Tetrahedron Letters,Vol.26,No.6,pp 705-708,1985
Printed in Great Britain

0040-4039/85 \$3.00 + .00

# Pd(II)-CATALYZED ACETAL/KETAL HYDROLYSIS/EXCHANGE REACTIONS

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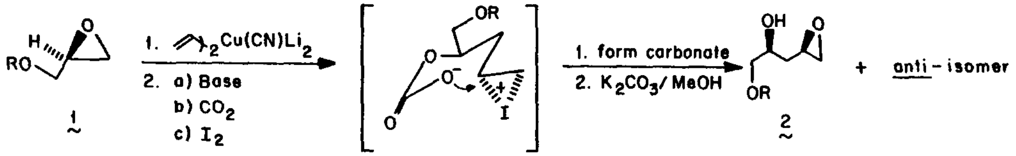
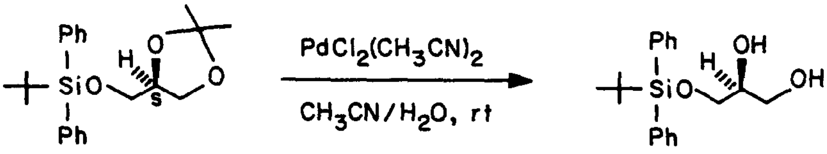
**Summary: $PdCl_2(CH_3CN)_2$ catalyzes the hydrolysis of dioxolane acetals and ketals in moist $CH_3CN$, while in acetone, efficient and more reproducible exchange reactions take place.**

We have recently described a strategy for preparing all syn-1,3-polyols in optically active form, key subunits of the polyene macrolide antibiotics.[2] This two-pot, reiterative route relies on a cuprate-mediated epoxide opening, reepoxidation sequence. The latter operation, which involves an iodocyclization, ultimately affords mixtures of syn : anti isomers 2 in ratios of 10-20:1. In attempting to improve these results, oxirane 1, R=t-BuPh$_2$Si was desired so as to compare the effects of this bulky group on the observed ratio relative to those originally obtained with 1, R=CH$_2$Ph. Epoxides of this type are commonly prepared via the acetonide of reduced D-glyceraldehyde, which subsequently involves etherification (to give, e.g., 3), hydrolysis, monotosylation, and treatment with base.[3] Unfortunately, all attempts to deprotect masked diol 3 (1.8 N $H_2SO_4$, 80°C, 5h; 80% HOAc, 100°C, 5h; TsOH, MeOH, rt, overnight) were completely unsuccessful,[4] as were conditions (HOAc/THF/$H_2O$, 3:1:1, 50°C, 5h) which straight-forwardly lead to the desired product when the benzyl ether is present.[2] This seemingly trivial reaction could be accomplished (82% isolated yield, 16% recovered start-





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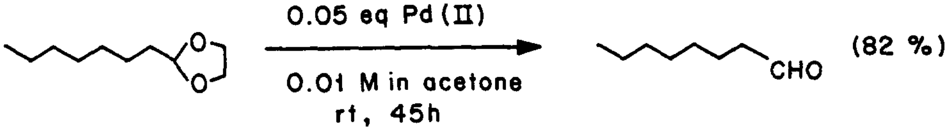
ing material), however, using a novel method based on Pd(II) catalysis.[5] Herein we report on our study of the generality of this potentially useful deblocking procedure.

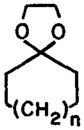
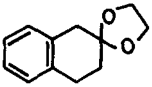
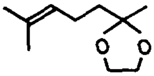
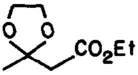
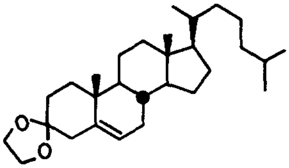
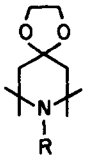
Initially, the reactivity patterns of several ketals[6] were examined in $CH_3CN$. Upon treatment with $PdCl_2(CH_3CN)_2$,[7] yields were oftentimes excellent; however, these hydrolyses were not consistently reproducible. Modifications which included using (a) freshly prepared catalyst; (b) other sources of Pd(II) [e.g., $Pd(OAc)_2$, $PdCl_2$]; (c) standardized amounts of $H_2O$, did little to improve the situation. Ultimately, simply switching to acetone as solvent,[8] which encourages transketalization, gave excellent results, as summarized in Table I. Perhaps the most salient feature associated with these several representative conversions, aside from the mildness of conditions and high yields, is that only 1 mol % Pd(II) need be utilized.

Dioxolane acetals also appear to undergo this exchange, as indicated in the case below. More dilute solutions and 5 mol % Pd(II), however, were needed to drive the reaction to completion.



The compatability of this soft Lewis acid[9] based deketalization with hydroxyl protecting groups was briefly investigated using substrate 5. As anticipated from the reaction of 3, *t*-$BuPh_2Si$ ethers are inert, as are MEM derivatives. By contrast, the *t*-$BuMe_2Si$ moiety suffers complete cleavage, an experimental finding which may provide a valuable alternative to both $H_3O^+$ and $F^-$ induced Si-O bond scissions.[4] THP derivatives also suffer competitive exchange, although moderate yields of selectively deprotected ketones may be obtained.

**Table I. Pd(II) Catalyzed Ketal Exchange Reactions in Acetone at Ambient Temperature**

| Entry | Substrate | Concentration(M) | Time(h) | Yield(%)[a] |
|---|---|---|---|---|
| 1 |  n = 0 | 0.10 | 0.33 | 100 |
| | n = 1 | 0.05 | 30 | 90 |
| | n = 1 | 0.10 | 30 | 88 |
| | n = 1 | 0.05 | 30 | 85 |
| | n = 7 | 0.10 | 1 | 96 |
| 2 |  | 0.10 | 23 | 86[b] |
| 3 |  | 0.24 | 4 | 82[c] |
| 4 |  | 0.10 | 1 | 100 |
| 5 |  | 0.10 | 23 | 97[d] |
| | | 0.10 | 11 | 93 |
| | | 0.10 | 24 | 92 |
| 6 |  | 0.1 | 21 | 82[c,e] |
| 7 |  R = H | 0.1 | 7 (days) | <2 |
| | R = $CO_2CH_3$ | 0.1 | 48 | >70[c] |

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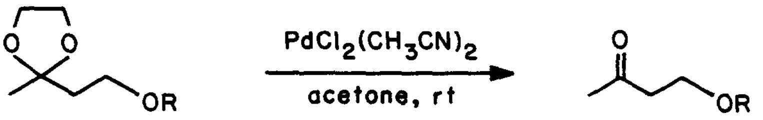
[a] By quantitative VPC, unless stated otherwise. [b] Consisted of 56% conjugated and 30% unconjugated enones. [c] Isolated yield. [d] 2 mol % Pd(II) was used. [e] The conjugated isomer was formed.



| 5, R | 6, Yield (%) |
|---|---|
| H | 98[a] |
| MEM | 87[b] |
| $SiMe_2$(t-Bu) | 0[c] |
| $SiPh_2$(t-Bu) | 97[b] |
| THP | 56[b] |

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[a] By quantitative VPC. [b] Isolated. [c] Compound 6, R = H was formed in 99% (VPC) yield.

**In summary, the use of catalytic quantities of $PdCl_2(CH_3CN)_2$ in acetone represents an attractive, simple technique for removing ethylene glycol derived acetals and ketals. The conditions are compatible with other functionality, including a number of routinely employed alcohol protecting groups.**

**Acknowledgment. Financial support provided by the National Science Foundation (CHE 83-02421) and the donors of the Petroleum Research Found, administered by the American Chemical Society, is gratefully acknowledged. We also thank Johnson-Matthey and Englehard Industries for the generous loans of palladium salts.**

## References and Notes

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6. **Dioxolane ketals were found to react faster than 1,3-dioxanes under $PdCl_2(CH_3CN)_2$ catalysis.**
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(Received in USA 5 November 1984)