Scheme II

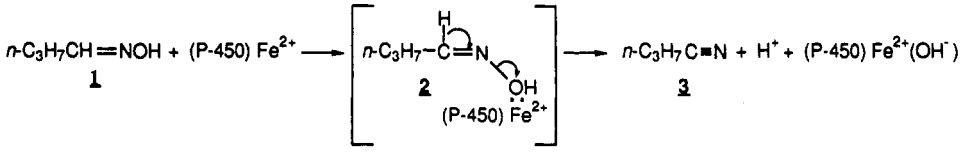

Table III. Conversion of *n*-Butyraldoxime (1) to Butyronitrile (3) Catalyzed by Sodium Dithionite (DT) Reduced Hematin under Anaerobic Conditions

Fe source (1.0 mM)	pH	N	butyronitrile (3) formed[a] (nmol/15 min)
hematin	6.0	6	<1
hematin	7.4	6	<1
hematin + DT	6.0	5	105 ± 5
hematin + DT	7.4	6	222 ± 8
$Fe_2(SO_4)_3$	6.0 (or 7.4)	3 (3)	<1
$FeSO_4$	6.0 (or 7.4)	3 (3)	<1

[a] Reaction mix containing 100 mM potassium phosphate buffer and an Fe source (as indicated) was preincubated for 5 min at 37 °C followed by the addition of sodium dithionite (DT; 10 μmol, where indicated) and 10 μmol of 1 in a total volume of 1.0 mL. After a 15-min incubation period under N_2, the reaction was stopped by the addition of 0.1 mL of 5.5 N $HClO_4$ and the samples were stored on ice until assayed by head space GC.

hematin (Fe^{2+}) also catalyzed this reaction, albeit at a rate of 0.04% of the NADPH-supported cytochrome P-450 reaction, based on nmol Fe. Hematin itself (Fe^{3+}), $Fe_2(SO_4)_3$, or $FeSO_4$ was ineffective in catalyzing this reaction (Table III). The difference spectra for 1 with Fe^{2+} cytochrome P-450 showed a trough at 411 nm, a characteristic of ligand binding to reduced cytochrome P-450,[11] and a peak at 444 nm demonstrating that substrate binding occurs with Fe^{2+} cytochrome P-450. The substrate binding spectra for 1 with Fe^{3+} cytochrome P-450 was reverse Type I.[12]

We envision this cytochrome P-450 catalyzed Beckmann-type dehydration to proceed via a mechanism involving the interaction of the oximino oxygen atom with ferrous iron of cytochrome P-450, as shown in Scheme II. The coordinated complex (hypothetical intermediate 2) provides the driving force for the elimination of H_2O from the oxime 1.

Although aldoximes are known to dehydrate to the corresponding nitriles under Beckmann conditions,[5] we are unaware of any aldoximes being converted to nitriles by cytochrome P-450. In the present case, 1 was converted to 3 with the latter nitrile product retaining the carbon skeleton of the original oxime. Highly branched ketoximes give abnormal Beckmann products, *including nitriles*, accompanied by fission of the carbon skeleton.[5] We present our preliminary observations at this time to encourage further studies (by others) with additional oxime substrates using purified isoforms of cytochrome P-450 and/or model cytochrome P-450 mimics.

Neither *n*-butyronitrile (3) nor nitrobutane (4) inhibited yeast AlDH directly or when coupled with the cytochrome P-450/NADPH system. These results suggest that another oxidative bioactivation pathway must exist for the generation of the active AlDH inhibitor from 1. We are presently attempting to identify this active species.

Acknowledgment. We thank Beth Redfern for technical assistance and Thomas P. Krick for the GC–MS analyses. The GC–MS facilities were provided by the Biochemistry Department of the University of Minnesota and maintained by the Minnesota Agricultural Experiment Station. This work was supported by the Department of Veterans Affairs.

Supplementary Material Available: GC–MS spectral data for authentic and enzyme-generated 3 (1 page). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(4) The GC–MS spectra of 3 are available as supplementary material.
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Metal-Catalyzed Decarbonylation of Primary Aldehydes at Room Temperature

Joseph M. O'Connor* and Junning Ma

Department of Chemistry (216), University of Nevada at Reno, Reno, Nevada 89557-0020

Received July 27, 1992

Summary: The metal-catalyzed decarbonylation of primary aldehydes has been achieved at room temperature in THF solvent by utilization of catalytic amounts of $Rh(PPh_3)_3Cl$ (2, 5 mol %), in conjunction with stoichiometric amounts of diphenylphosphoryl azide (DPPA, 4).

The development of a mild, efficient procedure for the decarbonylation of aldehydes would represent an impor-

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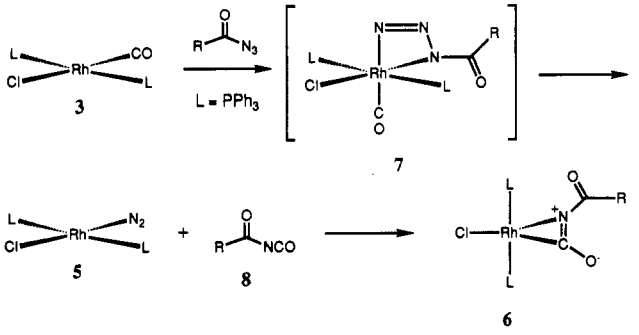
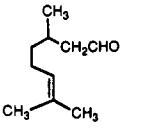
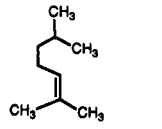
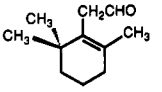
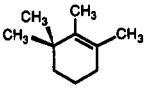
Scheme I



tant addition to existing methodology for the synthesis of fine chemicals[1] and isotopically enriched hydrocarbons.[2] Most existing decarbonylation catalysts function at elevated temperatures where substrate or product decomposition is problematic. For example, $[Rh(Ph_2P(CH_2)_3PPh_2)_2]^+ BF_4^-$ converts heptanal to hexane at 118 °C in only 39% yield, due to thermal decomposition, which also occurs in the absence of catalyst at that temperature.[3] The ruthenium porphyrin complex $Ru(tpp)(PPh_3)_2$ (1, tpp = dianion of tetraphenylporphyrin), and an iron analogue, catalyze decarbonylation of aldehydes at room temperature. However, these systems appear to involve radical mechanisms and thus suffer from undesired substrate rearrangement and problems with reproducibility.[4] Tsuji demonstrated over 25 years ago that $Rh(PPh_3)_3Cl$ (2) is effective for the *stoichiometric* decarbonylation of primary aldehydes at room temperature.[5,6] The formation of the stable rhodium containing product, *trans*-$[Rh(PPh_3)_2(CO)Cl]$ (3), prevents true catalysis by rhodium at or near room temperature. Thermal, photochemical, and chemical approaches toward clean reconversion of isolated 3 into a catalytically active species for aldehyde decarbonylation have met with little success.[7] Here, we describe the decarbonylation of primary aldehydes in a high-yield, room-temperature process which involves the use of catalytic amounts of 2 in conjunction with stoichiometric amounts of diphenylphosphoryl azide (DPPA, 4).

Table I. Yields for Decarbonylation of Primary Aldehydes at 24–25 °C by 2/DPPA[a]

substrate	product	time (h)	% yield[b]
$C_6H_5CH_2CH_2CHO$	$C_6H_5CH_2CH_3$	22	96
trans-$C_6H_5CH{=}CHCHO$	$C_6H_5CH{=}CH_2$	24	94
		45	99[c]
		45	90[d]
$C_6H_5CH_2CHO$	$C_6H_5CH_3$	31	95
$(CH_3)_3CCH_2\underset{\displaystyle CH_3}{\underset{\vert}{C}}HCH_2CHO$	$(CH_3)_3CCH_2CH(CH_3)_2$	46	97
$CH_3(CH_2)_4CH_2CHO$	$CH_3(CH_2)_4CH_3$	25	96

[a] Typical procedure: DPPA (0.30 mmol) is added by syringe pump to a degassed THF-d_8 (0.5 mL, 25 °C) solution of RCHO (0.30 mmol), 2 (0.014 mmol), and PhOMe (internal standard) under N_2. [b] Yields are based on aldehyde and determined by ^1H NMR integrals for substrate and product relative to internal standard. [c] Lewellyn, M. E.; Tarbell, D. S. *J. Org. Chem.* **1974**, *39*, 1407. [d] Naves, Y-R. *Helv. Chim. Acta* **1964**, *47*, 1833. Hamilton, R.; Mitchell, T. R. B.; Rooney, J. J.; McKervey, M. A. *J. Chem. Soc., Chem. Commun.* **1979**, 731.

Previously, Ukhin reported the reaction of butanoyl azide and 3 at −70 °C to give the dinitrogen complex 5, which decomposes in chloroform solution at room temperature (Scheme I).[8] Collman carried out extensive mechanistic work on the reaction of 3 and its iridium analogue with a variety of organic azides.[9] In the case of α-furoyl azide the isocyanate complex 6 was isolated. By analogy to Collman's mechanistic proposal for the iridium system, a plausible mechanism for the azide reaction involves initial formation of an oxidative adduct, 7, followed by rapid conversion to 5 and isocyanate 8.[10] Displacement of dinitrogen from 5 and 8 then leads to 6.[11]

The azide-mediated conversion of 3 into 5 has the potential for completing a catalytic cycle in the room-temperature decarbonylation of aldehydes by 2. We were initially disappointed to find that addition of α-furoyl azide to chloroform solutions of 3 under nitrogen resulted in

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(7) (a) Thermolysis of 3 in molten triphenylphosphine at 100 °C fails to displace the CO ligand.[5e] (b) Simple photoelimination of CO from 3 does not occur: Geoffroy, G. L.; Denton, D. A.; Keeney, M. E.; Bucks, R. R. *Inorg. Chem.* **1976**, *15*, 2382. (c) Complex 3 gives 2 in 73% yield upon reaction with α-chlorotoluene followed by treatment with excess triphenylphosphine in ethanol at reflux: Fries, R. W.; Stille, J. K. *Syn. Inorg. Met.-Org. Chem.* **1971**, *1*, 295. (d) Trimethylamine *N*-oxide fails to abstract CO from 3 at room temperature: O'Connor, J. M.; Ma, J., unpublished result.

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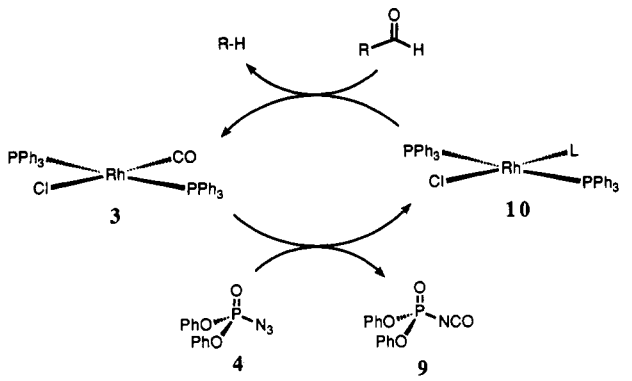
(11) The azide–carbonyl reaction may also be viewed as a [2 + 3] cycloaddition: Hessell, E. T.; Jones, W. D. *Organometallics* **1992**, *11*, 1496.

Scheme II



evolution of a gas (presumably N_2) with little change in the infrared spectrum of **3**.[12] It thus appears that **3** or a related species catalyzes azide decomposition. In an effort to retard the decomposition of azide we turned to the relatively stable azide, diphenylphosphoryl azide, DPPA (**4**), a readily available, nonexplosive, high-boiling azide used as a reagent in peptide synthesis.[13,14] Addition of a stoichiometric amount of **4** (0.30 mmol) to a room-temperature THF-d_8 solution of **2** (0.014 mmol, ~5 mol %) and 3-phenylpropanal (0.30 mmol) under nitrogen led to a 12% yield of ethylbenzene after 24 h. Encouraged by clear evidence of catalysis, a syringe pump was employed for the slow addition (24 h) of azide (0.30 mmol) to a room-temperature THF-d_8 solution of **2** (0.014 mmol) and 3-phenylpropanal (0.30 mmol, 0.6 M). ^{1}H NMR analysis of the reaction mixture indicated conversion of 3-phenylpropanal to ethylbenzene in 95% yield (~20 turnovers). Table I lists the yields for decarbonylation of selected primary aldehydes. Whereas the employment of **2**/DPPA for decarbonylation of cinnamaldehyde leads to styrene in 94% yield, the porphyrin complex **1** is ineffective with this substrate,[4] and the stoichiometric reaction of **2** with cinnamaldehyde gives an 83% yield of styrene *based on 2*.[5] In certain cases, the stoichiometric reaction of **2** with aldehydes leads to alkene side products. For example, at room temperature heptanal is converted to a ~6:1 ratio of hexane–hexene in 78% yield, based on **2**.[5b,e] For comparison, the **2**/DPPA method leads to decarbonylation of heptanal in 96% yield, with no evidence for formation of hexenes (<2%). In the case of decarbonylation with stoichiometric **2**, the formation of alkene byproducts has been attributed to the ready availability of an open coordination site for β-hydride elimination.[3] The reasons for the marked selectivity difference observed with **2**/DPPA are not presently known; however, the presence of potential ligands such as THF or diphenylphosphoryl isocyanate, **9**, may play a role in preventing alkene formation.

The mechanism for this new catalytic decarbonylation process is presumably similar to that proposed for the stoichiometric decarbonylation of aldehydes by **2**,[3,15] with the added feature of carbon monoxide abstraction from **3** by DPPA (Scheme II). The reaction of **3** with DPPA generates the known isocyanate **9** and a catalytically active rhodium complex of unknown composition (possibly **10** where L may be PPh_3, **9**, or THF). In a preparative-scale experiment in which 3-phenylpropanal was decarbonylated with **2**/DPPA, the diphenylphosphoryl isocyanate, **9**, was isolated from the reaction mixture in 95% yield and characterized by IR and NMR spectroscopy, as well as GC–MS analysis.[16] As anticipated, the **2**/DPPA decarbonylation method does not appear to involve radical species, as evidenced by decarbonylation of citronellal to give a 99% yield of 2,6-dimethyl-2-heptene with no observable formation of menthone or isomenthone (as is the case in the benzoyl peroxide decarbonylation of citronellal at 80 °C).[17] Preliminary evidence indicates that utilization of the **2**/DPPA method will be limited to primary aldehydes at room temperature, as expected from Tsuji's results with stoichiometric **2**.[5] Thus, cyclohexanecarboxaldehyde is decarbonylated in only 20% yield (four turnovers) after 60 h of reaction at 25 °C.

Studies are currently underway into the mechanism, scope, and limitations of this new metal-catalyzed decarbonylation process.[18] It may prove possible to extend this chemistry to other metal systems and carbonyl containing compounds.[4,19–22]

Acknowledgment. Support of the National Science Foundation (CHE-9116933) and a generous loan of rhodium trichloride from Johnson-Matthey-Aesar is gratefully acknowledged. We thank the American Cancer Society Junior Faculty Fellowship Program for support of our programs and Professor Robert Corcoran for helpful discussions.

(12) Only upon rapid addition of a large excess of azide was the CO stretch removed from the IR spectrum of $CHCl_3$ solutions of **3**. Collman reported[9a] that dinitrogen complex **5** undergoes an uncharacterized reaction with excess azide.

(13) Available from Aldrich Chemical Co. in kilogram quantities.

(14) DPPA undergoes reaction with **3** to give the urylene complex $RhCl(PPh_3)_2(RNCONR)$, R = $P(O)(OPh)_2$: Bartel, K.; Werner, K.; Beck, W. *J. Organomet. Chem.* **1983**, *243*, 79. This urylene product presumably arises from reaction of **9**, or a rhodium complex of **9**, with $H_2NP(O)(OPh)_2$, the hydrolysis product of **9**.

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(17) Kampmeier, J. A.; Harris, S. H.; Wedegaertner, D. K. *J. Org. Chem.* **1980**, *45*, 315. This work also reports that citronellal is decarbonylated by stoichiometric **2** in 90% yield at 80 °C.

(18) Potential interference of the acylazide with various functional groups has been partially addressed by the use of DPPA as a reagent in peptide synthesis. Similar concerns with the isocyanate byproduct may be circumvented by inter- and/or intramolecular traps. Efforts are currently underway to address these features more thoroughly.

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