Experimental Determination of the Antiaromaticity of Cyclobutadiene

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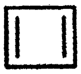
Photoacoustic calorimetry was used to quantify the antiaromaticity of 1,3-cyclobutadiene (CBD) by measuring the heat release accompanying its formation via photofragmentation of a polycyclic precursor. In combination with quantum yield measurements and thermochemical calculations, this measurement provides an enthalpy of formation for CBD of 114 ± 11 (2σ) kilocalories per mole (kcal/mol). The extraordinary reactivity of this prototypical antiaromatic hydrocarbon had previously made its heat of formation inaccessible except by theoretical calculations. Relative to a hypothetical strainless, conjugated diene reference, CBD is destabilized by a total of 87 kcal/mol, 32 kcal/mol of which can be attributed to ring strain and 55 kcal/mol to antiaromaticity (compared with 21 kcal/mol for the aromatic stabilization of benzene). Relative to a reference with isolated double bonds, CBD's antiaromaticity is 48 kcal/mol (compared with 32 kcal/mol for the aromaticity of benzene).

Aromaticity is one of the most widely recognized concepts of organic chemistry. To chemists, the term implies special thermodynamic stability, lack of characteristic alkene reactivity, absence of (or diminished) bond length alternation, and diamagnetic anisotropy ("aromatic ring current") (*1*). In the 1930s Hückel recognized the relation between the stability of aromatic compounds and the number of electrons in the cyclic, conjugated π system (*2*). Those with $4n + 2$ π-electrons, called aromatic, were predicted to be substantially more stable than those with $4n$ π-electrons ($n = 0, 1, 2, \ldots$). Members of the latter class, typified by 1,3-cyclobutadiene (CBD), were later called "antiaromatic" (*3*) because of their extraordinary instability, manifested by high reactivity that made them unusually difficult to prepare and isolate (*4*).

Not surprisingly, CBD has attracted intense theoretical interest, and most electronic structure calculations over the past 25 years have found π-system destabilizations of 30 to 60 kcal/mol (*5–11*). In an attempt to quantify CBD's destabilization experimentally, Breslow and co-workers performed a series of electrochemical and acidity measurements on highly substituted compounds containing the CBD moiety. These studies placed a lower limit of ~15 kcal/mol on the antiaromaticity of CBD (*12*), and later kinetic and electrochemical studies supported this estimate (*13, 14*). However, such measurements on the parent hydrocarbon are precluded by its extreme reactivity. For the same reason, the usual techniques of reaction calorimetry also cannot be applied.



Scheme 1. 1,3-Cyclobutadiene (CBD).

Experimental approach. We used photoacoustic calorimetry (PAC) to measure the enthalpy change accompanying the formation of CBD by pulsed-laser photolysis. Combining this enthalpy change with the heats of formation of the photochemical reactant and by-products—estimated from experimental data with the aid of semiempirical electronic structure calculations—provides the enthalpy of formation of CBD. Estimating CBD's antiaromaticity requires comparison of its heat of formation with that of a hypothetical reference, as well as subtraction of the angle strain of the four-membered ring, both of which are subject to interpretation.

PAC (*15*) is uniquely suited to acquiring energetic information for short-lived molecules like CBD. The reaction of interest is initiated by a nanosecond laser pulse, and the released heat causes an expansion of the irradiated region of the solution (changes in molecular volume can also contribute to this). The resulting pressure pulse is detected by an acoustic transducer as an oscillating voltage signal. Heat released on a time scale of a few nanoseconds or less—much faster than the frequency of our 0.25-MHz transducer—produces a signal whose amplitude is directly proportional to the amount of heat released. Such heat depositions can be quantified by simply comparing the PAC signal amplitude to that of a suitable standard. In the event that the measured heat release arises from two or more simultaneous processes, separating the enthalpy changes requires knowledge of photochemical and photophysical quantum yields. Heat released on time scales ranging from a few nanoseconds to several microseconds also causes a frequency shift in the transducer signal, from which both kinetic and thermodynamic information can be extracted (*15*). Any heat released on a time scale longer than ~10 μs is effectively invisible.

Our experiment required a photochemical CBD precursor that could reasonably be expected to provide CBD with high quantum efficiency, is stable at or near room temperature, and has an enthalpy of formation that is known or can be estimated with confidence from experimental data. Of the known photochemical CBD precursors (*4*), precursor **P** (Fig. 1) best met our criteria (*16*).

Photochemistry. We synthesized **P** in eight steps from cyclooctatetraene, using a modification of the literature procedure (*17*). Upon photolysis at 266 nm, the expected [2 + 2] cycloreversion of **P** to CBD and phthalan (*16*) was accompanied by a (formal) electrocyclic ring opening to tetraene **T** (Fig. 1) (*18*). The quantum yield for cleavage to CBD and phthalan, Φ_c, was 0.33 ± 0.02, and that for electrocyclic ring opening to **T**, Φ_e, was 0.34 ± 0.04 (error limits reported here and throughout are 2σ) (*19*). Because we were unable to detect fluorescence from photoexcited **P** ($\Phi_f < 10^{-3}$) (*20*), we attribute its remaining relaxation pathway to nonradiative decay with a quantum yield, Φ_{nr}, of 0.33.

Photoacoustic calorimetry. Typical PAC waveforms (*21*) acquired by pulsed-laser irradiation of separate solutions of **P** and a calibrant, *o*-hydroxybenzophenone, which is known to release all the absorbed photon energy by nonradiative relaxation within ~1 ns (*22*), show no frequency shift of the **P** wave with respect to the calibration wave (Fig. 2), implying that the two photochemical pathways (Fig. 1) and nonradiative relaxation all occur within a few nanoseconds. Because the concentration of CBD produced within

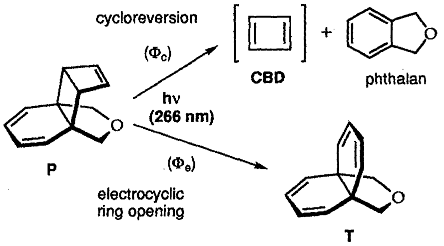


Fig. 1. Photochemistry of **P**. Quantum yields were determined using ferrioxalate actinometry, photolyzing to <5% conversion, and analyzing the product mixture by capillary GC (*39*).

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the irradiated volume is no more than 10^{-6} M, its dimerization (*4*) is expected to occur on a time scale of 100 μs or longer—too slow to be detected in our experiment.

To extract the thermal part of the PAC signal, it was necessary to account for the molecular expansion that accompanies the dissociation of **P** to CBD and phthalan. Volume changes in dissociative reactions typically range from 10 to 40 ml/mol (*23, 24*), and ignoring such effects can lead to significant errors in the reaction enthalpy change. The thermal and volume components can be separated by taking advantage of the dependence of the former on the thermal expansivity of the solvent, χ_s, as follows (*24*). The amplitude of the PAC signal is proportional to the total volume change, and the ratio of sample and calibrant signal amplitudes, *f*, is then simply the ratio of the volume changes. For **P**, the total volume change is the sum of that from thermal expansion, ΔV_{th}, and the reaction volume change, ΔV_{rxn}; the calibrant signal is entirely of thermal origin ($\Delta V_{th}'$). Thus,

$$f = (\Delta V_{th} + \Delta V_{rxn})/\Delta V_{th}' \qquad (1)$$

The thermal component, ΔV_{th}, is the product of the released heat, E_{th}, and the thermal expansivity of the solvent, χ_s. For the calibrant, E_{th} is just the photon energy, $E_{h\nu}$, so

$$f = (E_{th}/E_{h\nu}) + (\Delta V_{rxn}/E_{h\nu})(1/\chi_s) \qquad (2)$$

Within a series of *n*-alkane solvents, χ_s varies considerably, whereas the reaction enthalpies and quantum yields—and therefore E_{th}—can reasonably be expected to remain constant. A plot of *f* versus $1/\chi_s$ should therefore be linear and provide ΔV_{rxn} and E_{th} from the slope and intercept (*24*).

Values of *f* were measured in five alkane solvents as a function of $1/\chi_s$ (Fig. 3). From the slope and intercept of Fig. 3 and Eq. 2 (photon energy $E_{h\nu}$ = 107.5 kcal/mol), we find E_{th} = 110.5 ± 2.5 kcal/mol and ΔV_{rxn} = 16 ± 8 ml/mol. Because the intrinsic volume changes for nonradiative decay and for conversion of **P** to **T** should be nearly zero, ΔV_{rxn} can be attributed entirely to the cycloreversion pathway. Dividing by the quantum yield for this pathway ($\Delta V_{rxn}/\Phi_c$) provides a volume change for the dissociation of **P** to CBD and phthalan of 49 ± 25 ml/mol. Though large, this is not inconsistent with volume changes measured for similar reactions (*23, 24*).

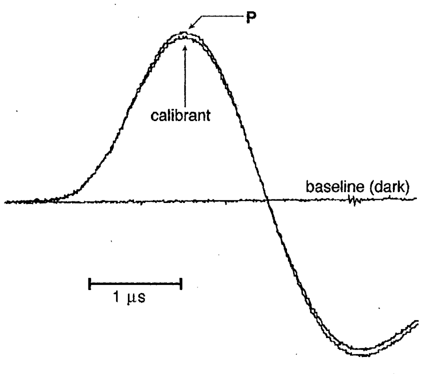

Fig. 2. PAC waveforms from irradiation (266 nm; ≤25 μJ per pulse; beam diameter ~2 mm; pulse width 8 to 9 ns) of separate solutions of **P** and *o*-hydroxybenzophenone in *n*-heptane, detected with a ~0.25-MHz acoustic transducer (*21*). The signals were corrected for small (<1%) differences in incident light intensity and absorbance.

Thermochemical calculations. The observed heat release, E_{th}, is the sum of those from the three thermal decay pathways (Fig. 4), which in turn are related to the reaction enthalpy changes for cycloreversion, ΔH_c, and electrocyclic ring opening, ΔH_e. Thus,

$$E_{th} = \Phi_{nr}E_{h\nu} + \Phi_c(E_{h\nu} - \Delta H_c) + \Phi_e(E_{h\nu} - \Delta H_e) \qquad (3)$$

Given that the quantum yields add to unity ($\Phi_{nr} = 1 - \Phi_c - \Phi_e$), this reduces to

$$E_{th} = E_{h\nu} - \Phi_c\Delta H_c - \Phi_e\Delta H_e \qquad (4)$$

Extracting the heat of formation of CBD from this equation requires formation enthalpies, ΔH_f°, for **P**, **T**, and phthalan (Fig. 1). The accuracy required, the nature of the compounds, and the quantities available made combustion calorimetry impractical. And although these compounds contain no particularly exotic structural features, their size and complexity precludes estimating their ΔH_f° values by a simple bond or group additivity scheme. Instead, we used a combination of experimental data and calculations on macroincrementation (MI) reactions (*25*). The MI principle entails building the compound of interest by what are assumed to be thermoneutral swaps of structural units among closely related species with known ΔH_f° values (Fig. 5).

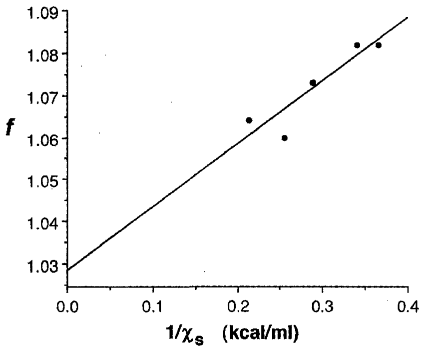

Fig. 3. Plot of *f* versus $1/\chi_s$ (kilocalories per milliliter) for photolysis of **P**. The solvents used were *n*-pentane, hexane, heptane, nonane, and decane (left to right). Least squares slope = 0.15 ± 0.08 ml/kcal; intercept = 1.028 ± 0.02. For maximal precision, the **P** and calibrant signal amplitudes (see Fig. 2) were plotted against incident laser energy (5 to 25 μJ per pulse) for each solvent, and the *f* value was obtained as the ratio of the slopes. The linearity of the plots ruled out interference from bimolecular reactions of CBD as well as any adventitious two-photon processes throughout the energy range used (*21*).

One could argue that the reactions in Fig. 5 should all be thermoneutral and derive the necessary ΔH_f° values purely from the available experimental data. However, we felt it important to allow for the possibility that the ΔH_f° values for **P** and **T** might be perturbed slightly by steric or electronic effects (or both) not present in the fragments. We therefore determined the ΔH° values for the MI reactions by AM1 and PM3 (*26*) semiempirical electronic structure calculations at MM3 (empirical force field)–optimized geometries (*27*) (Table 1). The reactions were designed to minimize any inherent computational errors associated with specific structural features (*28*). As expected, the deviations from thermoneutrality are small (Table 1).

Combining the experimental ΔH_f° values (Fig. 5) with the calculated ΔH° values (Table 1) provides the required ΔH_f° values. Reaction 1 in Fig. 5 yields $\Delta H_f^\circ(\mathbf{P})$ = 81 ± 5 kcal/mol. Reaction 2 yields $\Delta H_f^\circ(\mathbf{T})$ = 45 ± 6 kcal/mol; however, rather than amplify the errors by calculating ΔH_e° from these two values, we obtain a better estimate from reaction 3, ΔH_e° ($\mathbf{P} \rightarrow \mathbf{T}$) = −33 ± 4 kcal/mol. This agrees with the difference in the ΔH_f° values of **P** and **T** from reactions 1 and 2, −36 ± 8 kcal/mol. Reaction 4 yields ΔH_f°(phthalan) = −8.4 ± 2.3 kcal/mol (*29*).

Heat of formation of CBD. The measured quantum yields, $E_{h\nu}$, E_{th} from PAC, and the calculated ΔH_e° together provide ΔH_c = 25 ± 10 kcal/mol from Eq. 4. The heat of formation of CBD is then given by

$$\Delta H_f(\mathrm{CBD}) = \Delta H_c + \Delta H_f(\mathbf{P}) - \Delta H_f(\mathrm{phthalan}) \qquad (5)$$

Using the value for ΔH_c and the ΔH_f° values determined above, Eq. 5 gives ΔH_f(CBD) = 114 ± 11 kcal/mol.

Most early attempts to calculate CBD's

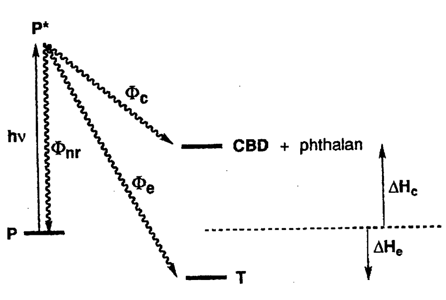

Fig. 4. Enthalpy diagram for photolysis of **P**. Excitation of **P** at 266 nm ($E_{h\nu}$ = 107.5 kcal/mol) produces an upper vibrational level of the excited singlet, **P***; fast vibrational relaxation cannot be distinguished from the other decay pathways. ΔH_c and ΔH_e are the enthalpy changes for cleavage and electrocyclic ring opening, respectively (see Fig. 1).

enthalpy of formation by semiempirical methods gave values ranging from 90 to 95 kcal/mol (*5*). Ab initio calculations have provided estimates of 103 to 114 kcal/mol, the most recent ranging from 103 to 107 kcal/mol (*6–8*). Presumably the best theoretical estimates come from G2 calculations, 100 to 102 kcal/mol (*9, 10*), or from density functional calculations, 106 kcal/mol (*11*). Although our value of 114 ± 11 kcal/mol clearly favors the higher end of the ab initio range, in view of our error limits, we cannot discount the lower ab initio or G2 values. Our disagreement with the G2 values is surprising, given the success of the method in reproducing experimental ΔH° values for reactions of small, strained organic molecules (*10, 30*). However, in the absence of experimental benchmark data for other molecules having exotic π systems (especially those with low-lying excited states), it is difficult to know what level of accuracy to expect for a species like CBD.

Antiaromaticity. We can quantify CBD's antiaromaticity by assessing how much less stable it is than a hypothetical version with simple conjugated or isolated π bonds, but lacking the special cyclic delocalization. Although crude from a theoretical standpoint, such an analysis is helpful in putting our experimental ΔH_f into chemically meaningful terms. The simplest reference structure consists of four CH units of an unstrained, conjugated polyene, and has a ΔH_f° of 27 kcal/mol (*31*). CBD is destabilized by 87 ± 11 kcal/mol relative to this "conjugated π-bond reference."

The total destabilization of CBD is not entirely due to antiaromaticity, but results in part from ring strain. We estimate the strain energy of CBD to be 32 ± 2 kcal/mol (*8*) from the fact that strain energies of four-membered-ring hydrocarbons increase by ~1.6 kcal/mol with each formal replacement of an sp^3 with an sp^2 ring carbon (*32*). Subtracting this strain energy yields a value of 55 ± 11 kcal/mol for the antiaromatic destabilization of CBD, relative to a conjugated reference (*33*). Essentially the same value can be derived (after subtracting the ring strain) from reaction 5 (Fig. 6), which is called homodesmotic (*34*) because it preserves the numbers of CC and CH bonds as well as their local bonding environments. In effect, this reaction measures the energetic cost of building CBD from the central =CH–CH= units of two butadienes. The analogous stabilization of benzene, derived by either the group increment or the homodesmotic procedure, is 21 kcal/mol. On a per-electron basis, the resonance stabilization energies of benzene and CBD are, respectively, 3.5 and −14 ± 3 kcal/mol.

Comparison of CBD with a nonconjugated reference is equivalent to determining a Hückel resonance energy. Creating the reference structure from four simple alkene carbons (*31*), we find a total destabilization of 80 kcal/mol, and thus an antiaromaticity of 48 ± 11 kcal/mol (the corresponding stabilization of benzene is 32 kcal/mol). This is equivalent to calculating a resonance energy from reaction 6 (Fig. 6), which is classified as isodesmic (*35*) because it preserves the numbers of CC and CH bonds. However, both this and the group-increment approach implicitly ignore the trade of a $C(sp^2)-C(sp^3)$ bond in the reference (alkene) for a $C(sp^2)-C(sp^2)$ bond in the cyclic polyene (*36*). Nevertheless, such an approximation clearly demonstrates that cyclic delocalization of its π electrons makes CBD much less stable than it would be if it had completely noninteracting π bonds. This has been called "absolute" antiaromaticity (as opposed to "relative" antiaromaticity versus a delocalized reference) (*14*).

Another interesting comparison that can be made within this framework is illustrated by the isodesmic reactions 7 and 8 (Fig. 6) for formation of CBD and benzene. Reaction 8 combines Kistiakowsky's famous measurements of the heats of hydrogenation of benzene and cyclohexene (*37*). Allowing for the small decrease in ring strain from 1.4 kcal/mol for cyclohexene (*31*) to zero for the products, the resonance energy of benzene is 32 kcal/mol, as calculated above. Assuming no change in strain energy (see above), the extreme endothermicity for the corresponding reaction of CBD (reaction 7) reconfirms the pronounced destabilization caused by its antiaromatic cycle.

Because the cyclic π component of the total energy is, of course, not directly measurable, any attempt to quantify aromaticity or antiaromaticity is subject to the reference chosen. Indeed, this is the source of much of the disagreement in the literature. Our subtraction of ring strain is also somewhat artificial, in that it ignores the extra bond-length distortion of the σ framework caused by the antiaromatic π system (*38*). Thus, our calculated antiaromaticity cannot be interpreted as localized to the π system. Nonetheless, with any reasonable choice of reference structure and ring strain, even a ΔH_f value on the lower end of our error range shows that CBD is dramatically destabilized by its four π-electron cycle. Although a

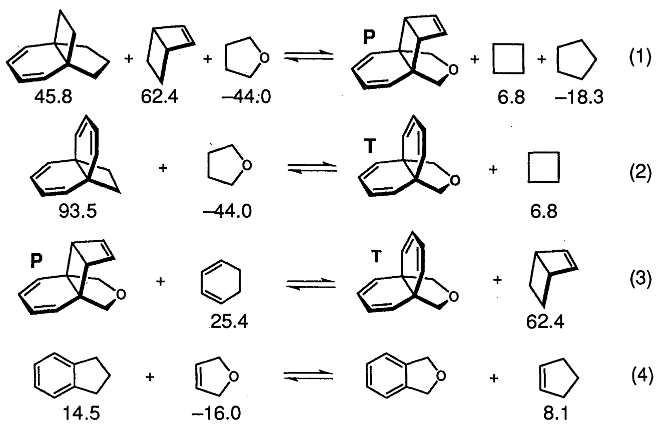

Fig. 5. Macroincrementation reactions used to calculate ΔH_f° values for **P** (reaction 1), **T** (reactions 2 and 3), and phthalan (reaction 4). Experimental ΔH_f° values given are in kilocalories per mole (*41, 42*).

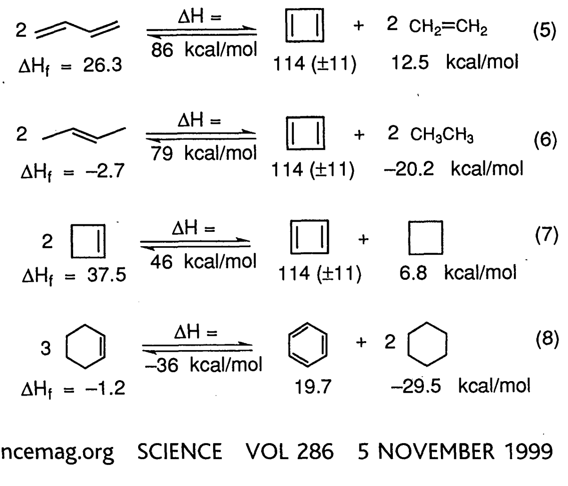

Fig. 6. Homodesmotic (*34*) (reaction 5) and isodesmic (*35*) (reactions 6 to 8) reactions used to evaluate the antiaromaticity of CBD. Experimental ΔH_f° values were taken from (*42*).

Table 1. Calculated reaction enthalpy changes for the macroincrementation reactions in Fig. 5.

Reaction	ΔH° (kcal/mol)		
	MM3	AM1//MM3*	PM3//MM3*
1	−1.47	5.21	5.39
2	0.56	2.61	2.07
3	−2.27	4.17	3.96
4	0.75	1.17	1.24

*From ΔH_f° values calculated by semiempirical methods at MM3-optimized geometries.

pronounced destabilization had long been evident from CBD's chemical behavior, it is gratifying to finally quantify its antiaromaticity by experimental measurement.

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18. The formation of **T** (12-oxatricyclo[4.4.3.0^{1,6}]trideca-2,4,7,9-tetraene) was established by GC–mass spectrometry (electron impact), mass-charge ratio *m/z* 172 (M^+), and ^{1}H nuclear magnetic resonance (NMR) δ 5.65 (8H, m, vinylic), 3.96 (4H, s, methylene) [J. Altman, E. Babad, J. Pucknat, N. Reshef, D. Ginsburg, *Tetrahedron* **24**, 975 (1968); J. J. Bloomfield and W. T. Quinlin, *J. Am. Chem. Soc.* **86**, 2738 (1964)]. The photolysis product was identical by GC (*39*) and NMR to an authentic sample of **T** produced by thermolysis of **P** [CD_3CN, 150°C, 1 to 2 hours; H.-D. Martin and M. Hekman, *Chimia* **28**, 12 (1974)].
19. Quantum yields were measured according to literature methods [C. G. Hatchard and C. A. Parker, *Proc. R. Soc. London Ser. A* **235**, 518 (1956); W. D. Bowman and J. N. Demas, *J. Phys. Chem.* **80**, 2434 (1976); S. L. Murov, I. Carmichael, G. L. Hug, *Handbook of Photochemistry* (Dekker, New York, ed. 2, 1993), p. 299]. We directed 266-nm laser light (*21*) into a sample cuvette containing a heptane solution of **P** and a long-chain alkane as an internal GC standard (*39*); 15 to 20% of the light was split off using a quartz flat and directed into a matched reference cuvette containing the ferrioxalate solution. Our final quantum yields include a small (<1%) correction for absorption by **T**. For additional experimental details, see (*40*).
20. We detected no fluorescence upon excitation of **P** at 260 nm in a fluorimeter. On the basis of the emission intensity of a naphthalene solution having the same absorbance, we estimate the fluorescence quantum yield to be $<10^{-3}$.
21. Our photoacoustic apparatus is similar to the one described previously [J. E. Rudzki, J. L. Goodman, K. S. Peters, *J. Am. Chem. Soc.* **107**, 7849 (1985)]. The frequency-quadrupled output of a Q-switched Quanta Ray DCR1 Nd:YAG laser was directed through a 2-mm pinhole and into the sample. A quartz flat reflected 15 to 20% of the light as a reference. To measure the sample absorbance and monitor the laser energy, we measured the transmitted and reference light intensities for both sample solution and pure solvent with Laser Precision RjP-735 pyroelectric energy probes connected to an Rj-7100 ratiometer. The sample cell was a quartz cuvette housed in an aluminum block. The output of a homemade lead-zirconate-titanate (PZT) piezoelectric transducer, clamped against the cuvette, was amplified with a Panametrics 5676 ultrasonic preamplifier and digitized using a 200-MHz Tektronix TDS 350 digital oscilloscope. Data were gathered and analyzed by a Power Macintosh 7100/80 computer equipped with a National Instruments interface board (GPIB). Alkane solvents were purified (washed with aq. H_2SO_4, $KMnO_4$; distilled from $LiAlH_4$) as necessary so that they gave no detectable PAC signal. Solutions of *o*-hydroxybenzophenone and **P** were prepared with 266-nm absorbances in the range of 0.1 to 0.3 and matched to within 1%. Solutions of **P** were deoxygenated thoroughly with a stream of N_2. Sample and calibrant PAC waves were acquired by averaging the results of 50 laser pulses and subtracting the (dark) baseline. Amplitudes were measured at the first crest (Fig. 2) after small absorbance and incident energy corrections.
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28. Applying this procedure to related reactions with known ΔH° values reproduced these values to within ~2 kcal/mol (*41*).
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