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The formation of 2-hydroxy-4-hydroxymethyl-3-(indol-3-yl)-cyclopent-2-enone derivatives from ascorbigens

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Abstract

A facile preparation is described of 3-(indol-3-yl)-2-hydroxy-4-hydroxymethylcyclopent-2-enone and its N-derivatives in 15–40% yields by the degradation of ascorbigen or its N-derivatives in a warm solution of L-ascorbic acid through a sequential domino reaction. The same cyclopentenone derivatives were obtained in 30–40% yields by the condensation of (*N*-alkylindol-3-yl)glycolic acids with ascorbic acid. 2,6-Dihydroxy-1-(indol-3-yl)hexa-1,4-diene-3-one and 2-hydroxy-4-hydroxymethyl-5-(indol-3-yl)cyclopent-2-enone were identified as intermediates in this reaction.

Keywords: Ascorbigen; L-Ascorbic acid; 2-Hydroxy-4-hydroxymethyl-3-(indol-3-yl)cyclopent-2-enone

1. Introduction

Ascorbigen, 2-*C*-[(indol-3-yl)methyl]-α-L-*xylo*-hex-3-ulofuranosono-1,4-lactone (**1a**), can be readily obtained by the interaction of 3-hydroxymethylindole and L-ascorbic acid. This reaction represents a rare example of C-alkylation of L-ascorbic acid under mild conditions (room temperature, buffer at pH 4.2).[1–3] Ascorbigen is the most abundant indole-derived dietary ingredient, which humans or animals obtain with cruciferous vegetables.[4,5] The anticarcinogenic properties reported for cruciferous vegetables,[6] makes studies on chemical and biological properties of ascorbigen important. Ascorbigen is a labile compound which undergoes various transformations under mild (even in biological nonenzymatic) conditions. Investigations of the products of ascorbigen transformations is thus important for understanding its biological properties.

Earlier we demonstrated that **1a**, by heating at pH < 3 in water, dissociates to L-ascorbic acid and an unstable salt of 3-methyleneindolenine, which oligomerizes to give di(indol-3-yl)methane, 5,11*H*-indolo[3,2-*b*]carbazole, and some other oligomers, or it interacts with another molecule of ascorbigen to yield 2′-[(indol-3-yl)methyl]ascorbigen.[7] These products are capable of further transformations in acid media.

At pH > 7 ascorbigen is also unstable: opening of the lactone ring leads to 2-*C*-[(indol-3-yl)methyl]-α-L-*xylo*-hex-3-ulofurano-

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sonic acid (**2**), which spontaneously decarboxylates and, after isomerization, produces a mixture of 1-deoxy-1-(indol-3-yl)-α-L-sorbopyranose (**3**) and 1-deoxy-1-(indol-3-yl)-α-L-tagatopyranose (**4**) (Scheme 1).[8]

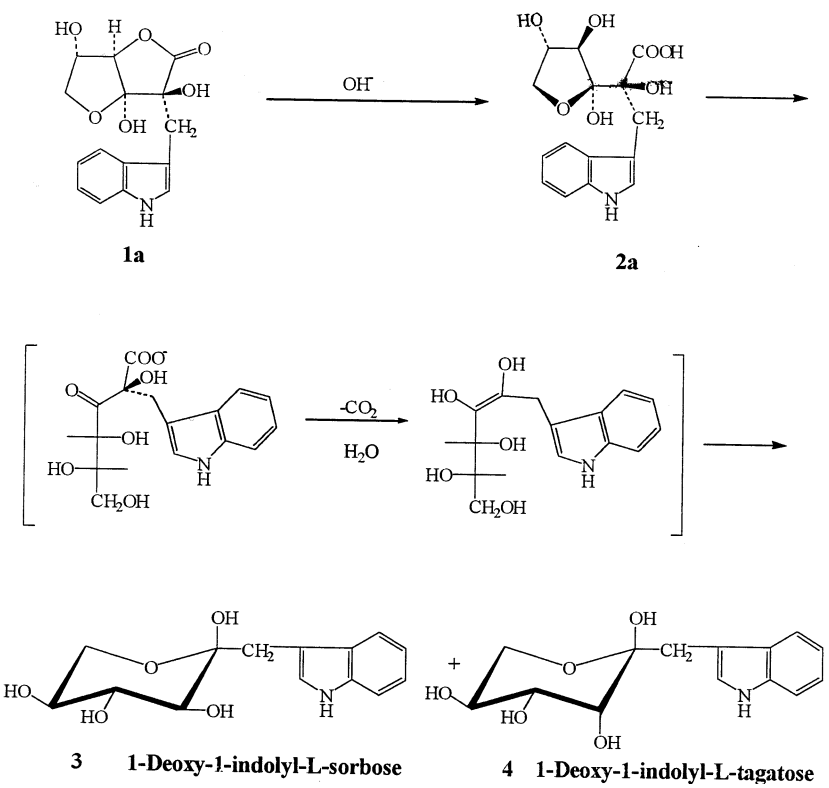
The goal of this work was to study the transformations of ascorbigen in acid media, which proceed without the release of L-ascorbic acid and lead to indole derivatives of a new type.

2. Results and discussion

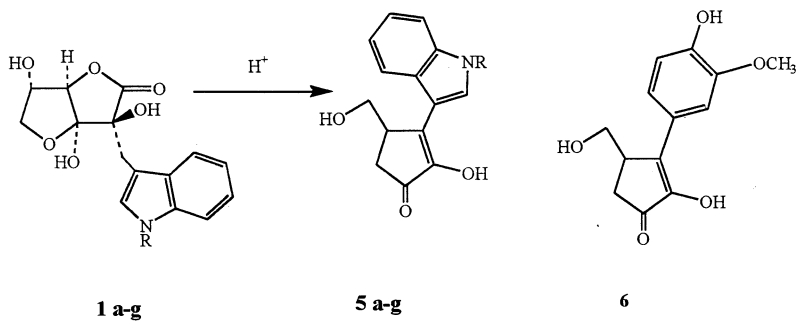
When ascorbigen is incubated in a warm L-ascorbic acid solution, the dissociation to L-ascorbic acid and 3-methylenindolenine oligomers is supressed. This facilitates a new type of reaction, which represents a sequential combination of such simple transformations as hydrolysis, CO_2 extrusion, dehydration, cyclization or Michael addition, and isomerization and is called a domino reaction.[9] When a solution of **1a** was heated at 60 °C in an aqueous solution of L-ascorbic acid (at a molar ratio 1:10–20) (Method A) racemic 2-hydroxy-4-hydroxymethyl-3-(indol-3-yl)cyclopent-2-enone (**5a**) was formed in 10–15% yield. Racemic N-substituted indolylcyclopentenone derivatives (*N*-methyl-, **5b**; *N*-benzyl-, **5c**; *N*-hexyl-, **5e**; and *N*-methoxy-, **5f**) were obtained under these conditions in higher yields (Scheme 2, Table 1).

Mild reaction conditions and the availability of reagents (starting ascorbigens and L-ascorbic acid) make these cyclopentenone derivatives **5** readily available, and the intense fluorescence of these compounds facilitated their TLC analysis and chromatographic purification. The presence of ascorbic acid in this reaction is crucial, as the heating of the unsubstituted ascorbigen (**1a**) or its *N*-benzyl- (**1c**) derivative at pH ≤ 1 in a 1:1 methanol–1 N HCl mixture (Method B) yielded strongly fluorescent cyclopentenones (**5a** and **5c**) in a very low yields (Table 1).

1-Alkoxyascorbigens, which were obtained by the methods reported in Refs. 10, 11, undergo similar transformations. In a boiling methanol–1 N HCl solution, **1f** and **1g** were converted into the corresponding highly fluorescent 2-hydroxy-3-(1-alkoxyindol-3-yl)-



Scheme 1.



1 a-g 5 a-g 6

Scheme 2. **5a** R = H; **5b** R = CH_3; **5c** R = $CH_2C_6H_5$; **5d** R = $CH_2CH{=}CH_2$; **5e** R = C_6H_{13}; **5f** R = OCH_3; **5g** R = OC_2H_5.

4-hydroxymethylcyclopent-2-enones (**5f** and **5g**) in 10–15% yields, whereas in a hot solution of L-ascorbic acid the yield of **5f** reached 27%. Earlier we have demonstrated that 1-alkoxyascorbigens are more stable in acids than ascorbigen **1a**, and need more drastic conditions for the release of L-ascorbic acid and the formation of 1-alkoxyindolylmethyl oligomers.[12] This explains the higher yields of cylopentenone derivatives **5f** and **5g** in acid conditions in comparison with **5a**. Comparison of yields of cyclopentenones obtained by Methods A and B shows that the presence of bulky N-substituents on the indole ring, which hinders the oligomerization reaction, facilitates the formation of cyclopentenones; the second important factor facilitating the cyclopentenone formation is the excess of L-ascorbic acid, which hinders the release of acid from ascorbigen.

Another method for preparation of indolylcyclopentenone derivatives uses (indol-3-yl)glycolic acids as starting compounds. Earlier we obtained 2-hydroxy-4-hydroxymethyl-3-(4-hydroxy-3-methoxyphenyl)cyclopent-2-enone (**6**) by the interaction of vanillomandelic and ascorbic acids.[13] By the treatment of indolylglycolic acids **7a–e** in a hot aqueous solution of L-ascorbic acid (10–12 equiv), we obtained cyclopentenone derivatives **5a–e** in 30–40% yields (Table 1, Method C). The presumed intermediate ascorbigens **8a–e** were not observed (Scheme 3). The starting (indol-3-yl)glycolic acid and its *N*-methyl-, *N*-benzyl-, and *N*-allyl- and *N*-*n*-hexyl derivatives **7a–e** were prepared from the corresponding (indol-3-yl)glyoxylic acids by the method described.[14]

When a reaction was performed with (indol-3-yl)glycolic acid methyl ester **9** and L-ascorbic acid, one of the isomers of the unstable 2-*C*-[(indol-3-yl)(methoxycarbonyl)methyl]-α-L-*xylo*-hex-3-ulosonic acid 1,4-lactone (**10**) was isolated (Scheme 4). This result supports the suggestion that carboxyascorbigen derivatives **8** are intermediates in the reactions of alkylindolylglycolic and ascorbic acids. Ester **10**, when stored for 1 h, underwent decomposition with the formation of several unidentified products. The ^{1}H NMR data correspond to an (indol-3-yl)methyl derivative of L-*xylo*-hex-3-ulosono-1,4-lactone, but do not establish whether the cyclic 3,6-hemiacetal furanose ring is present in compound **10**.

HR-MS of compounds **5a–g** revealed peaks for molecular ions. The ^{1}H and ^{13}C NMR spectral parameters of the cyclopentenone moieties in compounds **5** (Tables 2 and 3) are similar to those of the previously described 2-hydroxy-3-(4-hydroxy-3-methoxyphenyl)-4-hydroxy-methylcylopent-2-enone (**6**).[13]

To understand the mechanism of transformation of ascorbigens into cyclopentenone

Table 1
Comparison of yields of compounds **5** obtained by Methods A, B, and C

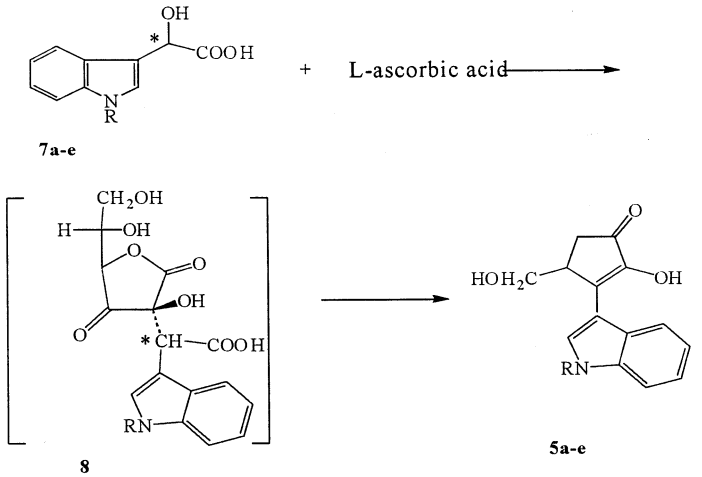
Compound	Yield (%)		
	Method A	Method B	Method C
5a	15	2	17
5b	25		30
5c	41	5	39
5d			32
5e	40		30
5f	27	15	
5g		15	

Table 2
^{1}H NMR spectral data (δ ppm, J Hz) for **5a**–**g** (CD_3OD)

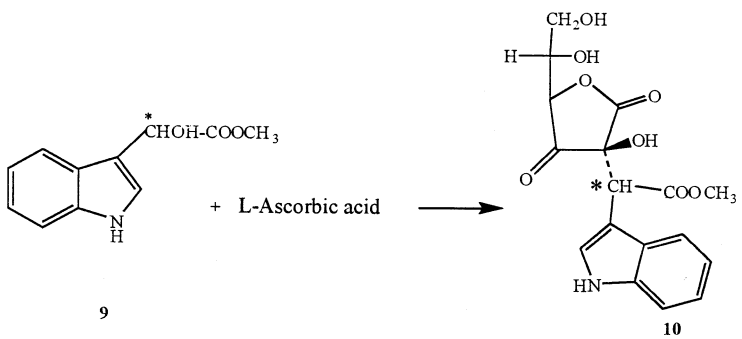
Signals	**5a**	**5b**	**5c**	**5d**	**5e**	**5f**	**5g**
4-CH	3.75 [a]	3.67 [a]	3.70 [a]	3.72 [a]	3.73 [a]	3.72 [a]	3.70 [a]
5-CH_2	2.56 [a]; 2.45 [a]; $J_{5a,5b}$ 18.6; $J_{4,5a}$ 1.0; $J_{4,5b}$ 6.0	2.61 [a]; 2.43 [a]; $J_{5a,5b}$ 18.6; $J_{4,5a}$ 0; $J_{4,5b}$ 6.2	2.63 [a]; 2.47 [a]; $J_{5a,5b}$ 18.8; $J_{4,5a}$ 0; $J_{4,5b}$ 6.1	2.65 [a]; 2.48 [a]; $J_{5a,5b}$ 18.6; $J_{4,5a}$ 0.9; $J_{4,5b}$ 6.3	2.65dd; 2.45d; $J_{5a,5b}$ 18.8; $J_{4a,5a} \sim 0$; $J_{4,5b}$ 6.0	2.68 [a]; 2.45 [a]; $J_{5a,5b}$ 18.6; $J_{4,5a}$ 0.8; $J_{4,5b}$ 6.2	2.64 [a]; 2.47 [a]; $J_{5a,5b}$ 18.3; $J_{4,5a}$ 0; $J_{4,5b}$ 6.1
6-CH_2	4.08 [a]; 3.42 [a]; $J_{6a,6b}$ 10.7; $J_{4,6a}$ 3.0; $J_{4,6b}$ 7.6	4.00 [a]; 3.41 [a]; $J_{6a,6b}$ 10.9; $J_{4,6a}$ 3.2; $J_{4,6b}$ 7.5	4.04 [a]; 3.50 [a]; $J_{6a,6b}$ 10.8; $J_{4,6a}$ 2.7; $J_{4,6b}$ 7.3	4.04 [a]; 3.51 [a]; $J_{6a,6b}$ 10.7; $J_{4,6a}$ 3.1; $J_{4,6b}$ 7.4	4.07dd; 3.41dd; $J_{6a,6b}$ 10.7; $J_{4,6a}$ 3.2; $J_{4,6b}$ 7.7	4.02 [a]; 3.43 [a]; $J_{6a,6b}$ 10.7; $J_{4,6a}$ 3.1; $J_{4,6b}$ 7.2	4.06 [a]; 3.41 [a]; $J_{6a,6b}$ 10.8; $J_{4,6a}$ 3.0; $J_{4,6b}$ 7.6
Indole protons [b]	7.13 (1 H, t, 5′-H); 7.18 (1 H, t, 6′-H); 7.43 (1 H, d, 7′-H); 7.95 (1 H, d, 4′-H); 8.12 (1 H, s, 2′-H).	7.14 (1 H, t, 5′-H); 7.21 (1 H, t, 6′-H); 7.30 (1 H, d, 7′-H); 7.84 (1 H, d, 4′-H); 7.95 (1 H, s, 2′-H).	7.10 (1 H, t, 5′-H); 7.15 (1 H, t, 6′-H); 7.30 (1 H, d, 7′-H); 7.90 (1 H, d, 4′-H); 8.08 (1 H, s, 2′-H).	7.18 (1 H, t, 5′-H); 7.24 (1 H, t, 6′-H); 7.33 (1 H, d, 7′-H); 7.88 (1 H, d, 4′-H); 8.00 (1 H, s, 2′-H).	7.19 (1 H, t, 5′-H); 7.22 (1 H, t, 6′-H); 7.46 (1 H, d, 7′-H); 7.95 (1 H, d, 4′-H); 8.10 (1 H, s, 2′-H).	7.22 (1 H, t, 5′-H); 7.32 (1 H, t, 6′-H); 7.53 (1 H, d, 7′-H); 7.95 (1 H, d, 4′-H); 8.24 (1 H, s, 2′-H).	7.17 (1 H, t, 5′-H); 7.26 (1 H, t, 6′-H); 7.45 (1 H, d, 7′-H); 7.93 (1 H, d, 4′-H); 8.18 (1 H, s, 2′-H).

[a] (1 H, m).

[b] N-substituents: **5b**, CH_3 3.77 (3 H, s); **5c**, $CH_2C_6H_5$ 5.32 (2 H, s), 7.30–7.15 (5 H, m); **5d**, $CH_2CH{=}CH_2$ 4.75 (2 H, bd, ^2J 5.5, H-1″), 5.20 (1 H, dd, ^3J 10.2, ^2J 1.1, H_a-3″); 5.11 (1 H, dd, ^3J 17.1, ^2J 1.1, H_B-3″); 5.96 (1 H, m, H-2″); **5e**, C_6H_{13} 0.88 (3 H, bs); 1.32 (8 H, m); 3.02 (2 H, t); **5f**, OCH_3 4.15 (3 H, s); **5g**, OC_2H_5 4.34 (2 H, q), 1.41 (3 H, t).



Scheme 3.



Scheme 4.

derivatives, the gradual transformation of ascorbigen under mild conditions was investigated. Compound **1a** was dissolved in an triethylamine–water solution; after its transformation into the salt of the acid **2a** was complete (as monitored by TLC), the mixture was acidified to pH 2 with HCl. This prevented the transformation of **2a** into 1-deoxy-1-indolylketoses **3** and **4** and resulted in several new products, which were separated by gel-column chromatography on Sephadex LH-20 with methanol as eluent. 2,5,6-Trihydroxy-1-(indol-3-yl)hex-1-en-3-one (**11**), 2,6-dihydroxy-1-(indol-3-yl)hexa-1,4-dien-3-one (**12**), and 2-hydroxy-4-hydroxymethyl-5-(indol-3-yl)cyclopent-2-enone (**13**) were isolated. When stored or heated, **12** formed **13**, which spontaneously gave cyclopentenone **5a**. The scheme of formation of **11**, **12**, and then **13** from the acid **2a** possibly includes an opening of the furanose ring, followed by decarboxylation and subsequent dehydrations (Scheme 5).

When ascorbigen is incubated in warm ascorbic acid solution, opening of the lactone ring as the first step of the reaction is not feasible. In this case, the furanose ring may open first to give lactone **14** (Scheme 6) followed by the extrusion of CO_2 and dehydrations, which give the key intermediate pentadienone **12**.

In conclusion, this work describes a new type of ascorbigen transformation that leads to (indol-3-yl)cyclopentenone derivatives.

3. Experimental

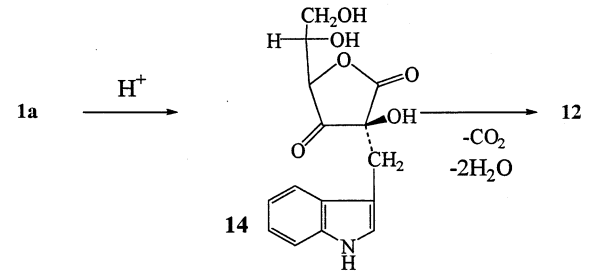
General methods.—NMR spectra were recorded with a Varian VXR-400 instrument operated at 400 MHz (^{1}H NMR) or at 100.6 MHz (^{13}C NMR). Chemical shifts were measured in CD_3OD or $CDCl_3$ using these solvents as internal standards ($CDCl_3$: δ ^{1}H (residual) 7.25 ppm, ^{13}C 77.00 ppm; CD_3OD:

Table 3
^{13}C NMR spectra of compounds **5b**,**e**,**f** (chemical shifts, ppm) [a]

	5b in $CD_3OD + CDCl_3$	**5e** in CD_3OD	**5f** in CD_3OD
Cyclopentenone ring			
C-1	200.55	202.34	202.51
C-2	146.25	148.21	148.77
C-3	137.16	141.65	140.19
C-4	38.68	40.06	40.10
C-5	36.46	37.63	37.69
C-6	65.28	66.44	66.18
Indole ring			
C-2′	125.78	127.41	127.23
C-3′	108.83	110.11	107.16
C-4′	120.99	122.40	122.7
C-4′a	131.21	129.84	130.54
C-5′	120.93	121.76	122.47
C-6′	122.30	123.22	124.14
C-7′	109.80	111.29	109.73
C-7′a	133.21	133.45	133.51

[a] N-Substituents: **5b** 33.05. **5e** 14.29; 23.57; 27.57; 31.06; 32.52; 47,55. **5f** 66.92 ppm.

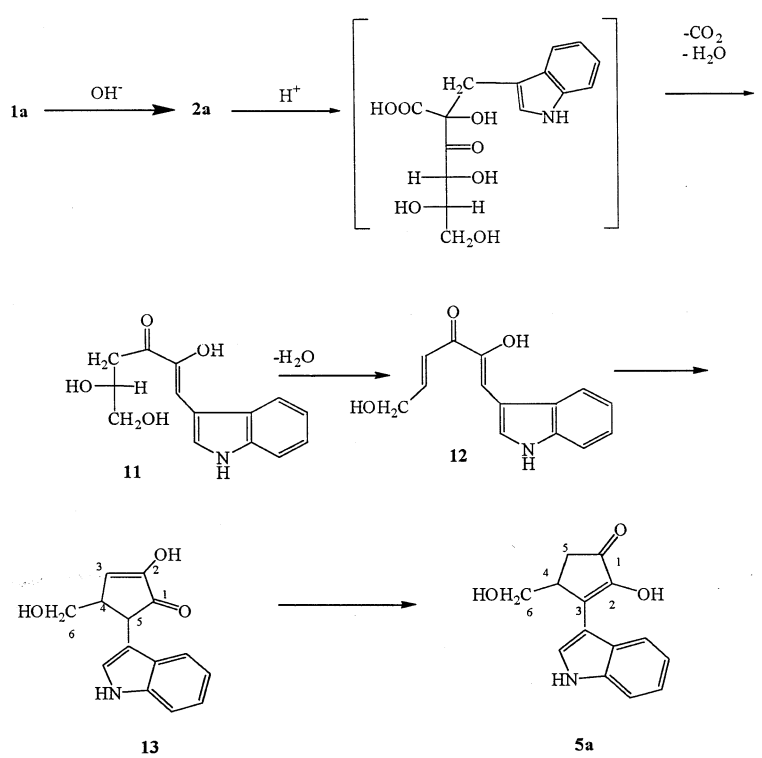
δ ^1H (residual) 3.32 ppm, ^{13}C 49.00 ppm). Analytical TLC was performed on Kieselgel F_{254} plates, and preparative TLC on plates (20×20 cm, 0.5 mm) with Kieselgel 60 F_{254}



Scheme 6.

(E. Merck), and column chromatography on Silica Gel Merck 60 (E. Merck) in the same system. Electron impact mass-spectra were obtained on an SSQ 710 Finnigan instrument.

2-Hydroxy-3-(indol-3-yl)-4-hydroxymethylcyclopent-2-enone (**5a**) *(Method A).*—An aqueous solution (20 mL) containing ascorbigen **1a** (0.1 g, 0.32 mmol) and L-ascorbic acid (1.15 g, 6.55 mmol) was stirred at 60 °C for 2 days. After cooling, the methyleneindolenine-derived polymeric side products were filtered off, and the filtrate was extracted with EtOAc. The extract was dried over Na_2SO_4 and evaporated, and the residue was purified by column chromatography, using as eluents consecutively $CHCl_3$ and $CHCl_3$–MeOH (25:1



Scheme 5.

and then 10:1) to afford 10 mg (12.5%) of **5a** as a greenish amorphous powder, R_f 0.45 (5:1, $CHCl_3$–MeOH); HR-MS, *m/z*: Found 243.0870, determined for $C_{14}H_{13}NO_3$ 243.0895; Anal. Calcd for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76. Found: C, 69.00; H, 5.49; N.5.59.

The EIMS of the per-(Me_3Si) derivative obtained from **5a** in boiling HMDS, *m/z*: 387 (3%) $[C_{14}H_{13}NO_3]^+$, 315 (35%) $[C_{14}H_{13}NO_3(SiMe_3)_2 - SiMe_3]^+$, 243 (4%) $[C_{14}H_{13}NO_3(SiMe_3)_2 - 2SiMe_3]^+$, 73 (100%) $[SiMe_3]^+$.

2-Hydroxy-4-hydroxymethyl-3-(1-methylindol-3-yl)-cyclopent-2-enone (**5b**) was obtained similarly and isolated as a greenish amorphous powder. R_f 0.47 (in EtOAc); HR-MS, *m/z*: Found 257.1062; Anal. Calcd for $C_{15}H_{15}NO_3$, 257.1052; MS of the per-(Me_3Si) derivative, *m/z*: 401 (5%) $[C_{15}H_{13}NO_3(SiMe_3)_2]^+$, 386 (5%) $[C_{15}H_{13}NO_3(SiMe_3)_2 - Me]^+$, 329 (60%) $[C_{15}H_{14}NO_3(SiMe_3)]^+$, 257 (20%) $[C_{15}H_{15}NO_3]^+$; 73 (100%) $[SiMe_3]^+$.

2-Hydroxy-4-hydroxymethyl-3-(1-benzylindol-3-yl)-cyclopent-2-enone (**5c**) was obtained similarly: R_f 0.60 (EtOAc). HR-MS, *m/z*: Found 333.1386; Anal. Calcd For $C_{21}H_{19}NO_3$ 333.1365; MS of the per-(Me_3Si) derivative, *m/z*: 477 (30%) $[C_{21}H_{17}NO_3(SiMe_3)_2]^+$, 405 (4%) $[C_{21}H_{18}NO_3(SiMe_3)]^+$, 332 (1%) $[C_{21}H_{19}NO_3 - H]^+$; 91 (80%) $[C_6H_5CH_2]^+$, 73 (100%) $[SiMe_3]^+$.

3-(1-Hexylindol-3-yl)-2-hydroxy-4-hydroxymethylcyclopent-2-enone (**5e**) was obtained similarly: R_f 0.63 (EtOAc); MS of the per-(Me_3Si) derivative, *m/z*: 471 (35%) $[C_{20}H_{23}NO_3(SiMe_3)_2]^+$, 456 (15%) $[C_{20}H_{23}NO_3(SiMe_3)_2 - Me]^+$, 399 (20%) $[C_{20}H_{24}NO_3(SiMe_3)]^+$, 370 (4%) $[C_{20}H_{24}NO_3(SiMe_3) - C_2H_5]^+$; 73 (100%) $[SiMe_3]^+$; Anal. Calcd for $C_{20}H_{25}NO_3$: C, 73.37; H, 7.70; N, 4.28. Found: C, 73.15; H, 7.80; N, 4.14.

2-Hydroxy-4-hydroxymethyl-3-(1-methoxylindol-3-yl)cyclopent-2-enone (**5f**) was obtained by the same method; R_f 0.60 (EtOAc); MS of the per-(Me_3Si) derivative, *m/z*: 417 (1%) $[C_{15}H_{13}NO_4(SiMe_3)_2]^+$, 402 (1%) $[C_{14}H_{10}NO_4(SiMe_3)_2 - Me]^+$, 387 (3%) $[C_{14}H_{10}NO_3(SiMe_3) - OMe + H]^+$, 345 (1%) $[C_{15}H_{11}NO_4(SiMe_3)]^+$; 73 (100%) $[SiMe_3]^+$; Anal. Calcd. for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13. Found: C, 65.99; H, 5.63; N, 5.10.

3-(1-Benzylindol-3-yl)-2-hydroxy-4-hydroxymethylcyclopent-2-enone (**5c**) *(Method C).*—A solution of (1-benzylindol-3-yl)glyoxyalic acid (170 mg, 0.6 mmol) in 80% aq EtOH (15 mL) was treated with a threefold excess of $NaBH_4$ (80 mg). After 1 h, the reaction mixture, containing **2c** was filtered and and the filtrate added dropwise to an aq solution (30 mL) of L-ascorbic acid (1 g, tenfold excess), and refluxed for 20 h. The solution was separated from oil drops, cooled, and extracted with $CHCl_3$. The organic layer was dried (Na_2SO_4) and evaporated to give the crude product, which was purified by flash chromatography in 5:1 petroleum ether–EtOAc and then in EtOAc to yield **5c** as an amorphous solid (39%); R_f 0.60 (EtOAc). The compound was identical to the sample obtained by Method A.

3-(1-Allylindol-3-yl)-2-hydroxy-4-hydroxymethylcyclopent-2-enone (**5d**) was obtained similarly; R_f 0.57 (EtOAc); HR-MS, *m/z*: Found 283.1200, Anal. Calcd for $C_{17}H_{17}NO_3$ 283.1208.

3-(1-Ethoxyindol-3-yl)-2-hydroxy-4-hydroxymethylcyclopent-2-enone (**5g**) *(Method B).*—A solution of **1g** (100 mg) in 10 mL of 1:1 MeOH–aqueous HCl was stirred at 60 °C for 6 h. Water and EtOAc were then added. The organic layer was dried (Na_2SO_4), evaporated in vacuo, and purified by TLC (R_f 0.60) to give 13 mg (15%) of an amorphous solid; R_f 0.60 (EtOAc); HR-MS, *m/z*: Found 287.1169, Anal. Calcd for $C_{16}H_{17}NO_4$ 287.1158; MS of the per-(Me_3Si) derivative, *m/z*: 431 (2%) $[C_{16}H_{15}NO_4(SiMe_3)_2]^+$, 387 (3%) $[C_{16}H_{15}NO_4(SiMe_3)_2\text{-}OEt + H]^+$, 359 (2%) $[C_{16}H_{16}NO_4(SiMe_3)]^+$, 73 (100%) $[SiMe_3]^+$.

2-C-[(Indol-3-yl)(methoxycarbonyl)methyl]-α-L-xylo-hex-3-ulofuranosonic acid 1,4-lactone (**10**).—The methyl ester (**9**) of (indol-3-yl)glycolic acid (102 mg, 0.5 mmol) was added to a solution of L-ascorbic acid (270 mg, 1.5 mmol) in aq MeOH. The mixture was stirred for 2 days at 50 °C, and then diluted with water and extracted with EtOAc. The extract was dried (Na_2SO_4) and the crude product, purified by TLC to give 15 mg (8%) of amorphous **10**; R_f 0.32 (8:1, $CHCl_3$–MeOH); ^1H

NMR in CD_3OD, indole moiety: 7.70 (1 H, d, H-4′), 7.50 (1 H, s, H-2′), 7.36 (1 H, d, H-7′), 7.11(1 H, t) and 7.05 (1 H, t) (H-5′ and H-6′); *CH*–COOMe: 4.51 (1 H, s); ascorbic acid moiety: 4.58 (1 H, d, $J_{4,5}$ 1.0 Hz, H-4), 4.40 (1 H, m, H-5), 4.16 (1 H, dd, $J_{5,6a}$ 5.6 Hz, H-6a), 4.00 (1 H, dd, $J_{5,6b}$ 3.6, $J_{6b,6a}$ 9.7 Hz, H-6b); 3.64 (3 H, s, OCH_3) ppm.

Gradual transformation of ascorbigen **1a**.—To a solution of ascorbigen **1a** (305 mg, 0.1 mmol) in 9 mL of 1:2 MeOH–water was added Et_3N (0.27 mL, 0.2 mmol). After the transformation of **1a** into the ascorbigen acid salt was complete (10–15 min, R_f of the acid salt ~ 0 in 7:2 $CHCl_3$–MeOH), 1 N HCl was added to pH 2 and the reaction mixture was stirred under heating at 50 °C for 45 min. The mixture was extracted with $CHCl_3$, the extract was washed repeatedly with brine until the washings came to neutral pH, dried (Na_2SO_4) and concentrated in vacuum. The residue was loaded onto a column of Sephadex LH-20 and the compounds **11**, **12**, and **13** were eluted with MeOH. The fractions containing **12** were evaporated to give, after evaporation, 50 mg (20%) of the amorphous 2,6-dihydroxy-1-(indol-3-yl)hexa-1,4-dien-3-one, which was stored under Ar at -17 °C; it was a bright orange powder; R_f 0.70 (7:2, $CHCl_3$–MeOH); HR-MS: 243.0880; Anal. Calcd for $C_{14}H_{13}NO_3$ 243.0895; ^{1}H NMR ($CD_3OD + CDCl_3$): 7.18 (1 H, s, H-1); 7.30 (1 H, dt, $J_{4,5}$ 15.42 Hz, H-4); 7.06 (1 H, dt, $J_{5,6}$ 3.98 Hz, H-5); 4.39 (2 H, q, $J_{6,4}$ 2.11 Hz, H-6); indole ring: 7.83 (1 H, d, H-4′); 7.41 (1 H, d, H-7′), 7.19 (1 H, td, H-6′), 8.04 (1 H, s, H-2′), 7.15 (1 H, td, H-5′) ppm. ^{13}C NMR ($CD_3OD + CDCl_3$): 185.60; 147.59; 146.71; 137.53; 130.65; 128.33; 123.34; 121.57; 121.22; 119.11; 112.58; 111.78; 110.08; 62.56 ppm.

2,5,6-Trihydroxy-1-(indol-3-yl)hex-1-en-3-one (**11**) was isolated in the amount of 40 mg (16%) as a yellow powder, R_f 0.52 (7:2, $CHCl_3$–MeOH). HR-MS Found 261.1020, Calc. for $C_{14}H_{15}NO_4$ 261.1001; ^{1}H NMR (CD_3OD): 7.08 (1 H, s, H-1); 4.21 (1 H, m, $J_{5,6}$ 5.45 Hz, H-5); 3.60 (2 H, d, H-6); 3.04 (2 H, m, $J_{4b,5}$ 7.73, H-4); indole ring: 8.70 (1 H, s. H-2′); 7.82 (1 H, d, H-4′); 7.40 (1 H, d, H-7′); 7.14 (1 H, m, H-6′); 7.17 (1 H, m, H-5′) ppm. ^{13}C NMR (CD_3OD): 195.61; 147.07; 137.54; 130.18; 128.38; 123.26; 121.07; 119.19; 112.53; 111.59; 109.79; 70.80; 66.89; 40.29 ppm; Anal. Calcd. for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N 5.36. Found: C, 64.48; H, 5.83; N 5.20. Likewise 20 mg (8%) of 2-hydroxy-4-hydroxymethyl-5-(indol-3-yl)cyclopent-2-enone (**13**) was isolated similarly as a slightly yellow powder. R_f 0.42 (7:2, $CHCl_3$–MeOH). HR-MS: 243.0876 Calc. for $C_{14}H_{13}NO_3$: 243.0895; ^{1}H NMR ($CD_3OD + CDCl_3$), cyclopentenone ring: 3.08 (1 H, m, $J_{4,5}$ 2.38 Hz, H-4); 3.55 (1 H, d, $J_{4,5}$ 2.38 Hz, H-5); 3.66 (1 H, dd, $J_{6a,6b}$ 10.84 Hz, H-6a); 3.79 (1 H, dd, $J_{6a,6b}$ 10.84 Hz, H-6b); 6.62 (1 H, d, $J_{3,4}$ 2.74 Hz, H-3); indole ring: 8.14 (1 H, s); 7.33 (1 H, t), 7.08 (2 H, m); 6.96 (1 H, t). Anal. Calcd for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76. Found: C, 68.90; H, 5.49; N.5.56. When the reaction mixture, after addition of HCl, was heated for 90 min at 50 °C, cyclopentenone **13** was isolated in an amount of 40 mg (16%). It was also obtained by heating or by storing of **12**.

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