gation was supported by the National Institutes of Health.

Appendix

For Scheme I, we may write

$$[E_t] = [E] + [EA] + [EB] + [EI] + [EAI] + [EBI] \tag{A1}$$

$$[EA] = ([A]/K_m)[E] \tag{A2}$$

$$[EB] = ([B]/K_m)[E] \tag{A3}$$

$$[EI] = ([I]/K_i)[E] \tag{A4}$$

$$[EAI] = \frac{[A][I]}{K_m \alpha K_i}[E] \tag{A5}$$

$$[EBI] = \frac{[B][I]}{K'_m \alpha' K_i}[E] \tag{A6}$$

Let

$$X = 1 + \frac{[A]}{K_m} + \frac{[B]}{K'_m} + \frac{[I]}{K_i} + \frac{[A][I]}{K_m \alpha K_i} + \frac{[B][I]}{K'_m \alpha' K_i} \tag{A7}$$

from which

$$[E_t] = [E]X \text{ or } [E] = [E_t]/X \tag{A8}$$

and

$$[EA] = \frac{[A]}{K_m}\frac{[E_t]}{X} \tag{A9}$$

$$[EB] = \frac{[B]}{K'_m}\frac{[E_t]}{X} \tag{A10}$$

$$[EAI] = \frac{[A][I]}{K_m \alpha K_i}\frac{[E_t]}{X} \tag{A11}$$

$$[EBI] = \frac{[B][I]}{K'_m \alpha' K_i}\frac{[E_t]}{X} \tag{A12}$$

The reaction velocity for A is

$$-d[A]/dt = v = k_{cat}[EA] + \beta k_{cat}[EAI] \tag{A13}$$

Substituting eq A9 and A11 into eq A13 and rearranging, we obtain

$$\frac{-d[A]}{dt} = v = \left(1 + \frac{\beta}{\alpha}\frac{[I]}{K_i}\right)\frac{k_{cat}}{K_m}\frac{[E_t]}{X}[A] \tag{A14}$$

Similarly, the reaction velocity for B is

$$\frac{-d[B]}{dt} = v' = \left(1 + \frac{\beta'}{\alpha'}\frac{[I]}{K_i}\right)\frac{k'_{cat}}{K'_m}\frac{[E_t]}{X}[B] \tag{A15}$$

Dividing eq A14 by eq A15, we obtain

$$\frac{d[A]}{d[B]} = \frac{[A]}{[B]}\frac{k_{cat}K'_m}{k'_{cat}K_m}\frac{1 + \frac{\beta}{\alpha}\frac{[I]}{K_i}}{1 + \frac{\beta'}{\alpha'}\frac{[I]}{K_i}} \tag{A16}$$

Integration of eq A16 gives

$$\frac{\ln \frac{[A]}{[A_0]}}{\ln \frac{[B]}{[B_0]}} = E^* \frac{1 + \frac{\beta}{\alpha}\frac{[I]}{K_i}}{1 + \frac{\beta'}{\alpha'}\frac{[I]}{K_i}} \tag{A17}$$

where

$$E^* = k_{cat}K'_m/k'_{cat}K_m \tag{A18}$$

Communications to the Editor

Liquid Xenon: An Effective Inert Solvent for C–H Oxidative Addition Reactions

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The C–H activating intermediate generated by irradiation of $Cp^*(PMe_3)IrH_2$ (**1**; $Cp^* = \eta^5\text{-}C_5Me_5$) reacts with all C–H bonds to which it is exposed.[1] This property is useful for inducing chemical transformations in normally unreactive substrates. However, such ubiquitous reactivity is also a problem because it prevents the employment of common organic liquids as inert solvents for C–H activation studies. This restriction has prevented investigation of C–H insertion in organic substrates that are available in limited quantity, prohibitively expensive, or difficult to liquify, such as low molecular weight gases and high-melting solids. Fluorocarbons have been used as inert solvents in some related C–H activation systems, such as those initiated by irradiation of $Cp^*Ir(CO)_2$.[2,3] However, their general applicability has been frustrated by the fact that intermediates generated from $Cp^*(PMe_3)IrH_2$ react even with these materials[4] and by the low solubility of many organic and organometallic compounds in fluorocarbons.

Liquified noble gases have been used as solvents in numerous spectroscopic investigations,[5] including many involving organometallic complexes, most notably by Poliakoff, Turner, and coworkers.[5e–h] However, noble gases have not previously been employed in preparative reactions. We now report that the noble gas xenon, which exists as a liquid under modest pressures in the temperature range from −100 to −60 °C (2–9 atm),[6] can be used successfully as an inert solvent[7] for preparative C–H oxidative

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[1] (a) Janowicz, A. H.; Bergman, R. G. *J. Am. Chem. Soc.* **1983**, *105*, 3929–3939. (b) Buchanan, J. M.; Stryker, J. M.; Bergman, R. G. *J. Am. Chem. Soc.* **1986**, *108*, 1537–1550.

[2] Hoyano, J. K.; McMaster, A. D.; Graham, W. A. G. *J. Am. Chem. Soc.* **1983**, *105*, 7190–7191.

[3] Marx, D. E.; Lees, A. J. *Inorg. Chem.* **1988**, *27*, 1121–1122.

[4] Sponsler, M. B.; Bergman, R. G., unpublished results.

[5] See, for example: (a) Bulanin, M. O. *J. Mol. Struct.* **1973**, *19*, 59–79. (b) Beattie, W. H.; Maier, W. B., II; Holland, R. F.; Freund, S. M.; Stewart, B. *Laser Spectros. S.P.I.E.* **1978**, *158*, 113–121. (c) Rentzepis, P. M.; Douglass, D. C. *Nature* **1981**, *293*, 165–166. (d) Andrea, R. R.; Luyten, H.; Vuurman, M. A.; Stufkens, D. J.; Oskam, A. *Appl. Spectrosc.* **1986**, *40*, 1184–1190. (e) Upmacis, R. K.; Poliakoff, M.; Turner, J. J. *J. Am. Chem. Soc.* **1986**, *108*, 3645–3651. (f) Jackson, S. A.; Upmacis, R. K.; Poliakoff, M.; Turner, J. J.; Burdett, J. K.; Grevels, F.-W. *Chem. Commun.* **1987**, 678–680. (g) Gadd, G. E.; Poliakoff, M.; Turner, J. J. *Organometallics* **1987**, *6*, 391–397. (h) Firth, S.; Klotzbücher, W. E.; Poliakoff, M.; Turner, J. J. *Inorg. Chem.* **1987**, *26*, 3370–3375.

[6] Theeuwes, F.; Bearman, R. J. *J. Chem. Thermodynamics* **1970**, *2*, 507–512.

[7] The term "inert solvent" is meant to indicate that the solvent does not give stable products with the intermediates generated by irradiation of $Cp^*(PMe_3)IrH_2$.

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Table I. Photolysis of **1** with Organic Substrates in Liquid Xenon[a]

substrate	conc[b] (M)	products	yields[c] (%)
cyclohexane	0.02–0.15	**2**	40–70
methane	0.67	**3**	50
adamantane	<0.08–0.14[d]	**4**	30–60
cubane	0.02–0.07	**5**	18–25
naphthalene	<0.06–0.1[d]	**6**, **7**, **8**	(8–10 each)
methanol	0.02	**11**	30
ethanol	0.01–0.02	**12**	50
isopropyl alcohol	0.02–0.03	**10**[e]	70–85
tert-butyl alcohol	0.08	**9**	90

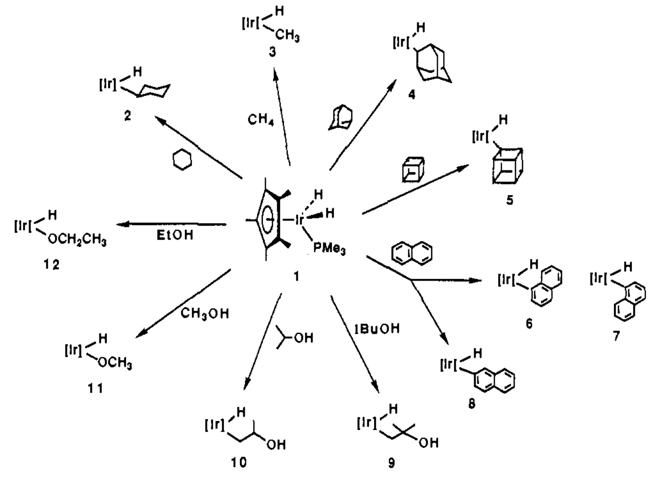
[a] A Hanovia medium-pressure 450-W mercury arc lamp was used, typically with 3 h irradiation. The concentration of **1** was 0.002–0.017 M. [b] The concentrations shown are simply calculated from the amount of substrate used, assuming that all was dissolved. These values are approximate. [c] Yields were determined by ^{1}H NMR integration. Yields were somewhat variable and should be viewed as qualitative. [d] The substrate was not completely dissolved. [e] 54:46 mixture of diastereomers.

addition reactions. This has allowed us to (a) carry out the activation of several new substrates, (b) demonstrate for the first time that alkane C–H oxidative addition can occur with a tertiary C–H bond, and (c) establish that under proper conditions, alcohols can undergo apparent insertion at either their C–H or O–H bonds.

Solutions of dihydride **1** and organic substrates (2–110 equiv) in liquid xenon were prepared by condensing the noble gas (1–3 mL of liquid) into Pyrex vessels[8] containing the reactants at 77 K, followed by warming to −78 °C and shaking.[9] (*Note*: *xenon liquified in glass containers is hazardous* and must be handled with great care to prevent pressure explosions. For safety purposes, a pressure relief valve was used, in case of accidental warming;[10] in addition, safety glasses, full face shields, and other protective clothing were worn at all times while working with the liquid.) Irradiation of the colorless solutions at −75 to −60 °C produced yellow solutions with tan precipitates. The xenon was then removed by freeze-drying (immersion in liquid nitrogen, followed by removal of the nitrogen bath and vacuum transfer of the xenon into a removable trap). The residues were then redissolved in organic solvents and either characterized spectroscopically or purified by low-temperature chromatography[1b] and characterized fully. Spectroscopic data are available as Supplementary Material.

All photochemical reactions of **1** and alkane substrates in xenon were found to yield alkyl hydride products. The results of a number of such experiments are summarized in Table I, and the structures of the products are depicted in Scheme I. The previously known oxidative addition products **2** and **3**, formed from cyclohexane and methane, respectively, were identified by comparison of their ^{1}H and ^{31}P{^{1}H} NMR spectra with those of authentic samples.[1b] The methane example represents the first generation of the methyl hydride **3** under kinetically controlled conditions by irradiation of dihydride **1**; in earlier studies, this product could be formed only under thermodynamic control by generation of the Cp*IrPMe$_3$ intermediate thermally from the cyclohexyl hydride.[11] The use of adamantane as a substrate gave the 2-adamantyl hydride complex **4** as a single product.[12] The selective activation of the secondary C–H bond is consistent with previously identified selectivities.[13] The photochemical reaction of **1** with cubane also gave a single product, identified as the cubyl hydride complex **5**. Although the cubane C–H bond is admittedly atypical, to our knowledge this reaction represents the first oxidative addition reaction involving an alkane tertiary C–H bond. Competition experiments carried out using mixtures of cyclohexane and cubane in liquid xenon showed preferential reaction with cubane, with a rate ratio of 2.4.[14]

Scheme I. Products Formed on Irradiation of Solutions of **1** and the Indicated Organic Molecules in Liquid Xenon at −60 to −75 °C



([Ir] = Cp*IrPMe$_3$)

Irradiation of **1** and naphthalene in xenon surprisingly gave a mixture of three aryl hydride products (by ^{1}H and ^{31}P NMR; purified as the mixture by room temperature chromatography), even though only two types of C–H bonds exist in the substrate. A likely explanation is that two of the products are rotamers of the α-naphthyl hydride complex (**6** and **7**), the third product being the β-naphthyl hydride complex **8** (with rapid rotation about the iridium–naphthyl bond).[15] No broadening of ^{1}H NMR bands was observed upon heating to 80 °C, indicating slow rotation in the α-naphthyl complex even at that temperature. Molecular modeling[16] supports the existence of a large 2-fold rotational barrier in **6**/**7** and a much smaller barrier in **8**.

Irradiation of dihydride **1** in alcohol solvents was found earlier to give rise to products resulting from preferential insertion of Ir into C–H rather than O–H bonds. For example, irradiation of **1** in *tert*-butyl alcohol gives the C–H insertion product Cp*(PMe$_3$)Ir(H)(CH$_2$C(Me)$_2$OH) (**9**),[17] and the use of isopropyl alcohol as solvent leads to Cp*(PMe$_3$)Ir(H)(CH$_2$CH(Me)OH) (**10**) as a mixture of diastereomers. The same reactivity is also observed in the irradiation of **1** in xenon with *tert*-butyl alcohol and isopropyl alcohol as substrates, which gives **9** and **10**, respectively.

The photochemistry with methanol and ethanol is more complicated. Irradiation of Cp*(PMe$_3$)IrH$_2$ in the neat alcohol solvents produces products that apparently arise from C–H insertion. Thus, irradiation of **1** in methanol gives primarily Cp*(PMe$_3$)Ir(CO), and the use of ethanol as solvent gives Cp*(PMe$_3$)Ir(H)(CH=CH$_2$) as the major product.[18,19] Both of these reactions can be rationalized by initial oxidative addition of the iridium center into a C–H bond in the alcohol, followed in the case of methanol by multiple dehydrogenation steps, or by loss of water in the ethanol insertion product. Strikingly, however, when **1** is irradiated in liquid xenon containing modest concentrations of methanol, the O–H insertion product Cp*(PMe$_3$)Ir-

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(8) Simple cylindrical heavy-walled Pyrex vessels were used (12 mm o.d., 8 mm i.d., 10 cm in length (not including stopcock)), equipped with single Teflon pressure-relief valves (see ref 10 for description).

(9) In some cases, the organic substrate was condensed after the xenon.

(10) Ace Glass part 8769-10 was used (illustration provided in catalogue), after replacing the spring with a stronger one (to give a release pressure of about 200 psi) and gluing the parts together with epoxy to allow manual opening of the valve. A similar valve based on Kontes stopcock K-826510 was also used.

(11) Wax, M. J.; Stryker, J. M.; Buchanan, J. M.; Kovac, C. A.; Bergman, R. G. *J. Am. Chem. Soc.* **1984**, *106*, 1121–1122.

(12) In some samples, a small amount of another product (possibly the tertiary adamantyl hydride) was observed (see Supplementary Material).

(13) Bergman, R. G. *Science* **1984**, *223*, 902–908.

(14) Adjusted statistically for the number of C–H bonds.

(15) For other examples of M–aryl hindered rotation in similar complexes, see: (a) Jones, W. D.; Feher, F. J. *Inorg. Chem.* **1984**, *23*, 2376–2388. (b) McGhee, W. D.; Bergman, R. G. *J. Am. Chem. Soc.* **1988**, *110*, 4246–4262.

(16) PCMODEL, version 1.1 for the Apple MacIntosh II, was used (Serena Software).

(17) Klein, D. P.; Hayes, J. C.; Bergman, R. G. *J. Am. Chem. Soc.* **1988**, *110*, 3704–3706.

(18) Stoutland, P. O.; Bergman, R. G. *J. Am. Chem. Soc.* **1988**, *110*, 5732–5744.

(19) We are grateful to L. J. Newman for carrying out preliminary experiments in ethanol.

(H)(OMe) (**11**) is reproducibly formed. The photoreaction of **1** with ethanol in xenon likewise gives $Cp^*(PMe_3)Ir(H)(OEt)$ (**12**),[20] although in this case significant amounts of other, unidentified products were sometimes observed.[21] The abrupt change in reactivity between ethanol and isopropyl alcohol is remarkable.

In summary, liquid xenon is a useful inert solvent for photochemically induced C–H oxidative addition reactions. Work is continuing aimed at examining the C–H insertion reactions of other substrates that cannot be liquified easily, using liquid xenon in fast kinetics experiments, and determining the cause of the dramatic substrate and solvent effects summarized above in the reactions of **1** with alcohols.

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Registry No. 1, 80146-01-6; **2**, 80145-83-1; **3**, 88548-54-3; **4**, 121618-77-7; **5**, 121618-78-8; **6**, 121618-79-9; **8**, 121618-80-2; **9**, 114326-78-2; **10** (isomer 1), 121701-52-8; **10** (isomer 2), 121618-81-3; **11**, 121618-82-4; **12**, 121618-83-5; CH_4, 74-82-8; *t*-BuOH, 75-65-0; *i*-PrOH, 67-63-0; CH_3OH, 67-56-1; EtOH, 64-17-5; xenon, 7440-63-3; cyclohexane, 110-82-7; adamantane, 281-23-2; cubane, 277-10-1; naphthalene, 91-20-3.

Supplementary Material Available: Spectroscopic data for complexes **4**, **5**, **6**/**7**/**8**, and **11** (2 pages). Ordering information is given on any current masthead page.

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[20] The ethoxy hydride **12** has been previously prepared in our group. Cf.: Newman, L. J. Ph.D. Dissertation, University of California, Berkeley, 1986. For the analogous triphenylphosphine-substituted complex, see: Newman, L. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1985**, *107*, 5314-5315.

[21] We have recently discovered that complex **11** can be independently synthesized by treating $Cp^*(PMe_3)IrCl_2$ (Isobe, K.; Bailey, P. M.; Maitlis, P. M. *J. Chem. Soc., Dalton Trans.* **1981**, 2003-2008) with sodium methoxide in tetrahydrofuran.

A New Synthesis of β-Lactams through Stereoselective Oxidative Coupling of the Dianions of Acyclic Amides

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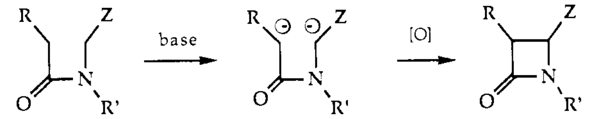
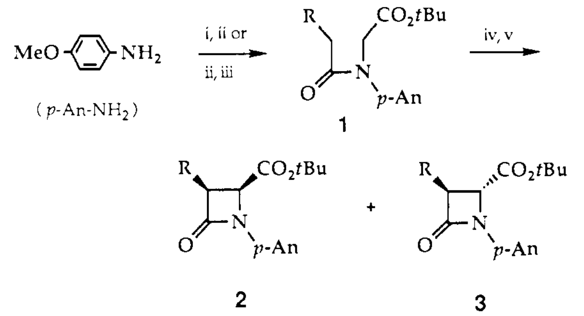
In view of steadily expanding chemotherapy with β-lactam antibiotics of a wide variety of structures,[1] development of a conceptually novel synthetic method is still of great importance.[2] We report herein that an intramolecular oxidative coupling reaction[3] of the dianions generated from acyclic amides affords β-lactams in synthetically useful yields (Scheme I). The stereochemical course of the ring closure is controllable by proper choice of the oxidant. Furthermore, asymmetric synthesis of β-lactams is achieved by introducing a chiral auxiliary attached to the amide nitrogen.

Scheme I



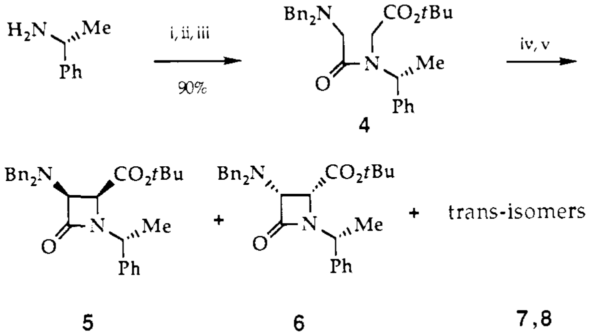
Scheme II[a]



a: R = H, b: R = Et, c: R = MeO, d: R = Bn_2N

[a] (i) $BrCH_2CO_2$-*t*-Bu, NEt_3; (ii) RCH_2COCl, NEt_3; (iii) $BrCH_2CO_2$-*t*-Bu, NaOH; (iv) RLi additive (see the footnote of Table I), THF, −78 °C; (v) $Cu(OAc)_2$, $Cu(OCOPh)_2$, or NIS, −70 to −95 °C.

Scheme III[a]



[a] (i) $BrCH_2CO_2$-*t*-Bu, NEt_3; (ii) $BrCH_2COBr$, NEt_3; (iii) Bn_2NH, NEt_3; (iv) *n*-BuLi, TMEDA; (v) NIS or $Cu(OAc)_2$.

The starting materials **1** are readily prepared by alkylation of *p*-anisidine with *tert*-butyl bromoacetate followed by acylation or vice versa as summarized in Scheme II. The overall yields fall in the range 68–93%. Dienolate formation of **1** was achieved quantitatively by treatment with slightly more than 2 equiv of butyllithium in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO) or *tert*-butyllithium alone in tetrahydrofuran (THF) at −78 °C. The dianions thus formed exist as such at low temperatures. The yields of the dianion formation were estimated to be >90% by deuteration with CD_3CO_2D and CD_3OD followed by MS and ^1H NMR spectrometry. The dianions were then treated with *N*-iodosuccinimide (NIS) or Cu(II) carboxylates[4]

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[3] Four-membered carbocyclic ring formation through an oxidative coupling reaction has been reported though in 15-37% yields. (a) Whitesides, G. M.; SanFilippo, J., Jr.; Casey, C. P.; Panek, E. J. *J. Am. Chem. Soc.* **1967**, *89*, 5302. (b) Kobayashi, Y.; Taguchi, T.; Morikawa, T.; Tokuno, E.; Sekiguchi, S. *Chem. Pharm. Bull.* **1980**, *28*, 262. (c) Minami, T.; Okada, Y.; Nomura, R.; Hirota, S.; Nagahara, Y.; Fukuyama, K. *Chem. Lett.* **1986**, 613. (d) Babler, J. H.; Sarussi, S. J. *J. Org. Chem.* **1987**, *52*, 3462.

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