Organometallics **2009,** *28,* 3303–3306

Notes

Kinetics of Reductive Elimination from Platinum(IV) as a Probe for Nonthermal Effects in Microwave-Heated Reactions

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Received September 14, 2008

*Summary: To test the hypothesis that microwave heating effects the nonthermal acceleration of reactions proceeding through polarized transition states, the kinetics and product ratios of the strongly medium-dependent thermolyses of $(DPPE)Pt(CH_3)_3O_2CCH_3$ (**1**) under microwave and conventional heating conditions were compared. No evidence of nonthermal effects was observed in this reaction, although failure to apply stirring resulted in significant differences in the thermal conditions and reaction rates achieved by the two heating methods.*

As microwave heating technology has matured over the last 20 years, the technique has proven to be a useful tool for the enhancement of many chemical reactions.[1−4] Although microwave reactors have been applied most enthusiastically to organic synthesis, they have also been employed in a variety of inorganic and organometallic systems,[5−8] and transition metal catalysis features prominently among the success stories in the field.[9,10] In many cases, the improvements conferred by microwaves are easily attributed to selective heating within heterogeneous mixtures, exceptionally rapid heating, or access to elevated temperatures facilitated by the microwave, but in other reactions the origins of the technique's evident benefits remain unclear.[11]

Some researchers have raised the intriguing possibility that in addition to heating reaction mixtures via dielectric loss, the microwave field may also interact with reagent molecules to accelerate reactions by other means.[11−13] Such nonthermal effects have been a subject of curiosity and controversy since early reports of microwave heating,[14,15] but this possibility was most thoroughly reviewed and framed as a hypothesis by Loupy and Perreux in a 2001 report.[16] Based on a survey of literature evidence, these authors proposed that nonthermal effects might result in the acceleration of reactions proceeding through transitions states of increased polarity and that these effects would be most pronounced when the reagents themselves (rather than the solvent) absorbed a large flux of microwave radiation. If valid, these oft-cited principles would be very useful in predicting which reactions may and may not stand to benefit from microwave heating.

Spurred by a desire to understand the origins of apparent microwave acceleration observed in our own laboratory,[17] we sought to test this hypothesis by comparing the microwave and oil-bath kinetics of a simple organometallic reaction likely, according to these two criteria, to exhibit nonthermal effects. Although a handful of recent studies have sought to assess the significance of such effects, these investigations have, with a few exceptions,[15,18,19] compared yield data. Kinetic parameters offer a more rigorous standard of comparison by which to evaluate suspected acceleration, and advances in microwave technology over the past few years now make possible the precise temperature control that meaningful studies of kinetics require. The demands of such a study called for a reaction possessing several characteristics: (1) a highly polarized rate-determining transition state; (2) a solvent with poor microwave absorptivity; (3) a nominally unimolecular, irreversible mechanism resulting in simple kinetic behavior; and (4) a slow reaction rate amenable to study by alternating microwave heating and concentration measurements.

These criteria led to the selection of the compound $(DPPE)Pt(CH_3)_3O_2CCH_3$ (**1**, DPPE = 1,2-bis(diphenylphosphino)ethane), which upon thermolysis undergoes reductive elimination to form C−C or C−O bonds at competitive rates (Scheme 1).[20,21] Goldberg and co-workers showed that this complex, like a variety of $(DPPE)Pt(CH_3)_3X$ analogues, decomposes by a

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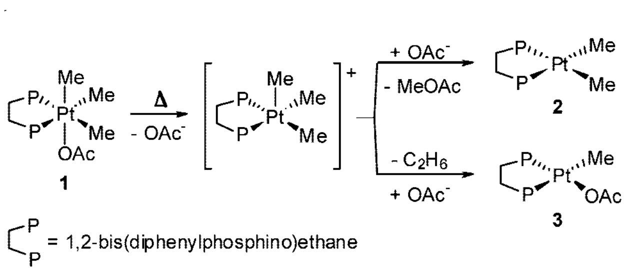
10.1021/om8008926 CCC: $40.75

Scheme 1. Thermolysis of (DPPE)Pt$(CH_3)_3O_2CCH_3$ (1)



mechanism involving initial dissociation of the acetate ligand to yield a five-coordinate platinum cation.[20] The resulting ions recombine in the transition state leading to C−O elimination, but remain separate prior to C−C elimination. As a result of both the ionic intermediate and the differences in the polarities of the product-forming transition states, the reaction exhibits a striking solvent effect: experiments in tetrahydrofuran or benzene yield 88−96% C−O elimination, and thermolyses in acetone or nitrobenzene yield almost exclusively ethane at an overall decomposition rate at least 50 times faster than that observed in THF. Both pathways are irreversible, and the overall process occurs with cleanly first-order kinetic behavior in THF, which is a poor microwave absorber with a tan(δ) value of only 0.047.[22] All these features render this system a very likely candidate to experience polarity-based nonthermal microwave effects, and a case in which these effects might be practically quantified by the magnitude of microwave-induced changes in both the rate and selectivity of the reaction. We thus set out to directly compare thermolysis reactions under otherwise identical microwave and conventional heating conditions, with the expectation that any nonthermal effects would accelerate the reaction and favor the more polarized C−C elimination pathway much as more polar solvents do.

Because of the poor microwave absorptivity of THF, high microwave powers (ca. 1200 W) were required to maintain reaction temperatures throughout most experiments. Comparisons of the temperature vs time profiles of mineral oil, anhydrous THF, and a 0.020 M (1.5 wt %) **1**/THF solution all heated at constant microwave power showed the reaction mixture to heat most quickly, confirming that microwave energy was absorbed primarily by the THF and also significantly by complex **1** itself (see Supporting Information). These conditions are thus consistent with the criteria laid out by other researchers as prerequisites for nonthermal microwave effects.

A total of 5 pairs of kinetic experiments, each set comprising microwave and conventional thermolyses of identical THF solutions of **1**, were monitored by ^{1}H NMR spectroscopy between heating periods over the course of 3 half-lives. The rate of each reaction consistently exhibited first-order dependence on [**1**], and products **2** and **3** were the only platinum-containing products observed (Figure 1). In each pair of experiments, which spanned a small range of temperatures, concentrations, and reaction volumes, the observed rate constants in microwave- and bath-heated samples were indistinguishable (Table 1). Results at 99 °C typically agreed closely with those previously reported for the complex, and variability was observed only between samples of starting material rather than between the two heating methods.[23]

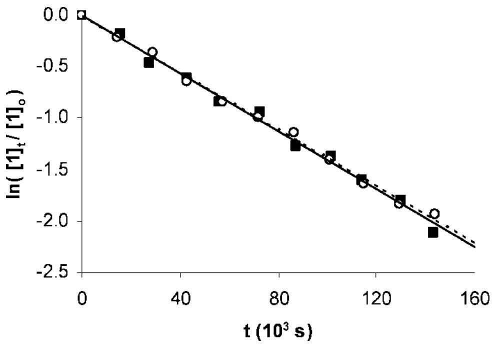


Figure 1. Plot of ln([**1**]$_t$/[**1**]$_o$) vs time for the stirred thermolyses of **1** in THF-d_8 under both microwave (○, • • • •) and oil-bath (■, —) heating conditions. Data correspond to entry 1 in Table 1.

Table 1. Observed Rate Constants and Selectivites for the Thermolyses of 1 by Microwave and Conventional Heating in THF-d_8

entry	T (°C)	conditions	microwave 10^5 k_{obs}/s^{-1}	oil bath 10^5 k_{obs}/s^{-1}
1	99	[a]	1.38	1.40
2	99	[b]	1.96	1.95
3	99	[c]	1.35	1.35
4	109	[d]	3.89	3.84
5	109	[e]	3.84	3.86

[a] 2.5 mL of 0.011 M **1** in a 3-cm-wide vessel. [b] 2.5 mL of 0.017 M **1** in a 2-cm wide vessel. [c] 1.5 mL of 0.031 M **1** in a 2-cm wide vessel. [d] 2.5 mL of 0.019 M **1** in a 3-cm wide vessel. [e] 7.5 mL of 0.011 M **1** in a 3-cm-wide vessel.

Table 2. Selectivities of the Thermolyses of 1 by Microwave and Conventional Heating[a]

entry	solvent	T (°C)	microwave % **2**	oil bath % **2**
1	THF-d_8	99	90	91
2	THF-d_8	99	86	84
3	THF-d_8	99	88	87
4	THF-d_8	109	78	79
5	THF-d_8	109	80	79
6	toluene	100	95	95
7[b]	$CDCl_3$	90	83	81
8[b]	CD_2Cl_2	70	17	18
9[b]	acetone	80	6	6
10	acetonitrile	70	<2	<2

[a] See Table 1 for specific conditions of entries 1−5. In entries 6−10, conditions were 2.0 mL of 0.0080 M **1** in a 3-cm-wide vessel except for entry 6, in which 0.020 M **1** was used. [b] In chlorinated solvents and in acetone, additional Pt(CH_3) resonances constituting <5% of total products were also observed.

Product ratios were also measured in these studies, and to extend the scope of selectivity data the relative quantities of products **2** and **3** were determined in thermolyses conducted in acetone, acetonitrile, chloroform, methylene chloride, and toluene under both oil-bath and microwave conditions (Table 2). These solvents represent the full range of the reaction's possible selectivity, varying from almost exclusive C−O elimination (toluene) to quantitative formation of ethane and **3** (acetonitrile). In all these experiments, the ratio between the reaction products showed no appreciable dependence on the heat source.

These data show no evidence of any nonthermal effect in this system, and given the very high microwave power applied and the sensitivity of the reaction to solvent polarity, this result

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(23) The original report of these reactions describes the use of polyvinylpyridine to scavenge acidic impurities that strongly affect rates; to avoid the potential for differential heating of phases in the microwave, this additive was not employed in these studies, and the rates reported here thus show some variance from one sample to another.

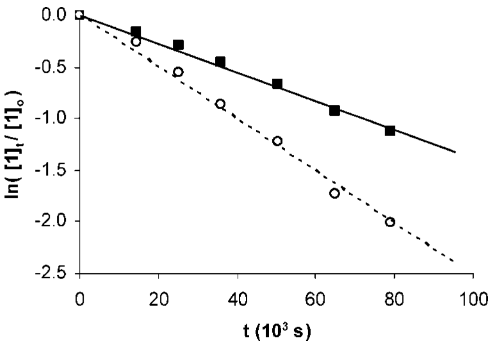

Figure 2. Plot of ln([**1**]$_t$/[**1**]$_o$) vs time for the *unstirred* thermolyses of **1** in THF-d_8 under both microwave (○, ••••) and oil-bath (■, —) heating conditions.

argues against the likelihood of polarity-based nonthermal microwave effects more generally. Other researchers have recently reported a similar absence of any nonthermal effects on the relative yields or rates of organic reactions heated by conventional and microwave equipment,[19,24,25] and this outcome is in agreement with those findings.

In addition to this result, this study also provided a cautionary example of how nonthermal effects may be incorrectly inferred from microwave heating results. In preliminary experiments, two pairs of kinetic runs were performed as described above, but without significant stirring of either reaction mixture. Interestingly, each of these experiments *did* result in significant differences between microwave and traditional heating conditions: the unstirred microwave reactions still exhibited consistently first-order behavior throughout monitoring, but proceeded with a higher rate constant, and with a higher fraction of C—C bond elimination, than their oil-bath counterparts (Figure 2). Both of these results would be consistent with the operation of a nonthermal acceleration particularly favoring the more polarized reaction mechanism to form **3**, but the outcomes of the stirred experiments illustrated in Figure 1 and Table 1 clearly demonstrate that this reaction is subject to no such effect. Temperature effects on the reaction pose an alternative explanation: both the product ratios and rate constants observed in unstirred reactions at 99 °C are consistent with a reaction occurring at a temperature closer to 105 °C.[26] Although the temperature was maintained at an average temperature of 99 °C at the internal fiber optic probe, the exponential rather than linear scaling of rate constants with temperature causes thermally heterogeneous mixtures to typically exhibit overall kinetic behavior more closely resembling that of their higher temperature regions. The altered rate constants and product ratios could thus be explained by the presence of higher temperature regions within the unstirred mixture. Such thermal gradients have recently been reported in other homogeneous microwave reactions,[24,27] and this result demonstrates that they may have noticeable consequences even in volumes as small as 2−3 mL.

This finding demonstrates that thermal differences even in small-scale homogeneous microwave systems may be unexpectedly significant, but that polarized transition states and high microwave power are insufficient conditions by which to predict any nonthermal effects. These results echo recent findings regarding microwave-assisted organic reactions and emphasize the caution with which apparent acceleration by microwave heating should be attributed to any factors more exotic than differences in the thermal conditions achieved by microwave and conventional heating.

Experimental Details

Materials and Methods. All starting materials were stored, dispensed, and manipulated in a N_2-filled inert atmosphere glovebox operating at or below 1 ppm O_2 and H_2O. All heating was conducted in closed vessels under air-free conditions. THF, THF-d_8, C_6D_6, and toluene were distilled under vacuum from purple Na/benzophenone ketyl before use. All other solvents were dried over 4 Å molecular sieves and vacuum transferred before use. *fac*-(DPPE)PtMe$_3$I was prepared by a literature method.[28] All other reagents were purchased from commercial suppliers and used as received. NMR spectra were recorded using a 300 MHz spectrometer, reported in ppm downfield from tetramethylsilane, and referenced to the chemical shift of residual solvent protons or to common external standards.

A 1600 W CEM MARS multimode instrument was used for all microwave heating, which was conducted at constant temperatures monitored and maintained by a fiber optic RTP-300 Plus probe immersed in the reaction mixture within a sapphire thermowell and calibrated to an oil bath at the desired reaction temperature. Each microwave reaction was conducted in a CEM GreenChem (85 mL) or GlassChem (25 mL) Pyrex vessel fitted with a thermowell, composite sleeve, and PFA Teflon cover. These vessels were held closed for the duration of the experiment by a polypropylene frame and/or screw assembly. Oil-bath heating was conducted in fully submereged Teflon-closed Pyrex tubes of similar dimensions (71 and 22 mL) submerged in a pre-equilibrated 1 L bath of stirred silicone oil heated by a thermocouple-controlled hot plate. The internal temperatures of reaction mixtures in oil-bath experiments were verified using the microwave's temperature sensor and found to match those of the oil-bath settings within the ±1 °C precision of the sensor. Microwave absorption by different materials was compared by alternately heating 3.0 mL each of mineral oil, pure THF, and 0.020 M **1** in THF with microwave heating at a constant power of 1600 W and monitoring the temperature over 10 min. These experiments showed the THF and THF solution of **1** to heat much more rapidly, confirming internal heating of the system. These data are included as a graph in the Supporting Information.

***fac*-(DPPE)Pt(CH$_3$)$_3$O$_2$CCH$_3$ (1).** This complex was prepared by modification of a literature method.[20] *fac*-(DPPE)PtMe$_3$I (0.945 g, 1.23 mmol) was suspended in 40 mL of toluene, AgOAc (0.207 g, 1.24 mmol) was added, and the resulting pale yellow suspension was stirred in the dark for 24 h at 20 °C. The resulting yellow-beige suspension was filtered through Celite, and the filtrate was evaporated to dryness *in vacuo*. The resulting light yellow foam was dissolved in THF, and this solution was allowed to stand at room temperature in ambient fluorescent light for 6 h, during which time it took on a darker, brownish color. This fine suspension was filtered twice through Celite to yield a clear, colorless solution that remained colorless on standing in the light and was layered with pentane and chilled to −35 °C. Blocky white crystals were isolated from this mixture after 48 h and further recrystallized from toluene and pentane at −35 °C to yield **1** as fine white crystals containing 1 equiv of toluene per formula unit (0.438 g, 45.1% overall yield). ^{1}H NMR (C_6D_6): δ 0.04 (t with ^{195}Pt satellites, 3H), 1.79 (t w/

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(26) In addition to the data already listed, a kinetic experiment at 89 °C was conducted to better correlate rate constant with temperature. These data also provided further confirmation of the reaction's dissociative mechanism, as the resulting Eyring plot indicated large positive $\Delta S^{\ddagger}$ and $\Delta H^{\ddagger}$ values. These data are included in the Supporting Information.

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^{195}Pt satellites, 6H), 1.83 (s, 3H), 2.5 (m, 2H), 3.3 (m, 2H), 6.9−7.3 (m, 12H), 7.7−7.8 (m, 8H); lit[20] 0.05, 1.80, 1.84, 2.5, 3.3, 6.9−7.3, 7.7−7.8 ppm. ^{31}P{^{1}H} NMR (C_6D_6): δ 23.1 ($^1J_{P-Pt} = 1150$ Hz); lit[20] 23.0 ($^1J_{P-Pt} = 1147$ Hz) ppm.

Thermolysis of 1: Rate Measurements. In a typical experiment, **1** (40.1 mg, 57.5 μmol), internal standard (1,3,5-trimethoxybenzene, 2.5 mg, 15 μmol), and THF-d_8 (5.0 mL) were combined, and the resulting solution was evenly divided between a microwave vessel and a glass reaction tube closed by a Teflon stopcock. Each vessel was equipped with a magnetic stir-bar, closed, and heated to 99 °C for 4 h by either microwave or oil bath. In microwave reactions an initial ramping time of ca. 7 min was observed, and the reaction temperature was subsequently maintained within a range of ±1 °C by a power of 1200−1400 W. The oil-bath temperature was also constant within ±1 °C. After heating, each reaction vessel was immediately chilled to −10 °C in a freezer. In an inert atmosphere glovebox, a sample of each reaction mixture was transferred to an NMR tube, and each sample was analyzed by ^{1}H NMR spectroscopy. NMR samples were then returned to their respective reaction mixtures, and the heating and analysis cycle was repeated at roughly 4 h intervals until less than 15% of starting material remained.

Product Ratios. The ratios of products **2** and **3**, when measured without the collection of full concentration vs time data, were determined by performing parallel heating experiments as described above. Mixtures were heated for a common duration to achieve 50−90% conversion and either analyzed directly by ^{1}H NMR or evaporated to dryness *in vacuo* and quantified in $CDCl_3$ solution.

Concentration Measurements. All concentrations were measured by comparison of ^{1}H NMR integrations of **1** (δ −0.42, t, 3H), **2** (δ 0.61, t, 6H), and **3** (δ 0.47, dd, 3H) to that of an internal standard such as trimethoxybenzene (δ 6.05, 3H). Due to overlap of the ^{195}Pt satellites of their Pt(CH_3) resonances, **2** and **3** were typically quantified by integration of their central Pt(CH_3) peaks and algebraic correction for the satellites that overlapped with those peaks. Alternatively, overlap was eliminated by phosphorus decoupling of ^{1}H NMR spectra, which caused all Pt(CH_3) resonances to appear as resolved singlets with satellites. The two approaches produced nearly identical data, and an example of each is included in the Supporting Information

Acknowledgment. The authors gratefully thank the ISU Faculty Research Committee for supporting this work with Research Grant 1003. C.K.L. and Z.H.P. also thank the ACS Project SEED for summer stipends.

Supporting Information Available: Kinetic plots for all experiments, microwave heating temperature profiles of control and reaction samples, details of concentration measurements, and a representative ^{1}H NMR spectrum. This material is available free of charge via the Internet at http://pubs.acs.org.

OM8008926