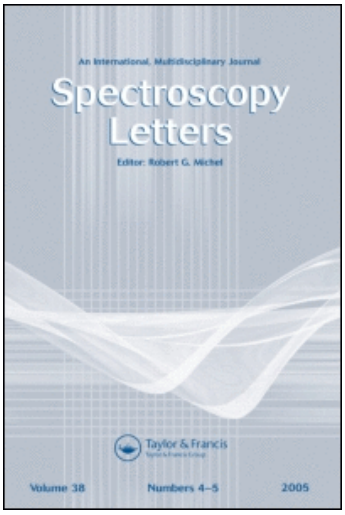

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NMR Studies of Hindered Rotation. The Diels-Alder Adduct of Phencyclone with *p*-Benzoquinone: Restricted Motion of Bridgehead Phenyls

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NMR STUDIES OF HINDERED ROTATION. THE DIELS-ALDER ADDUCT OF PHENCYCLONE WITH p-BENZOQUINONE: RESTRICTED MOTION OF BRIDGEHEAD PHENYLS.

Key Words: Dynamic NMR, ^{1}H NMR, One- and two-dimensional NMR, COSY, Restricted rotation, Anisotropy.

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ABSTRACT

The Diels-Alder adduct of phencyclone with p-benzoquinone has been examined by ^{1}H NMR at 300 MHz in $CDCl_3$ at ambient temperatures for evidence of hindered rotation of the unsubstituted bridgehead phenyl groups. The nearly first-order spectrum exhibits four approximate doublets and five approximate triplets in the aromatic

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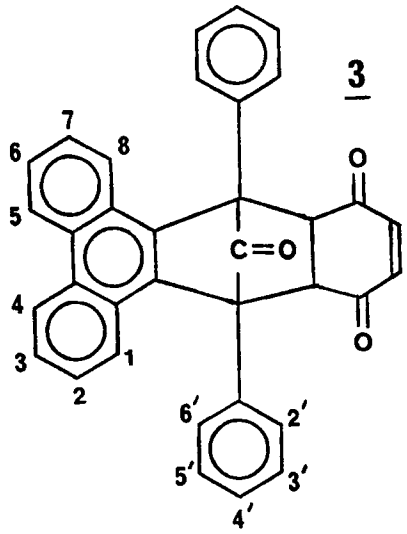

region, of roughly equal intensity (ca. 2H). This is consistent with a slow-exchange limit (SEL) spectrum of the hindered phenyls. For rapidly rotating phenyls, the predicted fast-exchange limit (FEL) spectrum would have shown two 2H doublets and one 4H doublet, in addition to three 2H triplets and one 4H triplet, in the aryl region. Full ^1H assignments have been made, based on the two-dimensional ^1H-^1H homonuclear chemical shift correlation spectrum (COSY) and expected magnetic anisotropy effects.

INTRODUCTION

The reactive Diels-Alder diene compound, phencyclone, 1, undergoes the cycloaddition reaction with both electron-poor and electron-rich olefins. Its reaction with p-benzoquinone, 2, to form an adduct, 3, has been reported (1). We had previously described ^1H

and ^{13}C NMR studies of the adduct, 4, formed by reaction of 1 with norbornadiene; this adduct exhibited hindered rotation of the unsubstituted bridgehead phenyl groups (2,3). Examination of Dreiding Stereomodels (4) for the phencyclone-norbornadiene adduct, 4, indicated potentially severe interactions between the phenyl ortho protons and H-1,8 of the phenanthrene moiety, with a closest approach distance of less than 0.2Å (2). If similar geometries and comparable interactions occurred in other Diels-Alder adducts of 1, the relatively unusual case of hindered rotation of an unsubstituted phenyl group about an sp^2-sp^3 bond (5) might potentially be demonstrated in these analogs. This present report describes such studies in the adduct, 3, from p-benzoquinone and 1. We had earlier reported NMR evidence for hindered rotation of the unsubstituted bridgehead phenyl group in the drug, ketazolam (6,7). The ^1H NMR data reported earlier for 3 were limited by use of a 60 MHz spectrometer (1) so that the aryl proton region had been reported simply as a 16H multiplet from 6.8-8.4 ppm (Table 6 in the Supplemental Data of ref. 1); the only other aryl resonance that was separately distinguishable was the low field doublet of the phenanthrene moiety's H-4,5. The superior dispersion of a higher field NMR spectrometer was expected by us to be essential.

EXPERIMENTAL

Chemicals were obtained from Aldrich Chemical Co., Inc. (Milwaukee WI 53233) and used as received except as noted. Melting points were determined on a Mel-Temp apparatus (Laboratory Devices, Cambridge MA 02139) and are uncorrected. NMR spectra were obtained with a General Electric QE300 spectrometer equipped with a Nicolet 1280 data system operating at a ^{1}H observe frequency of 300.152 MHz using a 5 mm switchable ^{1}H /^{13}C probe and thin wall NMR tube. Typical acquisition parameters (^{1}H, 1D) were: spectral width 20 ppm (6 KHz) from ca. +16 to -4 ppm, with 8 FIDs collected in 32K complex points for a digital resolution of 0.37 Hz/point and a 2.7 s acquisition time. Pulse widths were set to a 32° tip angle (3 μs) and a 1 s relaxation delay was used. No exponential multiplication or apodization was applied. For the ^{1}H-^{1}H homonuclear chemical shift correlation spectrum the macro "QUICK COSY" was used. Spectra were run at ambient temperatures in $CDCl_3$ (99.8 at % D, Aldrich) in the FT mode with quadrature detection.

Preparation of Phencyclone-p-Benzoquinone Adduct, 3. Phencyclone, 1, was prepared by base-promoted condensation of dibenzylketone with 9,10-phenanthrenequinone (99+%, Aldrich) as described previously (8,9) using KOH in refluxing methanol. The resulting near-black, powdery 1 was used directly for reaction with 2.

Thus, 250 mg of 1 (0.654 mmol) was suspended in 25 mL toluene and 70 mg of 2 (0.648 mmol) was added. After heating on a steam cone for 30 min with occasional swirling, the black mixture had cleared to a near-transparent yellowish color, indicating that the phencyclone had reacted. On standing at room temperature for 0.5 hr, crystals were formed. After an additional 2 days, filtration gave a 90% yield of 3 as slightly pale yellow powder with mp (dec) 265-266° [lit.(1) mp (dec) 272-273°]. This material was used directly for subsequent NMR analysis after dissolving in $CDCl_3$, with filtration performed as required to remove $CDCl_3$-insoluble particulates, using a cotton plug in a Pasteur filter-tip pipet.

RESULTS AND DISCUSSION

Our slightly simplified procedure for the preparation of 3 from 1 and 2, compared to that of Sasaki, et al. (1), yielded adduct with a ^1H NMR spectrum which showed signals in good agreement with the earlier reported spectrum (1). However, our higher spectrometer frequency rendered the aromatic region nearly first order, as shown in the expansion of the aryl region (Figure 1).

Fast rotation of the bridgehead phenyl groups of 3 would interconvert (and render equivalent) the phenyl ortho protons, H-2',6', to give a 4H intensity doublet

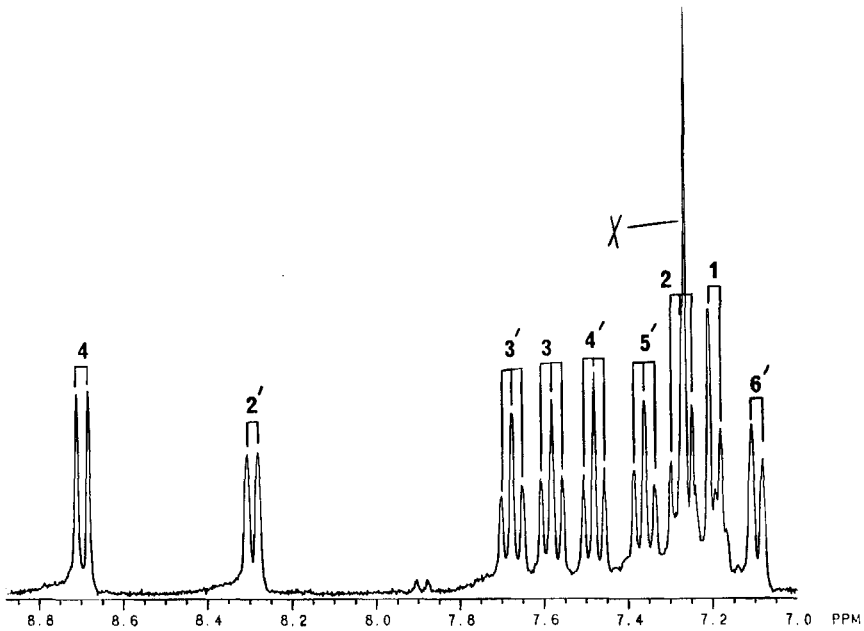

Figure 1. Expansion of part of aryl region of 300 MHz ^1H NMR spectrum of the phencyclone - 1,4-benzoquinone adduct in $CDCl_3$, from 7-9 ppm. The upfield singlets of the vinyl protons and sp^3 methines are not shown. The proton assignments are indicated, together with the gross multiplet structures. The $CHCl_3$ impurity peak is indicated by "X."

signal (due to single vicinal neighbors, with a first order approximation). Likewise, the meta protons of the phenyl, H-3',5', would be exchanged under conditions of fast phenyl rotation, and should give a 4H intensity triplet signal (due to two vicinal neighbors, with a first order approximation). The predicted aromatic region for 3 under fast exchange limit (FEL) conditions should thus consist of two 2H doublets and two 2H

triplets from the phenanthrene moiety, i.e., doublets for H-1,8 and H-4,5, and triplets for H-2,7 and H-3,6, together with a 4H doublet and a 4H triplet from the phenyl ortho and meta protons, respectively. Lastly, the phenyl para protons H-4' should appear as a 2H triplet. In total, the FEL spectrum should show only seven aryl resonances: two 2H doublets and one 4H doublet, three 2H triplets and one 4H triplet.

In fact, nine signals appear (in a near-first order spectrum), all of approximately equal intensity, comprised of four doublets and five triplets. This is fully consistent with a slow exchange limit (SEL) spectrum resulting from severely hindered phenyl groups rotating only slowly on the NMR time scale. Under slow rotation conditions, the phenyl ortho protons H-2' and H-6' must be nonequivalent and each should give rise to a 2H doublet. Similarly, the meta protons H-3' and H-5' should appear as two 2H triplets. The SEL spectrum should show (in the absence of accidental overlaps) nine equal intensity (2H) signals, being four doublets and five triplets. This is quite clearly seen in Fig. 1. One triplet (at 7.27 ppm) and one doublet (at 7.19 ppm) exhibit substantial leaning towards each other (see below); this triplet has slightly high intensity which we attribute to coincidence with the $CHCl_3$ signal (present as an impurity in the solvent $CDCl_3$). Otherwise,

excellent agreement is seen with the SEL prediction. Slow rotation of the bridgehead phenyls due to severe steric hindrance between the phenyl ortho protons H-2',6' and the phenanthrene H-1,8 protons must be present in the adduct 3 as was the case in the phencyclone-norbornadiene adduct examined earlier (2,3).

Additional NMR studies employed the ^{1}H-^{1}H 2D homonuclear chemical shift correlation experiment, "COSY", as shown in Figure 2. At the contour level selected for Fig. 2, seven clear, intense off-diagonal crosspeaks are seen for the aryl region from 7.0-8.8 ppm, corresponding to the expected seven ^{3}J vicinal couplings among the phenyl and phenanthrene moiety protons under SEL conditions. With a lower contour level (not shown) at least two additional weak crosspeaks are seen, consistent with long-range ^{4}J ("W") couplings, e.g., H-2/4, H-2'/6'. The COSY correlations of Fig. 2 thus permit straightforward analysis of the four spin system of the phenathrene moiety versus the five spin system of the bridgehead unsubstituted phenyls of 3.

The extreme lowfield doublet at 8.69 ppm is assigned to H-4,5 (10,11) of the phenanthrene moiety due to the major anisotropic deshielding experienced by these protons from the aryl rings. The connectivity is then mapped out from H-4 (d) - H-3(t) - H-2(t) - H-1(d). The rather highfield position of H-1 may result from its

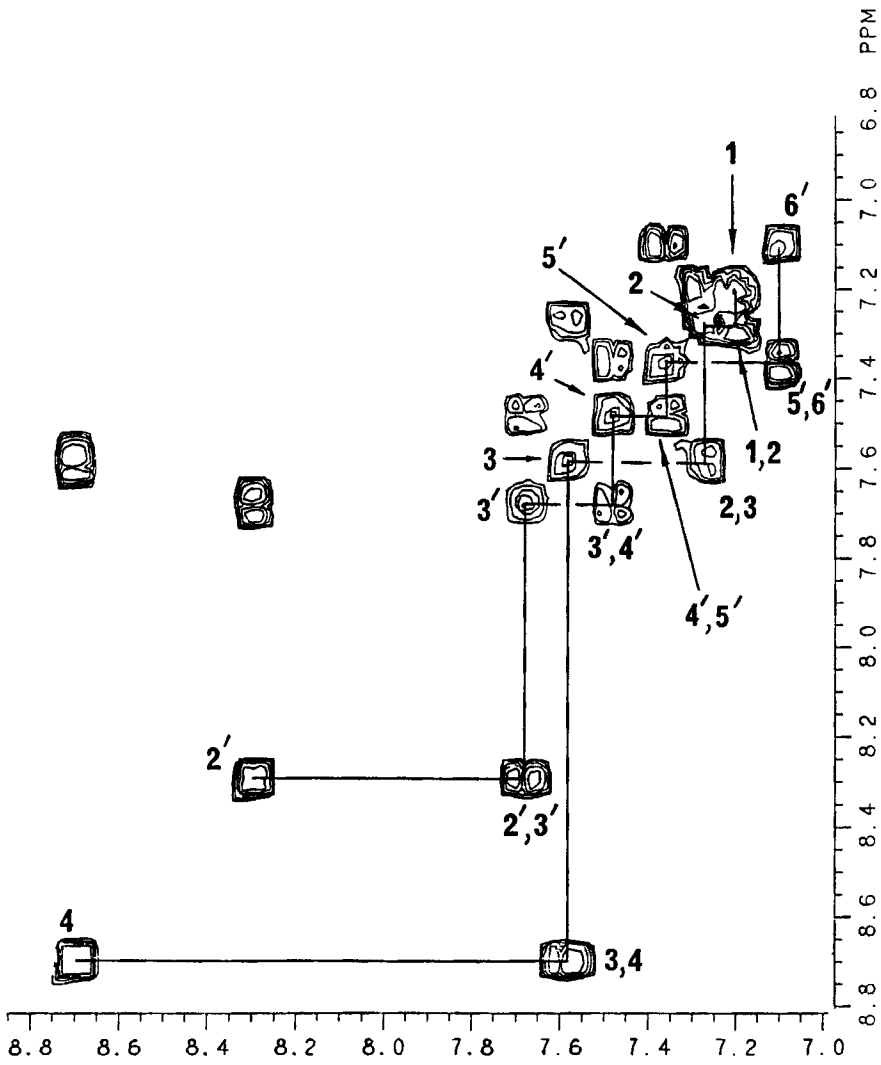

Figure 2. Two-dimensional homonuclear chemical shift correlation spectrum ("COSY") for the aryl region of the adduct, 3. Crosspeak correlations of vicinal couplings are indicated. With a more sensitive contour level setting (not shown), weak additional crosspeaks are seen for the ^4J H-2/4 and H-2'/6' correlations (see Results and Discussion).

Table 1. ^1H Assignments for Phencyclone - Benzoquinone Adduct in $CDCl_3$

Nucleus	δ (ppm) and J (Hz)[b]	Approx. Multiplicity [a]
1,8	7.19, J ~ 7.8	d
2,7	7.27, J ~ 7.3	t
3,6	7.58, J = 7.61	t
4,5	8.69, J = 8.39	d
2'	8.29, J = 7.58	d
3'	7.67, J = 7.60	t
4'	7.48, J = 7.40	t
5'	7.36, J = 7.55	t
6'	7.09, J = 7.97	d
HC=CH vinyl	5.75	s
HC(sp^3)	4.60	s

Notes a) Multiplicity: s(singlet), d(doublet), t(triplet);
b) Values of J estimated by difference from tables of peak frequencies.

location within the shielding cone of the bridgehead phenyl; in phenanthrene itself, in CCl_4, H-1 resonates at 7.80 ppm. The remaining five aryl signals of the bridgehead phenyls can be mapped out and assigned if H-2' is rationalized as being deshielded by proximity to, and near coplanarity with, the carbonyl. (Positioning the phenyls in this way would reduce repulsions with H-1,8 of the phenanthrene moiety). Carbonyl anisotropy has been discussed (12,13). The relative shifts of the four-proton series of the phenanthrene moiety of 3 and the five-proton set from the phenyl groups is similar to the relative shift sequences reported earlier for the phencyclone-norbornadiene adduct (2). The full assignments for 3 are summarized in Table 1. The leaning between the H-1 doublet and the H-2 triplet signals is consistent with the small magnitude of the chemical shift differences relative to the coupling constant, i.e., the presence of some second order effects.

CONCLUSIONS

The 300 MHz 1D ^1H and 2D COSY spectra for the phencyclone - p-benzoquinone adduct demonstrate hindered rotation about the $C(sp^3)$-$C(sp^2)$ bonds to the bridgehead unsubstituted phenyl groups at ambient temperatures. Full ^1H assignments have been made. Further studies are underway examining ^{13}C NMR of this and related hindered adducts.

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