

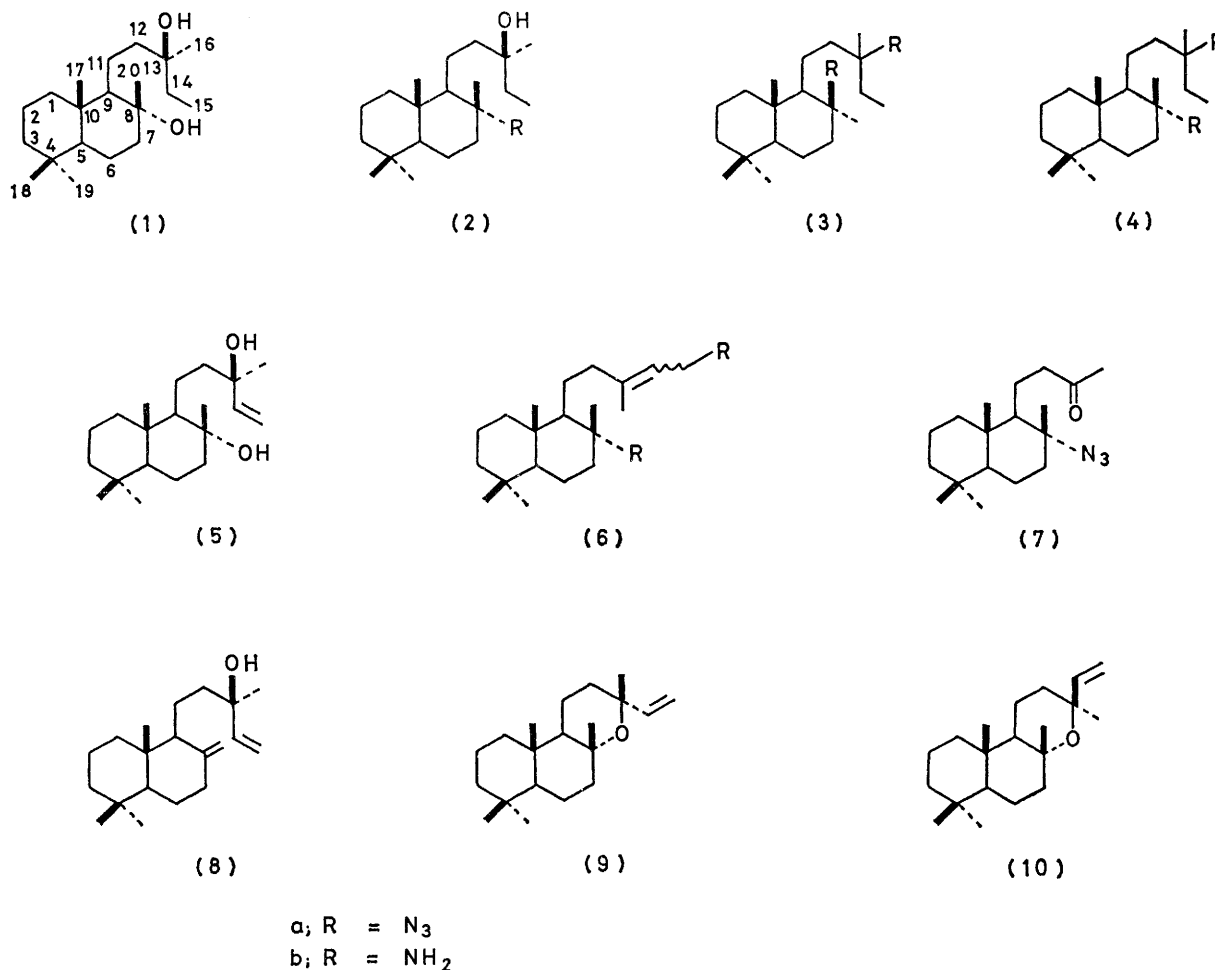
Azido- and Amino-labdanes. α - and β -Effects in ^{13}C Nuclear Magnetic Resonance Spectroscopy. The Problem of the Structure of Tertiary Azides

By Ange Pancrazi and Qui Khuong-Huu, Institut de Chimie des Substances Naturelles, C.N.R.S., 91190 Gif-sur-Yvette, France

The effect of the azido group in ^{13}C n.m.r. is useful in the determination of the configuration of tetrasubstituted carbon atoms bearing an azido group.

AZIDOLABDANES (2a)—(4a), (6a), and (7a) have been synthesized from dihydrosclareol (1) and sclareol (5), upon treatment with hydrazoic acid-boron trifluoride-ether.¹ Lithium aluminium hydride reduction of these

The correlation of the signals of the carbon atoms of the azido- and amino-labdanes was obtained by comparison with the known spectra of sclareol (5), manoöl (8), manoöl oxide (9),^{2,3} and the pimaradienes.⁴ Pre-



azides afforded the corresponding amines. The C-8 epimers need to be determined without ambiguity for a study of the mechanism of this reaction. A tertiary azide has no α -hydrogen and obviously ^1H n.m.r. analysis is not helpful for making stereochemical assignments; the downfield shift of the 17- and 20-Me signals in 8α - and 8β -azidolabdanes relative to the corresponding signals for sclareol (5) and dihydroscclareol (1) is not an argument for the determination of the configuration at C-8 (Table 1). This problem is resolved by ^{13}C n.m.r.

liminary analysis allowed the assignment of C-1—6, C-18 (δ 21.5 p.p.m.), and C-19 (δ 23.3 p.p.m.).

The chemical shift of C-8, which bears the nitrogen function in (2a)—(4a) and (6a) [δ 66.5 in (2) and (4); 63.6 in (3); 75.5 p.p.m. in (5) and (1)] is in agreement with the fact that α -effect of an azido or amino group is lower than those observed from the corresponding hydroxy group.^{5,6} The same relation is valid for C-13 of the azides (3a) and (4a) and the alcohol (1) [δ 73.0 in (1); 63.9 and 64.9 p.p.m. in (3) and (4)]. The determin-

TABLE I
 ^1H N.m.r. chemical shifts (δ) *
 Compound

	(4b)	(3b)	(2b)	(1)	(2a)	(3a)	(4a)	(7a)	(8)	(5)	(6a)	(6b)
16-H	1.05	1.02	1.13	1.17	1.17	1.20	1.22	2.13	1.28	1.27	1.75— 1.68	1.75— 1.67
20-H	1.02	0.98	1.02	1.15	1.22	1.25	1.22	1.22	4.52— 4.82	1.15	1.20	1.02
17-H	0.83	0.93	0.87	0.80	0.85	0.92	0.85	0.83	0.68	0.77	0.83	0.82

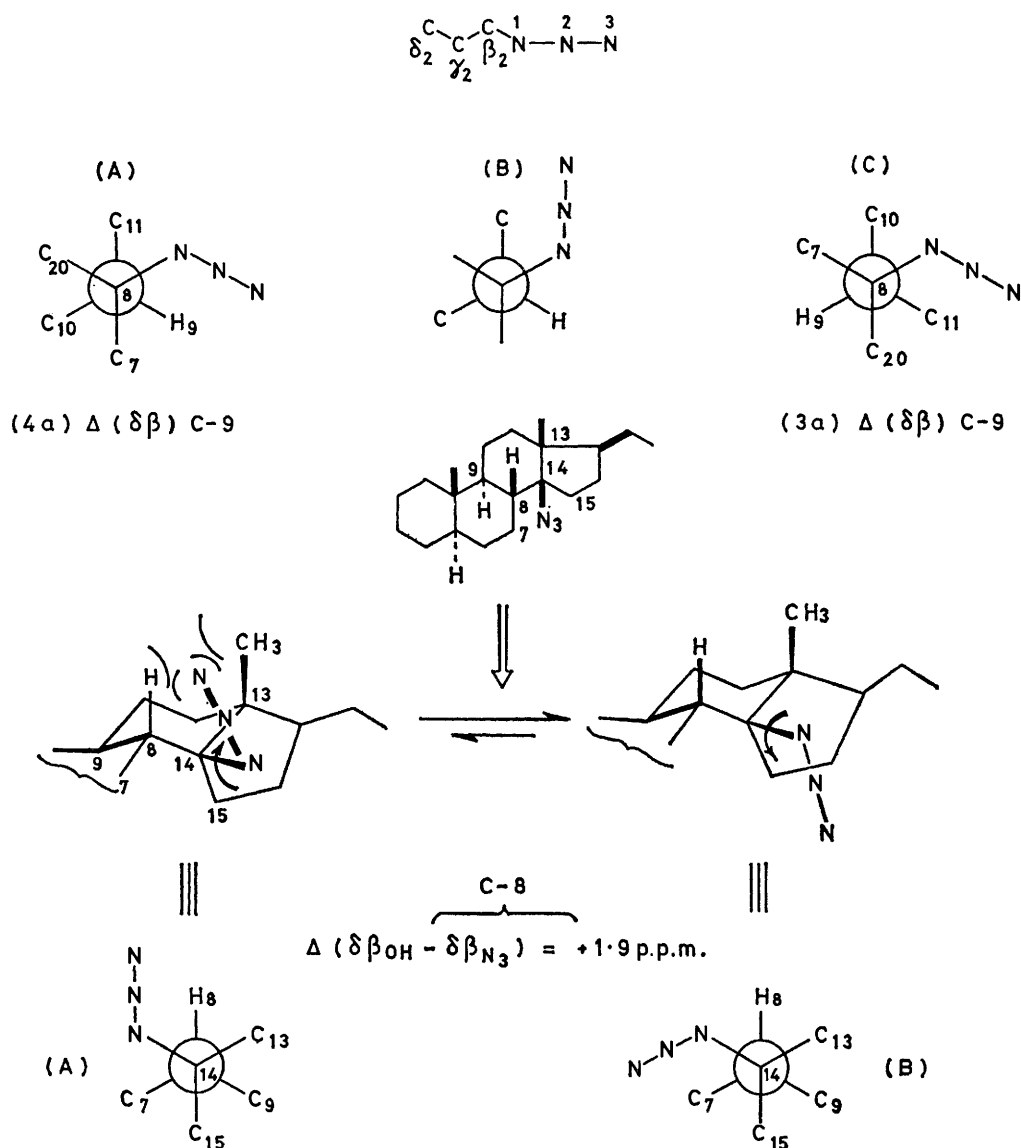
* Varian T60 instrument; solvent CDCl_3 ; 18-H, δ 0.82; 19-H, δ 0.88.

ation of the configuration of C-8 in (3a) and (4a) is deduced from the β -effect of the hydroxy, amino, and azido groups.

For a hydroxy or amino group, the β -effect is nearly the same and approximately independent of the nature of the substituent. But there is generally a lower β -effect for the azido group than for the hydroxy or amino group.⁶

These data and the fact that the chemical shift of the

equatorial methyl group is lower than for the corresponding axial methyl group,⁷ allowed the assignment without ambiguity of C-20 [δ 26.5 in (3a) and 20.8 p.p.m. in (4a)]. The epimeric azides (3a) and (4a) are, respectively, 8β and 8α . The β -carbon signal of an alcohol or an amine cannot be differentiated, whereas the β -carbons of the corresponding azide are shielded and easily identified. It has been reported⁸ that the lower β -effect of an azide compared with that of an alcohol or



SCHEME

TABLE 2
¹³C N.m.r. chemical shifts * of labdanes

	Compound											
	(4b)	(39)	(2b)	(1)	(2a)	(3a)	(4a)	(7)	(8)	(5a)	(6a)	(6b)
C-1	39.9	39.5	39.6	39.6	39.5	38.8	39.7	39.1	39.1	39.6	39.5	39.8
C-2	18.5	18.2	18.3	18.5	18.2	17.9	18.3	18.0	17.7	18.5	18.3	18.4
C-3	42.0	42.0	41.8	42.0	41.8	41.9	41.9	41.3	42.2	42.1	42.2	42.0
C-4	33.3	33.3	33.2	33.2	33.1	32.8	33.3	32.8	33.5	33.2	33.1	33.2
C-5	56.3	56.4	56.2	56.1	55.8	55.2	56.0	55.2	55.6	56.1	55.8	56.4
C-6	19.6	18.4	19.1	18.8	19.6	18.4	19.7	19.6	24.4	18.9	19.6	20.1
C-7	45.5	44.3	45.0	44.0	39.5	38.2	39.7	39.1	38.4	45.0	39.5	45.2
C-8	53.7	53.0	53.9	74.5	66.5	63.6	66.5	65.5	148.5	74.7	66.2	53.4
C-9	63.0	59.8	62.7	62.1	58.9	58.6	58.9	57.2	57.3	61.7	58.9	62.8
C-10	39.4	39.3	39.1	39.2	39.5	38.8	39.7	39.1	39.8	39.3	39.5	62.7
C-11	20.1	19.8	20.0	20.5	19.9	19.6	20.2	19.3	19.4	20.5	25.3	39.5
											24.9	24.8
C-12	46.7	46.3	46.0	44.0	43.9	41.4	41.6	45.7	41.4	44.0	41.8	43.9
											35.0	36.5
C-13	52.0	52.0	72.2	73.1	72.9	63.9	64.9	206.1	73.6	73.3	143.6	138.1
												137.2
C-14	35.4	34.7	35.9	36.3	34.0	31.3	32.3		145.1	146.8	117.5	125.6
	34.7						31.3				117.0	125.2
C-15	8.3	8.3	8.2	8.4	8.2	8.3	8.4		111.7	110.7	48.0	39.5
C-16 ^E	27.6	27.4	25.0	25.1	26.1	22.3	23.1	29.4	27.9	26.1	23.4	24.2
C-16 ^Z	27.3						22.5				16.4	16.4
C-17	15.7	15.7	15.5	15.5	15.7	14.6	15.9	15.4	14.4	15.4	15.8	15.6
C-18	21.5	21.6	21.4	21.5	21.4	21.4	21.5	21.2	21.7	21.6	21.4	21.5
C-19	33.3	33.3	33.0	33.4	33.1	33.0	33.3	32.8	33.5	33.2	33.1	33.2
C-20	24.0	32.4	23.7	24.2	20.7	26.5	20.8	20.3	106.5	24.2	20.7	23.9

* Carbon-13 shifts are in p.p.m. from internal Me₄Si. Solvent CDCl₃.

an amine is due to the additional γ -effect induced by the second nitrogen atom N(2) (Scheme). This γ -effect is a maximum when the N(1)-N(2) bond rotates parallel to the β -C-H bond [(A)]. But, due to the steric hindrance of the azide function, the probability of a conformer with an N(1)-N(2) bond parallel to the β -C-H bond is low [(B)] and the γ -effect is weak; this phenomenon was illustrated in the case of 14 β -azidopregnane in which the conformation with the N(1)-N(2) bond parallel to β -C-H is disfavoured by steric interaction between the azido group and the 18-methyl group of the steroid (Scheme). Obviously, an additional γ -effect does not exist when the azido group and the β -H are *trans*-diaxial in a rigid system. Hence, in azide (4a) [(A)] [C(7)-H(7 α) and C(9)-H(9 α) parallel N(1)-N(2)] with the β -effect at C-7 and -9 is lower than those observed for amine (4b) or hydroxy compound (1); C-7, $\Delta(\delta\beta_{\text{NH}_2} - \delta\beta_{\text{N}_3}) = 5.8$ p.p.m.; C-9, $\Delta(\delta\beta_{\text{NH}_2} - \delta\beta_{\text{N}_3}) = 4.1$ p.p.m. For the azide (3a), C-7, $\Delta(\delta\beta_{\text{NH}_2} - \delta\beta_{\text{N}_3}) = 6.1$ p.p.m. Parallelism can be observed between N(1)-N(2) and C(7)-H(7 β); for C-9, $\Delta(\delta\beta_{\text{NH}_2} - \delta\beta_{\text{N}_3}) = 1.2$ p.p.m. is in agreement with the fact that N(1)-N(2) and C(9)-H(9 α) are not parallel, which means the axial azido group is *trans*, relative to 9 α -H [(C)].

This phenomenon seems to be general. From the known stereochemistry of the cyclic azide, one can deduce the configuration of the β -methine function.

The epimeric *E*- and *Z*-azides (6a) were distinguished by the resolved C-12, -14, and -16 signals (Table 2). The signals of the allylic carbons in *Z*-olefin were upfield from those for the corresponding carbons in the *E*-olefin. For the azide (6a) in comparison with the amine (6b), one can observe the characteristic shielded β -ethylenic C-14, $\Delta(\delta_{\text{NH}_2} - \delta_{\text{N}_3}) = -8$ p.p.m. and the deshielded ethylenic C-13, $\Delta(\delta_{\text{NH}_2} - \delta_{\text{N}_3}) = +5.5$ p.p.m. This

effect is close to the 'allylic acetylation effect' observed by Wenkert *et al.*⁹ The isomeric *E*- and *Z*-olefins also reflect an effect on C-9 and -11 signals which are doublets in the spectrum.

In conclusion, ¹³C n.m.r. allowed the determination of the configuration of tertiary azides which show characteristic α - and β -effects. From the known configuration of the carbon bearing the azide group, the configuration of the β -methine carbon can also be deduced. The effect of the corresponding amines is not useful in this case.

EXPERIMENTAL

Instrumentation and Spectral Techniques.—Carbon-13 n.m.r. data were obtained using a Bruker HX 90 spectrometer, operating near 22.63 MHz; simultaneous proton decoupling was accomplished by irradiating the sample at 90.00 MHz. All samples were dissolved in CDCl₃ with *ca.* 10% tetramethylsilane added; *ca.* 2.1 ml of a 0.5M solution was usually used. ¹H Spectra were obtained using a Varian T60 instrument; all samples were run in CDCl₃ solution using tetramethylsilane as internal standard.

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