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SYNTHESES AND NMR SPECTRA OF 22,27-IMINO-17,23-OXIDOJERVANE DERIVATIVES[1]

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Abstract—A number of 22,27-imino-17,23-oxidojervane derivatives have been synthesized. The chemical shift values for all the Me groups of 65 derivatives of jervane are presented, and the effects of many different substituents on these chemical shifts are analysed. The additivity principle is shown to hold satisfactorily for the 19-Me protons of these C-nor-D-homosteroid alkaloids.

INTRODUCTION

In connection with a study aimed at the total synthesis of jervine, we have synthesized a number of jervine derivatives which would be useful as relay substances. In view of the close similarities of structure within these alkaloids, an intercomparison of the NMR spectra of a series of these compounds would be valuable in confirming certain stereochemical points as well as promoting the structure determination of new derivatives.[2] For these purposes we have carried out a study of the NMR spectra of 65 members of the group, including known compounds. While all the compounds discussed in the present paper contain a 22,27-imino-17,23-oxidojervane ring skeleton[3] and the data on the NMR spectra are confined to the correlation of the chemical shifts of Me groups with changes in their environment, the spectra of various compounds having a 22,27-iminojervane skeleton, in which no ether linkage is involved between C-17 and C-23, give a different result and will be reported later.

SYNTHESES OF 22,27-IMINO-17,23-OXIDOJERVANE DERIVATIVES

One of the reference compounds, 22,27-imino-17,23-oxidojervane (I), was synthesized as shown on Chart 1; the Wolff-Kishner reduction of 12α,13α-dihydrojervine[4] (II), prepared from jervine[5] (III),[6] gave 11-deoxo-12α,13α-dihydrojervine (IV). No

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[1] Part VII of C-*Nor-D-homosteroids and Related Alkaloids;* Part VI, T. Masamune, K. Orito and A. Murai, *Bull. Chem. Soc. Japan* **39**, 2503 (1966).

[2] For the NMR studies on the ceveratrum and fritillaria alkaloids having a C-nor-D-homosteroid skeleton, see the following Refs; [a] S. Ito, J. B. Stothers and S. M. Kupchan, *Tetrahedron* **20**, 913 (1964); and [b] S. Ito, M. Kato, K. Shibata and T. Nozoe, *Chem. Pharm. Bull. Japan* **11**, 1337 (1963).

[3] The designation "jervane" will be used to describe 17aβ-methyl-C-nor-D-homo-18-nor-13α-cholestane; cf. Ref. 1; J. Fried and A. Klingsberg, *J. Amer. Chem. Soc.* **75**, 4934 (1953); S. M. Kupchan and S. D. Levine, *ibid.* **86**, 701 (1964); W. F. Johns, *J. Org. Chem.* **29**, 2545 (1964).

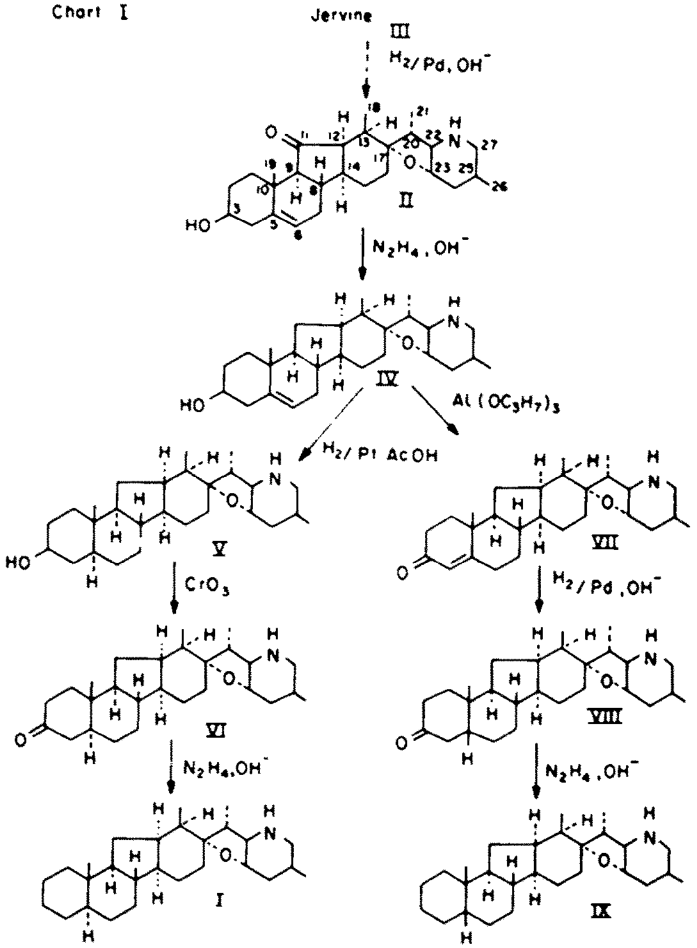
[4] [a] W. A. Jacobs and C. F. Huebner, *J. Biol. Chem.* **170**, 635 (1947); [b] The configurations of C-12 and C-13 in II have recently been established; O. Wintersteiner and M. Moore, *Tetrahedron* **20**, 1947 (1964).

[5] For the stereochemistry of jervine, see the following references; [a] T. Masamune, M. Takasugi and Y. Mori, *Tetrahedron Letters* 489 (1965); [b] O. Wintersteiner and M. Moore, *J. Org. Chem.* **29**, 262 (1964), the footnote 4.

[6] D. H. R. Barton, D. A. J. Ives and B. Thomas, *J. Chem. Soc.* 2056 (1956).

configurational change at C-9 and C-12 is considered to take place during the reduction, as II was recovered unchanged by vigorous treatments in strongly alkaline solutions. Hydrogenation of IV over Pt in acetic acid to 11-deoxo-5α,6,12α,13α-tetrahydrojervine (V) and subsequent oxidation with chromic anhydride afforded 22,27-imino-17,23-oxidojervan-3-one (VI), which in turn was submitted to the Huang-Minlon reduction to yield 22,27-imino-17,23-oxidojervane (I). On the other hand, an α,β-unsaturated ketone (VII) prepared by the Oppenauer oxidation of IV was hydrogenated over Pd in an alkaline solution[7] and produced 22,27-imino-17,23-oxido-5β-jervan-3-one (VIII), a 5β-isomer of VI, which was then converted into the corresponding 3-deoxo compound (IX) by the Huang-Minlon reduction. The configurations of C-5 in VI and VIII were deduced from the measurement of ORD curves; VI and VIII showed a positive and a negative Cotton effect, respectively.

Chart I



Synthesis of 12,13-dehydro derivatives of I and IX is shown on Chart II and

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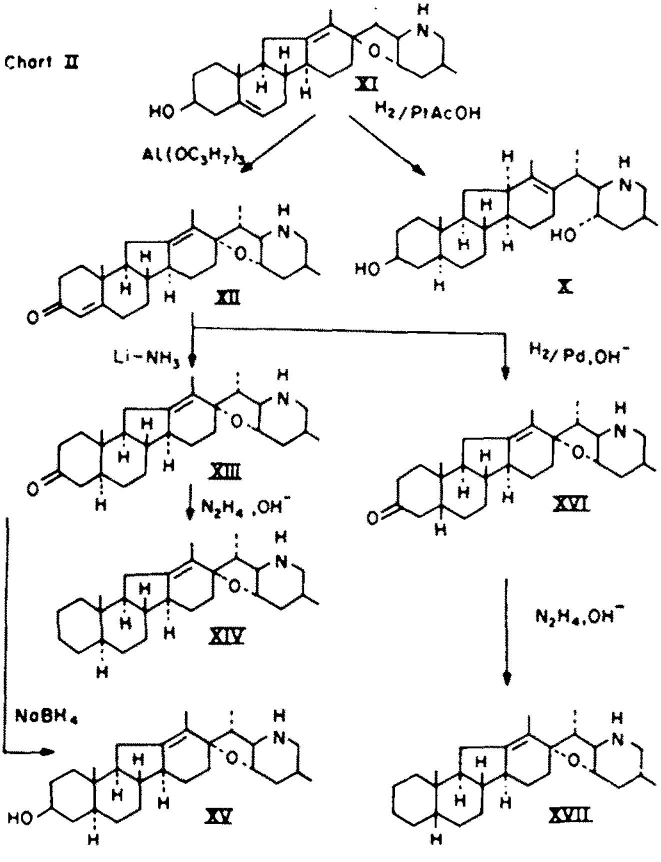
[7] cf. R. Yashin, G. Rosenkranz and C. Djerassi, *J. Amer. Chem. Soc.* 73, 4654 (1951); G. Slomp Jr., Y. E. Shealy, J. L. Johnson, R. A. Donia, B. A. Johnson, R. R. Holysz, R. L. Pederson, A. O. Jensen and A. C. Ott, *Ibid.* 77, 1216 (1955).

involves the sequence XI to XIV or to XVII. Since the hydrogenation of 11-deoxojervine[8] (XI) over Pt in acetic acid had led to the cleavage of the ether linkage with concomitant reduction of the 5,6-double bond and afforded 22,27-iminojerva-5,13(17)-diene-3β,23α-diol[1,6a] (X), reduction of the 5,6-double bond in XI was attempted in neutral or alkaline solutions. However, the starting material XI was only recovered unchanged. Hence, XI was first oxidized to "11-deoxo-Δ^4-jervone" (XII) by the Oppenauer method. Catalytic hydrogenation of XII under neutral or alkaline conditions produced 22,27-imino-17,23-oxido-5β-jerv-12-en-3-one (XVI), showing a negative Cotton effect, while the Birch reduction[9] of XII resulted in the formation of a 5α-isomer (XIII) of XVI, which gave a positive Cotton effect. The Huang-Minlon reduction of XIII and XVI produced the respective 3-deoxo derivatives (XIV and XVII), and hydride reduction of XIII with sodium borohydride gave 11-deoxo-5α,6-dihydrojervine[10] (XV) in good yield.

Next, stereospecific synthesis of 11-oxo derivatives of VI and VIII was undertaken

Chart II



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[8] T. Masamune, Y. Mori, M. Takasugi, A. Murai, S. Ohuchi, N. Sato and N. Katsui, *Bull. Chem. Soc. Japan* **38**, 1374 (1965).

[9] cf. G. Stork and S. D. Darling, *J. Amer. Chem. Soc.* **86**, 1761 (1964).

[10] Assignment for the β-configuration of the 3-OH group was deduced from analogous examples with normal steroids; cf. W. G. Dauben, E. J. Blanz, Jr., J. Jiu and R. A. Micheli, *J. Am. Chem. Soc.* **78**, 3752 (1956); O. R. Vail and D. M. S. Wheeler, *J. Org. Chem.* **27**, 3803 (1962).

and the process is summarized on Chart III. Normal Δ^4-3-ketosteroids which possess an 11β-hydroxyl[11] or 11-carbonyl group[11,12] are reduced by catalytic hydrogenation to the 5α,6-dihydro derivatives, whereas hydrogenation of 11α-hydroxy-Δ^4-3-ketones, specially in alkaline solutions, gives the corresponding 5β-isomers.[13] Thus, II was reduced to "12α,13α-dihydrojervin-11β-ol" (XVIII) with LAH and to the 11α-isomer (XXII) with sodium and butanol. According to the similar reduction methods, the 5α,6-dihydro derivatives (XXVII and XXVIII) of XVIII and XXII had already been prepared from 5α,6,12α,13α-tetrahydrojervine[4a,14,15] (XXVI). It is apparent that no epimerization takes place at C-9 and C-12 during the reductions, as II is stable to alkali as mentioned previously and, in addition, XVIII and XXII were oxidized smoothly to II in good yield. These alcohols XVIII and XXII were converted into the respective Δ^4-3-ketones (XIX and XXIII) by the Oppenauer oxidation. Hydrogenation of XIX over Pd-C in ethanol produced a 3-keto-11β-alcohol (XX) as a main product, the 5α-configuration of which was confirmed from the ORD curve (a positive Cotton effect). The keto-alcohol XX was oxidized with chromic anhydride to yield a diketone (XXI), which was also obtained by oxidation of the tetrahydrojervine XXVI. Since configurational change is unlikely to occur during such mild oxidations, XXI must be an 11-oxo analog of VI. Furthermore, a series of the above-mentioned transformations involve confirmation of the 5α-configuration of XXVI. On the other hand, treatment of XXIII with hydrogen in the presence of Pd in alkaline aqueous ethanol gave rise to a 3-keto-11α-alcohol (XXIV) as a major product, and the ORD curve (a negative Cotton effect) proved that XXIV had a A/B *cis* ring fusion. XXIV was oxidized smoothly to a diketone (XXV), which was a stereoisomer of XXI as well as an 11-oxo analog of VIII.

While XXI which possesses *trans* A/B and *trans* B/C linkages was recovered unchanged by treatment with potassium t-butoxide in refluxing t-butanol, it was anticipated that XXV which retains a *cis* A/B and *trans* B/C system would be epimerized at C-9 to give an isomer in which the B-ring is *cis*-fused with the C-ring. Such epimerizations have been observed with several hydrindanone derivatives[16] and also with analogs of XXV having a benzenoid D-ring.[17] Contrary to the expectation, XXV remained uneffected, when treated with potassium t-butoxide in refluxing t-butanol. However, a new compound was isolated in one run when XXV was refluxed in aqueous ethanol containing 20% potassium hydroxide for a long time. This compound (XXIX) was at first supposed to be an expected isomer, but it gave an O,N-diacetyl derivative on acetylation and was obtained from XXV in 70% yield by hydrogenation over Pt in an alkaline ethanol solution. Furthermore, XXIX was converted, in good yield, into the original diketone XXV by chromic anhydride oxidation. Thus, the

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[11] J. Pataki, G. Rosenkranz and C. Djerassi, *J. Biol. Chem.* **195**, 751 (1952).

[12] H. L. Mason, W. M. Hoen, B. F. Mckenzie and E. C. Kendall, *J. Biol. Chem.* **120**, 733 (1937); C. Djerassi, G. Rosenkranz, J. Pataki and S. Kaufmann, *Ibid.* **194**, 115 (1952).

[13] O. Mancera, C. Djerassi, H. J. Ringold, G. Rosenkranz and F. Sondheimer, *J. Amer. Chem. Soc.* **75**, 1286 (1953).

[14] B. M. Iselin, M. Moore and O. Wintersteiner, *J. Amer. Chem. Soc.* **78**, 403 (1956).

[15] cf. O. Wintersteiner and M. Moore, *Tetrahedron* **21**, 779 (1965).

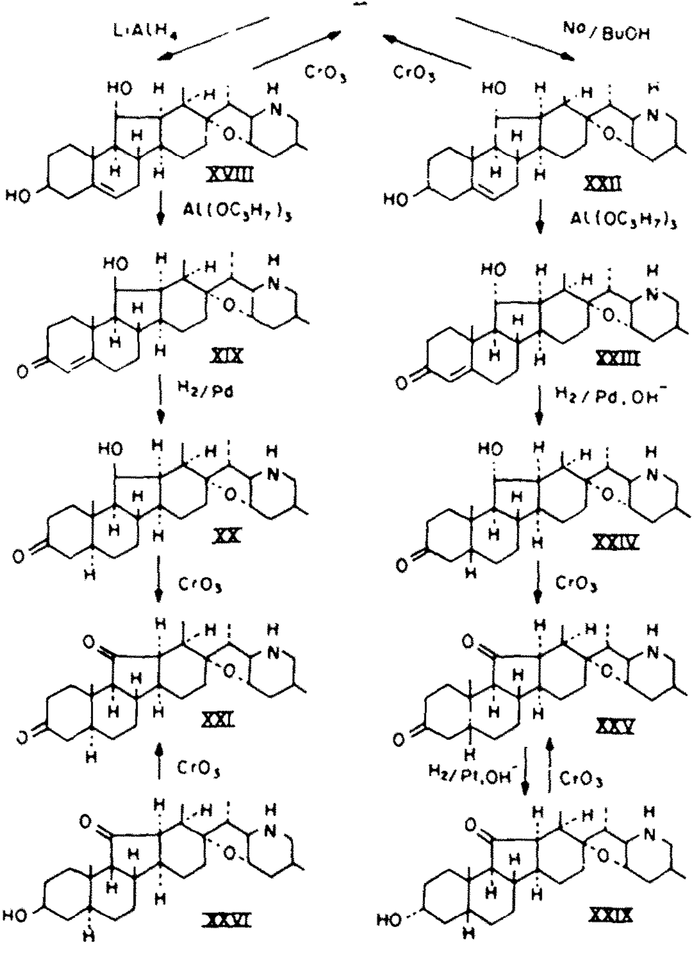
[16] Ref. 5*a*, footnote 8.

[17] [a] P. W. Schiess, D. M. Bailey and W. S. Johnson, *Tetrahedron Letters* 549 (1963); [b] D. M. Bailey, D. P. G. Hamon and W. S. Johnson, *Ibid.* 555 (1963).

compound could be formulated as XXIX,[18] and would have been formed by reduction of the Meerwein-Ponndorf type during the prolonged treatment with alkali.

Finally, synthesis of 11-oxo derivatives of XIII and XVI was carried out as shown on Chart IV. "Δ^4-Jervone"[4a] (XXX) was subjected to hydrogenation over Pd-C in ethanol or in alkaline aqueous ethanol. Fortunately, the hydrogenation led to only

Chart III



the reduction of a 4,5-double bond and yielded a mixture of stereoisomers, although the hydrogenation of III under similar conditions affords 12,13-dihydrojervine (II) in good yield.[19] By fractional recrystallizations of the product or of the N-acetyl derivative, stereoisomers (XXXI), m.p. 208–210°, and (XXXII), m.p. 208–210°, were isolated in the yields of 12% and 40%, respectively. Although both the compounds showed almost the same R_f on paper chromatograms and the closely similar pattern in the IR spectra, these could be distinguished each other by TLC and by the mixed

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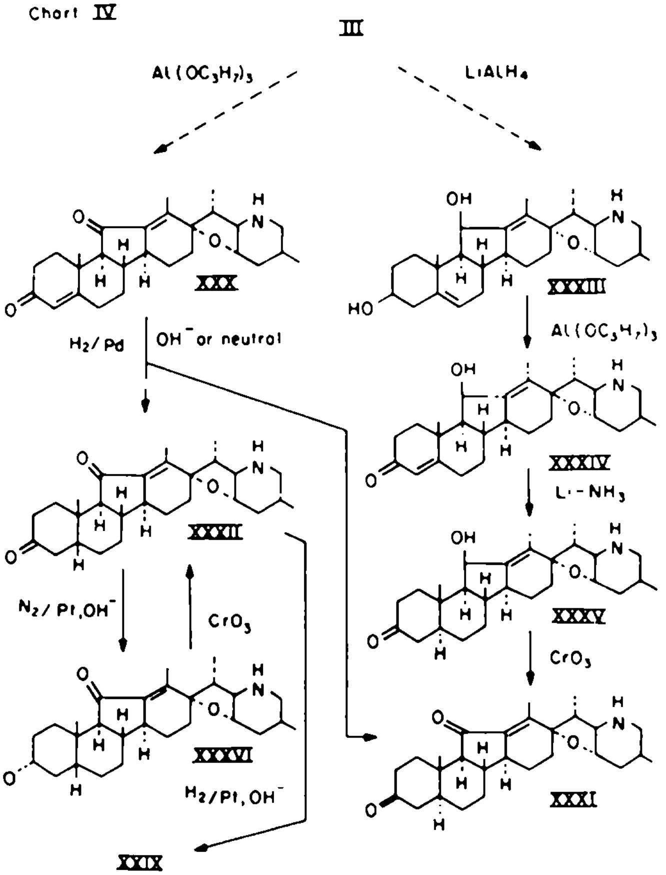
[18] The configuration of the 3α-OH group was assigned on the basis of analogous examples with normal steroids. cf. L. Ruzicka, H. Brungger, E. Eichenberger and J. Meyer, *Helv. Chim. Acta* 17, 1407 (1934).

[19] R. Anliker, H. Heusser and O. Jeger, *Helv. Chim. Acta* 35, 838 (1955).

m.p. method. In order to establish the configuration of these compounds, "jervine-11β-ol"[14,5a] (XXXIII), which has been proved to have the same configuration at C-9 as jervine, was converted into the corresponding Δ^4-3-ketone (XXXIV), which in turn was submitted to the Birch reduction to give a 3-keto-11β-alcohol (XXXV). The ORD curve of XXXV had a positive Cotton effect, indicating that it had a *trans* A/B ring fusion. Chromic anhydride oxidation of XXXV produced a 3,11-diketone, m.p. 205–208°, which was identical with XXXI. Since no epimerization is considered to occur during the oxidation, a series of the reactions from III to XXXI establish that XXXI is 3-dehydro-5α,6-dihydrojervine, an 11-oxo analog of XIII, and that XXXII is a 5β-isomer of XXXI. This was supported by the following reaction; XXXII was hydrogenated in the presence of Pt in alkaline aqueous ethanol and gave rise to XXIX already obtained from XXV (Chart III). With the purpose of preparation of compounds having a *cis* B/C ring fusion, XXXII and the 3-ethylene ketal (XXXIIb) were treated with potassium t-butoxide in refluxing t-butanol, but remained unaffected as in the case of XXV. The ethylene ketal XXXIIb having no ketonic group at C-3 was recovered unchanged also by prolonged treatment with potassium hydroxide in refluxing ethanol, whereas XXXII itself was reduced to yield a 12α,13α-dehydro derivative (XXXVI) of XXIX.

Chart IV



NMR SPECTRA, RESULTS AND DISCUSSIONS

The spectra of the steroid alkaloids examined in the present work were complex because of the presence of a number of alicyclic methylene and methine groups. However, the signals of Me groups were usually discernible as relatively sharp peaks, which appeared above the background of the methylene and methine protons The Me groups sometimes gave rise to overlapping signals, which made the assignment difficult. Then, the spectra were taken at two different magnetic fields (60 and 100 Mc) and interpreted, being compared each other. Assignment of the peaks to the respective Me groups and effects of structure on the peak positions are discussed in detail in the following. The results are summarized in tabular form; the chemical shift data for the various Me protons are shown in Tables 1 and 3 and the contributions of functional groups to chemical shifts of the 19- and 18-Me protons in Tables 2 and 4, respectively.

The 19-*methyl protons*. There is no ambiguity for almost all the assignments of the 19-Me protons (Table 1). The protons appear as sharp singlets over the range τ8·58 to 9·29 and give τ-values independent of change in the magnetic field. While the chemical shifts of the protons would not be expected to depend on substituents on the N atom and, in fact, it was the case, structural and configurational variations in the A, B and C rings cause change in the peak positions, just as observed in the similar studies of normal steroids and related compounds. In the NMR spectra of steroids[20] and triterpenoids,[21] the long range shielding effects of various substituents on the chemical shift of angular Me protons have been shown to be additive by many investigators. This "principle of additivity" has now been found to be applicable to the present series of compounds as well, and a detailed discussion follows.

In order to examine both additivity and magnitude of the shielding effects, all the compounds were classified into two groups, A and B, as usually done in the normal steroid series; the group A includes compounds having a *trans* A/B ring fusion (18 members) and those having a 4,5- or a 5,6-double bond (30 members), and the group B 17 compounds having a *cis* A/B linkage. 5α- and 5β-Iminooxidojervanes I and IX bearing no substituent were selected as reference compounds of the respective groups. The contributions of various functional groups (Table 2) were obtained by paring compounds which differ by only the single chemical group in question and by taking the average of differences of the chemical shifts. The values on the last column of Table 1 were calculated, having available the chemical shifts of the reference signals and the contributions listed in Table 2, and are in good agreement, within 0·02 ppm, with the observed chemical shifts, indicating that the shielding effects are really

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[20] [a] J. N. Shoolery and M. T. Rogers, *J. Amer. Chem. Soc.* **80**, 5121 (1958); G. Slomp, Jr. and B. R. McGarvey, *Ibid.* **81**, 2200 (1959); J. S. Cox, E. O. Bishop and R. E. Richards, *J. Chem. Soc.* 5118 (1960); K. Kawazoe, Y. Sato, N. Natsume, H. Hasegawa, T. Okamoto and K. Tsuda, *Chem. Pharm. Bull. Japan* **10**, 338 (1962); T. Okamoto and Y. Kawazoe, *Ibid.* **11**, 643 (1963); K. Tori and E. Kondo, *Tetrahedron Letters* 645 (1963); E. R. Malinowski, M. S. Manhas, G. H. Müller and A. K. Boxe, *Ibid.* 1161 (1963); A. I. Cohen and S. Rock, Jr., *Steroids* **3**, 243 (1964); K. Tori and T. Komeno, *Tetrahedron* **21**, 309 (1965); [b] R. F. Zürcher, *Helv. Chim. Acta* **44**, 1380 (1961); *Ibid.* **46**, 2054 (1963); [c] N. S. Bhacca and D. H. Williams, *Application of NMR Spectroscopy in Organic Chemistry* p. 14. Holden-Day, San Francisco (1964).

[21] A. T. Cohen, D. Rosenthal, G. W. Karkower and J. Fried, *Tetrahedron* **21**, 3171 (1965) and Refs. cited in the footnote *6a*.

TABLE 1. THE CHEMICAL SHIFT OF THE 19-METHYL PROTONS OF THE IMINOOXIDOJERVANES

Group A 5α-, Δ^4- *and* Δ^5-*Iminooxidojervanes*

		Substituents[b] at						Chemical	
No.	Compounds[a]	3	4	5	11	12	N	shifts[c]	(τ)
1	I						H	9·29	
2	Ia						Ac	9·29	(9·29)
3	II[d]	β-OH		Δ	O		H	8·98	(8·99)
4	IIa[d]	β-OAc		Δ	O		Ac	8·98	(8·98)
5	IIb	β-OH		Δ	O		CH_3	8.99	(8.99)
6	IIIa[e,f]	β-OAc		Δ	O	Δ	Ac	8·99	(8·98)
7	IIIb[e,f]	β-OH		Δ	O	Δ	Ac	9·00	(8·99)
8	IIIc[e]	β-OAc		Δ	O	Δ	H	9·00	(8·98)
9	IIId[e]	β-OAc		Δ	O	Δ	CH_3	8·97	(8·98)
10	IIIe	β-OAc		Δ	O	Δ	$(CH_3)_2$[g]	8·97	(8·98)
11	IV	β-OH		Δ			H	9·05	(9·06)
12	IVa	β-OAc		Δ			Ac	9·05	(9·05)
13	Va	β-OAc					Ac	9·26	(9·26)
14	VIa	O					Ac	9·08	(9·075)
15	VIb	$C_2H_4O_2$					H	9·26	(9·265)
16	VII	O	Δ				H	8·89	(8·89)
17	VIIa	O	Δ				Ac	8·89	(8·89)
18	XI[h]	β-OH		Δ		Δ	H	9·07	(9·06)
19	XIa[h]	β-OAc		Δ		Δ	Ac	9·06	(9·05)
20	XIb	β-OH		Δ		Δ	CH_3	9·07	(9·06)
21	XIc	β-OAc		Δ		Δ	CH_3	9·05	(9·05)
22	XII	O	Δ			Δ	H	8·89	(8·89)
23	XIII	O				Δ	H	9·08	(9·075)
24	XIV					Δ	H	9·30	(9·29)
25	XV	β-OH				Δ	H	9·27	(9·27)
26	XVa	β-OAc				Δ	Ac	9·26	(9·26)
27	XVIII	β-OH		Δ	β-OH		H	8·76	(8·765)
28	XVIIIa	β-OAc		Δ	β-OH		Ac	8·75	(8·755)
29	XVIIIb	β-OAc		Δ	β-OAc		Ac	8·84	(8·845)
30	XIX	O	Δ		β-OH		H	8·59	(8·595)
31	XIXa	O	Δ		β-OAc		Ac	8·69	(8·685)
32	XX	O			β-OH		H	8·78	(8·78)
33	XXI	O			O		H	9·01	(9·005)
34	XXIa[e]	O			O		Ac	9·02	(9·005)
35	XXII[d]	β-OH		Δ	α-OH		H	9·02	(9·03)

TABLE 1 (*Cont'd*)

		Substituents[b] at						Chemical	
No.	Compounds[a]	3	4	5	11	12	N	shifts[c]	(τ)
36	XXIIa	β-OAc		Δ	α-OH		Ac	9·00	(9·02)
37	XXIIb[i]	β-OAc		Δ	α-OAc		Ac	8·94	(8·96)
38	XXIII[i]	O	Δ		α-OH		H	8·88	(8·86)
39	XXIIIa	O	Δ		α-OAc		Ac	8·82	(8.80)
40	XXVI[d-f]	β-OH			O		H	9·19	(9·20)
41	XXVIa[f]	β-OAc			O		Ac	9·17	(9·19)
42	XXVII[g]	β-OH			β-OH		Ac	8·98	(8·975)
43	XXVIII[d,g]	β-OH			α-OH		Ac	9·24	(9·24)
44	XXX[d]	O	Δ		O	Δ	H	8·82	(8·82)
45	XXXI	O			O	Δ	H	9·00	(9·005)
46	XXXIIIa[e]	β-OAc		Δ	β-OH	Δ	Ac	8·77	(8·755)
47	XXXIV	O	Δ		β-OH	Δ	H	8·58	(8·595)
48	XXXV	O			β-OH	Δ	H	8·77	(8·78)
			Group B	*5β-Iminooxidojervanes*					
49	VIII	O					H	9·07	(9·075)
50	VIIIa	$C_2H_4O_2$					H	9.13	(9·13)
51	IX						H	9·17	
52	IXa						Ac	9·18	(9·17)
53	XVI	O				Δ	H	9·07	(9·07)
54	XVII					Δ	H	9·17	(9·17)
55	XXIV	O			α-OH		H	9·04	(9·04)
56	XXIVa	O			α-OAc		Ac	8·99	(8·99)
57	XXV	O			O		H	8·99	(8·99)
58	XXVa	O			O		Ac	8·98	(8·99)
59	XXIX	α-OH			O		H	9·07	(9·06)
60	XXIXa	α-OAc			O		Ac	9·06	(9·05)
61	XXXII	O			O	Δ	H	9·00	(8·99)
62	XXXIIa	O			O	Δ	Ac	9·00	(8·99)
63	XXXIIb	$C_2H_4O_2$			O	Δ	H	9·05	(9·05)
64	XXXVI	α-OH			O	Δ	H	9·04	(9·06)
65	XXXVIa	α-OAc			O	Δ	Ac	9·03	(9·05)

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[a] The suffix "a, b and so on" refers to acetyl, alkyl and/or ethylenedioxy derivatives. [b] The abbreviated words "O, $C_2H_4O_2$ and Δ" denote ketonic and ethylenedioxy groups and a double bond, respectively. [c] The figures in the parentheses refer to the values calculated from Table 2. [d] Ref. 4. [e] K. Saito, H. Suginome and M. Takaoka, *Bull. Chem. Soc. Japan* 11, 172 (1936). [f] W. A. Jacobs and L. C. Craig, *J. Biol. Chem.* **148**, 51 (1943). [g] Ref. 14. [h] Ref. 8. [i] W. A. Jacobs and Y. Sato, *J. Biol. Chem.* **175**, 57 (1948). [j] O. Wintersteiner, M. Moore and B. M. Iselin, *J. Amer. Chem. Soc.* **76**, 5609 (1954). [k] N-Methyl methiodide.

TABLE 2. THE CONTRIBUTION OF FUNCTIONAL GROUPS TO THE CHEMICAL SHIFT OF THE 19-METHYL PROTONS OF THE IMINOOXIDOJERVANES

Reference compounds[a] (τ)	Group A I 9·29 (9·208)		Group B IX 9·17 (9·075)	
Functional groups	No. of examples	Contribution[b] (ppm)	No. of examples	Contribution[b] (ppm)
3β-OH	12	−0·02 (−0·033)		
3β-OAc	17	−0·03 (−0·050)		
3α-OH			2	−0·03 (−0·008)
3α-OAc			2	−0·04 (−0·025)
3-Ethylenedioxy	1	−0·025 (−0·025)	2	−0·04 (−0·033)
3-Oxo	8	−0·215 (−0·242)	6	−0·10 (−0·117)
Δ^4-3-Oxo	9	−0·40 (−0·417)		
Δ^5	22	−0·21 (−0·233)		
11β-OH	8	−0·295 (−0·258)		
11β-OAc	2	−0·205 (−0·067)		
11α-OH	4	−0·03 (−0·117)	1	−0·03 (−0·117)
11α-OAc	2	−0·09 (−0·092)	1	−0·09 (−0·092)
11-Oxo	15	−0·07 (−0·217)	9	−0·08 (−0·217)
Δ^{12}	14	0·00	7	0·00
Substituents on N		0·00	6	0·00

[a] The values in the parentheses are the chemical shifts of the 19-Me protons in 5α,14α-and 5β,14α-androstanes. cf. Ref. 20b. [b] The negative sign denotes a downfield shift. The values in the parentheses are those of the corresponding effect with normal steroids. cf. Ref. 20*b*.

additive. In view of the low-field shifts of the 19-Me signal in the compounds possessing a B/C *cis*-fused ring (8β-H, and 9β-H),[17,22] it should be emphasized that the iminooxidojervane derivatives (and probably the iminojervane derivatives) whose 19-Me protons appear in accordance with the additivity rule (with minor deviations) must have a *trans*-fused B/C ring (8β-H, 9α-H). This "principle of additivity" would also be useful for determination of the stereochemistry of compounds without confirmatory chemical evidences for the configuration.[23]

On the results given in Table 2, some comments are presented in the following. (1) The 19-Me protons of I, the reference compound having a *trans* A/B ring fusion, appear at higher field than those of another reference compound IX having a *cis*-fused A/B ring system, and the difference (0·12 ppm) between their peak positions is equal to that (0·133 ppm) between the Me signals of 5α- and 5β-androstanes.[20b] On the other hand, when a pair of the reference compounds having the same A/B linkage, I and 5α-androstane or IX and 5β-androstane, are compared, the signals of I and IX are found at higher field by about 0·09 ppm than those of 5α- and 5β-androstanes, respectively. (2) Each functional group in the A and B rings provides almost the same deshielding effect as that of the corresponding group in the normal series. This indicates that the steric relation of various functional groups in the A and B rings to the 19-Me protons hardly suffers change in passing from the normal to the present modified ring skeleton, although the A and B rings were expected to undergo distortion

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[22] J. P. Kutney, A. By, T. Inaba and S. Y. Leong, *Tetrahedron Letters* 2911 (1965).

[23] For example, the 11-OH group of "jervine-11β-ol" (XXXIII) has been assigned to be β-oriented on the basis of a general rule that the hydride reduction of a CO group takes place from the less hindered side. However, the 11-epimer of XXXIII has not been prepared yet and no definite proof for the assignment appears to be reported.

due to the contraction of the ring C. (3) The substituents in the C ring display contributions different from those due to the corresponding functional groups in the normal steroid. It is interesting that the β-oriented OH and OAc groups at C-11 cause larger deshielding effects as compared with those in the normal steroid, while the 11α-OH group exerts a smaller deshielding effect. The spatial relation between the OH groups at C-11 and the 19-Me group would be different in the present modified steroid system from that in the normal steroids because mainly of the contraction of the C ring and partly of the deformation of the D ring discussed later. This alteration in the relative position between those groups would cause variation in the magnetic anisotropy[24] of the OH groups, involving C—O bond and O—H bond anisotropies and probable lone-pair electrons contribution, as well as in the van der Waals' compression[25] of the 1,3-diaxial disposed groups. These effects would lead to the variation of the deshielding effects in question, although no quantitative estimation was performed in the present case. (4) The deshielding effect (0·07 ppm) of the 11-CO group is remarkably small contrary to the large effect (0·217 ppm) shown in the normal steroids. It is well known[26] that protons lying in conical regions extending above and below the plane of the trigonal carbon atom of a CO group are shielded by this function, while those lying elsewhere and particularly those in the plane of the trigonal atom are deshielded. According to molecular models, substitution of a CO group at the position 11 does not affect the conformation of the D ring significantly (conformation A discussed later), and the plane of the 11-CO carbon is involved in the almost coplanar C ring. Thus, the 19-Me protons were far shifted from the plane as compared with the case when C ring is six-membered, and lie in the region where the CO group does not exert an important deshielding effect. The obtained result is, therefore, in good accord with the expectation. (5) There is no contribution from the 12,13-double bond. It is expected that introduction of the function into the D ring would lead to the change of conformation of the D ring. It should be mentioned that the double bond displays no shielding effect is a result of compensation of the effect due to the double bond itself and that due to the deformation of the D ring.

The 18-*methyl and other methyl protons.* The signals due to secondary Me groups other than the 19-Me group were usually discernible without much difficulty, although those signals appeared as overlapping signals in many cases or both the components of doublets were not clearly resolved in several cases. However, difficulty was encountered in the assignment of the appropriate signals to those Me groups. In an attempt to solve this problem, the spectra of compounds possessing a 12,13-double bond were first examined (Table 3, group D), because the signals of the 18-Me groups attached to the double bond appeared as singlets over the range τ 7·7 to 8·4, and could readily be distinguished from those of other Me groups. The absorptions of the 21- and 26-Me protons varied depending on a substituent at the N atom. In each of the spectra of compounds in which the N atom was substituted by a Me group or was not substituted, only one doublet involving six protons was observed and, therefore, the signals assignable to both the two Me groups coincided. The doublet was centered

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[24] [a]L. M. Jackman, *Application of NMR Spectroscopy in Organic Chemistry* p. 115. Pergamon Press, London (1959); [b] Ref. 20*b*.

[25] Cf. R. J. Abraham and J. S. E. Holker, *J. Chem. Soc.* 806 (1963); W. Nagata, T. Terasawa and K. Tori, *J. Amer. Chem. Soc.* **86**, 3746 (1964); T. Masamune, S. Ohuchi, S. Shimokawa and H. Booth, *Tetrahedron* **22**, 778 (1966).

[26] Ref. 24*a*, p. 122.

TABLE 3. THE CHEMICAL SHIFT OF THE 18-, 21- AND 26-METHYL PROTONS OF THE IMINOOXIDOJERVANES[a]

Substituents at 11	Substituents at N	No. of examples	Chemical shifts (τ) of methyl protons 21-	26-	18-
		Group C (without $\Delta^{12,13}$)			
H_2	Ac	6	9·18–9·19	8·99–9·00	9·08–9·10
H_2	H	7	9·08–9·10	9·08–9·10	
β-OH	Ac	2	9·17, 9·18	8·98, 8·99	8·98–8·99
β-OH	H	3	9·08–9·09	9·08–9·09	
β-OAc	Ac	2	9.18, 9·19	8·98, 8·99	9·11, 9·13
α-OH	Ac	2	9·17, 9·18	8·97, 8·98	8·98–9·02
α-OH	H	3	9·07–9·09	9·07–9·09	
α-OAc	Ac	3	9·15–9·16	8·97–8·98	9·15–9·16
O	Ac	5	9·16–9·18	8·97–8·99	9·06–9·08
O	H	5	9·06–9·08	9·06–9·08	
O	CH_3	1	8·97	8·97	
		Group D (with $\Delta^{12,13}$)			
H_2	Ac	2	9·15, 9·16	8·97, 8·99	8·29–8·39
H_2	H	7	9·06–9.08	9·06–9.08	
H_2	CH_3	2	8·93, 8·96	8·93, 8·96	
β-OH	Ac	1	9·15	8·98	8·10–8·14
β-OH	H	2	9·05, 9·06	9·05, 9·06	
O	Ac	4	9·10–9·13	8·94–8·96	7·74–7·85
O	H	6	9·04–9·06	9·04–9·06	
O	CH_3	1	8·94	8·94	
O	$(CH_3)_2$	1	(8·83 and 8·94)[b]		

[a] A part of this Table is described in one of the previous reports; Ref. 31. [b] Assignment was not possible.

in the narrow range τ 9·04 to 9·06 with latter compounds and in that τ 8·93 to 8·96 with former compounds, respectively, indicating that both the 26- and 21-Me signals were hardly affected by substituents in the C ring. On the other hand, when the N atom was substituted by an acetyl group, the signals due to the two Me groups appeared as separate doublets, one of them being always centered in the range τ 8·94 to 8·99 and the other in that τ 9·10 to 9·16. Again, the 21-Me signals appeared independently of substituents in the C ring. Thus, only from the available data, it was impossible to assign the signals to the Me groups in the N-acetyl compounds.

The spectra of compounds in which the D ring was saturated (Table 3, group C) were next examined with the following assumption; the signals of the 26-Me protons would appear in a narrow range irrespective of the presence of a 12,13-double bond and substituents in the C ring as far as the compounds have the same N-substituent. According to this assumption, the 26-Me signals should be centered either in the neighborhood of τ 8·97 or 9·13 in the N-acetyl derivatives. In most of the spectra examined, three doublets with spacings of 5·0 to 7·5 c/s were observed in the region τ 8·8 to 9·3. One of the three doublets was always centered in the range τ 8·97 to 9·00, and the other one in that τ 9·15 to 9·19. These chemical shifts are close to those of two doublets (τ 8·94 to 8·99 and 9·10 to 9·16) found in the spectra of the compounds included in the group D. Thus, it would be reasonable to assign the aforementioned two doublets to both the 26- and 21-Me protons (or *vice versa*). However, it was again difficult to assign the appropriate signals to the respective group. At this stage, the spectrum of "3O,N-diacetyl-Δ^{13}-jervine"[27] was examined. The absorptions of the three secondary Me groups appeared as doublets centered at τ 9·04, 8·99 and 8·92, and no signal regarded as components of a doublet was found in the field over τ 9·10. On the basis of this sole example and the assumption mentioned above, it might be proposed that the doublets found in the range τ 8·94 to 9·00 should be attributable to the 26-Me group, and those found in the region τ 9·10 to 9·19 to the 21-Me group,[28] though no other confirmatory evidence is not given in the present paper. Hence, the remaining one of the three doublets was assigned to the 18-Me group.

TABLE 4. THE CONTRIBUTION OF FUNCTIONAL GROUPS TO THE CHEMICAL SHIFT OF THE 18-METHYL PROTONS OF THE IMINOOXIDOJERVANES

Reference compounds (τ)		Group C 9·09[a]		Group D 8·34[b]
Functional groups	No. of examples	Contribution[c] (ppm)	No. of examples	Contribution[c] (ppm)
11β-OH	5	−0·11	3	−0·22
11β-OAc	2	+0·03		
11α-OH	5	−0·09		
11α-OAc	3	+0·07		
11-Oxo	11	−0·02	11	−0·45
Substituents in rings A and B and on N atom		0·00		~0·00

[a] The mean chemical shift of 18-Me protons in 13 compounds bearing no substituent at C-11 and C-12. [b] The mean chemical shift of 18-Me protons in 11 compounds bearing double bond at C-12–C-13 and no substituent at C-11. [c] The negative sign denotes a downfield shift.

In the spectra of most of the compounds in which the N atom was unsubstituted or Me substituted, two doublets were observed and one of them always involved six protons. The overlapping, two Me signals were centered in the range τ 9·06 to 9·10 and at τ 8·97 in the respective amines. The corresponding chemical shifts in the compounds of the group D were τ 9·04 to 9·06 and τ 8·93 to 8·96, respectively, which were almost the same as the above-mentioned values. Therefore, these signals were assigned to both the 26- and 21-Me protons. The remaining one doublet should be assigned to the 18-Me protons. While the 18-Me signals thus assigned varied depending on substituents at C-11, those were expected to remain unchanged by alteration of N-substituents. In fact, it was the case as shown in Table 3.

The contribution of several 11-substituents to the chemical shift of 18-Me protons is summarized in Table 4 and the following points should be noted for the compounds of the group C. (1) The deshielding effect (0·02 ppm) of the 11-CO group is negligibly small, indicating that the Me protons are located neither in the plane of the trigonal 11-carbon atom nor in the conical region extending above and below the plane. This disposition offers further support for the previous configurational assignment to C-12 and C-13[7b]; that is, it is satisfied only when both the 12- and 13-carbon atoms have

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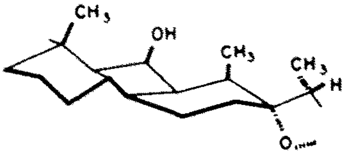
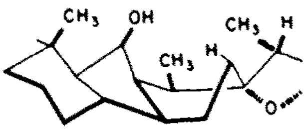
[27] B. M. Iselin and O. Wintersteiner, *J. Amer. Chem. Soc.* 77, 5318 (1955).

[28] In expectation of that evidences to support this assignment may be obtained, the spectra of several compounds have been measured in a mixture of deuterochloroform and benzene or in pyridine, and the result will be published in the near future.

α-oriented hydrogen atoms and the D ring possesses a slightly deformed chair conformation A discussed later. (2) In contrast to the contributions for the 19-Me protons, 11β-OH and OAc groups exhibited almost the same deshielding and shielding effects (−0·11 and +0·03 ppm) for the 18-Me protons as the corresponding 11α-groups (−0·09 and +0·07 ppm), although this does not always imply that the 18-Me group would have the similar steric relation for both the 11β- and 11α-OH groups. On the other hand, the deshielding effects of β-OH (and β-acetoxyl) groups at C-11 were remarkably small for the 18-Me group as compared with those (−0·295 and −0·205 ppm) for the 19-Me group, suggesting that the geometrical relation of the relevant groups at C-11 to the respective Me group is different each other. In view of that the D ring is *cis*-fused with the five-membered C ring, various conformations are possible for the D ring. Among them, the following two conformations A and B appear to be important.



A



B

In A, the D ring has a slightly deformed chair form with the C-11–C-12 and C-8–C-14 bonds being disposed equatorial and axial, respectively, in respect to the D ring. However, there would be severe non-bonded interaction between the 18-Me and the 11β-OH groups. To relieve this interaction, the ring D would be deformed, with the C-17–C-20 bond fixed equatorial, in a way that the C-11–C-12 bond is oriented pseudo-axial and the C-8–C-14 bond pseudo-equatorial. This deformation would lead to the boat form B, in which C-12 and C-16 correspond to a bowsprit and a flagpole. In this conformation B, there would be serious interference between the 18-Me and 21-Me groups besides that between the axial hydrogen at C-16 and 11β-OH group. Thus, it seems to us that iminooxidojervanes possessing an 11β-OH group would take an *intermediate* structure between conformations A and B, which might probably rationalize the difference of the deshielding effects in question. However, for want of any other experimental evidence supporting this structure, we prefer to leave the conformation of the D ring undefined. In relation to the above-mentioned discussion, the following fact is to be noted; photolysis of an 11-nitrite of 3O,N-diacetyl-11β-hydroxyiminooxidojerv-5-ene (XVIIIa) gave a 19-oximino derivative, but no 18-oximino compound could be detected.[29] The corresponding reaction in the normal steroid, in which the 11β-OH group exerts almost the same deshielding effects (−0·258 and −0·242 ppm) on the 19- and 18-Me groups,[30b] results in the formation of oximes at both C-19 and C-18.[30]

EXPERIMENTAL

All the m.ps are uncorrected. The homogeneity of each compound was always checked by paper chromatography[31] and/or by TLC on silica gel (Wakogel B-5), and the spots were developed with a bromophenol blue indicator, and with ceric sulfate in dil H_2SO_4 and I_2, respectively. The optical rotations and the UV spectra were measured at 23° in 95% EtOH and in 99% EtOH, respectively,

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[29] H. Suginome, N. Sato and T. Masamune, to be published.

[30] D. H. R. Barton and J. M. Beaton, *J. Amer. Chem. Soc.* **84**, 199 (1962).

[31] T. Masamune, M. Takasugi, M. Gohda, H. Suzuki, S. Kawahara and T. Irie, *J. Org. Chem.* **29**, 2282 (1964), footnote 40.

unless otherwise stated. The ORD curves were determined on a Nippon Bunko ORD/UV-5, in MeOH unless otherwise stated, and all of the IR spectra on a Nippon Bunko 401-G spectrophotometer in Nujol. The NMR spectra were obtained on a JEOL 3H-60 (60 Mc), a Varian A-60 (60 Mc) and/or a Varian HR-100 (100 Mc) spectrometer, $CDCl_3$ being used as a solvent. In most of the cases, 20–40 mg of the sample was dissolved in about 0·4 ml of the solvent. In a few cases, however, only 3–5 mg material was available and the samples were measured in a micro cell. The chemical shift data were given in τ-values and with TMS as an internal reference, and the precision was estimated to be within 0·02 ppm.

22,27-*Imino*-17,23-*oxidojerv*-5-*en*-3β-*ol* (IV)

Freshly-distilled diethylene glycol (330 ml) containing Na (7·8 g) was heated to 130° and cooled. To this soln was added anhyd hydrazine hydrate[31] (45 ml), and the mixture was refluxed for a while and then cooled. After the addition of II[4] (5·1 g), the entire mixture was heated at 180° for 48 hr. The condenser was removed and the soln was heated to 208° to remove the excess hydrazine. A condenser was replaced and the soln was again heated for another 24 hr at the temp. The cooled soln was diluted with water and extracted with chf. The chf extracts were washed with water, dried over Na_2SO_4 and evaporated to dryness. Recrystallization of the crystalline residue (5·6 g) from acetone–MeOH afforded a pure sample of IV (2·8 g), m.p. 248–250°; $[\alpha]_D$ −29.5°; IR, ν_{max} 3300 and 1055 cm^{-1}. (Found: C, 78·55; H, 10·36; N, 3·22. $C_{27}H_{43}O_2N$ requires: C, 78·40; H, 10·48; N, 3·39%.) A further quantity of IV (1·2 g), m.p. 239–241°, was obtained.

The compound IV (99 mg) was treated with Ac_2O (1 ml) and pyridine (1 ml) at room temp overnight and then heated on a water bath for 30 min. After removal of the solvents, the residue crystallized on trituration with 95% EtOH, and was recrystallized from the same solvent to yield IVa (91 mg), m.p. 179–181°; $[\alpha]_D$ +18.5°; IR, ν_{max} 3634 (EtOH), 3530 (EtOH), 1727, 1646, 1264 and 1030 cm^{-1}. (Found: C, 72·90; H, 9·57; N, 2·83. $C_{31}H_{47}O_4N \cdot C_2H_6O$ requires: C, 72·89; H, 9·82; N, 2·58%.)

22,27-*Imino*-17,23-*oxidojervan*-3β-*ol* (V)

The compound IV (0·50 g) was hydrogenated in the presence of Adams' Pt (0·20 g) at room temp in AcOH, and 24·3 ml of H_2 (1·03 moles) was absorbed for 8 hr. After removal of the catalyst and the solvent, the residue was diluted with water and then made alkaline (pH 8·6) with 5% Na_2CO_3aq (15 ml). The ppts thus obtained (0·51 g) were collected by filtration. Recrystallization from acetone–MeOH gave V (0·17 g), m.p. 231–232°; $[\alpha]_D$ +25.2° (MeOH); IR, ν_{max} 3548 and 1041 cm^{-1}. (Found: C, 76·10; H, 10·22; N, 3·16. $C_{27}H_{45}O_2N \cdot CH_4O$ requires: C, 76·34; H, 10·11; N, 3·31%). From the mother liquors, 0·13 g of V, m.p. 229–232°, was obtained.

Acetylation of V (59 mg) with Ac_2O (0·9 ml) and pyridine (0·6 ml) afforded Va (42 mg), m.p. 155–156° (from 95% EtOH); $[\alpha]_D$ +54·4° (MeOH); IR, ν_{max} 3622 (EtOH), 3510 (EtOH), 1723, 1643, 1257 and 1020 cm^{-1}. (Found: C, 74·11; H, 9·15; N, 2·83. $C_{31}H_{49}O_4N \cdot \frac{1}{2}C_2H_6O$ requires: C, 74·10; H, 9·24; N, 2·70%.)

22,27-*Imino*-17,23-*oxidojervan*-3-*one* (VI)

To a soln of V (0·92 g) in DMF (27 ml) were gradually added CrO_3 (92 mg) and conc H_2SO_4 (2 ml) under cooling. The soln was allowed to stand at room temp overnight, and 10% $NaHSO_3$aq (18 ml) was then added to reduce the excess oxidizing agent. The mixture was extracted with chf, and the chf soln washed with water, dried and evaporated to dryness. Recrystallization of the crystalline residue from acetone gave a pure sample of VI (0·25 g), m.p. 214–217°. From the mother liquors, crude V (0·33 g) of m.p. 207–209° was obtained. The pure sample showed $[\alpha]_D$ +46·5° (MeOH); IR, ν_{max} 1722 and 1030 cm^{-1}; ORD, $[\phi]^{peak}_{304}$ +2740°, $[\phi]^{trough}_{264}$ −1180°. (Found: C, 78·06; H, 10.04; N, 3·32. $C_{27}H_{43}O_2N \cdot \frac{1}{2}C_3H_6O$ requires: 78·00; H, 9·57; N, 3·19%.)

Acetylation of VI (56 mg) as mentioned above afforded VIa (49 mg), m.p. 225–229° (from 95% EtOH); IR, ν_{max} 1716, and 1658 cm^{-1}. (Found: C, 75·86; H, 9·35; N, 3·49. $C_{29}H_{45}O_3N \cdot \frac{1}{2}H_2O$ requires: C, 75·68; H, 9·14; N, 3·28%.)

The compound VI (190 mg) was dissolved in a mixture of toluene (10 ml) and ethylene glycol (1·5 ml), and to the soln was added *p*-toluenesulfonic acid hydrate (PTS, 12 mg). The mixture was

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[31] L. I. Smith and K. E. Howard, *Org. Synth*. 24, 53 (1944).

refluxed for 19 hr under stirring, water being removed under a Dean-Stock apparatus. After cooling the mixture was washed with 5% $NaHCO_3$aq and then with water, dried and evaporated to dryness, yielding a crystalline residue. Recrystallizations from ether–isopropyl ether gave an analytical sample of VIb (41 mg), m.p. 188–190°; IR, ν_{max} 1114, 1097, 1060 and 994 cm^{-1}. (Found: C, 75·86; H, 10·36; N, 3·23. $C_{29}H_{47}O_3N$ requires: C, 76·10; H, 10·35; N, 3·06%.)

22,27-*Imino*-17,23-*oxidojervane* (I)

To a diethylene glycol soln (20 ml) containing KOH (2·0 g) and 80% aqueous hydrazine (1.5 ml) was added VI (180 mg) dissolved in EtOH (2·0 ml). The soln was refluxed at 126° for 1·5 hr and then heated to distill the excess hydrazine, until the temp of the soln rose up to 200°. The soln was refluxed at the temp for 2 hr, cooled, diluted with water and extracted with ether. The ether soln yielded a crystalline substance, after being washed with water and dried. On recrystallization from EtOH, I (92 mg), m.p. 169–170°, was obtained; $[\alpha]_D$ +41·2° (MeOH). (Found: C, 81·27; H, 11·00; N, 3·62. $C_{27}H_{45}ON$ requires: C, 81·14; H, 11·35; N, 3·51%.)

Acetylation of I (100 mg) gave Ia (80 mg), m.p. 213–215° (from acetone); IR, ν_{max} 1678 cm^{-1}. (Found: C, 78·95; H, 10·45; N, 3·30. $C_{29}H_{47}O_2N$ requires: C, 78·86; H, 10·73; N, 3·17%.)

22,27-*Imino*-17,23-*oxidojerv*-4-*en*-3-*one* (VII)

A soln of IV (770 mg) in toluene (15 ml, redistilled) and dry cyclohexanone (15 ml, redistilled) was heated to distil about 70 ml of toluene to dry the system. To the stirred, refluxing soln was added a suspended mixture of aluminum isopropoxide (3·0 g) in toluene (15 ml, redistilled), and the mixture refluxed for 7 hr. After being cooled, the mixture was distilled with steam until most of the solvents had been removed, and the residue was extracted repeatedly with chf. The chf soln was evaporated to dryness *in vacuo* after drying and left a yellow resin, which was recrystallized from acetone. Recrystallization from acetone–MeOH afforded VII (150 mg), m.p. 116–117°; $[\alpha]_D$ +85·6° (MeOH); UV, λ_{max} 233·5 mμ (ϵ 24,400); IR, ν_{max} 3352, 1682, 1614 and 1038 cm^{-1}. (Found: C, 76·68; H, 9·61; N, 3·43. $C_{27}H_{37}O_2N{\cdot}CH_4O$ requires: C, 76·49; H, 9·40; N, 3·19%.) A further quantity (70 mg) of crude VII was obtained from the resinous mother liquors by trituration with water.

Acetylation of VII (80 mg) was carried out as usual, and VIIa (50 mg), m.p. 217–219°, was obtained after recrystallization from ether; UV, λ_{max} 233 mμ (ϵ 26,700); IR, ν_{max} 1677, 1612, 1040 cm^{-1}. (Found: C, 77·32; H, 9·07; N, 3·20. $C_{31}H_{41}O_4N$ requires: C, 77·46; H, 8·74; N, 3·13%.)

22,27-*Imino*-17,23-*oxido*-5β-*jervan*-3-*one* (VIII)

The compound VII (400 mg) in 0·02N alkaline ethanol (14 ml) was hydrogenated at room temp over 5% Pd-C (500 mg). The hydrogenation was stopped after 1·5 hr, at which time 24 ml of H (1·4 moles) had been taken up. The soln was neutralized with AcOH and then evaporated to dryness *in vacuo*. The residue was diluted with water, made alkaline to pH 9 with 6N NH_4OH and extracted with chf. The chf soln afforded, after drying and removal of the solvent, a yellow resin, which crystallized on trituration with acetone. On recrystallization from acetone, a pure sample of VIII (240 mg), m.p. 198–200°, was isolated as plates, and a further quantity (40 mg) of crude VIII, m.p. 195–198°, was obtained by concentration of the mother liquors. The pure sample showed $[\alpha]_D$ +58·7° (MeOH); IR, ν_{max} 3324, 1720, 1030 cm^{-1}; ORD, $[\phi]_{304}^{trough}$ +265°, $[\phi]_{265}^{peak}$ +2340°. (Found: C, 78·06; H, 9·74; N, 3·32. $C_{27}H_{39}O_2N{\cdot}\frac{1}{2}C_3H_6O$ requires: C, 78·00; H, 9·57; N, 3·19%.)

The compound VIII (170 mg) was dissolved in toluene (10 ml) containing PTS (8·5 mg) and ethylene glycol (1·5 ml), and the soln was stirred and refluxed for 16 hr under a Dean-Stock apparatus. The reaction was worked up as mentioned above, and VIIIa (105 mg), m.p. 189–191°, was obtained after recrystallization from ether–isopropyl ether; IR, ν_{max} 1096, 1080, 1050 and 1040 cm^{-1}. (Found: C, 75·88; H, 10·36; N, 3·49. $C_{29}H_{47}O_3N$ requires: C, 76·10; H, 10·35; N, 3·06%.)

22,27-*Imino*-17,23-*oxido*-5β-*jervane* (IX)

Compound VIII was reduced in a manner similar to VI; from 230 mg of VIII was obtained 150 mg of IX, m.p. 149–151° (from ether); $[\alpha]_D$ +36·3° (MeOH). (Found: C, 81·41; H, 11·06; N, 3·41. $C_{27}H_{45}ON$ requires: C, 81·14; H, 11·35; N, 3·51%.)

The compound IX (75 mg) was acetylated with pyridine (1·0 ml) and Ac_2O (0·8 ml) at room temp overnight, and gave IXa (50 mg), m.p. 190–193° (from acetone); IR, ν_{max} 1641 cm^{-1}. (Found: C, 78·65; H, 10·93; N, 3·01. $C_{29}H_{47}O_2N$ requires: C, 78·86; H, 10·73; N, 3·17%.)

22,27-*Imino*-17,23-*oxidojerva*-4,12-*dien*-3-*one* ("Δ^4-11-*deoxojervone*", XII)

The Oppenauer oxidation of XI[8] was similar to that of IV; a soln of XI (4·0 g) in dry toluene was treated with dry cyclohexanone (50 ml) in the presence of aluminum isopropoxide (3·0 g), and XII (3·1 g), m.p. 210–212°, was isolated after recrystallization from acetone; IR, ν_{max} 1671, 1611, 1021 cm^{-1}. (Found: C, 78·88; H, 9·40; N, 3·65. $C_{27}H_{39}O_2N$ requires: C, 79·17; H, 9·60; N, 3·42%.)

The compound XII (0·10 g) was heated with Ac_2O (1 ml) and pyridine (1 ml) for 3 hr on a steam bath. After removal of the solvents by azeotropization with benzene, the residue was crystallized from aqueous MeOH and then recrystallized from the same solvent to yield XIIa (80 mg), m.p. 182–184°. (Found: C, 77·00; H, 9·34; N, 3·28. $C_{29}H_{41}O_3N$ requires: C, 77·12; H, 9·15; N, 3·10%.)

22,27-*Imino*-17,23-*oxidojerv*-12-*en*-3-*one* (XIII)

To a refluxing soln of liquid NH_3 (100 ml) containing Li (46 mg) was added XII (500 mg) in dioxan (30 ml, redistilled) under stirring, and the mixture was continuously stirred for 8 min. NH_4Cl was added and the resulting colorless mixture was kept at room temp to remove the NH_3. The residue was diluted with water and shaken with chf repeatedly. The chf soln left a resinous substance after drying and removal of the solvent, which crystallized on trituration with AcOEt. Recrystallization from the same solvent afforded XIII (340 mg), m.p. 175–177°; IR, ν_{max} 1705 and 1033 cm^{-1}; ORD, $[\phi]^{peak}_{303}$ +1230°, $[\phi]^{trough}_{260}$ −2140°. (Found: C, 78·95; H, 9·95; N, 3·30. $C_{27}H_{41}O_2N$ requires: C, 78·78; H, 10·04; N, 3·40%.)

The ketone XIII (100 mg) was acetylated in a manner similar to XII and gave XIIIa (80 mg), m.p. 198–201° (from aqueous EtOH). (Found: C, 76·49; H, 9·70; N, 3·22. $C_{29}H_{43}O_3N$ requires: C, 76·78; H, 9·55; N, 3·09%.)

22,27-*Imino*-17,23-*oxidojerv*-12-*ene* (XIV)

The compound XIV was prepared by the Wolff-Kishner reduction of XIII practically in the same way as I was obtained from VI; from 207 mg of XIII, XIV (100 mg) was obtained and had m.p. 85–87° (from 95% EtOH); IR, ν_{max} 3375 and 1034 cm^{-1}. (Found: C, 81·30; H, 10·80; N, 3·40 $C_{27}H_{43}ON$ requires: C, 81·55; H, 10·90; N, 3·52%.)

22,27-*Imino*-17,23-*oxidojerv*-12-*en*-3β-*ol* (11-*deoxy*-5α,6-*dihydrojervine*, XV)[33]

The compound XIII (1·12 g) was treated with $NaBH_4$ (0·50 g) for 1·5 hr at room temp in abs EtOH under stirring. After decomposition of the excess $NaBH_4$ with acetone, the soln was evaporated to dryness and the residue shaken with chf and water. The chf soln gave a crystalline substance on drying and removal of the solvent, which was recrystallized from acetone to yield XV (0·79 g), m.p. 171–173°; IR, ν_{max} 3300 and 1040 cm^{-1}. (Found: C, 78·65; H, 10·30; N, 3·22; $C_{27}H_{43}O_2N$ requires: C, 78·40; H, 10·48; N, 3·39%.)

The alcohol XV (1·06 g) was treated with Ac_2O (5 m) and pyridine (10 ml) on a steam bath for 1 hr. The mixture was worked up as usual, and a pure sample of XVa (0·86 g), m.p. 193–195° (from aqueous MeOH), was obtained; IR, ν_{max} 1733, 1669 and 1027 cm^{-1}. (Found: C, 74·58; H, 9·47; N, 2·66. $C_{31}H_{47}O_4N$ requires: C, 74·81; H, 9·52; N, 2·81%.)

22,27-*Imino*-17,23-*oxido*-5β-*jerv*-12-*en*-3-*one* (XVI)

The compound XII (1·46 g) was hydrogenated over 5% Pd-C at room temp in EtOH (75 ml) and 96 ml of H_2 (1·2 mol) was consumed after 3 hr. After removal of the catalyst and the solvent, the residue was dissolved in AcOEt. On concentration and seeding with XIII, the soln yielded a crystalline substance (0·17 g), which was collected by filtration and had m.p. 165–171°. Recrystallization from AcOEt raised the m.p. to 174–176°, and the sample (0·12 g) was identified as XIII by the mixture m.p. and by comparison of the IR spectra. After removal of the crude sample of XIII by

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[33] Carried out by Akio Murai.

filtration, the filtrate was further concentrated to yield a crystalline substance (0·86 g), m.p. 201–204°. Recrystallization from AcOEt afforded a pure sample of XVI (0·48 g), m.p. 208–210°; IR; ν_{max} 1726 and 1032 cm^{-1}; ORD, $[\phi]^{trough}_{306}$ −350°, $[\phi]^{peak}_{266}$ −30°. (Found: C, 78·56; H, 10·18; N, 3·56. $C_{27}H_{41}O_2N$ requires: C, 78·78; H, 10·04; N, 3·40%.)

The compound XVI (100 mg) was treated with Ac_2O (1 ml) and pyridine (1 ml) on a steam bath for 3 hr, and the mixture was worked up as usual. Recrystallization from MeOHaq yielded the N-acetyl derivative (60 mg), m.p. 198–200°; IR, ν_{max} 1721 and 1663 cm^{-1}. (Found: C, 76·89; H, 9·76; N, 3·00. $C_{29}H_{43}O_3N$ requires: C, 76·78; H, 9·55; N, 3·09%.)

22,27-*Imino*-17,23-*oxido*-5β-*jerv*-12-*ene* (XVII)

The Wolff-Kishner reduction of XVI was similar to that of XIII; from 200 mg of XVI, XVII (70 mg) was obtained and had m.p. 100–102° (from EtOH); IR, ν_{max} 3580 and 1030 cm^{-1}. (Found: C, 81·78; H, 10·68; N, 3·42. $C_{27}H_{43}ON$ requires: C, 81·55; H, 10·90; N, 3·52%.)

22,27-*Imino*-17,23-*oxidojerv*-5-*ene*-3β,11β-*diol* (XVIII)

To a soln of II[4] (2·0 g) in dry THF (90 ml) was added LAH (1·5 g) in THF (20 ml), and the mixture was refluxed for 10 hr under N_2. The mixture was cautiously treated with EtOH (5 ml) and water (5 ml), and filtered. The filtrate was evaporated *in vacuo* and shaken with water and chf. The chf soln was washed with water, dried and evaporated to yield a crystalline substance. Recrystallization from acetone containing a small amount of MeOH afforded XVIII (1·6 g), m.p. 239–240°; $[\alpha]_D$ −5°; IR, no absorption in the CO region. (Found: C, 75·48; H, 10·09; N, 3·26. $C_{27}H_{43}O_3N$ requires: C, 75·67; H, 10·19; N, 3·16%.)

Compound XVIII (100 mg) was treated with Ac_2O (0·8 ml) and pyridine (0·8 ml) at room temp for 3 hr. Ofter removal of the solvents by azeotropization with benzene under reduced press, the residue was treated with water and chf. The chf soln was washed with water, dried and evaporated to yield a resin, which was crystallized on trituration with ether and amounted to 70 mg. Recrystallization from ether gave XVIIIa (50 mg), m.p. 206–207°: $[\alpha]_D$ +14°; IR, ν_{max} 3320, 1733 and 1620 cm^{-1}. (Found: C, 72·51; H, 9·16; N, 2·73. $C_{31}H_{47}O_5N$ requires: C, 72·32; H, 9·31; N, 2·91%.)

Compound XVIII (100 mg) was heated with Ac_2O (1·0 ml) and pyridine (1·0 ml) for 24 hr on a water bath. The soln was worked up as usual and yielded XVIIIb (70 mg), m.p. 219–221°; (from MeOH); $[\alpha]_D$ +5·2°; IR, ν_{max} 1730 and 1620 cm^{-1}. (Found: C, 71·28; H, 8·89; N, 2·52. $C_{33}H_{49}O_6N$ requires: C, 71·32; H, 8·89; N, 2·52%.)

To a soln of XVIIIa (30 mg) in acetone (redistilled over $KMnO_4$) was added two drops of Jones' reagent[34] (ca. 0·05 mol), and the mixture was stirred under cooling for 1 hr. After decomposition of the excess CrO_3 by addition of 10% $NaHSO_3$aq followed by removal of the solvent, the residue was made alkaline with 5% $NaHCO_3$aq and was repeatedly extracted with chf. On drying and removal of the solvent, the chf soln left a resinous substance, which was crystallized on trituration with ether. Recrystallization from EtOH gave a crystalline substance (20 mg), m.p. 210–212°, which was identified as IIa' by the mixed m.p. and by comparison of the IR spectra.

22,27-*Imino*-17,23-*oxidojerv*-4-*en*-11β-*ol*-3-*one* (XIX)

The Oppenauer oxidation of XVIII was similar to that of IV; a soln of XVIII (1·4 g) in dry toluene (500 ml) was refluxed with dry cyclohexanone (ca. 15 ml) in the presence of aluminum isopropoxide (3·0 g) for 9 hr. The mixture was worked up as usual and left a resinous substance, which crystallized on addition of AcOEt. Recrystallization from AcOEt afforded XIX (0·7 g), m.p. 231–232°; $[\alpha]_D$ +80°; UV, λ_{max} 238 mμ (ε21,400); IR, ν_{max} 3560, 3220 and 1665 cm^{-1}. (Found: C, 75·87; H, 9·66; H, 3·28. $C_{27}H_{41}O_3N$ requires: C, 75·88; H, 9·67; N, 2·95%.)

The compound XIX (100 mg) was acetylated with Ac_2O (0·8 ml) and pyridine (0·8 ml) on a water bath for 24 hr and gave XIXa (60 mg), m.p. 225–228° (from ether); $[\alpha]_D$ +129°; UV, λ_{max} 238 mμ (ε17,100); IR, ν_{max} 1730, 1672 and 1639 cm^{-1}. (Found: C, 72·67; H, 8·98; N, 2·73. $C_{31}H_{45}O_5N$ requires: C, 72·55; H, 8·83; N, 2·75%.)

22,27-*Imino*-17,23-*oxidojervan*-11β-*ol*-3-*one* (XX)

The compound XIX (0·49 g) was hydrogenated over 5% Pd-C at room temp in EtOH (50 ml), and 32 ml of H_2 (1·2 moles) was taken up after 1·5 hr. The mixture was worked up as usual and

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[34] K. Bowden, I. M. Heilbron, E. R. H. Jones and B. C. L. Weedon, *J. Chem. Soc.* 39 (1946).

gave a crystalline substance (0·35 g), m.p. 240–250°. Recrystallization from AcOEt afforded XX (0·25 g), m.p. 250–251°; $[\alpha]_D$ −19·5°; ORD (95% EtOH), $[\phi]_{306}^{peak}$ +2000°, $[\phi]_{266}^{trough}$ −60°. (Found: C, 75·61; H, 9·94; N, 3·49. $C_{27}H_{43}O_3N$ requires: C, 75·48; H, 10.00; N, 3·26%.)

22,27-*Imino*-17,23-*oxidojervane*-3,11-*dione* (XXI)

(1) To a soln of XX (230 mg) in DMF (33 ml) were added CrO_3 (230 mg) and conc H_2SO_4 (6 drops) under cooling, and the mixture was stirred at room temp for 2 days. The soln was treated with 10% $NaHSO_3$aq to decompose the excess CrO_3, made alkaline with 10% Na_2CO_3aq and extracted with 3 separate portions of chf (30 ml each). The chf soln left a resinous substance on drying and evaporation, which showed two spots (*R*, 0·8 and 0·3) on the paper chromatogram.[31] When the residue was dissolved in AcOEt and allowed to stand at room temp, 10 mg of a substance, having m.p. >280° and *R*, 0·3, separated as crystals. The mother liquor after removal of the substance by filtration was concentrated and gave crude XXI, which showed one spot (*R*, 0·8) on the paper chromatogram. Recrystallization from AcOEt afforded a pure sample of XXI (90 mg), m.p. 199–201°; IR, ν_{max} 1734 and 1725 cm⁻¹. (Found: C, 75·89; H, 9·82; N, 3·24. $C_{27}H_{41}O_3N$ requires: C, 75·83; H, 9·66; H, 3·28%.)

(2) Compound XXVI[4] (460 mg) was oxidized as mentioned above and yielded a diketone (240 mg), m.p. 198–201°, (from AcOEt), which was identified as XXI by the mixture m.p. and by comparison of the IR spectra.

Acetylation of XXI (30 mg) as usual yielded XXIa (20 mg), m.p. 269–271° (from ether); IR, ν_{max}, 1734, 1725 and 1640 cm⁻¹. (Found: C, 74·13; H, 9·31; N, 2·88. $C_{29}H_{43}O_4N$ requires: C, 74·16; H 9·23; N, 2·98%.)

22,27-*Imino*-17,23-*oxidojerv-5-ene-3β,11α-diol* ("*β-dihydrojervinol*", XXII)

The compound XXII (4·8 g) was prepared from II[4] (6·0 g) and had m.p. 284–285° after recrystallization from MeOH; $[\alpha]_D$ −5·2°; IR, no absorption in the CO region. (Found: C, 75·35; H, 10·03; N, 3·19. Calc. for $C_{27}H_{43}O_3N$; C, 75·48; H, 10·09; N, 3·26%.)

Compound XXIIa (75 mg) was obtained by treatment of XXII (90 mg) with Ac_2O and pyridine at room temp for 3 hr and had m.p. 233–235° on recrystallization from ether; $[\alpha]_D$ +31°; IR, ν_{max} 3370, 1732, 1629 and 1240 cm⁻¹. (Found: C, 72·40; H, 9·38; N, 2·91. $C_{31}H_{47}O_5N$ requires: C, 72·51; H, 9·16; N, 2·78%.)

The oxidation of XXIIa (50 mg) to IIa was similar to that of XVIIIa mentioned above, and the main product (25 mg), m.p. 210–212° (from EtOH), proved to be identical with IIa in all respects.

Compound XXIIb (70 mg) was prepared by heating XXII (100 mg) with Ac_2O and pyridine on a water bath for 6 hr and had m.p. 247–248° on recrystallization from MeOHaq; $[\alpha]_D$ ÷27°; IR, ν_{max} 1729, 1724, 1639 and 1240 cm⁻¹. (Found: C, 71·24; H, 8·63; N, 2·61. $C_{33}H_{49}N_6O$ requires: C, 71·32; H, 8·89; N, 2·52%.)

22,27-*Imino*-17,23-*oxidojerv-4-en*-11α-*ol*-3-*one* (XXIII)

The Oppenauer oxidation of XXII was similar to that of IV; a soln of XXII (4·0 g) in dry toluene (550 ml) was refluxed with dry cyclohexanone (ca. 20 ml) in the presence of aluminum isopropoxide (4·0 g) for 9 hr, and XXIII (2·1 g), m.p. 214–216°, was obtained after recrystallization from AcOEt; $[\alpha]_D$ +98°; UV, λ_{max} 238 mμ (ε 17,100); IR, ν_{max} 3340 and 1671 cm⁻¹. (Found: C, 75·52; H, 10·00; N, 3·38. $C_{27}H_{41}O_3N$ requires: C, 75·87; H, 9·66; N, 3·28%.)

Compound XXIIIa (60 mg) was prepared by heating XXIII (100 mg) with Ac_2O (1·0 ml) and pyridine (1·0 ml) on a water bath for 6 hr, and had m.p. 225–228° (from MeOH); $[\alpha]_D$ +118°; UV, λ_{max} 238 mμ (ε 19,400); IR, ν_{max} 1733, 1639 and 1250 cm⁻¹. (Found: C, 72·29; H, 8·81; N, 2·80. $C_{31}H_{45}O_5N$ requires: C, 72·67; H, 8·98; N, 2·73%.)

22,27-*Imino*-17,23-*oxido*-5β-*jervan*-11α-*ol*-3-*one* (XXIV)

The compound XXIII (1·5 g) in EtOH (210 ml) containing KOH (0·7 g) was hydrogenated over 5% Pd-C (0·15 g) at room temp and 90 ml of H_2 (1·2 moles) was taken up after 45 min. The mixture was worked up as usual and crude XXIV (0·9 g), m.p. 240–248°, was obtained. Recrystallization from AcOEt afforded a pure sample of XXIV (0·6 g), m.p. 250–251°; $[\alpha]_D$ +70°; IR, ν_{max} 1709 cm⁻¹; ORD (95% EtOH), $[\phi]_{300}^{trough}$ +14°, $[\phi]_{266}^{peak}$ +1700°. (Found: C, 75·34; H, 10·16; N, 3·44. $C_{27}H_{43}O_3N$ requires: C, 75·48; H, 10·09; N, 3·26%.)

Compound XXIVa (50 mg) was prepared by treatment of XXIV (100 mg) with Ac_2O (1·0 ml) and pyridine (1·0 ml) at room temp overnight and had m.p. 223–225° after recrystallization from ether containing a small amount of MeOH; $[\alpha]_D$ +39°; IR, ν_{max} 1735, 1710 and 1640 cm^{-1}. (Found: C, 72·48; H, 9·13; N, 2·71. $C_{31}H_{47}O_5N$ requires: C, 72·48; H, 9·22; N, 2·73%.)

22,27-*Imino*-17,23-*oxido*-5β-*jervane*-3,11-*dione* (XXV)

To a soln of XXIV (0·50 g) in DMF were added CrO_3 (1·8 g) and conc H_2SO_4 (30 drops) under cooling, and the mixture kept at room temp for 48 hr under stirring. The reaction product was worked up as usual and crude XXV (0·25 g), m.p. 164–175°, was obtained. Recrystallization from ether-acetone gave a pure sample (0·20 g), m.p. 183–185°; $[\alpha]_D$ −4·6°; IR, ν_{max} 1725 and 1713 cm^{-1}. (Found: C, 75·88; H, 9·79; N, 3·26. $C_{27}H_{41}O_3N$ requires: C, 75·83; H, 9·66; N, 3·28%.)

Compound XXVa (42 mg) was prepared by treatment of XXV (60 mg) with AC_2O (0·5 ml) and pyridine (0·5 ml) at room temp overnight, and had m.p. 236–238° after recrystallization from ether-acetone; $[\alpha]_D$ +16°; IR, ν_{max} 1725, 1710 and 1640 cm^{-1}. (Found: C, 74·17; H, 9·23; N, 2·88. $C_{29}H_{43}O_4N$ requires: C, 74·16; H, 9·29; N, 2·98%.)

22,27-*Imino*-17,23-*oxido*-5β-*jervan*-3α-*ol*-11-*one* (XXIX)

(1) A soln of XXV (30 mg) in EtoH (20 ml) was treated with KOH (160 mg) in the presence of pre-reduced Adams' catalyst (150 mg) at room temp for 4 hr under N_2. The mixture was worked up as usual and left a resin, which crystallized on addition of acetone. Recrystallization from the same solvent gave XXIX (21 mg), m.p. 273–275°; $[\alpha]_D$ −6·5°; IR, ν_{max} 3200 and 1730 cm^{-1}. (Found: C, 75·35; H, 10·18; N, 3·06. $C_{27}H_{43}O_3N$ requires: C, 75·48; H, 10·09; N, 3·26%.)

(2) The compound XXV (70 mg) was refluxed in 20% ethanolic KOH soln for 10 hr under a stream of N_2. After removal of the solvent *in vacuo*, the residue was diluted with water and extracted with chf. The chf soln left a resin after drying and evaporation, which was dissolved in MeOH–acetone and allowed to stand at room temp. Crude crystals of XXIX (30 mg) separated out and were collected by filtration, m.p. 264–270°. Recrystallization from acetone yielded a pure sample (21 mg), m.p. 273–275°.

(3) Compound XXXII (100 mg) described later was hydrogenated in the presence of pre-reduced Adams' catalyst (40 mg) at room temp in EtOH (14 ml) containing KOH (50 mg), and 10 ml of H_2 (1·2 moles) was consumed after 5 hr. The mixture was worked up as usual and left a resin, which crystallized on trituration with AcOEt. Recrystallization from acetone gave XXIX (55 mg), m.p. 271–275°.

Compound XXIXa (30 mg) was prepared from XXIX (50 mg) in the usual manner and had m.p. 197–199° (from acetone); $[\alpha]_D$ +40·0°; IR, ν_{max} 1730, 1240 and 1040 cm^{-1}. (Found: C, 72·38; H, 9·20; N, 2·63. $C_{31}H_{47}O_5N$ requires: C, 72·48; H, 9·22; N, 2·73%.)

The compound XXIX (30 mg) was oxidized with Jones' reagent as mentioned previously and yielded XXV (20 mg), m.p. 184–185° (from ether-acetone).

Hydrogenation of 22,27-*imino*-17,23-*oxidojerva*-4,12-*diene*-3,11-*dione* ("Δ^4-*jervone*", XXX)

(1) A soln of XXX[4] (5·26 g) in EtOH (110 ml) was hydrogenated in the presence of 5% Pd-C (5·26 g) at room temp and 358 ml of H_2 was taken up after 5·5 hr. After filtration of the catalyst and removal of the solvent *in vacuo*, the residue was crystallized on trituration with AcOEt. Recrystallization from AcOEt gave as the first crop a mixture (1·10 g), m.p. 164–166°, of XXXI and XXXII. While XXXI and XXXII gave practically the same spot on the paper chromatogram,[20] they showed different R_f values (0·5 and 0·45) on the TLC (solvent, ether). Two recrystallizations of the mixture from the same solvent gave a single substance (0·62 g) having m.p. 205–208° and a R_f value of 0·5, which was further recrystallized to yield an analytical sample of XXXI, m.p. 208–210°; $[\alpha]_D$ −110°; UV, λ_{max} 248 mμ (ε 16,000); IR, ν_{max} 1703, 1630 and 960 cm^{-1}. (Found: C, 76·44; H, 9·25; N, 3·14. $C_{27}H_{39}O_3N$ requires: C, 76·23; H, 9·18; N, 3·29%.)

The mother liquor after removal of the above-mentioned first crop was concentrated to yield a mixture (1·59 g), m.p. 155–157°, of XXXI and XXXII, which resisted further purification by recrystallization. The filtrate obtained on filtration of the second crop was further concentrated to yield the third crop (1·47 g), m.p. 204–206°, which showed one spot (R_f 0·45). Two recrystallizations afforded an analytical sample of XXXII, m.p. 208–210°; $[\alpha]_D$ −80°; UV, λ_{max} 248 mμ (ε 16,000); IR, ν_{max} 1710 and 1628 cm^{-1}. (Found: C, 76·14; H, 9·16; N, 3·18. $C_{27}H_{39}O_3N$ requires: C, 76·23;

H, 9·18; N, 3·29%.) The filtrate obtained on removal of the third crop was evaporated to dryness, leaving a crystalline substance (0·55 g), m.p. 180–190°, which consisted mainly of XXXI and XXXII and could not be purified by recrystallization.

The compound XXXI (90 mg) was acetylated as usual and yielded XXXIa (75 mg), m.p. 229–231° (from acetone); UV, λ_{max} 249 mμ (ε 18,000); IR, ν_{max} 1718, 1708 and 1630 cm^{-1}. (Found: C, 74·38; H, 8·89; N, 2·66. $C_{29}H_{41}O_4N$ requires: C, 74·52; H, 8·78; N, 2·99%.)

The compound XXXII (80 mg) was acetylated as usual and yielded XXXIIa (70 mg), m.p. 192–194° (from acetone); UV, λ_{max} 248 mμ (ε 17,000); IR, ν_{max} 1710 and 1633 cm^{-1}. (Found: C, 74·80; H, 8·56; N, 2·95. $C_{29}H_{41}O_4N$ requires: C, 74·52; H, 8·78; N, 2·99%.)

The compound XXXII (3·20 g) was dissolved in toluene (160 ml) containing PTS (0·32 g) and ethylene glycol (6·5 ml), and the soln was refluxed for 20 hr under a Dean-Stock apparatus. The reaction mixture was worked up as usual and XXXIIb (2·88 g) was obtained on recrystallization from isopropyl ether, having m.p. 218–220°; $[\alpha]_D$ −83°; IR, ν_{max} 1710, 1630, 1090 and 1055 cm^{-1}. (Found: C, 73·96; H, 9·10; N, 3·01. $C_{29}H_{43}O_4N$ requires: C, 74·20; H, 9·17; N, 2·99%.)

(2) The compound XXXI was obtained by oxidation of XXXV described later; to a soln of XXXV (200 mg) in DMF (30 ml) were added CrO_3 (250 mg) and conc H_2SO_4 (9 drops), and the soln was stirred at room temp for 44 hr. The reaction mixture was worked up as usual and yielded a resin which crystallized on trituration with AcOEt. Recrystallization from AcOEt afforded XXXI (84 mg), m.p. 205–208°, which was identified by mixed m.p., comparison of the IR spectra and by the TLC.

22,27-*Imino*-17,23-*oxidojerva*-4,12-*dien*-11β-*ol*-3-*one* (XXXIV)

The Oppenauer oxidation of XXXIII[14] was similar to that of IV. A soln of XXXIII (3·12 g) in dry toluene (600 ml) was refluxed with dry cyclohexanone (40 ml) in the presence of aluminum isopropoxide (3·5 g) for 7 hr. The reaction mixture was worked up as usual and gave a resin, which was crystallized on trituration with acetone. Repeated recrystallizations afforded a crystalline substance (1·32 g), m.p. 248–250°. Further recrystallization from acetone afforded an analytical sample of XXXIV, m.p. 248–250°; $[\alpha]_D$ −4°; UV, λ_{max} 237 mμ (ε 23,000); IR, ν_{max} 3400, 1670, 1620 and 1050 cm^{-1}. (Found: C, 76·11; H, 9·42; N, 3·37. $C_{27}H_{39}O_3N$ requires: C, 76·23; H, 9·18; N, 3·29%.) The mother liquors obtained on removal of the crystalline substance mentioned above were combined, evaporated to dryness and amounted to 1·05 g, having m.p. 180–190°. The resulting substance was found to consist mainly of XXXIV by TLC, but was not further purified.

22,27-*Imino*-17,23-*oxidojerv*-12-*en*-11β-*ol*-3-*one* (XXXV)

To a soln of liquid (80 ml) containing Li (100 mg) was added XXXIV (0·3 g) in dioxan (10 ml) under stirring and cooling with dry ice-acetone, and the mixture was further stirred for 30 min. After addition of NH_4Cl (1·0 g) and evaporation of the solvents, the residue was extracted with chf. The chf soln gave a resinous substance after drying and evaporation, which crystallized on addition of AcOEt. Recrystallization from AcOEt afforded XXXV (0·15 g), m.p. 235–237°; $[\alpha]_D$ −60°; IR, ν_{max} 3400, 1707 and 1040 cm^{-1}; ORD, (dioxan), $[\phi]_{316}^{\text{peak}}$ +470°, $[\phi]^{\text{trough}}$[illegible] −3680°. (Found: C, 75·72; H, 9·69; N, 3·16; $C_{27}H_{41}O_3N$ requires: C, 75·88; H, 9·60; N, 3·28%.)

Alkaline treatment of 22,27-*imino*-17,23-*oxido*-5β-*jerv*-12-*en*-3-*one* (XXXII)

(1) To t-butanol (40 ml) containing potassium t-butoxide (prepared from 1·6 g K) was added XXXII (0·1 g) in t-butanol (8 ml), and the soln was refluxed for 1 hr in a stream of N_2. After cooling, the mixture was diluted with water (120 ml) and extracted 3 separate portions of chf (30 ml each). The chf soln gave a resin after being washed with water, dried and evaporated to dryness under reduced press. The resin was crystallized when dissolved in acetone and allowed to stand at room temp, and was collected by filtration. The crystalline substance, m.p. 204–207°, amounted to 83 mg and was identified as the starting material XXXII in all respects. The mother liquor showed the same spot and IR spectrum as XXXII after evaporation to dryness.

(2) A soln of XXXII (100 mg) in EtOH (25 ml) containing KOH (5·0 g) was refluxed for 20 hr under a stream of N_2. After removal of the solvent under reduced press, the residue was shaken with water and chf. The chf soln left a resin after drying and evaporation, which showed 2 spots on the paper chromatogram, and was chromatographed on acid-washed alumina (2·0 g). While fractions eluted with a mixture of ether and chf (3:1) consisted mainly of the starting material (checked by

the paper chromatogram and by the IR spectrum), those eluted with chf gave a crystalline substance, which was recrystallized from acetone to yield XXXVI (30 mg), m.p. 284–285°; $[\alpha]_D$ −64°; UV, λ_{max} 248 mμ (ε 12,700). (Found: C, 75·83; H, 9·66; N, 3·27. $C_{27}H_{41}O_3N$ requires: C, 76·02; H, 9·79; N, 3·28%.)

The compound XXXVI (90 mg) was acetylated as usual and yielded XXXVIa (70 mg), m.p. 202–205° (from acetone); $[\alpha]_D$ −26°; UV, λ_{max} 248 mμ (ε 15,100). (Found: C, 72·66; H, 8·83; N, 2·70. $C_{31}H_{45}O_5N$ requires: C, 72·76; H, 8·86; N, 2·74%.)

The compound XXXVI (26 mg) was oxidized with Jones' reagent and yielded XXXII (15 mg), m.p. 208–210° (from acetone–ether), which was identified by mixture m.p., comparison of the IR spectra and by TLC.

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