Iodide has an immeasurably small permeation of the bilayer[7] and is able to discriminate between molecules free in solution from those located in the interior of the membrane. While camptothecin free in solution was quenched readily by iodide ($V = 1.8\ M^{-1}$; $K_{SV} = 44.3\ M^{-1}$), drug bound to DMPC membranes was much more difficult to quench ($V = 0\ M^{-1}$; $K_{SV} = 6.2\ M^{-1}$). Membrane-bound drug is thus much less accessible to quenching by iodide, presumably because the fluorochrome locates deep with the bilayer.

In summary, the important anticancer drug camptothecin has been shown here to be stable when harbored within liposomal bilayers of DMPC and DMPG. Because liposomes have been shown to be useful clinically in the delivery of other anticancer drugs such as doxorubicin, daunorubicin, and *cis*-platinum complexes (see refs 8–10 and references therein), and because liposome suspensions stabilize the pharmacologically active form of camptothecin, liposomal drug delivery systems may be of potential utility for introducing camptothecin (or related lipophilic analogues) to cancer victims. Studies of such formulations in experimental models are presently in progress.

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Geometry and Dynamics of Benzene Chemisorbed on a Pt/η-Al_2O_3 Catalyst: A ^{13}C Dipolar NMR Study

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Received June 4, 1992

It has been suggested from infrared investigations of benzene chemisorbed on alumina-supported platinum catalysts that the symmetry of the molecule is C_{3v}.[1,2] This result was found to be consistent with earlier infrared studies of benzene adsorbed on a Pt(111) single-crystal surface,[3] in which a C_{3v} symmetry was also assigned.[4] Since molecular distortion may be a precursor to catalytic activity, and since highly disperse metal-supported particles may result in an increase of reactivity in structure-sensitive processes involving carbon–carbon bonds,[5] the measurements reported in this communication were performed using 95%-disperse Pt/η-Al_2O_3. Given that infrared studies provide only indirect information about a possible alternation of short and long C–C bond lengths, a direct NMR determination of the C–C distances would constitute a more stringent test of such a distortion. We report here the results of a dipolar NMR study which indicates the absence of significant distortion of benzene chemisorbed on highly disperse Pt/η-Al_2O_3 as well as rapid ring reorientation at temperatures as low as 6 K.

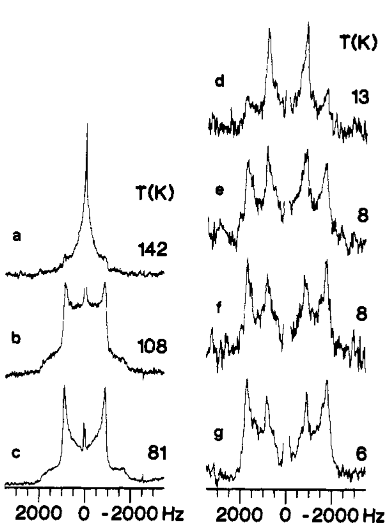

Figure 1. ^{13}C spectra of doubly-labeled benzene (1,2-$^{13}C_2$) chemisorbed on Pt/η-Al_2O_3 obtained at 15 MHz (1.4 T) using a Carr–Purcell–Meiboom–Gill (CPMG) pulse sequence with π pulses of width 9.6 μs (B_{1C} = 4.86 mT) and 15.4% rf duty factor. The narrow central peak cropped for clarity in the spectra shown in Figure 1b–g is partially due to spin-locking by the average rf field.

Nutation NMR spectroscopy[5] is especially suited for measuring interatomic distances in orientationally disordered solids and has been used to confirm bond alternation in *trans*-polyacetylene.[6] In that case, a superposition of two Pake doublet patterns permitted unambiguous confirmation of two C–C bond lengths. The Pake doublet splitting is proportional to the inverse third power of the ^{13}C–^{13}C internuclear distance and is the parameter used to measure bond lengths in this experiment.[5] In this work, we used the Carr–Purcell–Meiboom–Gill (CPMG) sequence,[7] which in principle offers twice the spectral resolution of a nutation experiment and thus a better chance of detecting two nearly equal bond lengths. We recently showed theoretically as well as experimentally that the Pake splitting measured using the CPMG pulse sequence scales linearly with the radio frequency (rf) duty factor and that appropriate extrapolation of a plot of doublet splitting versus duty factor yields C–C distances accurate to ~1%.[8]

The ^{13}C CPMG spectra of benzene-$^{13}C_2$ chemisorbed on Pt/η-Al_2O_3 obtained with cross polarization and proton decoupling[5] are shown in Figure 1.[9] The spectra change significantly with temperature, indicating dynamical behavior which is very different from what is observed in bulk solid benzene. In the latter at temperatures >90 K, the molecule is known to reorient rapidly about the hexad axis, and the doublet splitting should be reduced to one-half the rigid-lattice value.[10] However, as Figure 1 shows,

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(9) The 0.2-g sample contained 5 wt % platinum, as determined by X-ray fluorescence spectroscopy. The catalyst was prepared from chloroplatinic acid by reduction in H_2 at 593 K for 2 h, followed by outgassing for 3 h at the same temperature. Subsequently it was cooled and outgassed at 298 K for 2 h. The catalyst thus activated was then equilibrated with doubly-^{13}C-labeled benzene (benzene-*1,2*-$^{13}C_2$ from Isotech) at ambient temperature. The sample was then outgassed at 298 K for 6 h. This procedure leaves benzene molecules chemisorbed on the Pt surface, removing most of the physisorbed material, see: ref 1 and Tirendi, C. F.; Mills, G. A.; Dybowski, C. R. *J. Phys. Chem.* **1984**, *88*, 5765. The N_2 BET surface area of the catalyst before reduction was 179 m^2/g. The amount of benzene chemisorbed under these conditions, as determined by uptake measurements, was estimated to be 0.11 mmol of benzene per gram of catalyst. The dispersion of the Pt as measured by hydrogen uptake experiments is high, ~95%.

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for benzene chemisorbed on 95%-disperse $Pt/\eta\text{-}Al_2O_3$, a doublet indistinguishable from that observed in bulk benzene at temperatures >90 K (where rapid reorientation prevails) is observed at 80 K. At temperatures above 80 K (Figure 1a,b), an initially broad central component becomes apparent and grows in at the expense of the Pake doublet pattern. The spectrum becomes a single line at 160 K and rapidly narrows at higher temperature. This motional behavior has also been observed in a recent deuterium NMR study over a higher temperature range ($T > 75$ K) of a monolayer of benzene adsorbed on $Pt/\eta\text{-}Al_2O_3$ and has been attributed to fluctuations of the direction of the hexad rotational axis.[11,12]

In order to determine the carbon–carbon bond length, we measured the doublet splitting at 80 K over a wide range of rf duty factors for benzene-*1,2*-$^{13}C_2$ in the catalyst sample and found a C–C distance of 1.42 Å (uncorrected for vibrational motion[13]), the same result obtained for doubly-^{13}C-labeled benzene diluted in benzene with ^{13}C in natural abundance. This value is slightly larger than the 1.398 Å C–C distance in crystalline benzene determined by neutron diffraction,[14] but the difference may be accounted for in large part by a vibrational correction to the NMR splitting.

At temperatures below 80 K (Figure 1d–g), outer peaks appear with twice the splitting of the doublet observed at 80 K. This pair of doublets cannot be due to distorted benzene molecules with C–C bond lengths of 1.42 and 1.80 Å (i.e., $2^{1/3} \times 1.42$ Å). If this were the case, the intensities of the two doublets would be equal under all experimental conditions since polarization of the benzene protons, which determines the intensity of the signal, is independent of the distance between ^{13}C spins. The intensity behavior we observe is completely different, as shown in Figure 1e–g. When the recycle delay time is increased at constant temperature (Figure 1e,f), the relative intensity of the outer doublet increases, indicating a longer relaxation time for ^{13}C spins responsible for the larger splitting. This is consistent with assignment of the outer doublet to benzene rings moving slowly on the NMR time scale ($\sim 10^{-4}$ s). Moreover, as the temperature is lowered and the recycle delay time is kept constant (Figure 1e,g), the relatively intensity of the outer doublet again increases, indicating that the fractional number of static molecules is increasing. We conclude from both of these results that the inner and outer doublets arise from molecules on different sites which are rapidly reorientating or are static, a conclusion consistent with the 2:1 ratio of the splittings.

The observation of a single Pake doublet at 80 K does not rule out the possibility of a thermally-induced rotational average of two bond lengths with an average C–C distance of 1.42 Å. However, the single outer doublet observed at 6 K (Figure 1g), corresponding to static molecules, rules out that possibility and constitutes convincing evidence for the absence of such a distortion of the benzene ring in these samples.

We conclude that a distorted structure for benzene chemisorbed on a highly disperse $Pt/\eta\text{-}Al_2O_3$ catalyst, involving long and short C–C bonds, is not consistent with our experimental results. Although a rapid equilibration of structures of lower symmetry not involving a rotation of the whole molecule cannot be ruled out, some restrictions are suggested by our data. For example, the possibility of two C–C bonds with an average length considerably greater than that in bulk benzene as proposed for benzene co-adsorbed with CO on Pt(111)[15] would not be in agreement with our experimental results. The motional behavior of benzene chemisorbed on highly disperse $Pt/\eta\text{-}Al_2O_3$ is drastically different from that of bulk benzene, with rapid motion on the NMR time scale still present at temperatures even close to liquid helium.[16]

Acknowledgment. The authors especially thank R. D. Kendrick for assistance with the instrumentation to make Carr–Purcell measurements and Kurt Zilm and Nazeer Bhore for helpful discussions. They are also grateful to D. Neiman (IBM) for TEM studies of the Pt particles. Partial funding for this project was provided by IBM Brazil (M.E.), by the National Science Foundation (Grant No. CHE-9013926), and by the sponsors of the Center of Catalytic Science and Technology.

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Triple-Helix Formation by Oligodeoxynucleotides Containing the Carbocyclic Analogs of Thymidine and 5-Methyl-2′-deoxycytidine

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Received July 15, 1992

Sequence specific triple-helix formation of an oligodeoxynucleotide (ODN), via the parallel binding motif, requires recognition of 2′-deoxyadenosine by thymidine and recognition of 2′-deoxyguanosine (dG) by 2′-deoxycytidine.[1,2] Recognition of dG is complicated by the need to protonate the N-3 of the cytosine nucleobase to form a hydrogen bond with the N-7 of the guanine heterocycle.[3] 5-Methyl-2′-deoxycytidine has been shown to be a useful substitute for 2′-deoxycytidine,[4] and while it extends the pH range of triple-helix formation, protonation at physiological pH of this heterocycle is still problematic. A recent approach to overcome this problem has been the introduction of analogs which emulate the hydrogen-bonding face of a N-3-protonated cytosine without the need for protonation.[5] Another approach is to increase the pK_a of the 2′-deoxycytidine nucleobase and therefore facilitate protonation at neutral pH, but no analog of this type has been introduced. Formation of double-helix structures with the carbocyclic analog of polythymidylic acid have been reported,[6,7] but no triple-helix complexes were demonstrated. Reported herein

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