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THE EFFECT OF THE PHENYLHYDRAZINE MOIETY ON THE SUBSTITUTION AT THE CARBONYL RESIDUE IN PHENYLHYDRAZONES OF ISOHYDROCORIAMYRTIN AND ALLETHROLONE

T. OKUDA and K. KONISHI

Faculty of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto, Japan

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Abstract—The effect of the phenylhydrazine moiety at C-14 over the substitution reaction of the allylic OH group at C-11 in isohydrocoriamyrtin phenylhydrazone and analogues has been studied in an attempt to prove the participation of this effect in the formation of the unusual reaction product II. Marked influence of the substituents on the Ph ring of the phenylhydrazine moiety across —NH—N= bond was shown by the comparison of the methoxylation of phenylhydrazone and α-methyl-, *p*-nitro-, 2,4-dinitro-, and α-methyl-2,4-dinitro-phenylhydrazone of isohydrocoriamyrtin. The methoxylation of *o*-nitro-, *p*-nitro-, and 2,4-dinitro-phenylhydrazone of allethrolone also showed appreciable effect by each group on the Ph ring.

THE effects of the substituents in the phenylhydrazine analogues on their reactions with isohydrocoriamyrtin (I) were proposed in the preceding paper.[1] 11-Methylphenylhydrazino-isohydrocoriamyrtin-methylphenylhydrazone (II) should have been formed by the substitution of the OH group at C-11 in isohydrocoriamyrtin-methylphenylhydrazone (VI) initially produced, since the latter is obtained upon the reaction of equimolar α-methylphenylhydrazine with I. The production of II, then may be partially attributed to the effect of the methylphenylhydrazine moiety at C-14 across the —NH—N= linkage upon the substitution at C-11. The difference in behaviour between isohydrocoriamyrtin phenylhydrazone and its analogues may also be attributable to the effects of the substituents in the phenylhydrazine moiety at C-14, besides the effects of the substituents in the phenylhydrazine molecule which attacks at C-11.

It is considered probable on the basis of the UV and visible spectra of the 2,4-dinitrophenylhydrazones derived from various carbonyl compounds[2] that the 2,4-dinitrophenyl group has some influence across the —NH—N= linkage upon the chemical reactions in the carbonyl residue. The facile elimination of the halogen in α-halo-2,4-dinitrophenylhydrazones has been reported.[3] The authors have now obtained chemical evidence which shows that the substitution reaction at C-11 in isohydrocoriamyrtin is strongly promoted through formation of phenylhydrazones at C-14, and that this effect is markedly reduced by the nitro groups on the phenylhydrazine moeity. Analogous effects in the derivatives of allethrolone (III) have also been proved.

The initial experiments—an attempted reaction of α-methylphenylhydrazine with isohydrocoriamyrtin 2,4-dinitrophenylhydrazone (IV) in acetic acid—resulted in recovery of IV. However, the reactions of isohydrocoriamyrtin phenylhydrazone (V) with methylphenylhydrazine or with 2,4-dinitrophenylhydrazine, and the reactions of

isohydrocoriamyrtin methylphenylhydrazone (VI) with phenylhydrazine or 2,4-dinitrophenylhydrazine etc, which were carried out in the attempt to get evidence of the effect by the substituent in the phenylhydrazine molecule which attacks at C-11 resulted in the production of intractable mixtures.

The comparison of the influence by the substituents in the C-14 phenylhydrazine moiety on the substitutions at C-11 was made by the methoxylation of isohydrocoriamyrtin phenylhydrazone and analogues in acidic media. The methylphenylhydrazone VI and the phenylhydrazone V were methoxylated in methanol containing weak acid to produce VII and VIII respectively. Besides the structure of VII which was already confirmed,[1] the structure of VIII was also confirmed by UV, IR and NMR spectra, which showed introduction of a OMe group, and retention of the conjugated system. However, the 2,4-dinitrophenylhydrazone IV was recovered unchanged even on the treatment with 1% methanolic sulphuric acid. Elevated temperature was required for the production of 11-O-methyl-2,4-dinitrophenylhydrazone IX. The attempted methoxylation of I and tetrahydrocoriamyrtin (X)[4] in 1% methanolic sulphuric acid at room temperature also resulted in recovery of the starting materials.

Investigation of the processes of the methoxylations, with 0·025%, 0·1% and 1% methanolic sulphuric acid and with a mixture of methanol and acetic acid, on TLC are summarized in the Table which shows that the time required for the first appearance of the spot of the 11-OMe derivative, and the time spent before the spot of 11-OH compound was no longer detected were markedly different depending on the structure

TABLE 1. TIME REQUIRED FOR METHOXYLATION OF PHENYLHYDRAZONE ANALOGUES DERIVED FROM ISOHYDROCORIAMYRTIN AND ALLETHROLONE

Compounds	H_2SO_4–MeOH (r.t.)[a]			AcOH–MeOH (1:1)	
	0·025%	0·1%	1%	r.t.	Δ[b]
VI	1 min[c] (12 min)	(i)[d]	(i)	5 min (2 hr)	
V	1 min (30 min)	i	(i)	10 min (4 hr)	
XII	30 min (73 hr)	20 min (17 hr)	3 min (2 hr)	15 hr	
XIII	3 hr (197 hr)	1 hr (48 hr)	5 min (4 hr 15 min)	X[e]	1 hr
IV	X	X	20 min (1 week)	X	X
XVIII	X	2 min (2.5 hr)	i (55 min)		
XVII	X	5 min (51 hr)	1 min (4 hr)		
XVI	X	8 hr (200 hr)	20 min (94 hr)		

[a] r.t.: Room temperature, ca. 20°.

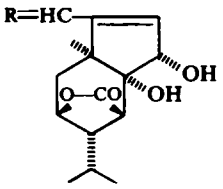
[b] Heated on a boiling water-bath.

[c] The number without the parentheses shows the time within which partial methoxylation was observed. The number in the parentheses shows the time within which methoxylation was completed.

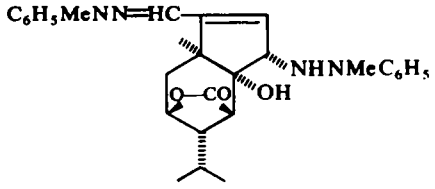
[d] i: The methoxylation occurred instantly.

[e] X: No reaction occurred for 24 hr.

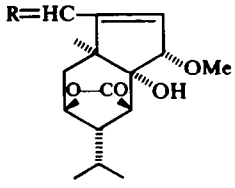
CHART 1



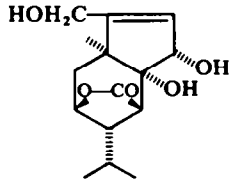
I: R = O
IV: R = $NNHC_6H_3(NO_2)_2$
V: R = $NNHC_6H_5$
VI: R = $NNMeC_6H_5$
XII: R = $NNHC_6H_4NO_2(p)$
XIII: R = $NNMeC_6H_3(NO_2)_2$



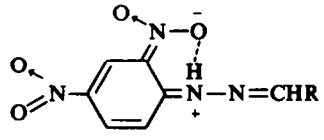
II



VII: R = $NNMeC_6H_5$
VIII: R = $NNHC_6H_5$
IX: R = $NNHC_6H_3(NO_2)_2$
XIV: R = $NNHC_6H_4NO_2(p)$
XV: R = $NNMeC_6H_3(NO_2)_2$



X



XI

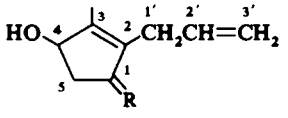
of the phenylhydrazine moiety at C-14. It is deducible from these results that the Ph—NR—N= group at C-14 gives intense activating influence on the substitution at C-11, and that this influence is appreciably reduced by the nitro groups on the Ph ring. Although ready transformation of phenylhydrazones in solutions into azo or hydroperoxyazo derivatives has been reported in recent years making a comparison with the methylphenylhydrazones which do not tautomerize,[5] the difference in the results observed with IV, V and VI upon the methoxylation and the reactions with excess phenylhydrazine reagents[1] are not attributable to the tautomerization since the UV spectrum of V, λ_{max} (log ε): 248 (3·88), 303 (4·07), 336 mμ (4·35), measured after leaving the solution overnight, or after adding sulphuric acid, acetic acid, or ammonia showed no recognizable difference from the spectrum of the fresh solution.

The effect by *o*-nitro group should include the steric effect and the effect by the chelation with NH as depicted by XI,[2a] which is substantiated by the NMR signal of NH at $-1{\cdot}48\ \tau$ in IV measured in DMSO. The *p*-nitrophenylhydrazone (XII), $C_{21}H_{25}O_6N_3$, and α-methyl-2,4-dinitrophenylhydrazone (XIII), $C_{22}H_{26}O_8N_4$, were prepared from I as amorphous solids, and then transformed into the corresponding crystalline methoxides, XIV, $C_{22}H_{27}O_6N_3$, and XV, $C_{23}H_{28}O_8N_4$, respectively. These methoxides show UV absorption maxima at almost the same wave length [397 mμ (log ε 4·44) for XIV, and 396 mμ (log ε 4·26) for XV]. These absorption maxima

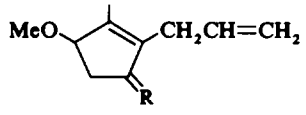
are about 20 mμ longer than that of 11-O-methylisohydrocoriamyrtin 2,4-dinitrophenylhydrazone (IX) which shows the UV absorption maximum at 375 mμ. The UV data of these compounds are in agreement with Bohlmann's observation who attributed the coincidence of the absorption maxima of *p*-nitrophenylhydrazones and α-methyl-2,4-dinitrophenylhydrazones of some conjugated carbonyl compounds to the absence of the H-bonding in *p*-nitrophenylhydrazones and α-methyl-2,4-dinitrophenylhydrazones.[2a] It is therefore predictable that there could be appreciable difference in the reactions between the 2,4-dinitrophenylhydrazone IV and the α-methyl-2,4-dinitrophenylhydrazone XIII.

The comparison by TLC on the methoxylation of IV, XII and XIII, as shown in Table 1, indicates that the effect on the substitution reaction is in accord with the prediction based on the UV spectra. The significant difference between the phenylhydrazone V and the *p*-nitrophenylhydrazone XII, between the methylphenylhydrazone VI and the α-methyl-2,4-dinitrophenylhydrazone XIII, and also between the *p*-nitrophenylhydrazone XII and the 2,4-dinitrophenylhydrazone IX shows that the inductive and resonance effects which are transmitted across the —NH—N= linkage are reflected on the substitution reactions at C-11. The total effects by the phenylhydrazine moiety at C-14 over the substitution at C-11 of isohydrocoriamyrtin would be shown in the order as follows:
$(NO_2)_2C_6H_3NHN = R < (NO_2)_2C_6H_3NMeN = R < p\text{-}NO_2C_6H_4NHN = R < C_6H_5NHN = R < C_6H_5NMeN = R$ [O = R: isohydrocoriamyrtin (I)].

CHART 2



III: R = O
XVI: R = $NNHC_6H_3(NO_2)_2$
XVII: R = $NNHC_6H_4NO_2(o)$
XVIII: R = $NNHC_6H_4NO_2(p)$



XIX: R = $NNHC_6H_3(NO_2)_2$
XX: R = $NNHC_6H_4NO_2(o)$
XXI: R = $NNHC_6H_4NO_2(p)$

Analogous effects have also been shown in the methoxylations of *o*-nitro, *p*-nitro, and 2,4-dinitrophenylhydrazone of allethrolone in which the conjugated system is similar to that in isohydrocoriamyrtin. Allethrolone 2,4-dinitrophenylhydrazone (XVI), $C_{15}H_{16}O_5N_4$, allethrolone *o*-nitrophenylhydrazone (XVII), $C_{15}H_{17}O_3N_3$, and allethrolone *p*-nitrophenylhydrazone (XVIII), $C_{15}H_{17}O_3N_3$, were prepared, and treated with methanol containing sulphuric acid to produce 4-O-methylallethrolone 2,4-dinitrophenylhydrazone (XIX), $C_{16}H_{18}O_5N_4$, 4-O-methylallethrolone *o*-nitrophenylhydrazone (XX), $C_{16}H_{19}O_3N_3$, and 4-O-methylallethrolone *p*-nitrophenylhydrazone (XXI), $C_{16}H_{19}O_3N_3$, respectively. The time required for the completion of the methoxylation, as shown in the Table 1, indicates that the nitro groups on the Ph ring of the phenylhydrazine moiety have appreciable effects on the substitution reaction at C-4 in allethrolone. The difference between XVII and XVIII shows that the effect of the *o*-nitro group is stronger than that of *p*-nitro group as presumed on the basis of the UV spectral investigation.[2c] The difference between XVI and XVII also indicates that the inductive and resonance effect of the *p*-nitro group is transmitted strongly across the —NHN= linkage to the carbonyl residue. The comparison of

isohydrocoriamyrtin 2,4-dinitrophenylhydrazone (IV) with allethrolone 2,4-dinitrophenylhydrazone (XVI) shows that there is only a slight difference in the reactivity of IV and XVI, and that the latter is somewhat faster on the methoxylation. Although no strict comparison can be made here between these compounds which have been derived from different parent carbonyl compounds, the participation by the lactone carbonyl which might be considered as one of the factors in causing the stereospecificity of the substitution at C-11 in isohydrocoriamyrtin phenylhydrazone and analogues as described in the preceding paper is rather unlikely.

These data concerning the methoxylation support the presumption that the production of II is partially due to the activating effect by the C-14 methylphenylhydrazine moiety, and also would be indicative of the generality of the marked effects by the substituents on the Ph ring on the phenylhydrazine moiety on the reactions at the carbonyl residues which have analogous partial structures.

EXPERIMENTAL

M.ps are uncorrected. UV spectra were measured in EtOH, and IR spectra were taken in KBr. Unless otherwise stated, NMR spectra were determined in $CDCl_3$ with TMS as an internal standard on a Varian A-60 spectrometer, and coupling constants are given in c/s. TLC was developed on Silica Gel acc. to Stahl (E. Merck, 0·25 mm) in $CHCl_3$–MeOH (95:5), which induced satisfactory separation of the C-11 hydroxy hydrazones from corresponding C-11 substituted derivatives. The elution chromatography was run on Mallincrodt's silicic acid (100 mesh) in $CHCl_3$. The ratios of the mixed solvents are shown by vol/vol, and the concentrations of the compounds and the acids are shown by g/vol.

11-O-*Methylisohydrocoriamyrtin phenylhydrazone* (VIII)

To a soln of V (24·1 mg) in MeOH (1 ml), 1% H_2SO_4 in MeOH (0·1 ml) was added. After leaving at room temp for 30 min, the reaction mixture was concentrated *in vacuo* to give a crystalline ppt which was filtered off and recrystallized from MeOH to yield almost colourless needles (5·3 mg), m.p. 181–182° (dec); λ_{max} (log ε): 248 (3·89), 303 (4·07), 337 mμ (4·36); ν_{max} 3470, 3290 (OH, NH), 1765 (γ-lactone) cm^{-1}; NMR 0·04 (d, $J = 6$), 8·87 (d, $J = 6$) (8-Me_2), 8·61 (s, 1-Me), 6·54 (s, 11-OMe), 5·87 (d, $J = 3$ 11-H), 4·07 τ (d, $J = 3$, 12-H). (Found: C, 68·73; H, 7·63; N, 7·37. $C_{22}H_{28}O_4N_2$ requires: C, 68·72; H, 7·34; N, 7·29%). The same product was obtained by the treatment of V in 0·025% H_2SO_4–MeOH for 20 min at room temp.

Reactions of tetrahydrocoriamyrtin (X), *isohydrocoriamyrtin 2,4-dinitrophenylhydrazone* (IV), *and isohydrocoriamyrtin* (I) *with* 1% H_2SO_4–MeOH

(a) Tetrahydrocoriamyrtin (6·3 mg) was dissolved in 1% H_2SO_4–MeOH (1 ml). After standing at room temp for 1 hr, the soln was neutralized with NaOMe in MeOH, and concentrated *in vacuo*. $CHCl_3$ (5 ml) was added to the concentrated soln, and ppt was filtered off. The filtrate was dried over $MgSO_4$ and filtered. On evaporation of the filtrate, colourless crystals were obtained which were recrystallized from $CHCl_3$–pet. benzin, and identified as X by IR comparison and mixed m.p.

(b) Analogous treatment of isohydrocoriamyrtin 2,4-dinitrophenylhydrazone resulted in recovery of IV.

(c) Isohydrocoriamyrtin (4·6 mg) was treated with 1% H_2SO_4–MeOH (0·3 ml) at room temp for 90 min, and a soln of 2,4-dinitrophenylhydrazine (3% soln in H_2SO_4–water–EtOH, 28:20:70) was added, and then ppt was recrystallized from MeOH. This product was identified as isohydrocoriamyrtin 2,4-dinitrophenylhydrazone.

TLC examination of the reaction mixtures in (a), (b) and (c) did not show any product.

Examination of methoxylations of phenylhydrazone and analogues derived from isohydrocoriamyrtin and allethrolone

The phenylhydrazone and analogues were dissolved to make 0·2% solns in 0·025%, 0·1%, and 1% H_2SO_4–MeOH, or in AcOH–MeOH (1:1), at room temp (ca. 20°). The solns of isohydrocoriamyrtin 2,4-dinitrophenylhydrazone and isohydrocoriamyrtin methyl-2,4-dinitrophenylhydrazone in AcOH–

MeOH, which did not show the methoxylation at room temp, were heated on a boiling water-bath. The reaction mixture, corresponding to 4γ of each compound was spotted on the chromato-plate every three to 5 min for the first hr, every 10 min for the second hr, and then every 1 hr for a day, unless the methoxylation was observed instantly or within one min. It was necessary to develop TLC immediately after the sample soln was spotted. Otherwise, hydrolysis of the methoxide on the silica gel plate occurred.

Reaction of isohydrocoriamyrtin 2,4-*dinitrophenylhydrazone* (IV) *with* α-*methylphenylhydrazine in* AcOH

A 10% soln of α-methylphenylhydrazine in 67% AcOH aq (0·03 ml) was added to a soln of the 2,4-dinitrophenylhydrazone IV (6·6 mg) in AcOH (0·5 ml). The mixture was heated on a boiling water-bath for 10 min, and after cooling, water was added to produce a yellow crystalline ppt which was identified as IV by IR spectra and TLC.

Isohydrocoriamyrtin p-*nitrophenylhydrazone* (XII)

A soln of *p*-nitrophenylhydrazine (24·8 mg) in 1% HCl–tetrahydrofuran was added to a soln of I (43·5 mg) in tetrahydrofuran. After leaving at room temp for 2 hr, water was added, and ppt was filtered off (54·5 mg). The ppt was dissolved in $CHCl_3$ and extracted with 2N HCl 6 times. The $CHCl_3$ soln was dried over $MgSO_4$ and distilled. Pet. ether was added to the concentrated soln, and ppt was filtered off. This ppt was shown on TLC contaminated by the reagent, and was stirred in 2N HCl for 3 hr. After filtration, the solid was chromatographed (0·7 × 12 cm column). Yellow needles of XII were obtained from 1% MeOH–$CHCl_3$ eluate, m.p. 219–221° (dec); λ_{max} (log ε) 251 (3·78), 294·5 (3·76), 326 (3·70), 393 mμ (4·38); ν_{max} 3425, 3250, 1756 cm^{-1}.

Isohydrocoriamyrtin methyl-2,4-*dinitrophenylhydrazone* (XIII)

A soln of α-methyl-2,4-dinitrophenylhydrazine (31·3 mg) in 0·5% HCl in a mixture of tetrahydrofuran and water (1:1, 1 ml) was added to a soln of I (42·1 mg) in tetrahydrofuran (0·3 ml). The mixture was heated on a boiling water-bath for a few min, and ppt was filtered off (58·3 mg). After reprecipitating from $CHCl_3$–pet. ether, this ppt was dissolved in $CHCl_3$, and extracted with 2N HCl 6 times, and then washed with water. The $CHCl_3$ layer was dried over $MgSO_4$ and evaporated under reduced press. The residue was chromatographed (0·9 × 14·5 cm column) to afford orange powder, m.p. 139–144° (dec); λ_{max} (log ε) 267 (3·76), 283 (3·69), 396 mμ (4·03); ν_{max} 3450, 1762 cm^{-1}. (Found: C, 56·19; H, 5·86. $C_{22}H_{26}O_8N_4$ requires: C, 55·69; H, 5·52%).

11-O-*Methylisohydrocoriamyrtin* p-*nitrophenylhydrazone* (XIV)

A soln of *p*-nitrophenylhydrazine (24·7 mg) in 0·3% HCl–MeOH was added to a soln of I (44·3 mg) in MeOH, and the mixture was left at room temp for 1 hr, and then heated on a boiling water-bath for 5 min. After concentration, water was added and ppt was collected, and washed with 2N HCl and then with water. This product, which showed presence of XII on TLC, was dissolved in 0·3% HCl–MeOH and heated on a boiling water-bath for 15 min. Crystals appeared on cooling were filtered and recrystallized from MeOH 3 times, m.p. 226–228° (dec); λ_{max} (log ε) 251 (3·71), 295·5 (3·65), 326 (3·46), 397 mμ (4·44); ν_{max} 3475, 3300, 1762 cm^{-1}; NMR 6·52 (s, 11-OMe), 5·88 (d, J = 3, 11-H), 3·97 τ (d, J = 3, 12-H). (Found: C, 61·75; H, 6·49; N, 9·92. $C_{22}H_{27}O_6N_3$ requires: C, 61·52; H, 6·34; N, 9·79%).

11-O-*Methylisohydrocoriamyrtin methyl*-2,4-*dinitrophenylhydrazone* (XV)

To a suspension of α-methyl-2,4-dinitrophenylhydrazine (33·0 mg) in 1% HCl–MeOH, 2N HCl was added until clear soln was effected, and this soln was added to a soln of crude I (43·3 mg) in 3 drops of 1% HCl–MeOH. The mixture was left at room temp for 90 min, and ppt was filtered off. The ppt was then dissolved in 0·3% HCl–MeOH and heated on a boiling water–bath for 15 min to complete the methoxylation. The ppt appeared on addition of water was filtered off and washed with water (19·8 mg). Recrystallization from MeOH–water, then from MeOH afforded yellow needles, m.p. 192·5–194° (dec); λ_{max} (log ε) 267 (3·96), 283 (3·94), 396 mμ (4·26); ν_{max} 3500, 1767 cm^{-1}; NMR 6·58, 6·50 (s, OMe, NMe), 5·88 (d, J = 3, 11-H), 3·85 τ (d, J = 3, 12-H). (Found: C, 56·47; H, 6·08. $C_{22}H_{28}O_8N_4$ requires: C, 56·55; H, 5·78%).

Allethrolone 2,4-*dinitrophenylhydrazone* (XVI)

A soln of 2,4-dinitrophenylhydrazine (300 mg) in EtOH–water–H_2SO_4 (14:4:5·6, 10 ml) was added to a soln of allethrolone* (250 mg). The ppt was filtered and recrystallized from $CHCl_3$ three times to afford red

* Supplied by Sumitomo Chemical Company Ltd. Purity: 77·3%.

crystals (40·6 mg), m.p. 204·5–205° (dec); λ_{max} (log ε) 255·5 (4·21), 287 (3·94), 380 mμ (4·42). ν_{max} 3290, 1613 cm^{-1}; NMR (in pyridine) 7·88 (s, 3-Me), 7·22 and 6·82 (AB part of ABX, J_{AB} = 18, J_{AX} = 2, J_{BX} = 7, 5-H_2), 4·87–5·16 (m, X part of ABX, 4-H), 6·75 (d, J = 6, 1'-H_2), 5·03–4·54 (m, 3'-H_2), 4·30–3·57 τ (m, 2'-H). (Found: C, 54·49; H, 4·84; N, 16·58. $C_{15}H_{16}O_5N_4$ requires: C, 54·21; H, 4·85; N, 16·86%).

Allethrolone o-nitrophenylhydrazone (XVII)

Allethrolone (520 mg) in MeOH (8 ml) was treated with a soln of *o*-nitrophenylhydrazine (400 mg) in MeOH (15 ml). Three hr later, the mixture was concentrated *in vacuo*, and pet. ether was added to yield ppt which was collected and recrystallized from MeOH to afford red needles, m.p. 144° (dec); λ_{max} (log ε) 267 (4·24), 306 (4·38), 455 mμ (3·91); ν_{max} 3450, 1613 cm^{-1}. NMR 8·03 (s, 3-Me), 7·53 and 7·00 (AB part of ABX, J_{AB} = 18, J_{AX} = 2, J_{BX} = 6, 5-H_2), 6·88 (d, J = 6, 1'-H_2), 5·34–5·00 (m, X part of ABX, 4-H), 5·12–4·70 (m, 3'-H), 4·42–3·82 (m, 2'-H), 3·43–1·80 (m, Ar-H), −0·52 τ (s, NH). (Found: C, 62·96; H, 6·06; N, 14·46. $C_{15}H_{17}O_3N_3$ requires: C, 62·70; H, 5·96; N, 14·63%).

Allethrolone p-*nitrophenylhydrazone* (XVIII)

To a suspension of *p*-nitrophenylhydrazine (808 mg) in MeOH (10 ml), a soln of allethrolone (1·05 g) in MeOH (0·5 ml) was added. After stirring for 12 hr, then standing at room temp for 30 hr, ppt was collected (1·33 g). Recrystallization from ether–pet. ether provided yellow crystals, m.p. 180–181° (dec). λ_{max} (log ε) 284·5 (3·96), 3·18 (3·61), 4·08 mμ (4·44). ν_{max} 3280, 1603 cm^{-1}. (Found: C, 62·55; H, 5·84; N, 14·39. $C_{15}H_{17}O_3N_3$ requires: C, 62·70; H, 5·96; N, 14·63%).

4-O-*Methylallethrolone* 2,4-*dinitrophenylhydrazone* (XIX)

A soln of XVI (359 mg) in 0·7% H_2SO_4–MeOH (30 ml) was refluxed for 1 hr, and kept at room temp for another hr. Collected crystals were recrystallized from MeOH to afford red needles, m.p. 146° (dec); λ_{max} (log ε) 256 (4·20), 287 (3·92), 380 mμ (4·40); ν_{max} 3300, 1619 cm^{-1}; NMR 8·00 (s, 3-Me), 7·47 and 7·07 (AB part of ABX, J_{AB} = 18, J_{AX} = 2, J_{BX} = 6, 5-H_2), 6·82 (d, J = 7, 1'-H_2), 6·57 (s, OMe), 5·54 (m, X part of ABX, 4-H), 5·12–4·69 (m, 3'-H_2), 4·46–3·83 (m, 2'-H), 2·24–0·85 (ArH), −0·88 τ (s, NH). (Found: C, 55·68; H, 5·22; N, 16·27. $C_{16}H_{18}O_5N_4$ requires: C, 55·48; H, 5·24; N, 16·18%).

4-O-*Methylallethrolone* O-*nitrophenylhydrazone* (XX)

(a) Allethrolone (378 mg) in MeOH (5 ml) was treated with a soln of *o*-nitrophenylhydrazine hydrochloride (375 mg) in MeOH (15 ml) at room temp. Five hr later, deposited crystals were collected and recrystallized from MeOH to yield red crystals of XX, m.p. 94–96°; λ_{max} (log ε) 270 (4·13), 306·5 (4·22), 455 mμ (3·76); ν_{max} 3270, 1613 cm^{-1}; NMR 8·05 (s, 3-Me), 7·52 and 7·10 (AB part of ABX, J_{AB} = 18, J_{AX} = 2, J_{BX} = 6, 5-H_2), 5·58 (m, X part of ABX), 6·85 (d, J = 6, 1'-H_2), 6·62 (s, OMe), 5·18–4·72 (m, 3'-H_2), 4·43–3·68 (m, 2'-H), 3·50–1·75 (m, ArH), −0·55 τ (s, NH). (Found: C, 63·82; H, 6·27; N, 13·86. $C_{16}H_{19}O_3N_3$ requires: C, 63·77; H, 6·36; N, 13·95%).

(b) Allethrolone *o*-nitrophenylhydrazone (40 mg) was dissolved in 3 ml warm 1% H_2SO_4–MeOH. Three hr later, the soln was concentrated *in vacuo* to ½ vol. Red needles were collected and identified as XX.

4-O-*Methylallethrolone* p-*nitrophenylhydrazone* (XXI)

To a soln of allethrolone *p*-nitrophenylhydrazone (352·1 mg) in MeOH (10 ml) was added 1% H_2SO_4–MeOH (6 ml). After standing at room temp for 1 hr, the soln was concentrated *in vacuo*, and ppt was filtered off. Recrystallization from MeOH and subsequent elution chromatography (15·7 × 1·7 cm column) afforded yellow needles, m.p. 157° (dec); λ_{max} (log ε) 286 (3·94), 318 (3·62), 408 mμ (4·45); ν_{max} 3270, 1600 cm^{-1}; NMR 8·07 (s, 3-Me), 7·57 and 7·20 (AB part of ABX, J_{AB} = 17, J_{AX} = 2, J_{BX} = 6, 5-H_2), 5·56 (m, X part of ABX, 4-H), 6·87 (d, J = 6·5, 1'-H_2), 5·22–4·72 (m, 3'-H_2), 4·43–3·70 (m, 2'-H), 2·95 and 1·90 (ABq, J_{AB} = 9, ArH), 2·37 τ (s, NH). (Found: C, 63·57; H, 6·43; N, 13·79. $C_{16}H_{19}O_3N_3$ requires: C, 63·77; H, 6·36; N, 13·95%).

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