Total Assignment of the ¹³C-NMR Spectra of 5H-Indolo[1,7-ab][1]benzazepine and 6,7-Dihydro-5H-indolo[1,7-ab][1]benzazepine Using Two-Dimensional Proton-Carbon Chemical Shift Correlation Experiments

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¹³C-nmr chemical shift assignments for 5H-Indolo[1,7-ab][1]benzazepine and 6,7-Dihydro-5H-indolo-[1,7-ab][1]benzazepine, made on the basis of two-dimensional ¹H-¹³C chemical shift correlation experiments are reported.

Tetracyclic dibenzazepines, 5H-indolo[1,7-ab][1]benzazepine (1) and 6,7-dihydro-5H-indolo[1,7-ab][1]benzazepine (2) are important intermediates for our synthesis of new conformationally restricted antidepressant agents related to imipramine [2]. During the course of our investigation of 1, we found that it underwent an unusually facile photodimerization under ordinary light conditions [3]. We have
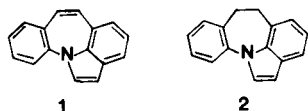
also recently reported the mass spectral fragmentation [4] and the total assignment of the ¹H-nmr spectra of 1 and 2 [5]. We now wish to report the total assignment of the ¹³C-nmr spectra of these compounds through the use of two-dimensional nmr techniques, which have provided an unequivocal means of obtaining resonance assignments.

Structurally, since neither 1 or 2 is symmetric, a total of sixteen carbon resonances were expected in the fully decoupled nmr spectrum of each. In the specific case of the decoupled spectrum of 1 at lower field (25.2 MHz), this observation was not met, the downfield quaternary carbon resonance resolving into a pair of signals resonating at 141.59 and 141.54 ppm at 75.46 MHz. From our previous work on the related pyrrolo[3,2,1-kl]phenothiazine [6,7], it was clear that chemical shift arguments alone could not be relied upon for the successful assignment of the spectra of 1 and 2. Thus, we resorted to two-dimensional proton-carbon chemical shift correlation [8-10], this providing a ready means of making assignments since the proton spectra of both molecules had been previously assigned [5].

Decoupled spectra were obtained for 1 and 2 in deute-

Table I

¹³C-NMR Chemical Shift Assignments for 5H-Indolo[1,7-ab][1]-benzazepine (1) and 6,7-Dihydro-5H-indolo[1,7-ab][1]benzazepine (2) in Deuteriochloroform at 25°

position	δ ¹³C	
	1	2
1	124.72	126.86
2	105.79	105.18
3	120.68	118.86
4	122.20	119.97
5	123.57	122.86
6	131.79	34.93
7	130.79	34.34
8	133.68	130.48
9	125.06	124.47
10	130.41	127.26
11	120.04	122.08
2a	131.24	130.29
2b	141.54	134.67
5a	126.50	117.89
7a	129.42	119.43
11a	141.59	140.37

riochloroform at 25°, the longer relaxation times of the quaternary carbons providing a convenient means of distinguishing these resonances from their protonated counterparts. The two-dimensional proton-carbon chemical shift correlation spectra of 1 and 2 are shown in Figures 1A and 1B respectively. Both are presented as contour plots and are flanked by their corresponding proton spectra (F_1 axis) and the carbon spectrum (recovered by projection, F_2 axis). Beginning with the pyrrole resonances of 1,
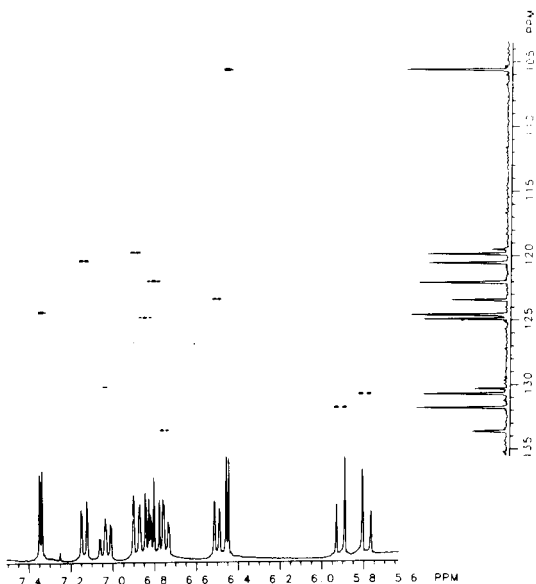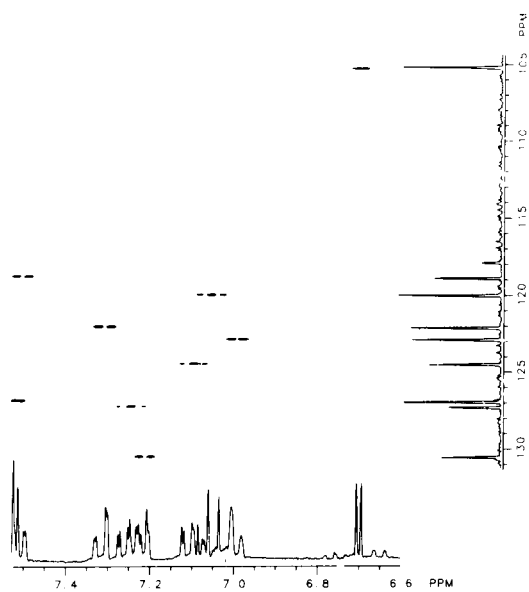
Figure 1a

Figure 1b

Figure 1. Four level contour plots of the two-dimensional proton-carbon chemical shift correlation spectra. The F_2F_1 data matrix is plotted and consisted of 256 × 512 real data points flanked by the conventional proton spectrum which is shown along the F_1 axis and by a ^{1}H-decoupled ^{13}C-nmr spectrum shown along F_2 obtained by a 90° projection of the F_2F_1 data matrix: A) spectrum of 5H-indolo-[1,7-ab][1]benzazepine (1); B) spectrum of 6,7-dihydro-5H-indolo[1,7-ab][1]benzazepine (2).

the H1 and H2 resonances are clearly identifiable in the spectrum along the F_1 axis as the AX pair resonating at 7.35 and 6.45 ppm respectively. The corresponding carbons are then readily assigned as the resonances observed at 124.72 and 105.79 ppm, the latter resonating considerably upfield of the other resonances as would be expected on the basis of related work [6,7]. Having assigned the pyrrole resonances, the remaining two-spin system resonating at 5.92/5.79 ppm and attributed to the etheno bridge protons [5], could then be correlated with the carbon resonances at 131.79 and 130.79 ppm respectively. Remaining to be assigned are the carbons associated with the protons of the three- and four-spin systems. Beginning with H3-H5, which constituted an AMX spin system, the H4 resonance appears as a "triplet" (overlapped doublet of doublets due to equal couplings to H3 and H5) resonating in the congested region of the spectrum between 6.73-6.91 ppm. Specifically, the resonance centered at 6.81 ppm correlating with the carbon resonance at 122.20 ppm was assigned at H4/C4. The H3 resonance at 7.14 ppm provided the assignment for the resonance at 120.68 ppm as C3, the remaining member of this spin system resonating at 6.71 ppm and corresponding to the signal at 123.57 ppm, these assigned as H5/C5. Remaining to be assigned at this point were the carbon resonances corresponding to the H8-H11 four spin system. Again, both H9 and H10 would initially be expected to appear grossly as some form of double doublets or as triplets if the vicinal couplings were equal. Thus, the H9 resonance at 6.85 ppm and the H10 resonance at 7.04 ppm provided the means of assigning the carbons resonating at 125.06 and 130.41 ppm as C9 and C10 respectively. Finally, the H8 resonance at 6.75 ppm correlated with the carbon resonance at 133.68 ppm while the H11 resonance at 6.88 ppm was associated with the carbon resonance at 120.04 ppm.

Assignments for the protonated carbon resonances of 2 were made in a similar fashion. For the most part, these assignments were completely straightforward and are not worthy of elaboration with the exception of the assignments for the H8 and H10 resonances and their corresponding carbons. The previously reported assignments for H8 and H10 at 250 MHz [5] were 7.28 and 7.24 ppm respectively, the multiplets for these resonances contained in a congested region of the spectrum at that observation frequency. In contrast, from the two-dimensional proton-carbon chemical shift correlation spectrum of 2 which is shown in Figure 1B, there can be no doubt that the "triplet" contour associated with H10 is downfield of the "doublet" contour response associated with the H8, these resonating at 7.25 and 7.22 ppm respectively. Slight differences in chemical shift of the type observed in this case may be attributable to differences in concentration from the conventional high resolution proton sample to that em-

ployed for the proton-carbon chemical shift correlation study. Differences of this type do, however, underscore the need for care to be taken in making assignments even from chemical shift correlation spectra as "crossover" can still lead to erroneous assignments.

Through the use of two-dimensional proton-carbon chemical shift correlation experiments, the resonance assignments for 5H-indolo[1,7-ab][1]benzazepine (1) and 6,7-dihydro-5H-indolo[1,7-ab][1]benzazepine (2) can be made in a convenient and unequivocal manner. Had the proton resonance assignments been unavailable they could have been made either through the prior acquisition of a two-dimensional autocorrelated proton (COSY) [11,12] spectrum or through the acquisition of two-dimensional relayed coherence transfer experiments [13-16] which have recently been applied in the assignment of peptide [17], oligosaccharide [18], and polynuclear aromatic thiophene [19] carbon spectra. Since these techniques can be performed on modest quantities of material and since they are furthermore unequivocal, they should be utilized whenever possible, especially if the assignments produced are to be subsequently utilized in determining structures of metabolites or in related structural applications.

EXPERIMENTAL

The two-dimensional experiments on 1 and 2 were performed using the pulse sequence originally described by Freeman and Morris [8] with phase cycling to povide the equivalent of quadrature detection in F_1 [9], the coherence transfer echo detected to provide enhanced sensitivity in the presence of magnetic field inhomogeneities [10]. Samples were prepared containing approximately 100 mg of compound dissolved in 0.4 ml of deuteriochloroform. The data was collected using a Nicolet NT-300 wide bore spectrometer equipped with a MIC-1280 computer interfaced through a Model 293-C pulse programmer, the sample observed in a 5 mm dual tuned $^1H/^{13}C$ probe. Total data collection on each sample required less than four hours for the $256 \times 1K$ data point matrix. Data were processed in the usual fashion using double exponential apodization in both directions to povide 256×512 real data points which are presented in Figures 1 and 2 as four level contour plots [20]. All chemical shifts are referenced to the residual protiochloroform resonance or to the center line of the deuteriochloroform multiplet as appropriate.

REFERENCES AND NOTES

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