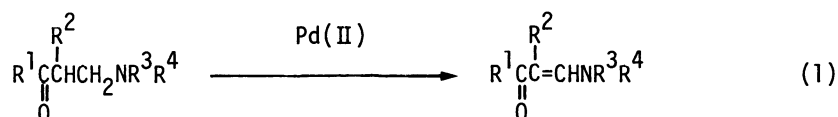


SYNTHESIS OF ENAMINONES BY Pd(II) INDUCED DEHYDROGENATION OF β -AMINO KETONES

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The reaction of β -amino ketones with bis(acetonitrile)dichloro-palladium(II) in the presence of triethylamine gives enaminones regioselectively.

Palladium inserts into the carbon-hydrogen bond α to the nitrogen of tertiary amines to give enamine hydride complexes.¹⁾ During the course of the study concerning enamine complexes, we have found that tertiary amines which have a carbonyl group at the β -position undergo dehydrogenation to give enaminones as depicted in Eq. 1.



Enaminones are versatile synthetic intermediates²⁾ because of their regioselective reactions with either electrophiles³⁾ or nucleophiles.⁴⁾ The synthesis of enaminones has been performed by the limited methods which include condensation of 1,3-diketones with amines⁵⁾ and the other methods.⁶⁾ The present palladium induced reaction of β -amino ketones provides a new strategy, because the starting β -amino ketones are readily available by either Mannich reactions of carbonyl compounds or Michael addition of amines to α,β -unsaturated ketones.

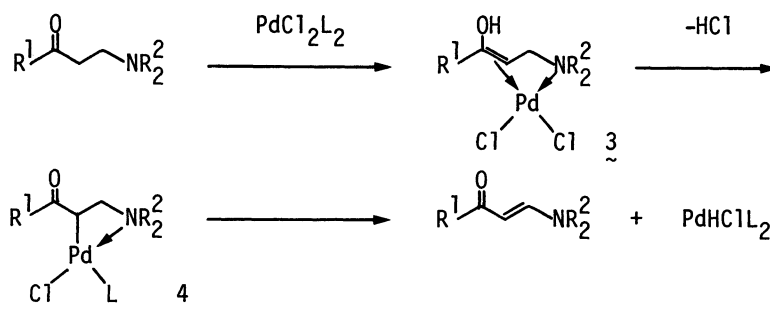
Typically, the preparation of (E)-4-diethylamino-3-buten-2-one (1) was performed as follows. To a suspension of $\text{PdCl}_2(\text{CH}_3\text{CN})_2$ (208 mg, 0.8 mmol) in dry acetonitrile (10 mL) were added dry triethylamine (162 mg, 1.6 mmol) and 4-diethylamino-2-butanone (114 mg, 0.8 mmol). The mixture was heated at reflux for 30 min under nitrogen. After cooling, the palladium metal precipitated was filtered off. The filtrate was poured into water. The ether extract was dried

over Na_2SO_4 , and concentrated in vacuo. Bulb to bulb distillation gave enaminone 1 (78 mg, 70% yield), bp 101-110 °C/1.6 mmHg, NMR (CDCl_3 , δ), 1.20 (6H, t, $J = 7.2$ Hz, CH_3), 2.07 (3H, s, COCH_3), 3.22 (4H, q, CH_2), 5.07 (1H, d, $J = 13.0$ Hz, COCH), and 7.41 (1H, d, CHN).

The method affords moderate to very good yields of a number of enaminones. The representative results are summarized in Table 1. The structure of the enaminones was established by the IR, NMR, and Mass spectral data and elemental analyses. The stereochemistry was established to be trans by the NMR spectra.⁷⁾ $\text{PdCl}_2(\text{CH}_3\text{CN})_2$ gave the best results. $\text{Pd}(\text{OAc})_2$ showed high reactivity, but the yield was low. The solvent effect is important for the enaminone formation. Acetonitrile gave the best result (95%) for the formation of enaminone 1 in comparison with the other solvents examined, such as THF (37%) and acetone (47%). The present reaction requires a base to trap hydrogen chloride generated. Using triethylamine, enaminone 1 and (E)-3-dimethylamino-1-phenyl-2-propen-1-one (2) were obtained in 95% and 81% yields, respectively. In the absence of a base, 1,3,5-triacetyl and 1,3,5-tribenzoylbenzenes were obtained in 32% and 35% yields, respectively. These triacylbenzenes seem to be derived from the acid catalyzed condensation of the enaminones formed. Indeed, the treatment of enaminone 2 with hydrogen chloride in acetonitrile at reflux gave 1,3,5-tribenzoylbenzene in 95% yield.

The Pd(II) induced dehydrogenation of carbonyl compounds has been performed directly from ketones⁸⁾ and indirectly from silyl enol ethers⁹⁾ and Sn(II) enolates.¹⁰⁾ Since the regioselectivity of the direct transformation is poor, the latter indirect methods have been used for the synthesis of various cyclic compounds.¹¹⁾ In these reactions, oxo- π -allyl complex and/or acyl palladium complex has been postulated as a key intermediate.

The mechanism which involves the enamine complex derived from the activation of the C-H bond α to the nitrogen¹⁾ seems to be unlikely, because the palladium(0)



Scheme 1.

reaction could not be detected under the reaction condition.¹²⁾ The present reaction can be rationalized by assuming the Scheme 1; formation of π -complex of enol (3), insertion of palladium into the enol to give β -carbonyl palladium complex (4), which undergoes β -elimination of PdHClL_2 to give enaminones. The initial coordination of the Pd(II) compound to the amino group is crucial to control the regioselectivity. The stable conformer of 4, in which the carbonyl group is trans to the amino group, undergoes cis-elimination of [PdH] species to give (E)-enaminones.

Table 1. Conversion of β -Amino Ketones to Enaminones^{a)}

Entry	β -Amino ketone	Time/h	Product	Yield/% ^{b)}
1		0.5		70(95) ^{c)}
2		12		81 ^{d)}
3		4 ^{f)}		78 ^{d)}
4		0.5		71 ^{e)}
5		0.5 ^{f,g)}		74 ^{c)}
6		0.5		47 ^{d)}
7		0.25		95 ^{c)}

a) All reactions were carried out using β -amino ketone (0.8 mmol) and $\text{PdCl}_2 \cdot (\text{CH}_3\text{CN})_2$ (0.8 mmol) in the presence of triethylamine (1.6 mmol) in acetonitrile at reflux under nitrogen unless otherwise noted. b) Isolated yields and VPC yields in parentheses. c) Bulb to bulb distillation. d) Preparative TLC (silica gel). e) Chromatographic separation (alumina). f) $\text{Pd}(\text{OAc})_2$ was used. g) Na_2CO_3 was used as base.

References

- 1) S.-I. Murahashi and T. Watanabe, *J. Am. Chem. Soc.*, 101, 7429 (1979).
- 2) J. V. Greenhill, *Chem. Soc. Rev.*, 1977, 277.
- 3) M. Yoshimoto, N. Ishida, and T. Hiraoka, *Tetrahedron Lett.*, 1973, 39; A. I. Meyers, A. H. Reine, and R. Gault, *J. Org. Chem.*, 34, 698 (1969); H. Iida, Y. Yuasa, and C. Kibayashi, *J. Am. Chem. Soc.*, 100, 3598 (1978).
- 4) R. F. Abdulla and K. H. Fuhr, *J. Org. Chem.*, 43, 4248 (1978); A. I. Meyers and S. Singh, *Tetrahedron Lett.*, 1967, 5319.
- 5) P. G. Baraldi, D. Simoni, and S. Manfredini, *Synthesis*, 1983, 902 and references cited therein.
- 6) Reaction of enamines with ketenes, R. H. Hasek and J. C. Martin, *J. Org. Chem.*, 28, 1468 (1963); Addition of amines to ethynyl ketones, R. Mestres, *J. Chem. Soc., Perkin Trans. 1*, 1972, 805; Oxidative amination of α,β -unsaturated ketones, J. J. Bozell and L. S. Hegedus, *J. Org. Chem.*, 46, 2561 (1981); Reaction with formamide acetals, R. F. Abdulla and R. S. Brinkmeyer, *Tetrahedron*, 35, 1675 (1979); Condensation of silyl enol ethers with oxime mesylate, Y. Matsuyama, J. Fujiwara, K. Maruoka, and H. Yamamoto, *J. Am. Chem. Soc.*, 105, 6312 (1983).
- 7) C. Kashima, H. Aoyama, Y. Yamamoto, and T. Nishio, *J. Chem. Soc., Perkin Trans. 2*, 1975, 665.
- 8) B. Bierling, K. Kirschke, H. Oberender, and M. Schulz, *J. Prakt. Chem.*, 314, 170 (1972); R. J. Theissen, *J. Org. Chem.*, 36, 752 (1971).
- 9) Y. Ito, T. Hirao, and T. Saegusa, *J. Org. Chem.*, 43, 1011 (1978).
- 10) T. Mukaiyama, M. Ohshima, and T. Nakatsuka, *Chem. Lett.*, 1983, 1207.
- 11) Y. Ito, H. Aoyama, and T. Saegusa, *J. Am. Chem. Soc.*, 102, 4519 (1980); A. S. Kende, B. Roth, P. J. Sanfilippo, and T. J. Blacklock, *ibid.*, 104, 5808 (1982).
- 12) The treatment of tributylamine with palladium black in the presence of a hydrogen acceptor of diphenylacetylene gave dibutylamine (27%), N,N-dibutyl-2-ethylhexylamine (27%) which was derived from the enamine intermediate (S.-I. Murahashi, K. Ito, and T. Watanabe, the 41st National Meeting of the Chemical Society of Japan, Osaka, April 1980, Abstr., No. 3025).

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