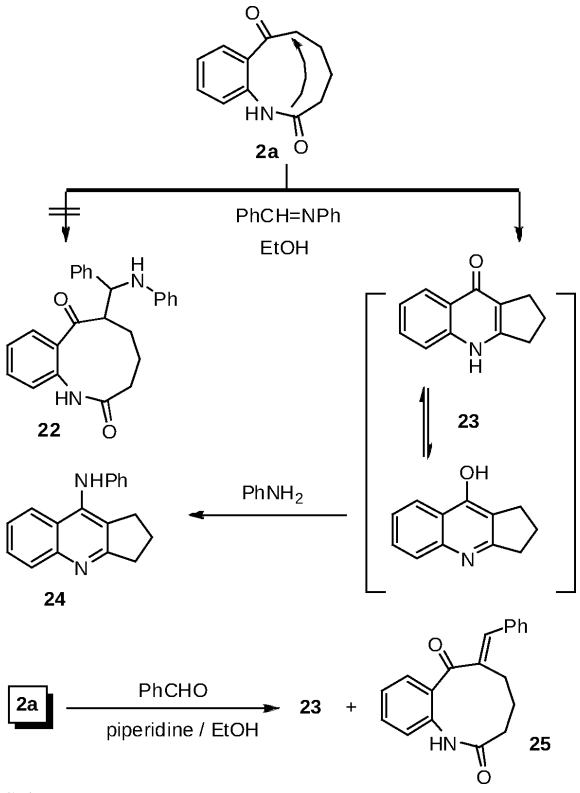

Scheme 7.

On the other hand, the reaction of aldimines with cyclic ketones has opened routes to the corresponding Mannich bases [37, 38]. Thus, the synthesis of the bis-(Mannich base) **21** has been achieved by treating compound **2a** with *N*,*N*′-bis(*p*-methoxybenzylidene)ethylenediamine (Scheme 6). It is interesting in this connection that attempted reaction of benzalaniline with **2a** failed to give the required base **22**, leading instead to the formation of 9-phenylamino-1*H*-cyclopenta[*b*] quinoline (**24**) (Scheme 7). The IR spectrum of **24** revealed the absence of carbonyl groups and showed a strong band at 3290 cm^{-1} (NH). Its mass spectrum exhibited a molecular ion peak at *m/z* = 260 (65 %); the base peak at *m/z* = 259 (100 %) is due to the $[M–1]^+$ ion. The ^1H NMR spectrum revealed a multiplet at δ = 2.02 – 2.50 (1-H_2, 2-H_2 and 3-H_2) and a broad singlet at δ = 3.28 (Ph-N*H*).

The formation of **24** rather than **22** may be attributed to the tendency of **2a** to cyclize readily under mild basic conditions to give 1,2,3,4-terahydro-cyclopenta[*b*] quinolin-9-one (**23**), as reported earlier by Witkop *et al*. [39]. Further reaction of **23** with aniline, resulting from the decomposition of benzalaniline, afforded **24**. In line with this, compound **23** was obtained as the main product (66 %) besides the 6-benzylidene derivative **25** (12 %), on treating **2a** with benzaldehyde in the presence of piperidine as a catalyst.

Experimental Section

All melting points were determined on a Gallenkamp electric melting point apparatus and are uncorrected. Elemental microanalyses were carried out at Microanalytical Unit, Faculty of Science, Cairo University. Infrared spectra were measured on a Mattson 5000 FTIR spectrometer. ^1H NMR data were obtained in $CDCl_3$ or [D_6]DMSO solution on a Varian XL 200 MHz instrument using TMS as internal standard. Chemical shifts are reported in ppm (δ) downfield from internal TMS. Mass spectra were recorded on a GC-MS QP-1000 EX Shimadzu instrument. The course of the reaction and the purity of the synthesized compounds were monitored by TLC using EM science silica gel coated plates with visualization by irradiation with an ultraviolet lamp. Due to the limited solubility of the products in common solvents, the ^1H NMR spectra were recorded for compounds **3**, **5a**, **10**, **11**, **16**, **20**, **24**, and **25** as representative examples. Compounds **1** [40] and **2a** [20] were prepared as previously described.

*7-(Phenylhydrazono)-1,3,4,5,6,7-hexahydro-benzo[b] azonin-2-one (**2b**)*

To a solution of **2a** (1 g, 5 mmol) in ethanol (10 mL), phenylhydrazine (0.54 g, 5 mmol) and acetic acid (0.2 mL) were added. The reaction mixture was heated on a water bath for 5 min and stirred for 90 min at r. t. The product obtained on cooling was filtered and crystallized from ethanol to give **2b**. M. p. 192 °C. Yield 40 % (yellow leaflets). – IR (KBr): ν = 3445 (NH hydrazone), 3399 (NH lactam), 1709 (CO), 1431, 1322, 1120 cm^{-1}. – $C_{18}H_{19}N_3O$ (293.36): calcd. C 73.69, H 6.53, N 14.32; found C 73.64, H 6.48, N 14.19.

*5,6,7,8-Tetrahydro-9H-indolo[2,3-d]benzo[b]azonin-6-one (**3**)*

A solution of **2b** (0.59 g, 2 mmol) in 20 % sulfuric acid (10 mL) was heated on a water bath for 30 min, poured onto water (30 mL) and basified with NH_4OH. The obtained product was filtered and crystallized from ethyl acetate-pet. ether 40 – 60 °C (2 : 1) to give **3**. M. p. 221 °C. Yield 58 % (greenish crystals). – IR (KBr): ν = 3447 (NH indole), 3390 (NH lactam), 1705 (CO), 1613 (C=C), 1420, 1210 cm^{-1}. – ^1H NMR (200 MHz, [D_6]DMSO, 25 °C, TMS): δ = 1.83 – 1.98 (m, 6H, 7-H_2, 8-H_2, 9-H_2), 6.97 – 7.53 (m, 8H, aromatic), 8.95 (s, 1H, CON*H*), 10.87 (s, 1H, N*H* indole). – MS (EI, 70 eV): *m/z* (%) = 276 (100) $[M]^+$, 248 (25) $[M–CO]^+$, 233 (53), 219

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(87), 77(12). – $C_{18}H_{16}N_2O$ (276.33): calcd. C 78.24, H 5.85, N 10.14; found C 78.02, H 5.80, N 10.07.

*8,9-Dihydrodibenzo[b,f][1,5]diazacyclododecene-6,10,16 (5H,7H,15H)-trione (**4**)*

A solution of **3** (0.55 g, 2 mmol) in methanol (80 mL) and acetone (40 mL) was added to a solution of sodium periodate (0.85 g, 4 mmol) in water (5 mL). After standing at r. t. for 13 h, the solvent was removed at reduced pressure, and the product was washed successively with water (3 × 10 mL) and boiling chloroform (3 × 10 mL) to give **4**. M. p. > 350 °C. Yield 41 % (pale green powder). – IR (KBr): ν = 3422 (NH lactam), 1770 and 1753 (CON), 1655 (CO), 1533, 1212 cm^{-1}. – MS (EI, 70 eV): *m/z* (%) = 306 (17) $[M–2]^+$, 305 (26) $[M–3]^+$, 213 (39), 144 (100), 121 (36), 92 (19), 77 (26). – $C_{18}H_{16}N_2O_3$ (308.33): calcd. C 70.12, H 5.33, N 9.09; found C 70.06, H 5.11, N 8.99.

*6-Arylhydrazono-3,4,5,6-tetrahydro-1H-benzo[b]azonin-2,7-diones **5a**, **b***

Diazotized *p*-toluidine or *p*-nitroaniline (5 mmol) was added with stirring to a cold solution of **2a** (1 g, 5 mmol) in pyridine (15 mL). The reaction mixture was stirred for 30 min at 5 – 10 °C and for 2 h at r. t. The reaction mixture was diluted with water (20 mL) and extracted with ethyl acetate, washed with water and dried over sodium sulfate. The solvent was removed at reduced pressure to give **5a**, **b**.

*6-(p-Tolylhydrazono)-3,4,5,6-tetrahydro-1H-benzo[b] azonin-2,7-dione (**5a**)*

M. p. 244 °C (ethanol). Yield 33 % (red needles). – IR (KBr): ν = 3420 (NH lactam), 3240 (NH hydrazone), 1720 (CON), 1680 (CO), 1333, 1210 cm^{-1}. – ^{1}H NMR (200 MHz, [D$_6$]DMSO, 25 °C, TMS): δ = 1.40 – 1.71 (m, 6H, 3-*H*$_2$, 4-*H*$_2$, 5-*H*$_2$), 2.20 (s, 3H, Ar-C*H*$_3$), 7.12 – 7.53 (m, 8H, aromatic), 9.21 (s, 1H, CON*H*), 10.53 (s, 1H, N*H* hydrazone). – MS (EI, 70 ev): *m/z* (%) = 321 (17) $[M]^+$, 244 (4), 200 (16), 184 (8), 138 (20), 122 (100), 76 (50). – $C_{19}H_{19}N_3O_2$ (321.37): calcd. C 71.01, H 5.96, N 13.08; found C 70.97, H 5.90, N 12.97.

*6-(p-Nitrophenylhydrazono)-3,4,5,6-tetrahydro-1H-benzo [b]azonin-2,7-dione (**5b**)*

M. p. 205 °C (chloroform). Yield 15 % (dark green powder). – IR (KBr): ν = 3432 (NH lactam), 3269 (NH hydrazone), 1733 (CON), 1670 (CO), 1517, 1341 (NO_2), 1210 cm^{-1}. – MS (EI, 70 eV): *m/z* (%) = 353 (1) $[M+1]^+$, 230 (2) $[M–C_6H_4NO_2]^+$, 229 (4), 200 (16), 150 (55), 122 (100) $[M–C_{12}H_{12}N_3O_2]^+$. – $C_{18}H_{16}N_4O_4$ (352.34): calcd. C 61.36, H 4.58, N 15.90; found C 61.29, H 4.44, N 15.87.

*6,6′-(1,4-Phenylenedihydrazono)-bis(3,4,5,6-tetrahydro-1H-benzo[b]azonin-2,7-dione) (**6**)*

This compound was obtained from **2a** (1 g, 5 mmol) and bis(diazotized) *p*-phenylenediamine (2.5 mmol) in pyridine (15 mL), following the same procedure as described above. The product was purified by preparative chromatography on Al_2O_3 using chloroform – methanol (2 : 1) as eluent. M. p. > 350 °C. Yield 35 % (dark brown powder). – IR (KBr): ν = 3404 (NH lactam), 3330 (NH hydrazone), 1709 (CON), 1680 (CO), 1585, 1315, 1210 cm^{-1}. – MS (EI, 70 eV): *m/z* (%) = 534 (5) $[M–2]^+$, 533 (4) $[M–3]^+$, 336 (8) $[M–C_{12}H_{11}NO_2]^+$, 232 (41), 214 (7), 210 (10), 184 (100), 136 (18). – $C_{30}H_{28}N_6O_4$ (536.58): calcd. C 67.15, H 5.26, N 15.66; found C 67.09, H 5.14, N 15.57.

*8,13-Dihydro-10-methyl-indolo[2,3-e]benzo[b]azonin-6,14 (5H,7H)-dione (**7**)*

This compound was obtained by treating **5a** (0.8 g, 2.5 mmol) with hot 20 % sulfuric acid (10 mL), following the procedure described above for the synthesis of **3**. The product was purified by crystallization from DMSO to give **7**. M. p. 235 °C. Yield 15 % (dark brown powder). – IR (KBr): ν = 3410 (NH indole), 3340 (NH lactam), 1715 (CON), 1670 (CO), 1576, 1330, 1212 cm^{-1}. – MS (EI, 70 eV): *m/z* (%) = 306 (17) $[M+2]^+$, 305 (26) $[M+1]^+$, 291 (14), 264 (15), 240 (16), 215 (22), 201 (20), 144 (100), 77 (26). – $C_{19}H_{16}N_2O_2$ (304.34): calcd. C 74.98, H 5.30, N 9.20; found C 74.89, H 5.26, N 9.16.

*7,8,10,18,19,21-Hexahydro-benzo[b]azonino[5″,6″ : 4′,5′] pyrrolo[2′,3′ : 5,6]indolo[2,3-e]benzo[b]azonin-6,11,17,22 (5H,16H)-tetraone (**8**)*

A mixture of **6** (0.4 g, 0.7 mmol) and 20 % sulfuric acid (10 mL) was heated on a water bath for 30 min, poured onto water (25 mL) and basified with NH_4OH. The product was filtered and washed with boiling pyridine to give **8**. M. p. > 350 °C. Yield 40 % (dark brown powder). – IR (KBr): ν = 3475 (NH indole), 3420 (NH lactam), 1709 (CON), 1670 (CO), 1322, 1212 cm^{-1}. – MS (EI, 70 eV): *m/z* (%) = 502 (2) $[M]^+$, 337 (27), 274 (16), 260 (26), 216 (20), 184 (100), 166 (35), 154 (21), 92 (17). – $C_{30}H_{22}N_4O_4$ (502.52): calcd. C 71.70, H 4.41, N 11.15; found C 71.63, H 4.33, N 11.02.

*18-Methyl-2,11-diaza-tricyclo[14.4.0.0^{5,10}]eicosa-1(20), 5(10),6,8,16,18-hexaene-3,4,12,15-tetraone (**9**)*

A solution of **7** (0.2 g, 0.65 mmol) in pyridine (10 mL) was added to a solution of sodium periodate (0.28 g, 1.3 mmol) in water (5 mL). After standing at r. t. for 18 h, the solvent was removed at reduced pressure, and the product was washed successively with water (3 × 10 mL) and boiling pyridine (3 × 10 mL) to give **9**. M. p. > 350 °C. Yield 55 %

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(white powder). – IR (KBr): ν = 3420 (NH lactam), 1730 (CON), 1710 (CO), 1690 (CO), 1620 (C=C), 1210 cm^{-1}. – MS (EI, 70 eV): *m/z* (%) = 338 (59) $[M+2]^+$, 311 (40), 310 (100), 309 (80), 247 (17), 203 (18), 179 (36), 76 (66). – $C_{19}H_{16}N_2O_4$ (336.34): calcd. C 67.85, H 4.79, N 8.33; found C 67.79, H 4.71, N 8.28.

*1,3,4,5,6,8-Hexahydro-benzo[b][1,4]diazecin-2,7-dione (**10**)*

To a solution of **2a** (0.5 g, 2.5 mmol) in chloroform (30 mL) containing 90 % sulfuric acid (4 mL) at 0 °C was added sodium azide (0.16 g, 2.5 mmol). After stirring for 1 h at 0 °C and 4 h at 25 °C, the reaction mixture was diluted with ice water (50 mL) and basified with NH_4OH. The product was filtered and crystallized from ethyl acetate – pet. ether 40 – 60 °C (2 : 1) to give **10**. M. p. 191 °C. Yield 53 % (white powder). – IR (KBr): ν = 3399 (NH), 1708 (CON), 1613, 1425, 1315, 1212 cm^{-1}. – ^{1}H NMR (200 MHz, [D_6]DMSO, 25 °C, TMS): δ = 1.83 (t, *J* = 7.5 Hz, 4H, 4-H_2, 5-H_2), 2.12 (t, *J* = 7.5 Hz, 4H, 3-H_2, 6-H_2), 7.15 – 7.24 (m, 4H, aromatic), 9.22 (s, 2H, 2 × CON*H*). – MS (EI, 70 eV): *m/z* (%) = 218 (6) $[M]^+$, 200 (12), 171 (25), 145 (84), 134 (30), 119 (13), 108 (100) $[M–C_6H_8O_2]^+$, 93 (9), 77 (70). – $C_{12}H_{14}N_2O_2$ (218.25): calcd. C 66.04, H 6.47, N 12.84; found C 66.15, H 6.33, N 12.79.

*9,9′-Methylenebis(2,3,4,9-tetrahydro-1H-carbazole) (**11**)*

A solution of **1** (3.42 g, 20 mmol) and formalin (37 %, 1.2 mL, 15 mmol) in acetic acid (40 mL) was heated on a steam bath for 15 min. The reaction mixture was chilled and diluted with water (50 mL). The product obtained was filtered and crystallized from 1,2-dichloroethane to give **11**. M. p. 188 °C. Yield 32 % (yellow powder). – IR (KBr): ν = 1620 (C=C), 1525, 1410, 1225, 1109 cm^{-1}. – ^{1}H NMR (200 MHz, [D_6]DMSO, 25 °C, TMS): δ = 1.88 – 2.76 (m, 16H, 2 × (CH_2)$_4$), 6.17 (s, 2H, NCH_2N), 7.13 – 7.52 (m, 8H, aromatic). – MS (EI, 70 eV): *m/z* (%) = 354 (12) $[M]^+$, 184 (100), 170 (6), 156 (21), 143 (9), 115 (12). – $C_{25}H_{26}N_2$ (354.48): calcd. C 84.63, H 7.33, N 7.89; found C 84.59, H 7.25, N 7.80.

*1,1′-Methylenebis(3,4,5,6-tetrahydro-1H-benzo[b]azonin-2,7-dione) (**12**)*

This compound was obtained from **11** (0.42 g, 1.2 mmol) in pyridine (10 mL) and sodium periodate (0.58 g, 2.7 mmol) in water (5 mL), following the procedure described above for the synthesis of **9**. The product was purified by washing with boiling pyridine (3 × 10 mL) to give **12**. M. p. > 350 °C. Yield 25 % (white powder). – IR (KBr): ν = 1750 (CON), 1701 (CO), 1535, 1345, 1220 cm^{-1}. – MS (EI, 70 eV): *m/z* (%) = 416 (7) $[M–2]^+$, 361 (7), 202 (10), 149 (16), 119 (8), 105 (29), 91 (27), 77 (33), 55 (100). – $C_{25}H_{26}N_2O_4$ (418.48): calcd. C 71.75, H 6.26, N 6.69; found C 71.70, H 6.21, N 6.62.

*6,6′-Methylenebis(3,4,5,6-tetrahydro-1H-benzo[b]azonin-2,7-dione) (**13**)*

A solution of **2a** (0.5 g, 2.5 mmol) and paraformaldehyde (0.042 g, 1.4 mmol) in acetic acid (15 mL) was heated on a water bath at 90 °C for 15 min. The precipitated solid was filtered and washed with boiling chloroform to give **13**. M. p. > 350 °C. Yield 35 % (white powder). – IR (KBr): ν = 3347 (NH lactam), 1720 (CON), 1680 (CO), 1210, 1105 cm^{-1}. – MS (EI, 70 eV): *m/z* (%) = 416 (6) $[M–2]^+$, 361 (3), 208 (12), 202 (13), 149 (20), 105 (35), 91 (37), 77 (27), 55 (100). – $C_{25}H_{26}N_2O_4$ (418.48): calcd. C 71.75, H 6.26, N 6.69; found C 71.72, H 6.23, N 6.65.

*1-Methylene-9-(1,2,3,4-tetrahydro-9H-carbazol-9-yl-methyl)-2,3,4,9-tetrahydro-1H-carbazole (**16**)*

A solution of **1** (3.42 g, 20 mmol), benzylamine (2.14 g, 20 mmol) and formalin (37 %, 2.2 mL, 30 mmol) in acetic acid (40 mL) was heated on a steam bath for 1 h. The product obtained on cooling and dilution with water (70 mL) was filtered and crystallized from chloroform – pet. ether 40 – 60 °C (1 : 1) to give **16**. M. p. 169 °C. Yield 75 % (redish powder). – IR (KBr): ν = 3074, 2933, 1611, 1515, 1225 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.85 – 2.69 (m, 14H, 7 × CH_2), 5.24 (s, 2H, CH_2=), 6.01 (s, 2H, NCH_2N), 7.12 – 7.49 (m, 8H, aromatic). – MS (EI, 70 eV): *m/z* (%) = 368 (84) $[M+2]^+$, 367 (62) $[M+1]^+$, 352 (88) $[M–CH_2]^+$, 196 (30) $[M–C_{12}H_{12}N]^+$, 184 (100), 171 (43), 156 (42), 143 (58), 129 (15), 90 (10), 77 (2). – $C_{26}H_{26}N_2$ (366.50): calcd. C 85.21, H 7.15, N 7.64; found C 85.17, H 7.05, N 7.57.

*1-[(2,7-Dioxo-2,3,4,5,6,7-hexahydro-1H-benzo[b]azonin-yl)methyl]-3-methylene-3,4,5,6-tetrahydro-1H-benzo[b]azonin-2,7-dione (**17**)*

This compound was obtained from **16** (0.51 g, 1.4 mmol) in pyridine (10 mL) and sodium periodate (0.7 g, 3.2 mmol) in water (5 mL), following the procedure described above for the synthesis of **12**. The product was purified by washing with boiling pyridine (3 × 10 mL) to give **17**. M. p. > 350 °C. Yield 18 % (white powder). – IR (KBr): ν = 1774 (CON), 1754 (CON), 1719 (CO), 1702 (CO), 1213, 1110 cm^{-1}. – MS (EI, 70 eV): *m/z* (%) = 430 (73) $[M]^+$, 361 (50), 332 (72), 215 (100), 184 (70), 104 (78), 76 (64). – $C_{26}H_{26}N_2O_4$ (430.50): calcd. C 72.54, H 6.09, N 6.51; found C 72.50, H 6.11, N 6.44.

*Attempted Mannich reaction with **2a**: Synthesis of compounds **19** and **20***

A solution of **2a** (0.5 g, 2.5 mmol), piperidine (0.26 g, 3 mmol) and paraformaldehyde (0.1 g, 3 mmol) in acetic acid

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(15 mL) was heated on a water bath at 90 °C for 90 min. The reaction mixture was diluted with ice water (40 mL), basified with NH_4OH, and subjected to preparative thin layer chromatography on Al_2O_3 using ether-chloroform (2 : 1) as eluent to give **19** and **20**.

*6-Methylene-3,4,5,6-tetrahydro-1H-benzo[b]azonin-2,7-dione (**19**)*

M. p. 179 °C. Yield 8 % (white powder). – IR (KBr): ν = 3395 (NH lactam), 1705 (CON), 1678 (CO), 1325, 1212, 1105 cm^{-1}. – MS (EI, 70 eV): *m/z* (%) = 215 (13) $[M]^+$, 187 (12) $[M–CO]^+$, 169 (35), 144 (22), 127 (53), 113 (16), 91 (25), 77 (16), 55 (100). – $C_{13}H_{13}NO_2$ (215.25): calcd. C 72.54, H 6.08, N 6.51; found C 72.51, H 6.00, N 6.47.

*4,4a′,5,5′,6′,7′,9′,13b′-Octahydro-3′H-spiro[1-benzazonine-6,2′-pyrano[3,2-f][1] benzazonin]-4,7,8′(1H,3H,4′H)-trione (**20**)*

M. p. 210 °C. Yield 53 % (white powder). – IR (KBr): ν = 3450 (NH lactam), 3410 (NH lactam), 1780 (CON), 1768 (CON), 1678 (CO), 1335, 1222, 1100 cm^{-1}. – ^{1}H NMR (200 MHz, [D$_6$]DMSO, 25 °C, TMS): δ = 1.63 – 2.10 (m, 14H, 7 × CH_2), 2.5 (t, 2H, CH_2), 7.15 – 7.53 (m, 8H, aromatic), 8.9 (s, 1H, CON*H*), 9.4 (s, 1H, CON*H*). – MS (EI, 70 eV): *m/z* (%) = 430 (4) $[M]^+$, 412 (21) $[M–18]^+$, 230 (14), 214 (28), 186 (70), 146 (40), 120 (56), 105 (7), 92 (50), 77 (25), 50 (100). – $C_{26}H_{26}N_2O_4$ (430.50): calcd. C 72.54, H 6.09, N 6.51; found C 72.52, H 6.03, N 6.48.

*N,N′-Bis[(3,4,5,6-tetrahydro-2,7-dioxo-1H-benzo[b]azonin-6-yl)-(4-methoxyphenyl)-methyl]ethane-1,2-diamine (**21**)*

A solution of **2a** (1 g, 5 mmol) and *N*,*N*′y-bis(4-methoxybenzylidene)ethane-1,2-diamine (0.74 g, 2.5 mmol) in ethanol (15 mL) and 2 drops of conc. hydrochloric acid was heated on a water bath for 5 min. The precipitated solid was filtered and washed with boiling ethanol to give **21**. M. p. > 350 °C. Yield 15 % (white powder). – IR (KBr): ν = 3344 (NH lactam), 3316 (NH), 3176 (NH), 1766 (CON), 1668 (CO), 1213, 1115 cm^{-1}. – MS (EI, 70 eV): *m/z* (%) = 703 (14) $[M]^+$, 362 (17), 263 (14), 214 (19), 109 (21), 139 (31), 117 (18), 83 (41), 77 (20), 57 (100). – $C_{42}H_{46}N_4O_6$ (702.84): calcd. C 71.77, H 6.60, N 7.97; found C 71.70, H 6.58, N 7.87.

*9-Phenylamino-1H-cyclopenta[b]quinoline (**24**)*

A solution of **2a** (1 g, 5 mmol) and benzalaniline (0.91 g, 5 mmol) in ethanol (15 mL) and one drop of conc. hydrochloric acid was heated on a water bath for 5 min. After standing at r. t. for 8 h and neutralization with NH_4OH, the solvent was removed at reduced pressure, and the product was crystallized from ethanol to give **24**. M. p. 186 °C. Yield 43 % (pale yellow powder). – IR (KBr): ν = 3290 (NH), 1634 (C=N), 1611, 1312, 1225, 1100 cm^{-1}. – ^{1}H NMR (200 MHz, CD_3OD, 25 °C, TMS): δ = 2.02 – 2.50 (m, 6H, 1-H_2, 2-H_2, 3-H_2), 3.28 (br s, 1H, N*H*), 6.90 – 8.10 (m, 9H, aromatic). – MS (EI, 70 eV): *m/z* (%) = 260 (65) $[M]^+$, 259 (100) $[M–1]^+$, 167 (26), 128 (17), 77 (18). – $C_{18}H_{16}N_2$ (260.33): calcd. C 83.04, H 6.19, N 10.76; found C 82.99, H 6.12, N 10.70.

*Base-catalyzed condensation of **2a** with benzaldehyde: Synthesis of **23** and **25***

A solution of **2a** (1 g, 5 mmol), benzaldehyde (0.53 g, 5 mmol) and 2 drops of piperidine in ethanol (15 mL) was refluxed on a water bath for 2 h. After cooling to r. t., the reaction mixture yielded two products which were separated by their different solubility in ethanol. The insoluble component was identified as **23**, and the soluble one as **25**.

*1,2,3,4-Tetrahydro-cyclopenta[b]quinolin-9-one (**23**)*

M. p. 326 °C (327 °C [39]) (benzene). Yield 66 %, colorless crystals. The structure was confirmed by a comparison of IR data, m. p. and TLC with an authentic sample obtained from **2a** and 2 N NaOH solution as previously reported [39].

*6-Benzylidene-3,4,5,6-tetrahydro-1H-benzo[b]azonin-2,7-dione (**25**)*

M. p. 195 °C (ethanol). Yield 12 % (yellow crystals). – IR (KBr): ν = 3407 (NH lactam), 1765 (CON), 1670 (CO), 1315, 1220, 1110 cm^{-1}. – ^{1}H NMR (200 MHz, [D$_6$]DMSO, 25 °C, TMS): δ = 1.60 – 1.80 (m, 6H, 1-H_2, 2-H_2, 3-H_2), 4.5 (s, 1H, Ph-C*H*=), 6.90 – 7.40 (m, 9H, aromatic), 9.2 (s,1H, CON*H*). – MS (EI, 70 eV): *m/z* (%) = 291 (16) $[M]^+$, 200 (94), 170 (12), 91 (53), 77 (12), 55 (100). – $C_{19}H_{17}NO_2$ (291.34): calcd. C 78.33, H 5.88, N 4.81; found C 78.28, H 5.82, N 4.77.

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