

CARBON-13 SPIN-LATTICE RELAXATION TIME (T_1) FOR ASSIGNMENT OF BROMINATED CARBONS

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Abstract - T_1 values can be used to distinguish a brominated quaternary carbon for other quaternary carbons, because the former carbon shows the T_1 value which is generally much smaller than the values of the latter carbons.

During our continuing search for pharmacologically active secondary metabolites from marine organisms, we isolated from the brittle stars *Ophiocoma erinaceus* the known polybrominated *N*-methylindoles (**1** and **2**), which had been obtained from the red alga *Laurencia brongniartii*.¹ Since the assignments of the ^{13}C NMR signals for these compounds have not been reported, we analyzed their 2D NMR spectra, mainly HSQC and HMBC spectra, in detail. However, carbons-3a and 6 of **1** and carbons-3a, 5, and 6 of **3** were indistinguishable from the 2J and/or 3J -cross peaks. We, therefore, turned attention to ^{13}C spin-lattice relaxation time (T_1). Because the predominant relaxation mechanism of protonated ^{13}C is ^{13}C - ^1H dipole-dipole interaction, carbon T_1 relaxation times are widely used to determine the local mobility of molecules. In the case of nonprotonated carbons other relaxation mechanisms become more important. The spin-lattice relaxation behavior of bromobenzene indicates that scalar relaxation completely dominates the relaxation of ^{13}C nuclei bonded to ^{79}Br nuclei and the scalar and/or dipole-dipole interaction between ^{13}C and ^{81}Br nuclei excludes ^{13}C - ^1H dipole-dipole relaxation for ^{13}C nuclei bonded to the ^{81}Br isotope.² As a result carbon-13 nuclei bound to Br relax relatively fast.³ There were a few application of this method to assign brominated quaternary carbons.⁴

Prior to application of this T_1 method, we assigned all the quaternary carbons of **1** and **2** with the aid of heteronuclear H-C NOE difference spectroscopy (H-C NOEDS)⁴ as shown in Figure 1. Irradiation at 7-H (δ 7.34) of **1** increases the signal intensity of two carbons (δ 116.5 and 136.7). Because the latter carbon was already assigned as C-7a, the former one must be C-6, which led the assignment of C-3a resonating at 125.7. Actually, irradiation at 4-H (δ 7.25) enhances this carbon (δ 125.7, 3a position). Two nonprotonated carbons (δ 92.9 and 115.5, 2 and 3 position) were not affected in these NOE experiments. The same NOE experiments were performed on **2**, which resulted in full assignment of the carbon signals of **2**.

Carbon T_1 values, determined by the inversion recovery method, show good agreement with the assignments: The T_1 values of the brominated carbons, C-2, 3, and 6 (7.6, 7.9, and 9.6 sec), of **1** are about a half of those of the nonbrominated quaternary carbons (15.6 and 16.7 sec). Also, the T_1 values of

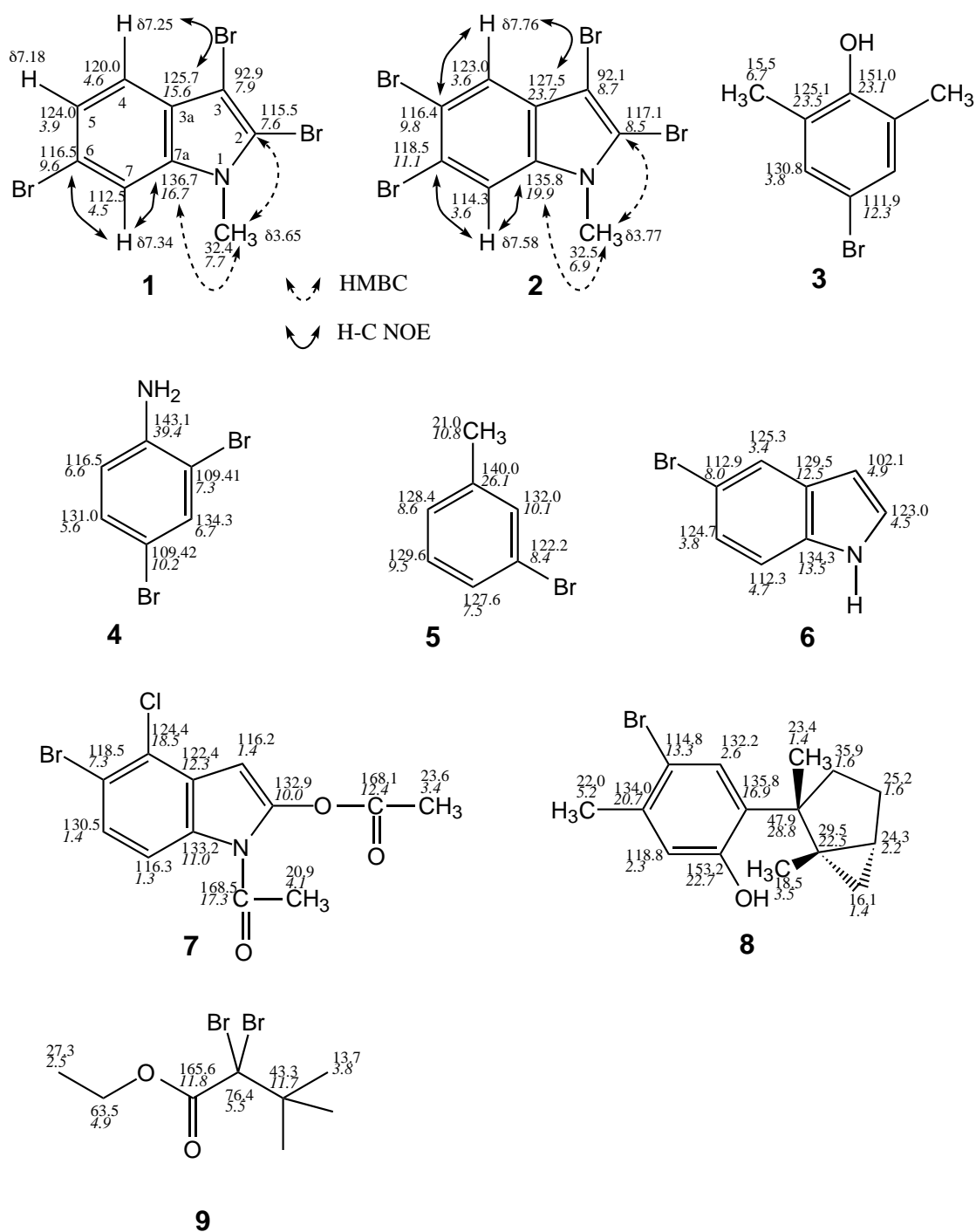


Figure 1. ^{13}C chemical shifts (δ/ppm) and T_1 values (sec) of brominated compounds.⁵

C-2, 3, 5, and 6 (8.5, 8.7, 9.8, and 11.1 sec) are significantly smaller than those of C-3a and C-7a (23.7 and 19.9 sec).

To confirm the general utility of carbon T_1 values to assign the brominated carbons, T_1 s of other bromo compounds (**3-9**) were measured, and the results are shown in Figure 1.⁴ The brominated sp^2 carbons have T_1 s which are roughly half or less of those observed for the nonbrominated quaternary carbons in each

compound without exception. Other atoms, oxygen, nitrogen and chlorine, have no effect on the relaxation times of the bonded carbons. It should be noted that the T_1 of the brominated sp^3 carbon of **9** showed one fourth of the values obtained for the nonbrominated quaternary carbons. Because there has been no practical method to detect the brominated quaternary carbons, the present method using T_1 values may become more useful means to distinguish quaternary C-Br from other quaternary carbons.

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5. All NMR experiments were carried out on a Bruker ARX-400 spectrometer (^1H : 400 MHz, ^{13}C : 100 MHz) at 300 K. Samples were 50-300 mg/mL CDCl_3 solution, deoxygenated by argon bubbling and sealed. Carbon-13 T_1 values were measured by the inversion recovery method, with a Bruker program of "T1ir". As no clear ^{79}Br and ^{81}Br isotope difference was observed because of experimental temperature and/or incomplete deoxygenation, T_1 values were calculated as the averages of them.