groups, it does not permit deblocking of *O*-benzyl serine residues.
(9) Formation of succinimide derivatives in peptides containing β esters in an aspartyl residue was reported several times in the literature (cf. footnote 14 in ref 7). Ring closure was generally thought to be less likely when the side chain of aspartyl residues is unprotected. However, succinimide derivatives formed during the attempted purification of the peptide antibiotic amphomycin: M. Bodanszky, G. F. Sigler, and A. Bodanszky, *J. Am. Chem. Soc.*, **95**, 2353 (1973). Yet, since a readiness to accept two acyl residues on its amino group is characteristic for glycine, only Asp-Gly sequences were considered prone to this side reaction.
(10) S. K. Freeman, "Interpretive Spectroscopy", Reinhold, New York, N.Y., 1965, p 104.
(11) M. Bodanszky, *Nature (London)*, **175**, 685 (1955).
(12) M. Bodanszky, M. L. Fink, K. W. Funk, M. Kondo, C. Y. Lin, and A. Bodanszky, *J. Am. Chem. Soc.*, **96**, 2234 (1974).
(13) J. Piess and R. A. Boissonnas, *Helv. Chim. Acta*, **46**, 1609 (1963).
(14) M. Bodanszky, "Peptides-1968", E. Bricas, Ed., North-Holland Publishing Co., Amsterdam, 1968, p 150.
(15) M. Bodanszky and A. Bodanszky, *Chem. Commun.*, 591 (1967).
(16) J. T. Sheehan, U.S. Patent 3,196,144.
(17) M. Bodanszky and M. A. Ondetti, "Peptide Synthesis", Wiley-Interscience, New York, N.Y., 1966, p 104.
(18) The following abbreviations were used: DMF, dimethylformamide; TFA, trifluoroacetic acid; DIEA, diisopropylethylamine.
(19) D. P. Schwartz and M. J. Pallansch, *Anal. Chem.*, **30**, 219 (1958).
(20) T. Ziminski and E. Borowski, *J. Chromatogr.*, **23**, 480 (1966).
(21) D. H. Spackman, W. H. Stein, and S. Moore, *Anal. Chem.*, **30**, 1190 (1958).
(22) M. Bodanszky and V. duVigneaud, *J. Am. Chem. Soc.*, **81**, 5688 (1959).
(23) S. Guttmann, *Helv. Chim. Acta*, **44**, 721 (1961).
(24) M. Bodanszky, M. Kondo, C. Y. Lin, and G. F. Sigler, *J. Org. Chem.*, **39**, 444 (1974).
(25) E. Scoffone, F. Marchiori, A. M. Tamburro, and R. Rocchi, *Gazz. Chim. Ital.*, **94**, 695 (1974).
(26) Prepared according to the general procedure described in *Biochem. Prep.*, **9**, 110 (1962): mp 114–116°; $[\alpha]^{25}D$ +1.4° (*c* 2, DMF containing 1% AcOH).
(27) W. König and R. Geiger, *Chem. Ber.*, **106**, 3626 (1973).
(28) E. Sandrin and R. A. Boissonnas, *Helv. Chim. Acta*, **46**, 1637 (1963).
(29) K. Samejima, W. Dairman, and S. Udenfriend, *Anal. Biochem.*, **42**, 222 (1971); K. Samejima, W. Dairman, J. Stone, and S. Udenfriend, *ibid.*, **42**, 237 (1971).
(30) M. Bodanszky, K. W. Funk, and M. L. Fink, *J. Org. Chem.*, **38**, 3565 (1973); cf. also ref 24.

Carbon-13 Nuclear Magnetic Resonance Spectral Analysis of Quassinoid Bitter Principles[1]

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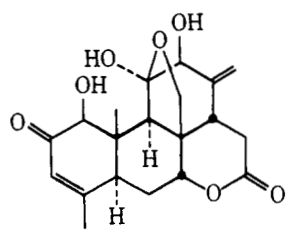
The ^{13}C NMR spectra of several types of quassinoid terpenic substances are presented and all chemical shifts assigned. The data are used for the corroboration of the structure of a new quassinoid principle.

The bitter principles of the plant family Simaroubaceae are a group of structurally complex, highly oxygenated, triterpene degradation products which have attracted attention especially since the advent of ^1H NMR spectroscopy.[3] The latter and mass spectroscopy have been the major tools of structure analysis in this field of terpene chemistry in recent times. In view of the diagnostic power of ^{13}C NMR spectroscopy this new analytical method now has been utilized for the analysis of quassinoid compounds of several structure types and the data applied to the confirmation of the structure of a new substance from *Perriera orientalis* Courchet.

The ^{13}C NMR investigation was initiated by an inspection of the proton-decoupled as well as single-frequency, off-resonance decoupled spectra of ailanthone (**1**), chaparrinone (**2**), and glaucarubinone (**3a**), three compounds differing from each other only in rings C and D.

The chemical shifts of the carbonyl carbons of **1**, **2**, and **3a** are deduced from known ^{13}C NMR parameters of 2-cyclohexenones, δ-lactones, and branched esters.[1,4,5] Similarly, the olefinic carbon shifts are derived from those of 2-cyclohexenone and methylenecyclohexane models. The methyl shifts of the three compounds are based on the differentiation of the 4- and 10-methyl groups of **1** by the use of 1-methylcyclohexene as a model, and 13-methyl group of **2** being recognized by default and the two methyl groups of the side chain of **3a** differing from each other by their being the equivalent of neopentyl and homoneopentyl carbons. The 2.3-ppm difference of the chemical shift of C(18) in **2** vs. **3a** is a reflection of the δ effect[6] exerted by the interaction of the peri C(13) and C(15) substituents. As a comparison of the high-field C(19) shifts of compounds **1–3** with



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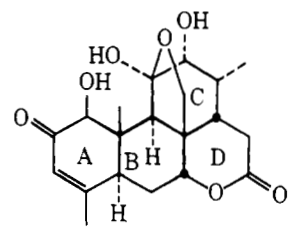

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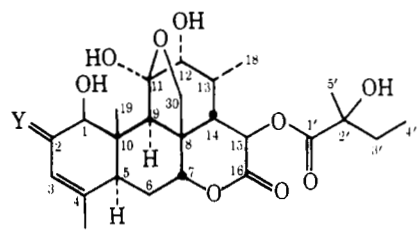


3a, Y = O
b, Y = α-OH, β-H

those of substances possessing an 8β-methyl group instead of the oxymethylene bridge (vide infra) indicates, shielding of up to 2 ppm is due to the heterocycle spanning C(8) and C(11).

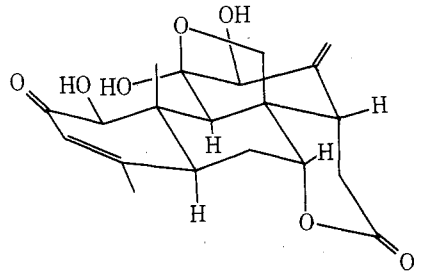
The methylene shifts of ailanthone (**1**) and chaparrinone (**2**) are distinguished easily from each other in view of one being associated with an expectedly low-field oxymethylene, another with a ketomethylene and, finally, one with an unsubstituted, upfield methylene function. In accord with conformations **4** and **5** for ailanthone and chaparrinone, respectively, one of the ketomethylene hydrogens, H(15β), experiences a peri interaction with C(18) in the lat-

Table I
Carbon Chemical Shifts[a]

	1	2	3a	3b
C(1)	82.5	82.5	82.6	82.6
C(2)	197.2	197.1	196.8	71.3
C(3)	125.0	124.7	124.8	125.7
C(4)	162.5	162.3	162.5	133.8
C(5)	43.3	43.1	43.9	40.1
C(6)	25.1	25.0	24.7	24.9
C(7)	77.7	77.6[b]	77.4	77.9
C(8)	44.5	44.9[c]	46.8	46.7
C(9)	46.1	41.1	41.1	40.9
C(10)	44.5	44.3[c]	44.5	44.1[d]
C(11)	108.9	108.9	108.9	109.1
C(12)	79.1	77.9[b]	78.4	78.5
C(13)	146.6	30.4	31.4	31.4
C(14)	41.1	41.1	44.5	44.6[d]
C(15)	34.3	29.4	69.8	69.5
C(16)	169.1	167.6	166.8	167.1
C(18)	119.7	12.5	14.8	14.8
C(19)	9.5	9.4	9.9	10.1
C(30)	71.2	70.1	70.0	70.1
4-Me	22.2	22.1	22.1	20.9
C(1′)			174.4	174.4
C(2′)			73.9	73.9
C(3′)			32.5	32.6
C(4′)			7.6	7.7
C(5′)			24.7	24.9

[a] The δ values are in parts per million downfield from Me_4Si; $\delta(Me_4Si) = \delta(Me_2SO\text{-}d_6) + 39.5$ ppm. [b-d] Signals within any vertical column may be reversed.

ter but not in the former. This phenomenon is reflected by a difference of 4.9 ppm of the C(15) shifts, chaparrinone (**5**)



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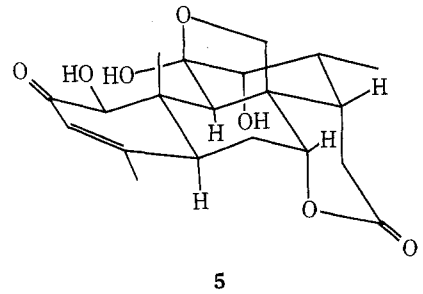
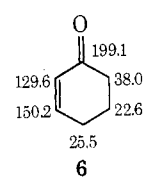


5

being more shielded. The ketomethylene signal is replaced in glaucarubinone (**3a**) by one for its side chain methylene group.

Differentiation of the oxymethines of compounds **1**, **2**, and **3a** is founded on the C(1) and C(7) shifts being constant and C(1) being deshielded by its α-keto group. The assignment of the C(1) shift and its distinction from the C(7) shift is confirmed by the C(1) shift perturbation on acetylation (vide infra). The extra oxymethine signal of **3a** is that of C(15). The designation of the nonoxygenated methine shifts is more difficult. The appearance of an extra methine signal in the spectra of **2** and **3a** in comparison with the spectrum of **1** reveals the C(13) resonance in the former. Since the change of stereochemistry of the 12-hydroxy group from **1** to **2** or **3a** imposes a 1,3-diaxial interaction and hence a γ effect of up to 7 ppm on C(9) in the latter two substances, only the 46.1-ppm shift can be assigned to C(9) of **1** and the 41.1-ppm shift to the same carbon of **2** and **3a**. Furthermore, since C(5) is least affected by the ring C changes, the constant 43–44-ppm shift can be related to it. This leaves the C(14) shift by default. Its identity in **1** and **2** is in conformity with the known minimal difference of the shift of a cyclohexyl methine vicinal to an exo methylene vs. equatorial methyl group[7] and the lower field position of C(14) in **3a** as contrasted to **2** is related to the added β and γ effects of the C(15) substituent of the former. Among the nonprotonated, saturated sites of the three substances the oxy carbon of the side chain of **3a** is unique. Dioxygenated C(11) shows a constant downfield signal. Carbon 10 exhibits similar shift constancy, leaving C(8) by default. All carbon shifts of ailanthone (**1**), chaparrinone (**2**), and glaucarubinone (**3a**) are listed in Table I.

^{13}C NMR analysis of glaucarubin (**3b**), a simaroubaceous substance differing from the aforementioned glaucarubinone (**3a**) only by the replacement of the 2-keto group by an equatorial hydroxy function, had to be based on solely a proton-decoupled spectrum because of the low sample size. This limitation necessitated, inter alia, differentiation of the trigonal carbons 3 and 4 by line width characteristics, i.e., the C(4) signal being considerably slimmer than the C(3) line in view of the slower relaxation of C(4) and the absence of one-bond, carbon–hydrogen residual coupling in its signal. All carbon shifts of glaucarubin (**3b**) are nearly identical with those of glaucarubinone (**3a**) except those of carbons 2, 3, 4, and 5 and the 4-methyl shift. The difference of the olefinic carbon shifts of the ketone and alcohol are reminiscent of the $\Delta\delta$ values of related carbons of 2-cyclohexenone (**6**)[8] and 2-cyclohexenol (**7**).[9] Carbon 5, whose



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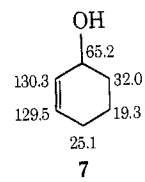

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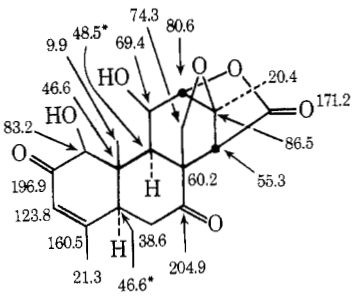
equivalent site in the models is unperturbed, is shielded in the alcohol (**3b**). This shift change affects also the 4-methyl group and may reflect subtle conformational modification of ring A perhaps due to greater ring puckering in the compound of fewer trigonal carbon sites.

Samaderine B (**8**) is a C_{19} quassinoid product whose ring A retains the substitution pattern of compounds **1**, **2**, and **3a**, C(7) has the lactone oxygen terminus replaced by a double-bonded oxygen, and whose remaining skeleton is modified drastically. The ring A identity is reflected in the shift similarity of C(1), C(2), C(3), C(4), and the 4-methyl group. The 10-methyl group is also unaffected, even though the two-atom bridge across ring C now is at a different location. The assignment of the shifts of C(11) and C(12) is based on the shifts of the same oxymethines of the bruceines (vide infra) and the expected deshielding of C(12) when part of a lactone ring. It is worth noting that the C(18) signal is diagnostic for the samaderine B ring system in view of the C(13) attachment of the oxymethylene bridge foisting a β effect upon C(18) and thus strongly deshielding this methyl group. All chemical shifts of samaderine B are denoted on formula **8**.[10]

In contrast to the quassinoid substances described thus



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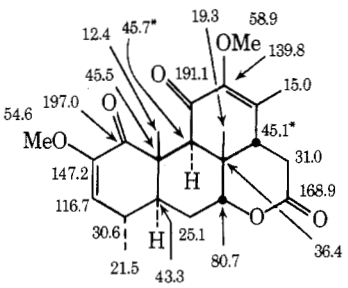
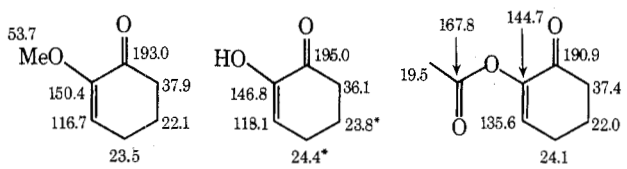


9

far, quassin (**9**) possesses two 2-methoxy-2-cyclohexenone chromophores. Hence one major task is the differentiation of the trigonal carbon shifts. The lactone carbonyl shift is nearly the same as that of ailanthone (**1**), while the two other carbonyl groups differ from each other and from the carbonyl shift of model **10** by C(1) being deshielded (i.e., a β effect) by the neighboring angular methyl group and C(11) being shielded (i.e., γ effects) by the angular methyl functions. The olefinic oxy carbons, C(2) and C(12), are distinguishable by the former being characterized by the oxy carbon shift of model **10** to which is added a mildly shielding γ effect by C(19) and C(12) experiencing stronger shielding from its vicinal, olefinic methyl group. Carbon 3 is a unique olefinic center and the C(13) signal was obscured. While the shift of the 2-methoxy group is normal, when compared with the methoxy shift of model **10**, the 12-methoxy group is deshielded by ca. 4 ppm, reminiscent of the deshielding effect on the methoxy shift of anisoles by two ortho substituents,[7,11]

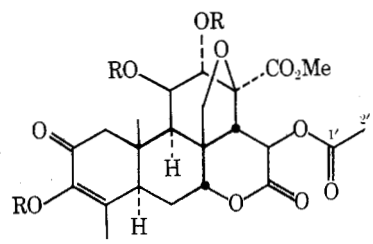


10 **11** **12**

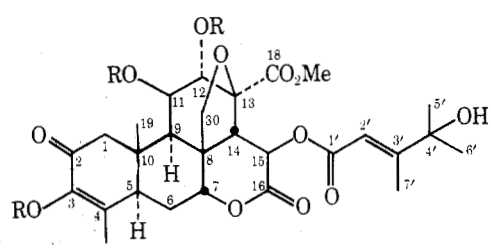
The four *C*-methyl groups of quassin (**9**) can be recognized in the following manner. The 4-methyl unit can be expected to exhibit a shift similar to that of the like carbons in compounds **1–3**. The C(18) shift differs from that of the 4-methyl group by the addition of a strong shielding component due to the neighboring methoxy group. This added shift must be of a magnitude between the ca. 6-ppm difference of the *C*-methyl shifts of toluene and *o*-cresyl methyl ether and the ca. 9-ppm difference for the 2-methyl group of *o*-xylene and 2,3-dimethylanisole.[4] The added γ effect is predictably closer to the smaller $\Delta\delta$ value, since C(18) experiences less compression from its methoxy neighbor and C(15) in a C/D cis ring system than the methyl group of a 2,6-disubstituted toluene. While no direct evidence can be brought to bear upon the distinction of C(19) and C(30), only a minimal shift change can be expected for C(19) from the δ value of the angular methyl group of compounds **1–3** and **8**. Being an olefinic methyl group, C(18) can be differentiated from the other methyl functions by a simple single-frequency, off-resonance decoupling technique. Since the C(18) hydrogens are downfield from those of the remaining methyl groups in the ^1H NMR spectrum, the residual one-bond, carbon–hydrogen coupling of C(18) is distinctly larger than that of the other methyl groups, when the decoupling frequency is placed at the far upfield end of the ^1H NMR spectral range. This simple confirmation of the C(18) shift was applied also to the corroboration of the 4-methyl shifts of compounds **1**, **2**, **3a**, and **8**.

The removal of the β effect due to the oxygen bridge on the one-carbon unit attached to C(8) in the previous compounds shields this quaternary carbon in quassin (**9**). The C(5) shift can be selected on the assumption of its invariancy throughout the quassinoid series alongside the constancy of the 4-methyl, C(6), and C(10) shifts and is confirmed by smaller residual coupling in the single frequency off-resonance decoupled (sford) spectrum. The remaining nonoxygenated methine signals of quassin (**9**) consist of one upfield and two nearly identical, downfield peaks. Since the difference between the two allylic methines, C(4) and C(14), lies in the former feeling a γ effect from C(19) and the latter experiencing no such shielding influence but strong deshielding by at least its neighboring methyl groups, C(4) is represented by the upfield signal and C(9) and C(14) by the indistinguishable downfield peaks. All chemical shifts of quassin are delineated on formula **9**.

Brucein B (**13a**) and brucein C (**14a**) are simaroubaceous compounds whose oxymethylene bridge is samaderine-like,



13a, R = H
b, R = Ac



14a, R = H
b, R = Ac

whose ring D is of the glaucarubinone (**3a**) type, and whose C(18) is in the high oxidation state of a carboxylic ester. Their ^{13}C NMR analysis was undertaken with the use of their triacetates, **13b** and **14b**, respectively, and 2-oxy-2-cyclohexenones **11** and **12** acting as models. While brucein B (**13a**) and its triacetate (**13b**) were run in hexadeuteriodimethyl sulfoxide and brucein C (**14a**) and its triacetate (**14b**) in deuteriochloroform solution, respectively, the solvent-induced shift changes were minimal and the sford spectra in both solvents useful for facilitating the interpretation of multiplets under solvent signals. Since the difference between the two bruceins is limited to the C(15) side chain, the ^{13}C NMR analysis of brucein C (**14a**) is a simple extension of the interpretation of the spectra of brucein B (**13a**). All δ values of **13a**, **13b**, **14a**, and **14b** are listed in Table II.

All carbonyl shifts of the bruceins and their acetates are

Table II
Carbon Chemical Shifts

	13a[a]	13b[a]	14a[b]	14b[b,c]
C(1)	48.7	49.9	47.8[i]	49.9
C(2)	192.9	188.6	193.0	188.3
C(3)	144.1	140.7	144.3	141.6
C(4)	128.3	148.3	129.4	146.0
C(5)	39.9[d]	39.5[e]	42.1[j]	42.0[k]
C(6)	28.7	27.6	29.1	28.2
C(7)	82.8	81.4	83.2	82.3
C(8)	44.7	43.9	45.5	44.8
C(9)	40.4[d]	41.4[e]	41.6[j]	40.5[k]
C(10)	40.9	38.4	41.1	40.0
C(11)	71.4	68.2	71.2	69.0
C(12)	74.7	70.9	75.4	71.0
C(13)	81.4	79.0	81.6	79.8
C(14)	48.7	48.8	49.7[i]	51.6
C(15)	67.3	66.4	66.7	65.3
C(16)	167.0	166.5	168.0	168.1
C(18)	169.9	168.8[f]	168.0	168.1
C(19)	15.0	14.8	15.2	15.6
C(30)	72.3	73.1	73.6	73.7
4-Me	13.3	14.0	13.1	14.5
OMe	52.3	52.4	52.7	52.7
C(1′)	168.7	168.6[f]	165.9	164.9
C(2′)	20.4	20.0	111.5	111.0
C(3′)			171.3	166.6[m]
C(4′)			73.6	73.7
C(5′)			27.9	28.2
C(6′)			27.9	28.2
C(7′)			15.2	15.6
3-OAc		167.5, 21.0[h]		167.4, 21.5[l]
11-OAc		168.1,[g] 20.0[h]		168.1, 20.2[l]
12-OAc		168.3,[g] 20.0[h]		168.1, 20.8[l]

[a] The δ values are in parts per million downfield from Me_4Si. In Me_2SO-d_6 solution; $\delta(Me_4Si) = \delta(Me_2SO\text{-}d_6) + 39.5$ ppm. [b] In $CDCl_3$ solution; $\delta(Me_4Si) = \delta(CDCl_3) + 76.9$ ppm. [c] Some CD_3OD was added for dissolution of the compound. [d-l] Signals within any vertical column may be reversed. [m] This signal may be interchanged with the signal of one of the acetyl carbonyl groups.

Table III
Carbon Chemical Shifts[a]

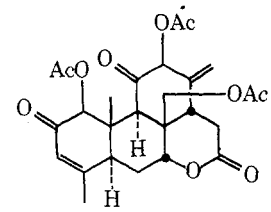
	15	16	17a	17b
C(1)	83.3	83.2	83.2	79.1
C(2)	191.3	191.7	191.2	72.9
C(3)	125.1	124.7	124.7	119.3
C(4)	162.6	162.3	162.3	138.2
C(5)	40.8[b]	40.6	39.2	38.6
C(6)	24.0	24.5	24.1	23.5
C(7)	78.4[c]	76.9	76.5	76.7
C(8)	41.3	43.4	46.7	46.6
C(9)	49.7	46.4	46.4	47.7
C(10)	43.6	43.4	43.7	41.9
C(11)	201.8	204.8	204.6	204.5
C(12)	75.0[c]	81.3	81.8	80.7
C(13)	140.7	33.6[d]	30.4[e]	30.0
C(14)	39.5[b]	34.8[d]	34.1	34.1
C(15)	30.5	27.8	70.1	69.8
C(16)	170.1	170.0	170.5[f]	170.4[f]
C(18)	115.5	12.8	14.6	14.5
C(19)	10.4	11.0	11.5	11.2
C(30)	63.9	60.9	60.5	60.9
4-Me	21.7	21.9	21.8	20.4 ± 0.2[g]
C(1′)			166.2[f]	166.2[f]
C(2′)			80.0	80.0
C(3′)			30.6[e]	30.0
C(4′)			7.0	7.0
C(5′)			20.4 ± 0.2[g]	20.4 ± 0.2[g]

[a] The δ values are in parts per million downfield from Me_4Si; $\delta(Me_4Si) = \delta(Me_2SO\text{-}d_6) + 39.5$ ppm. [b-e] Signals within any vertical column may be reversed. [f] Any of these signals may be interchanged with an acetate carbonyl signal. [g] This signal cannot be differentiated from that of an acetate methyl group.

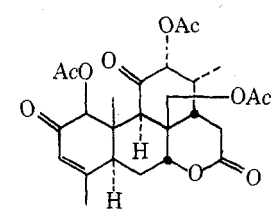
based on comparisons among the four compounds, glaucarubinone (**3a**) and models **11** and **12** and the carbon shifts of the C(15) side chain of **14a** and **14b** rely on calculations from models.[4] As the shift distribution of the enol-one chromophore of **11** and **12** indicates, acetylation of a cyclic α-diketone monoenol shields mildly the olefinic oxy carbon and more strongly the carbonyl group, while exerting a powerful deshielding influence on the nonoxygenated, olefinic site. This phenomenon permits the shift assignment of C(2), C(3), and C(4) in compounds **13** and **14**. The nuclear methyl groups, C(19) and the 4-methyl group, in the bruceins and their acetates are differentiatable by the size of the residual coupling in their sford spectra. Carbon 19 of brucein B (**13a**) is 5.6 ppm downfield of the same carbon of chaparrinone (**2**) in view of the removal of at least a γ effect of the latter's 1-hydroxy group. The 4-methyl group, on the other hand, is shielded by 8.9 ppm when compared with that of chaparrinone (**2**). This influence of the 3-hydroxy function on its neighboring methyl group is reminiscent of and greater than the impact of the 12-methoxy group on its vicinal methyl function in quassin (**9**) (vide supra). The increased size of this shielding effect in brucein B (**13a**) must be due to the greater compression felt by the methyl group from the 3-hydroxy unit and equatorial C(6) (with respect to ring A).

The oxymethines can be characterized as those impervious to acetylation and those experiencing shielding. The former group is composed of C(7) and C(15), whose shifts are similar to those of the same carbons in glaucarubinone (**3a**), while the latter category is made up of C(11) and C(12). The C(11) shift of the bruceins is similar to that of C(11) of samaderine B (**8**), while the C(12) shift can be calculated approximately from the δ value of C(12) in chaparrinone (**2**) by the substitution of an equatorial, oxygen β effect by one of an axial variety. Being under the influence of a large number of β effects and minimal number of γ effects, C(14) can be expected to be downfield of the remaining, undifferentiatable methines, C(5) and C(9). Quaternary centers C(8) and C(10) are shielded relative to glaucarubinone (**3a**), but C(10) more so in view of the lack of a β effect from a 1-hydroxy group.

Acetylation of ailanthone (**1**), chaparrinone (**2**), glaucarubinone (**3a**), and glaucarubin (**3b**) unravels their hemiacetals liberating 11-keto compounds **15, 16, 17a,** and **17b,** respectively. Their ^{13}C NMR spectra were analyzed, only

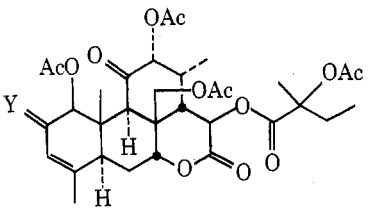


15



16

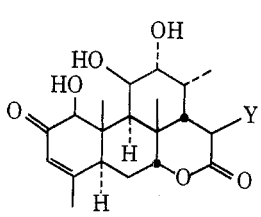
the proton-decoupled spectrum having been inspected in the case of **17a,** and the chemical shifts are listed in Table III. All acetate methyl and carbonyl shifts fall into the range of 20.4 ± 0.2 and 169.4 ± 0.3 ppm, respectively.



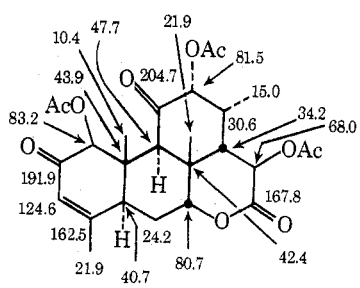
17a, Y = O
b, Y = α-OAc,β-H

Shift assignment of the methyl and methylene groups, olefinic centers, and carbonyl groups, except for the difficult differentiation of C(16) from C(1′), can be made on the basis of all the arguments made thus far. Recognition of the individual quaternary carbon shifts is based on the expectation of the δ values of **15** and **16** reflecting minimal structural change in the C(10) environment and the quaternary carbon shifts of **17a** and **17b** showing the same relationship for C(8). Comparison of the oxymethine shifts of the four compounds reveals the C(7) shift of **16, 17a,** and **17b** to be nearly identical, the C(15) shifts to be associated only with **17a** and **17b** and to be the same as those of the natural products, **3a** and **3b,** respectively, themselves, and the C(2) shift of glaucarubin pentaacetate (**17b**) to be unique. Distinction of the α-keto oxymethines, C(1) and C(12), depends on the expected invariance of the C(1) shift of **15, 16** and **17a** and of the C(12) shift of **16, 17a** and **17b.** The C(7) and C(12) shifts of ailanthone triacetate (**15**) are difficult to distinguish. Among the nonoxygenated methine signals that of the α-ketomethine, i.e., C(9), is recognized readily because of its downfield position and its ca. 3-ppm upfield move on experiencing an added γ effect by the C(12) inversion of an equatorial acetoxy group in **15** to an axial substituent in the other compounds. The next low-field signal is that of C(5), its position being similar to its location in the spectra of the natural products. Finally, a distinction of the C(13) and C(14) shifts is made on the basis of C(14) being expected to undergo a shift change on the introduction of the C(15) side chain into compounds **17a** and **17b.** It is noteworthy that acetylation of glaucarubin (**3b**) produces ring A shift changes previously associated with allyl alcohol to allyl acetate conversions.[12] Thus C(3) and C(4) of glaucarubin pentaacetate (**17b**) are shielded and deshielded strongly, respectively.

Recently there was isolated a new quassinoid substance from the simaroubaceous plant *Perriera orientalis* Courchet whose infrared, ultraviolet, ^{1}H NMR, and mass spectral analyses showed it to be the 15β-hydroxy derivative of klaineanone (**18a**).[3,13] Structure **18b** of the new natural substance was revealed also by comparison of the ^{1}H NMR spectra of its derivative **19** and the 15-deoxy equivalent derived from klaineanone (**18a**).[13] A ^{13}C NMR analysis of



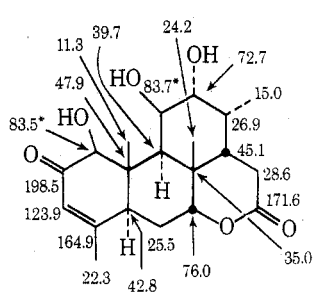
18a, Y = H
b, Y = OH



19

18a, the new quassinoid principle, and compound **19** now was undertaken. While the usual two spectra could be run on 15β-hydroxyklaineanone (**18b**), the investigation was limited solely to proton-decoupled spectra of klaineanone (**18a**) and compound **19** owing to the availability of only small quantities of material.

Comparison of the ^{13}C NMR spectra of **18a** and **18b** reveals all except two signals to be nearly identical. Since the sford spectrum of **18b** exhibits the carbon type of each signal and since the nonidentical signals can be associated with a methine and an oxymethine unit, changes expected for the modification of the C(15) environment, the correlation of the klaineanone (**18a**) signals and its carbon types can be considered established. A spectral comparison of klaineanone (**18a**) with chaparrinone (**2**) shows strong shift alteration, especially in ring C, some of which are readily explicable. Thus C(8) and C(12) of klaineanone (**18a**) are shielded owing to missing β effects, C(14) is deshielded in view of a missing γ effect, the C(13) shift is modified as a consequence of alteration of the groups exerting γ effects, and C(11) and C(30) are shifted dramatically owing to their different substitution pattern. A comparison of the carbon shifts of klaineanone (**18a**) and 15β-hydroxyklaineanone (**18b**) reveals the influence of the new hydroxy group in the form of a 36.8-ppm α effect on C(15) and a 9.8-ppm β effect on C(14). This is in full accord with the previously proposed structure for 15β-hydroxyklaineanone (**18b**).[3,13] Furthermore, confirmation of the structure is revealed by comparison of the ^{13}C NMR spectra of **19** and glaucarubinone tetraacetate (**17a**). All shifts are nearly the same except those of C(7) and C(30). Both shift changes are due to the removal of the 30-acetoxy group in **19** and suggest a rotamer population preference of this group in **17a** favoring a gauche interaction with H(7). The carbon shifts of the acetyl groups of **19** are within the range cited for **17a** (vide supra). All shifts for compounds **18a, 18b,** and **19** are listed on formulas **20, 21,** and **19,** respectively.[10]



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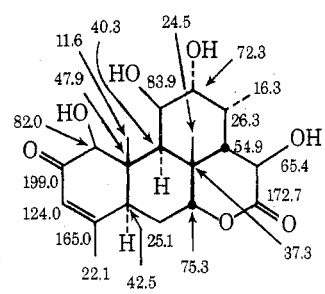

21

In view of the ease of detection of nonprotonated carbon sites in structurally complex organic compounds by application of the noise off-resonance decoupling technique (nord)[14,15] it is possible to obtain directly the C(8) and C(10) shifts and to analyze them in terms of a specific quassinoid structure type. The above shift determinations of the naturally occurring substances reveal three diagnostically distinct shift patterns. All compounds exhibit a signal within the 40–50-ppm range. Those showing the other signal within the same range represent the 7,30-dioxy structure type, those with 5–10-ppm upfield signal the 7-oxy-30-deoxy type, and those with a 10–15-ppm downfield signal the 7-oxo-30-oxy type. In view of there being an oxygen bridge emanating from C(30) in the first and third kinds of natural quassinoid substances, the oxycarbon signal in the nord spectrum differentiates the C(11) from the C(13) terminus of this bridge.

Experimental Section

The carbon shifts denoted on various formulas and in Tables I–III were recorded on a Varian DP-60 spectrometer operating at 15.08 MHz or a Varian XL-100-15 spectrometer functioning at

25.20 MHz. All spectra were obtained with the use of Fourier transform techniques. The δ values portrayed on formulas **8, 9, 19, 20,** and **21** refer to Me_2SO-d_6 solutions, those on formulas **6** and **7** to deuteriochloroform solutions, and those on formulas **10, 11** and **12** imply chloroform [δ (Me_4Si) = δ($CHCl_3$) + 77.2 ppm] as solvent.

Registry No.—**1,** 981-15-7; **2,** 22611-34-3; **3,** 1259-86-5; **3a,** 1448-23-3; **13a,** 25514-29-8; **13b,** 37746-38-6; **14a,** 25514-30-1; **14b,** 55606-57-0; **15,** 990-35-2; **16,** 990-33-0; **17a,** 55658-68-9; **17b,** 55606-58-1.

References and Notes

(1) Carbon-13 Nuclear Magnetic Resonance Spectroscopy of Naturally Occurring Substances. XXXI. For Part XXX see S. G. Levine, R. E. Hicks, H. E. Gottlieb, and E. Wenkert, *J. Org. Chem.*, **40,** 2540 (1975).
(2) Address correspondence to Department of Chemistry, Rice University, Houston, Texas 77001.
(3) J. Polonsky, *Prog. Chem. Org. Nat. Prod.*, **30,** 101 (1973).
(4) J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York, N.Y., 1972; G. C. Levy and G. L. Nelson, "Carbon-13 Nuclear Magnetic Resonance for Organic Chemists", Wiley-Interscience, New York, N.Y., 1972.
(5) The lactone carbonyl carbon and several other sites in the quassinoid skeleta show appreciable shift variability indicative of subtle conformational transmission of the effect of configurational changes through especially rings B, C, and D. Strong bond angle distortions are noted in the X-ray analysis of glaucarubin (**3b**) *p*-bromobenzoate: G. Kartha and D. J. Haas, *J. Am. Chem. Soc.*, **86,** 3630 (1964).
(6) S. H. Grover, J. P. Guthrie, J. B. Stothers, and C. T. Tan, *J. Magn. Reson.*, **10,** 227 (1973).
(7) E. Wenkert, B. L. Buckwalter, I. R. Burfitt, M. J. Gašić, H. E. Gottlieb, E. W. Hagaman, F. M. Schell and P. M. Wovkulich, in G. C. Levy, "Topics in Carbon-13 NMR Spectroscopy", Vol. II, Wiley, New York, N.Y., in press.
(8) Cited in ref 1.
(9) F. Fringuelli, H. E. Gottlieb, E. W. Hagaman, A. Taticchi, E. Wenkert, and P. M. Wovkulich, *Gazz. Chim. Ital.*, in press.
(10) The starred numbers indicate possible shift reversal.
(11) K. S. Dhami and J. B. Stothers, *Can. J. Chem.*, **44,** 2855 (1966).
(12) G. Lukacs, F. Piriou, S. D. Gero, D. A. van Dorp, E. W. Hagaman, and E. Wenkert, *Tetrahedron Lett.*, 515 (1973); N. J. Bach, H. E. Boaz, E. C. Kornfeld, C.-J. Chang, H. G. Floss, E. W. Hagaman, and E. Wenkert, *J. Org. Chem.*, **39,** 1272 (1974); E. Wenkert, M. J. Gašić, E. W. Hagaman, and L. D. Kwart, *Org. Magn. Reson.*, **7,** 51 (1975).
(13) J. Polonsky, Z. Baskévitch-Varon, and M. Debray, *C. R. Acad. Sci., Ser. C,* **280,** 1149 (1975).
(14) E. Wenkert, A. O. Clouse, D. W. Cochran, and D. Doddrell, *J. Am. Chem. Soc.*, **91,** 6879 (1969).
(15) This technique is one of various possible methods of generating low-power noise modulation over the ^1H NMR spectral range. As a consequence it is not surprising that several experimental variations to achieve the goal initially described in ref 14 have been published recently: E. W. Randall, *Chem. Br.*, **7,** 371 (1971); I. H. Sadler, *J. Chem. Soc., Chem. Commun.*, 809 (1973).

Equilibrium in the Behrend Rearrangement of Nitrones

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A group of α-phenyl-*N*-benzylnitrones bearing one of the substituents nitro (*o*-, *m*-, or *p*-), chloro (*o*- or *p*-), methyl (*p*-), methoxy (*o*-, *m*-, *p*-), as well as the *p*-methoxy-*p*-nitro derivative and α,α-diphenyl-*N*-benzylnitrone, were made to undergo Behrend rearrangement to the isomeric nitrone resulting from 1,3-prototropic shift by treatment with sodium methoxide in refluxing ethanol. It was demonstrated that an equilibrium mixture was obtained in each case by approaching the equilibrium from either side. Equilibrium compositions were determined by NMR spectroscopy. All para substituents favored the isomer with substituent on the α-phenyl group. *m*-Methoxy as a substituent was almost without effect on the equilibrium, and a *m*-nitro group slightly favored the isomer with the substituent on the *N*-benzyl group. The ortho substituents strongly favored the isomer with the substituent on the *N*-benzyl group, presumably for steric reasons. α-Phenyl-*N*-benzhydrylnitrone was favored over its isomer, α,α-diphenyl-*N*-benzylnitrone (K = 0.57). The results with the para substituents are consistent with an electronically amphoteric capability of the nitrone group for conjugation.

Isomerization of nitrones by a 1,3-prototropic shift has been called the Behrend rearrangement after its discoverer[2] (eq 1). The closely related isomerization of imines has

$$RCH_2\overset{O}{\overset{\uparrow}{N}}{=}CHR' \longrightarrow RCH{=}\overset{O}{\overset{\uparrow}{N}}{-}CH_2R' \qquad (1)$$

been extensively studied, owing to its importance in biological transamination,[3] but the Behrend rearrangement has received only casual attention.

The initial work on the Behrend rearrangement was essentially qualitative,[2,4-6] directed mainly to the question of whether or not a given nitrone would rearrange. Neubauer[4] investigated a number of substituted α-phenyl-*N*-benzylnitrones, examining the products by fractional crystallization. According to his work and that of Behrend, two such systems (*p*-chloro and *p*-nitro) underwent the 1,3-prototropic shift reversibly, one of them (α-*m*-nitrophenyl) underwent irreversible rearrangement, and many (*p*-methoxy, *p*-hydroxy, *o*-hydroxy, *o*-chloro, *o*-nitro) were inert to attempted rearrangement catalyzed by alcoholic sodium ethoxide. The confusing inconsistency of the observations was noted much later by Lamchen.[7]

The Behrend rearrangement may occur during the preparation or isolation of nitrones, as first noticed by Behrend and König.[2] Cope and Haven prepared[8] α,α-diphenyl-*N*-benzylnitrone (**2**) successfully from benzophenone imine and *N*-benzylhydroxylamine hydrochloride when they used ammonia as the base, but use of sodium ethoxide brought about isomerization to α-phenyl-*N*-benzhydrylnitrone (**1**).

$$PhCH{=}\overset{O}{\overset{\uparrow}{N}}{-}CHPh_2 \rightleftharpoons PhCH_2{-}\overset{O}{\overset{\uparrow}{N}}{=}CPh_2 \qquad (2)$$

1 **2**

Smith and Robertson[9] encountered rearrangement of certain nitrones during a study of the site of alkylation of oxime anions. The collected reports point to catalysis by strong base, an unelucidated dependence of both the ease and direction of rearrangement on structure, and a susceptibility to rearrangement equal to or greater than that of imines. The mechanism is presumed to involve abstraction of a proton to form a delocalized carbanion (eq 3).[7,9]

$$R_2CH{-}\overset{O}{\overset{\downarrow}{N}}{=}CR_2' \rightleftharpoons R_2C{-}\overset{O}{\overset{\downarrow}{N}}{-}CR_2' \rightleftharpoons R_2C{=}\overset{O}{\overset{\downarrow}{N}}{-}CHR_2' \qquad (3)$$