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IONIC HYDROGENATION OF 8-AZA-16-THIAGONA-1,3,5(10),13-TETRAENE-12,17-DIONES. SYNTHESIS AND PROPERTIES OF 8-AZA-16-THIAGONA-1,3,5(10),13-TETRAEN-17-ONES

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Ionic hydrogenation of 8-aza-16-thiagona-1,3,5(10),13-tetraene-12,17-diones has been carried out by regioselective reduction of the carbonyl part of the aminovinylketothiolactone group to give 8-aza-16-thiagona-1,3,5(10),13-tetraen-17-ones.

Keywords: 8-aza-16-thiagonanes, benzo[*a*]thieno[*f*]quinolizines, ionic hydrogenation.

Heterocyclic analogs of steroids, in particular the aza-, oxa-, and thia- analogs, are of interest for a study of structure activity relationships in a series of steroids and they have an important practical value in the development of novel pharmacological agents for regulating and maintaining biochemical homeostasis in man and domestic animals [1-3]. We have previously reported the annelation of 3,4-dihydroisoquinolines by 3-acylthiotetronic acids which leads to 8-aza-16-thiagona-1,3,5(10),13-tetraene-12,17-diones (benzo[*a*]thieno-[*f*]quinolizines) [4, 5] which are promising immunomodulating agents [6, 7].

In a continuation of our investigation of the synthesis and study of the properties of heterocyclic analogs of steroids we considered it of interest to carry out some reactions of the pharmacophoric aminovinylketothiolactone group of 8-aza-16-thiasteroids. We aimed to prepare derivatives not readily available in terms of direct synthesis and to analyse the effect of such conversions on the physicochemical properties and biological function of compounds of this type. We further kept in mind the results of bioscreening [6, 8] of compounds prepared by the modification of the aminovinyldicarbonyl, aminovinylketolactone, and aminovinylketolactam groups of 8-aza- [9-11], 8-aza-16-oxa- [8], and 8,16-diazasteroids [12, 13].

As remarked earlier [4], the 8-aza-16-thiagona-12,17-diones **1a-c**, despite their isostericity with 8-aza-, 8-aza-16-oxa-, and 8,16-diazagona-12,17-diones [3], differ significantly from the latter. Hence, experiments to prepare the oximes **2** at the carbonyl in position 12 of the 8-aza-16-thiagonanes **1** were unsuccessful, and this may be due to the extremely low solubility of the investigated compounds thus making impossible the general methods for preparing oximes [14]. Carrying out the same oximation in trifluoroacetic acid led exclusively to a complex mixture of products which did not yield to chromatographic separation. Attempts to dehydrogenate the 8-aza-16-thiagonanes **1** with the aim of introducing a 9,11-double bond (compound **3**) were also unsuccessful. In particular, the reactions with chloranil, dichlorocyano-*p*-benzoquinone, and cupric chloride using known methods [15, 16] proved ineffective.

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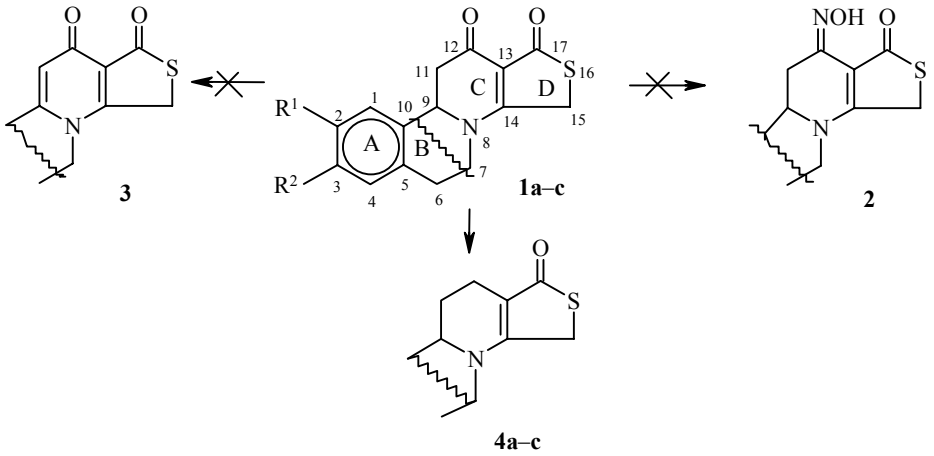


4a–c

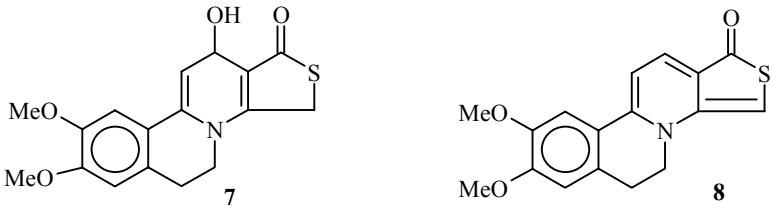
1 a $R^1 = R^2 = H$, **b** $R^1 = H$, $R^2 = OMe$, **c** $R^1 = R^2 = OMe$

With this in mind, and also with the data for the regiospecific reduction of aminovinyldicarbonyl [11], aminovinylketolactone [8], and aminovinylketolactam [12, 13] groups using ionic hydrogenation [17], we have made attempts of prepare the 12-desoxy derivatives of the 8-aza-16-thiasteroids **4a-c** *via* a direct ionic hydrogenation of the aminovinylketothiolactone group in compounds **1a-c**.

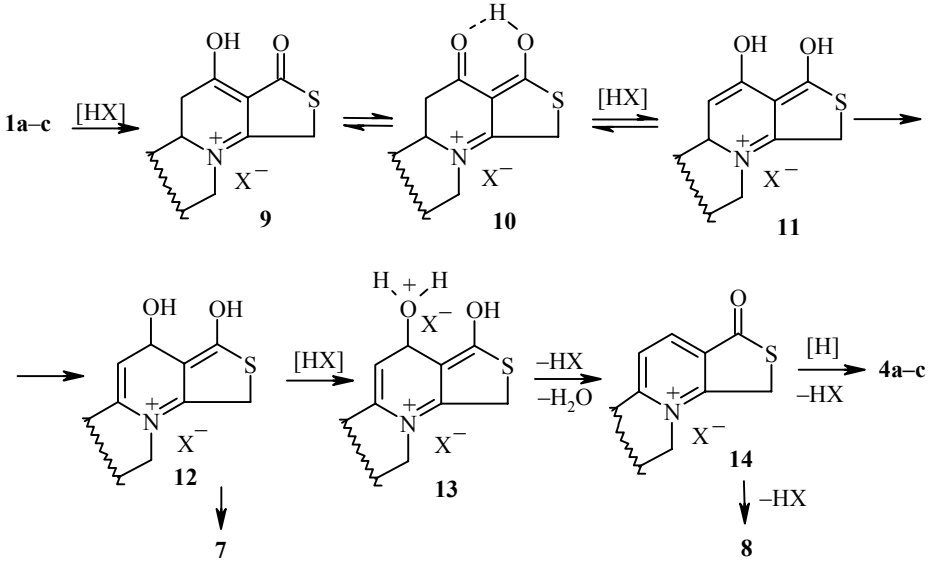
The hydrogenolysis of the carbonyl group in the 12 position of compounds **1a-c** was carried out in trifluoroacetic acid solution using triethylsilane in the presence of boron trifluoride etherate or lithium perchlorate. The use of lithium perchlorate as catalyst shortened the reaction time and led to higher yields of the target 12-desoxy derivatives **4a-c**. Apparently, the reduction products **4a-c** form extremely stable, and hard to separate complexes [18] with the boron trifluoride and this contaminates the target materials. The use of lithium perchlorate as catalyst removes such a complication and results in a shorter work up of the reaction mixture and an increase in the yield of the product. We were not able to reduce the 8-aza-16-thiagonanes **1a-c** to the 12-hydroxy derivatives **5** or **6** using sodium borohydride in aqueous methanol (by analogy with the reduction of the 8-aza-16-oxasteroids [11]).

It should be noted that the mechanism of reduction of the carbonyl group at position 12 in compounds **1a-c** under hydride transfer reaction conditions as, indeed with other 8-aza steroid compounds [8, 11-13], while not fully defined (but made on the basis of earlier findings) is of a hypothetical nature.

The chromatographic mass-spectrometric analysis of the reaction mixture and of the dry product of reduction of the 8-aza steroid **1c** has shown that, both in the reaction mixture and in the dry product, there are present both the target derivative **4c** and also side (intermediate) products which could be assigned the structures of the alcohol **7** and the 12-desoxy derivative **8** from the mass spectrometric results.



With this data in mind we propose that the dicarbonyl substrates **1a-c** in trifluoroacetic acid (pK_a = 0.23) are protonated to form the pseudo salts **9-11**. As a result of either intramolecular oxidative-reductive rearrangement or intermolecular hydride transfer they are converted to the onium derivatives **12** which are precursors of the alcohols **7**. As a result of protonation, the oxonium cations **13** formed can be dehydrated to the onium derivatives **14** and these are synthetic precursors of the derivatives **8**. On the other hand, the derivatives **14** can be hydrogenated *via* a hydride transfer process and converted to the target 12-desoxy derivatives **4a-c** after removal of acid.



The products of the ionic hydrogenation of the 8-aza-16-thiagonanes **1a-c** are the 12-desoxy derivatives **4a-c** and are crystalline materials melting with decomposition in the range 180-210°C (Table 1). Analytical samples of these materials were prepared by chromatography of the reaction mixtures on Al_2O_3 (ethyl acetate–hexane, 6:4) with crystallization of the products from the mixture of ethyl acetate with hexane. According to elemental analytical data the synthesized compounds correspond to the proposed structures for the aminovinylthiolactones **4a-c**.

The IR spectra of compounds **4a-c** (Table 2) show an extremely characteristic set of absorption band (AB) signals in the region 1700-1400 cm^{-1} which differ significantly from those of the starting materials [4, 5]. Hence the AB at ~ 1670 cm^{-1} is due to the carbonyl stretching vibration of the thiolactone fragment, the bands at ~1600 and ~1580 cm^{-1} to the stretching vibrations of the $C_{(13)}$=$C_{(14)}$ bond and the aromatic ring A, and the bands at 1470-1430 cm^{-1} to the deformation vibrations of the methylene groups [19].

The UV spectra of the 12-desoxy derivatives **4a-c** (Table 2), in contrast to their synthetic precursors **1a-c** (which are characterized by three strong AB at ~230, ~265, and 304-309 nm [4]), show the presence of one strong AB at ~310 nm and bands of medium intensity at 230-240 nm. The strong, long wavelength AB is evidently due to the π-π* electronic transitions of the aminovinylcarbonyl $N_{(8)}$–$C_{(14)}$=$C_{(13)}$–$C_{(17)}$=O chromophore and the short wavelength AB at 230-240 nm to electronic transitions of the thiolactone group. It is important to note that differentiation of the spectroscopic curves of the long wavelength AB splits it into three bands with maxima at ~270, ~311, and ~345 nm. The complex composition of the long wavelength AB may be explained either by conformational effects of the molecular framework changing the extent of conjugation of the aminovinylthiolactone chromophore, or by a "mesomeric tautomer" situation [20].

The ^{1}H and ^{13}C NMR spectra of the 12-desoxy derivatives **4a-c** (Table 3) are the most informative and decisive for structural assignment. In the ^{1}H NMR spectra of these compounds (and in contrast to the spectra of the starting compounds) there are present at 2.38 and 1.70 ppm the resonance signals for the methylene groups

TABLE 1. Physicochemical Characteristics for Compounds **4a-c**

Compound	Empirical formula	Found, % / Calculated, %				mp, °C (dec.)	$[M]^+$	Yield, %
		C	H	N	S			
4a	$C_{15}H_{15}NOS$	69.94 / 70.01	5.68 / 5.87	5.26 / 5.44	12.61 / 12.46	187-189	257.36	100*
4b	$C_{16}H_{17}NO_2S$	66.68 / 66.87	5.82 / 5.96	4.76 / 4.87	10.94 / 11.16	200-203	287.38	95*
4c	$C_{17}H_{19}NO_3S$	64.19 / 64.33	5.94 / 6.03	4.29 / 4.41	10.31 / 10.10	187-190	317.39	92*[2]

* Prepared using $LiClO_4$.
*[2] Prepared using $BF_3 \cdot Et_2O$.

in the 12 and 11 positions respectively, observed as complex, two-proton resonance signals. The resonance signals for the methylene group at position 15 is observed at ~3.96 ppm as broadened, two-proton singlets whereas in the spectra of compounds **1a-c** they are seen at about 4.66 ppm as a strongly coupled AB type spin system ($\Delta\delta$ (H_AH_B) 23 Hz, J ~ 17.5 Hz).

The resonance signals for the protons at position 9 are observed at ~4.51 ppm as a pair of poorly resolved doublets due to spin-spin interactions with the protons of the methylene group at $C_{(11)}$. The structure of the compounds obtained was also confirmed by the presence in the expected regions of the ^{1}H NMR spectra of resonance signals for the $C_{(6)}$ and $C_{(7)}$ protons of the ethylene fragment, the aromatic ring, and the methoxy substituted ring A.

The ^{13}C NMR spectra of the 12-desoxy derivatives **4a-c** show the number of resonance ^{13}C NMR signals required by the assigned structure. Thus the spectra of these derivatives are characterized by the presence of five resonance signals in the region 20-45 ppm corresponding to the methylene groups. In the low field region at 192-194 ppm there are resonance signals for the $C_{(17)}$ of the thiolactone carbonyl. The signals of the polarized vinyl fragment are observed at ~109.7 ($C_{(13)}$) and ~178.1 ppm ($C_{(14)}$) and the resonance signal for the $C_{(9)}$ atom is seen at ~60.4 ppm. The signals for the carbon atoms of the aromatic ring and the methoxy substituents are seen in the anticipated regions of the spectrum at ~109-160 and ~56 ppm respectively.

With the aim of a more exact comparison of the NMR spectra for the starting and prepared compounds and an explanation of the effect of acid on the spectroscopic characteristics of the 12-desoxy derivatives for compound **4c** the ^{1}H NMR and ^{13}C NMR spectra were recorded in CF_3COOD solution. Evidently, in the presence of the acid the 8-aza-16-thiagonanes **4a-c** can be protonated at the three nucleophilic centers in the aminovinylthiolactone fragment (N, S, O) and, in the case of compounds **4b,c** even at the oxygen atoms of the methoxy groups in positions 2 and/or 3. The protonation at the oxygen atoms of the methoxy groups conjugated to the aromatic ring should be accompanied by a low field shift of the signals for the carbon atoms of the aromatic ring and the methoxy groups. In fact, in CF_3COOD the signals for the carbon atoms of the aromatic ring in compound **4c** are shifted to the low field region by 1.5-2.9 ppm and the signals for the methoxy groups by ~ 1.5 ppm relative to the chemical shifts of the corresponding carbon atoms for this compound in $CDCl_3$. Upon exchanging $CDCl_3$ for CF_3COOD the most marked low field shifts are observed for $C_{(14)}$ (11.8), $C_{(15)}$ (5.6), $C_{(7)}$ (5.3), $C_{(13)}$ (4.0), and $C_{(9)}$ (3.8) ppm and this points to the realization of the pseudo salt structure **15** in CF_3COOD solution. Such a shift for the signal of the $C_{(14)}$ atom points to a predominating contribution to the resonance structure of the cation from the limiting structure **A** when compared with the structure **B**. Exchange of $CDCl_3$ for CF_3COOD has virtually no effect on the chemical shift of the signals for the thiolactone $C_{(17)}$ atom and the $C_{(6)}$, $C_{(11)}$, and $C_{(12)}$ methylene group atoms. If the absence of a change in the chemical shift of the $C_{(11)}$ methylene group is explained by its remoteness from the protonated p,π-electronic fragments then the stability

TABLE 2. IR, UV, and Mass Spectra of Compounds **4a-c**

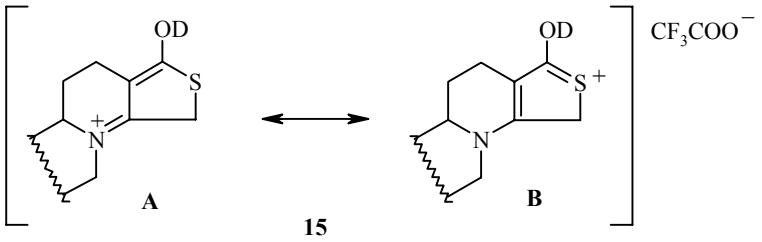
Com-pound	IR spectrum ν, cm^{-1}	UV spectrum, λ, nm (ε)		Mass spectrum, *m/z* (*I*, %)
		λ_{max}	λ_{min}	
4a	3100-2820, 1672, 1590, 1570, 1470-1435, 1366, 1329, 1286, 1225, 922, 753	239.4 (6 870), 310.0 (17 735)	224.7 (4 855), 267.7 (2 030)	259.20 (5.97); 258.20 (18.62); 257.20 (100.00); 256.20 (36.82); 229.20 (4.93); 228.20 (14.99); 225.20 (7.70); 224.20 (46.27); 214.20 (6.18); 210.20 (4.45); 197.15 (12.17); 196.15 (58.55); 194.15 (13.31); 183.10 (4.02); 182.10 (18.95); 181.10 (5.46); 180.10 (6.48); 168.10 (7.75); 167.10 (8.49); 152.05 (5.78); 141.05 (4.24); 132.10 (10.25); 131.10 (8.11); 130.10 (32.99); 129.10 (11.36); 128.10 (15.58); 127.00 (8.48); 117.10 (12.45); 116.00 (11.91); 115.00 (37.51); 105.05 (6.68); 104.05 (8.56); 103.05 (15.34); 102.05 (6.46); 97.85 (4.02); 96.95 (8.21); 91.05 (15.21); 90.15 (4.70); 89.00 (7.50); 83.60 (9.64); 79.00 (4.07); 78.00 (8.17); 77.00 (20.90); 76.00 (4.49); 65.95 (4.28); 64.95 (12.70); 62.95 (7.78); 53.05 (8.23); 52.05 (5.28); 51.05 (10.82); 44.95 (6.48)
4b	3000-2830, 1672, 1605, 1595, 1518, 1495, 1324, 1290, 1224, 1041, 930, 916, 830	230.9 (15 650), 310.0 (2 3365), 385.0 (3 165)	217.3 (12 720), 263.7 (5 315), 342.8 (985)	289.25 (6.17); 288.25 (20.78); 287.25 (100.00); 286.25 (69.73); 272.20 (4.01); 258.20 (11.14); 256.20 (6.04); 255.30 (4.03); 254.20 (20.51); 244.15 (5.33); 227.20 (15.57); 226.20 (58.80); 224.20 (6.98); 213.20 (6.93); 212.20 (37.36); 211.20 (4.39); 210.20 (5.51); 184.15 (4.40); 182.10 (5.27); 168.10 (4.12) 167.10 (4.00); 162.10 (7.27); 161.10 (7.98); 160.10 (25.96); 159.15 (4.94); 147.05 (6.60); 146.05 (10.46); 145.05 (7.50); 143.85 (6.85); 135.00 (5.04); 134.10 (6.51); 131.00 (6.96); 130.10 (5.24); 129.00 (5.24); 128.00 (8.17); 127.00 (9.64); 118.10 (5.95); 117.10 (16.93); 116.00 (7.53); 115.00 (18.17); 113.70 (4.13); 105.05 (4.60); 104.05 (5.34); 103.05 (13.04); 102.05 (6.41); 96.95 (7.46); 91.05 (18.61); 90.00 (5.41); 89.00 (8.73); 79.00 (4.13); 78.00 (7.39); 77.00 (14.64); 65.95 (4.39); 64.95 (14.06); 53.05 (8.10); 52.05 (4.81); 51.05 (8.28); 44.95 (6.06)
4c	3050-2830, 1660, 1605-1570, 1530, 1475-1450, 1360 1325, 1291, 1261, 1224, 1211, 1200, 1132, 1100, 1072, 848, 770	234.6 (14 520), 310.4 (25 305)	220.8 (11 350), 263.9 (2 320)	319.20 (6.51); 318.30 (22.31); 317.20 (100.00); 316.20 (78.81); 302.20 (11.56); 288.25 (9.28); 286.25 (13.49); 284.25 (18.10); 274.20 (5.75); 257.30 (12.09); 256.30 (49.43); 242.25 (22.16); 240.15 (7.50); 212.20 (4.01); 207.10 (4.61); 198.15 (4.50); 192.15 (4.44); 191.15 (8.24); 190.15 (17.78); 189.15 (4.27); 177.10 (9.46); 176.10 (10.90); 175.10 (5.50); 174.10 (7.33); 165.10 (7.00); 164.10 (5.33); 158.65 (7.79); 154.05 (4.05); 147.15 (4.86); 146.05 (15.64); 145.05 (4.64); 133.00 (7.49); 131.00 (10.48); 130.00 (4.32); 129.00 (6.27); 127.80 (10.87); 127.10 (11.17); 121.00 (5.74); 120.10 (5.63); 119.00 (5.06); 118.00 (5.67); 117.00 (8.93); 116.10 (6.72); 115.00 (15.48); 112.05 (4.14); 105.05 (7.87); 104.05 (7.40); 103.05 (12.76); 102.05 (5.14); 98.95 (4.10); 96.95 (7.58); 91.05 (15.90); 90.00 (6.16); 89.00 (8.38); 83.70 (4.71); 80.00 (4.17); 79.00 (5.78); 78.00 (8.20) ; 77.00 (17.99); 76.00 (4.45); 67.10 (4.47); 65.95 (5.24); 65.05 (16.03); 62.95 (6.21); 53.05 (9.41); 52.05 (5.28); 51.05 (8.70); 44.95 (6.46); 44.05 (10.41)

TABLE 3. ^{1}H and ^{13}C NMR Spectra of Compounds **4a-c**

Com-pound	^{1}H NMR spectrum, δ, ppm (*J*, Hz)	^{13}C NMR spectrum, δ, ppm
4a	1.62-1.82 (2H, m, $C_{(11)}H_2$); 2.32-2.46 (2H, m, $C_{(12)}H_2$); 2.84 (1H, tt, *J* = 15.0; 3.0; 3.0, $C_{(6)}H_e$); 3.04 (1H, dtd, *J* = 15.0; 12.5; 5.0, $C_{(6)}H_a$); 3.39 (1H, ddd, *J* = 12.5; 12.5; 3.0, $C_{(7)}H_a$); 3.86 (1H, qq, *J* = 12.5; 5.0; 3.0, $C_{(7)}H_e$); 3.96 (2H, s, $C_{(15)}H_2$), 4.55 (1H, dd, *J* = 10.0; 1.5, $C_{(9)}H_a$); 7.10-7.32 (4H, m, $C_{(1)}H$, $C_{(2)}H$, $C_{(3)}H$, $C_{(4)}H$)	20.18 ($C_{(11)}$); 29.66 ($C_{(12)}$); 29.79 ($C_{(6)}$); 31.88 ($C_{(15)}$); 43.62 ($C_{(7)}$); 57.21 ($C_{(9)}$); 106.76 ($C_{(13)}$); 126.12; 126.80; 126.89; 128.78; 133.86; 135.81; 164.08 ($C_{(14)}$); 192.51 ($C_{(17)}$)
4b	1.53-1.84 (2H, m, $C_{(11)}H_2$); 2.30-2.44 (2H, m, $C_{(12)}H_2$); 2.80 (1H, tt, *J* = 15.5; 3.0; 3.0, $C_{(6)}H_e$); 3.00 (1H, dtd, *J* = 15.5; 12.0; 4.0, $C_{(6)}H_a$); 3.38 (1H, ddd, *J* = 12.0; 12.0; 3.0, $C_{(7)}H_a$); 3.82 (3H, s, OCH_3); 3.85 (1H, qq, *J* = 12.0; 4.0; 3.0, $C_{(7)}H_e$); 3.96 (2H, s, $C_{(15)}H_2$); 4.50 (1H, dd, *J* = 10.0; 2.0, $C_{(9)}H_a$); 6.68 (1H, d, *J* = 2.5, $C_{(4)}H$); 6.84 (1H, dd, *J* = 8.5; 2.5, $C_{(2)}H$); 7.18 (1H, d, *J* = 8.5, $C_{(1)}H$)	20.69 ($C_{(11)}$); 30.37 ($C_{(12)}$); 30.51 ($C_{(6)}$); 32.50 ($C_{(15)}$); 44.27 ($C_{(7)}$); 55.92 (OCH_3); 57.47 ($C_{(9)}$); 107.47 ($C_{(13)}$); 113.71; 113.99; 127.83; 128.60; 135.80; 158.84($C_{(3)}$); 164.69 ($C_{(14)}$); 193.13 ($C_{(17)}$)
4c	1.58-1.84 (2H, m, $C_{(11)}H_2$); 2.31-2.43 (2H, m, $C_{(12)}H_2$); 2.73 (1H, tt, *J* = 15.0; 3.0; 3.0, $C_{(6)}H_e$); 2.97 (1H, dtd, *J* = 15.0; 12.0; 5.0, $C_{(6)}H_a$); 3.34 (1H, ddd, *J* = 12.0; 12.0; 3.0, $C_{(7)}H_a$); 3.86 (1H, qq, *J* = 15.0; 5.0; 3.0, $C_{(7)}H_e$); 3.88 (6H, s, $2OCH_3$); 3.95 (2H, s, $C_{(15)}H_2$); 4.48 (1H, dd, *J* = 10.5; 1.5, $C_{(9)}H_a$); 6.63 (1H, s, $C_{(4)}H$); 6.72 (1H, s, $C_{(1)}H$) [1.88 (1H, dddd, *J* = 12.0; 11.0; 11.0; 5.0, $C_{(11)}H_a$); 2.50-2.83 (2H, m, $C_{(11)}H_e$, $C_{(12)}H_a$); 2.94 (1H, tt, *J* = 12.0; 5.0; 5.0, $C_{(12)}H_e$); 3.00 (1H, tt, *J* = 14.0; 4.0; 4.0, $C_{(6)}H_e$); 3.14 (1H, ddd, *J* = 12.0, 4.0, 4.0, $C_{(6)}H_a$); 3.77 (1H, ddd, *J* = 12.0; 12.0; 4.0, $C_{(7)}H_a$); 4.00 (6H, s, $2OCH_3$); 4.12 (1H, tt, *J* = 12.0; 12.0; 4.0. $C_{(7)}H_e$); 4.54 (2H, s, $C_{(15)}H_2$); 4.86 (1H, dd, *J* = 11.0; 3.0, $C_{(9)}H_a$); 6.90 (1H, s, $C_{(4)}H$); 6.96 (1H, s, $C_{(1)}H$)]*	20.23 ($C_{(11)}$); 29.23 ($C_{(12)}$); 30.17 ($C_{(6)}$); 31.90 ($C_{(15)}$); 43.78 ($C_{(7)}$); 55.97 (OCH_3); 56.12 (OCH_3); 57.08 ($C_{(9)}$); 106.85 ($C_{(13)}$); 109.13($C_{(4)}$); 111.41($C_{(1)}$); 125.99 ($C_{(10)}$); 127.65 ($C_{(5)}$); 147.94 ($C_{(2)}$); 148.12 ($C_{(3)}$); 164.12 ($C_{(14)}$); 192.58 ($C_{(17)}$) [20.78 ($C_{(11)}$); 29.78 ($C_{(12)}$); 30.49 ($C_{(6)}$); 37.50 ($C_{(15)}$); 49.07 ($C_{(7)}$); 57.42 (OCH_3); 57.75 (OCH_3); 60.87 ($C_{(9)}$); 110.79 ($C_{(13)}$); 112.01 ($C_{(4)}$); 114.04 ($C_{(1)}$); 128.38 ($C_{(10)}$); 129.10 ($C_{(5)}$); 149.82 ($C_{(2)}$); 150.05 ($C_{(3)}$); 175.92 ($C_{(14)}$); 192.47 ($C_{(17)}$)]*

* Spectra recorded in CF_3COOD.

of the $C_{(6)}$ and $C_{(12)}$ methylene group chemical shifts is evidently due to an insignificant change upon protonation in the electronic structure of the $C_{(5)}$ and $C_{(13)}$ atoms bonded to them. The retention of the chemical shift for the thiolactone $C_{(17)}$ atom upon exchanging the aprotic $CDCl_3$ for the protogenic CF_3COOD is not fully clear and is evidently connected with the absence of a change in electron density on the indicated carbon atom. It can be suggested that for compound **4c** in trifluoroacetic acid solution, along with the O-protonated salt of structure **15**, there also exist the N- and S-protonated structures **16** and **17** respectively. However, the experimental data obtained does not provide direct proof for their realization.



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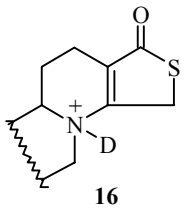

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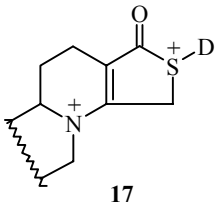

17

Hence the combined data for the spectroscopic investigation of compounds **4a-c** confirms the structure assigned and shows that, in the presence of powerful acids, they are protonated at the thiolactone oxygen atom to form the pseudo salt **15**.

The lability of the derivatives obtained should also be mentioned. Thus continued exposure of alcoholic solutions of the 12-desoxy derivatives to light (5-10 days) in the presence of atmospheric oxygen leads to a marked change in their UV spectra and points to a disruption to the chromatographic homogeneity of the samples. The most important property of the compounds obtained is their solubility in chloroform, ethanol, and other solvents and this makes their study significantly easier.

The obtained 12-desoxy derivatives **4a-c** are obviously of interest. Firstly as intermediates in the synthesis of benzo[*a*]- and benzo[*a*]thieno[*f*]quinolizines difficult to obtain by known methods, secondly as potentially biologically active compounds which are of promise in developing novel pharmacological agents, and finally as model structures for the study of structure-biological function correlations amongst hetero analogs of steroids.

EXPERIMENTAL

Monitoring of the reaction course and purity of the products was carried out using the TLC method (Silufol UV-254, chloroform–methanol, 9:1) and visualized using UV light or iodine vapor with subsequent heating at 250-300°C and also by using chromatography mass spectrometry on an HP 5890/5972 GC/MS instrument (1 μl sample of ~ 200 μg/ml solution of the sample in CH_2Cl_2 with vaporizer temperature 280°C, HP 5 MS quartz capillary column 30 m × 0.25 mm × 0.2μm, stationary phase 5% PhMe silicone, helium gas carrier 0.7-1.0 ml/min, temperature program 40-300°C at 6°C/min, and electron ionization energy 70 eV). Melting points were determined on a Boetius heating block. IR spectra were taken on a UR-20 instrument for KBr

tablets, and UV spectra on a Specord M-400 spectrophotometer using ethanol. Differentiation of the UV spectra was carried out using a mathematical procedure incorporated in the program control of the instrument. ^{1}H and ^{13}C NMR spectra were taken on a Bruker AC-200 instrument (200 MHz for ^{1}H and 50 MHz for ^{13}C). Chemical shifts were measured relative to TMS (internal standard) with a measurement accuracy of 0.5 (for ^{1}H) and 3.0 Hz (for ^{13}C). The regimes and conditions for recording the spectra corresponded to those given in the study [15]. ^{13}C and $^{13}C–\{^{1}H\}$ NMR spectra were recorded using the PGD and GD programs included in the control of the instrument.

General Method for Ionic Hydrogenation. A solution of the 8-aza-16-thiagonane **1a-c** (0.2 g) in trifluoroacetic acid (1.5-2.0 ml) was treated with 1.5 ml of a 6% solution of boron trifluoride etherate in trifluoroacetic or several crystals of lithium perchlorate and 0.50-0.75 ml of triethylsilane. The reaction mixture was held for 1 day at room temperature and triethylsilane (0.25 ml) was added. With lithium perchlorate the reaction was complete within 2 days and with boron trifluoride etherate 3-4 days. The reaction mixture was then evaporated under reduced pressure and the residue was treated with saturated $NaHCO_3$ solution and extracted with chloroform. The extracts were dried over Na_2SO_4, evaporated and chromatographed on Al_2O_3 eluting with a mixture of ethyl acetate and hexane (6:4). The eluates were evaporated and the residue was crystallized from a mixture of ethyl acetate and hexane.

8-Aza-16-thiagona-1,3,5(10),13-tetraen-17-one (4a). Use of boron trifluoride etherate gave 0.17 g (90%) as light yellow crystals with mp 185-188°C (decomp.) and of lithium perchlorate gave 0.19 g as colorless crystals.

8-Aza-3-methoxy-16-thiagona-1,3,5(10),13-tetraen-17-one (4b). Use of boron trifluoride etherate gave 0.17 g (90%) as light yellow crystals with mp 199-203°C (decomp.) and of lithium perchlorate gave 0.18 g as grayish crystals.

8-Aza-2,3-dimethoxy-16-thiagona-1,3,5(10),13-tetraen-17-one (4c). Use of boron trifluoride etherate gave 0.176 g of light yellow crystals and of lithium perchlorate gave 0.17 g (89%) as yellow crystals with mp 188-191°C (decomp.).

8-Aza-2,3-dimethoxy-16-thiagona-1,3,5(10),9(11),12,14-hexaen-17-one (8). Mass spectrum, *m/z* (*I*, %): 315.20 (6.91) $[M+2]^+$; 314.20 (21.81) $[M+1]^+$; 313.20 (100) $[M]^+$; 313.20 (85.49); 298.15 (24.53); 297.15 (7.70); 296.15 (19.50); 284.25 (10.03); 281.25 (7.64); 270.20 (12.34); 269.10 (5.65); 268.20 (13.39); 255.10 (8.68); 254.20 (6.92); 240.05 (5.60); 239.05 (6.07); 227.10 (6.47); 226.15 (13.35); 210.10 (7.27); 209.10 (8.31); 208.10 (10.16); 207.10 (34.94); 198.05 (10.21); 197.05 (6.71); 194.05 (5.50); 191.05 (6.40); 178.10 (7.86); 167.10 (9.01); 166.10 (10.93); 165.10 (8.44); 154.05 (8.60); 153.15 (6.96); 152.05 (5.18); 140.05 (7.56); 139.05 (7.55); 126.90 (8.71); 126.10 (7.68); 115.00 (7.54); 114.00 (5.12); 112.95 (5.62); 105.05 (8.68); 102.95 (5.23); 101.95 (5.71); 95.95 (5.99); 89.00 (9.99); 86.80 (5.77); 83.20 (5.08) 77.00 (10.45); 76.00 (6.63); 75.00 (8.20); 73.0 (8.64); 62.95 (11.79); 50.95 (9.11); 44.95 (7.05); 44.05 (41.08).

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