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PALLADIUM CATALYZED SYNTHESIS OF TERTIARY ALLYLAMINES. UTILIZATION OF α-NITRO OLEFINS AS ALLYLIC NITRO COMPOUNDS

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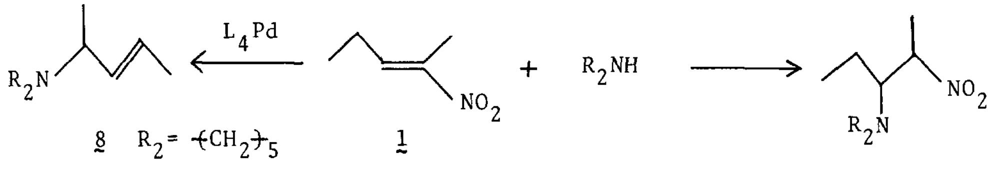
Summary: Reaction of α-nitro olefins with secondary amines in the presence of palladium(0) catalyst affords allylic amines.

α-Nitro olefins are easily prepared in good yields by numerous procedures[1] and have proven to be versatile synthetic intermediates.[2] Meanwhile, allylic nitro compounds, the isomer of α-nitro olefins, have been demonstrated to be useful substrates for palladium(0) catalyzed allylic alkylation and amination reactions[3] and for alkylation with lithium dialkylcuprates.[4] However, the procedures for preparation of allylic nitro compounds are limited to several.[5] We have recently reported that stable tertiary allylic nitro compounds are prepared by the base-catalyzed 1,4-addition of α-nitro olefins to conjugated enones.[3a] In general it is rather difficult to convert α-nitro olefins to the corresponding allylic nitro compounds by the base-catalyzed isomerization due to the thermodynamical stability of α-nitro olefins.[6] Therefore it is of value to induce the isomerization in situ and utilize the resulting allylic nitro compounds for further reactions.

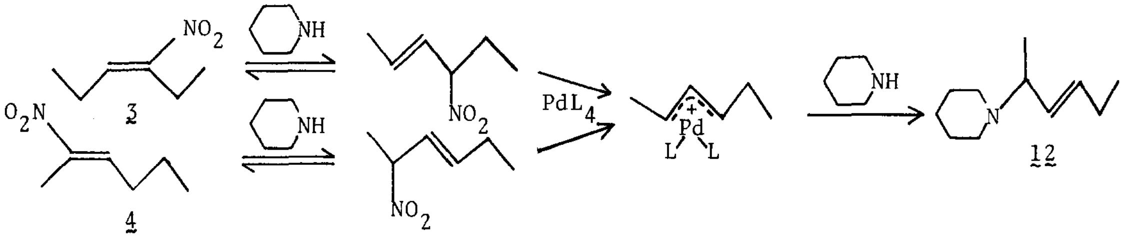
We now describe a new and convenient method to prepare tertiary allyl amines directly from α-nitro olefins and secondary amines in the presence of a catalytic amount of palladium(0). It is well-known that α-nitro olefins undergo the Michael addition of secondary amines to give 2-nitroalkylamines.[7] When this reaction was carried out in the presence of palladium(0) catalyst, however, the reaction products were found to be tertiary allyamines.



In a typical experiment, a mixture of 2-nitro-2-pentene (1) (0.228g, 2.0 mmol), piperidine (0.59ml, 6.0mmol), $(Ph_3P)_4Pd$ (0.116g, 0.10mmol) and 1,2-bis-(diphenylphosphino)ethane (dppe) (0.040g, 0.10mmol) in DMF (4.0ml) was stirred at 75° for 1 hr. Working up the reaction mixture in the usual way followed by bulb-to-bulb distillation (120-125°/14 Torr) gave pure N-(1-methyl-2-butenyl)-piperidine (8) in 75% yield. The stereoselective product was E-isomer.[8]

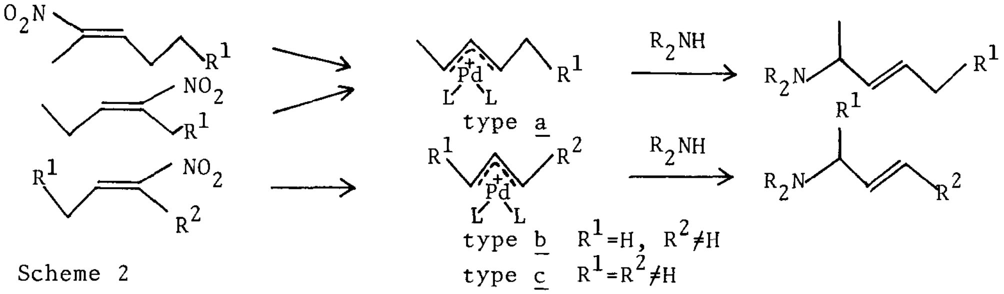
The results of the reactions using various α-nitro olefins, amines, and solvents are summarized in the Table. The remarkable solvent effects on this reaction were observed, i.e., the replacement of the solvent from THF and benzene to acetonitrile and DMF resulted in a great enhancement of the yield of 8 (entries 1-4) and the best yields of the allylic amines in all cases were obtained in DMF. Piperidine was the suitable secondary amine for this reaction, while with di-n-propylamine and pyrrolidine the yields of the allylic amines were lowered and no allylic amine was obtained with di-iso-propylamine and N-methylaniline (entries 1, 5-8). Polymerization occurred with 1-nitropropene (7) (entry 15).

The reactions of two isomeric α-nitro olefins, 3 and 4, gave a useful suggestion on the reaction mechanism (entries 10 and 11). That is, the fact that the same sole product (12) was obtained from both reactions indicates that the reaction intermediate should be an identical π-allyl palladium complex and that the nucleophilic attack of piperidine occurred exclusively at the less hindered site to afford the regio- and stereoselective product (Scheme 1).[3a] Above solvent effects can be explained in terms of the acceleration by polar solvents of the amine-catalyzed isomerization of α-nitro olefin 1 to the allylic nitro compound, so that the Michael addition of piperidine to 1 can be suppressed.



Scheme 1

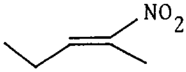
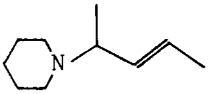
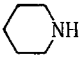
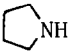
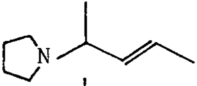
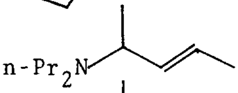
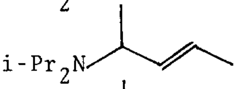
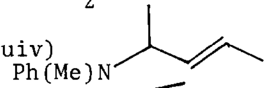
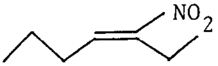
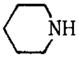
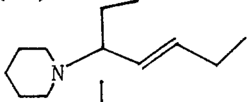
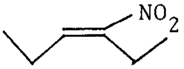
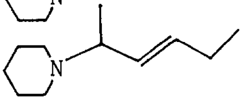
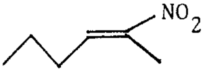
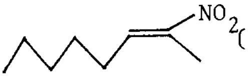
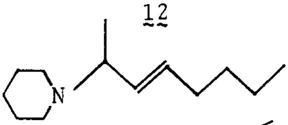
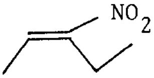
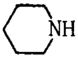
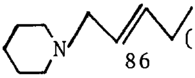
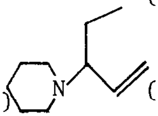
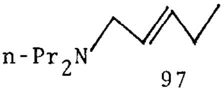
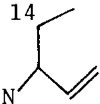
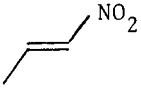
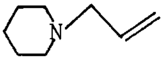
The palladium-catalyzed synthesis of allylic amines described here is useful in the following cases: (i) when the π-allyl palladium complex intermediate is type a, which can be derived from two different α-nitro olefins, or type b, the regio- and stereoselective products being obtained (entries 10-14), and (ii) when the intermediate is symmetrical type c, the stereoselective products being produced (entries 1 and 9)(Scheme 2).



Scheme 2

Since these α-nitro olefins are easily available from primary nitro alkanes via an aldol-type addition with aldehydes (the Henry reaction)[9] followed by dehydration[10] and arbitrary primary nitro alkanes can be prepared

Table. Reaction of α-Nitro Olefins and Secondary Amines with $(Ph_3P)_4Pd$ and dppe[a]

Entry	α-Nitro Olefin	Amine	Condition[b]	Product (E-isomer)	Isolated Yield (%)
1	 (1)		A		(8) 75(92)^c
2	1		CH_3CN,80°,2hr	8	40
3	1		THF,65°,20hr	8	5^c
4	1		PhH,80°,18hr	8	7^c
5	1		A		(9) 48
6	1	n-Pr_2NH	A		(10) 53
7	1	i-Pr_2NH	DMF, 75°,4hr		0
8	1	Ph(Me)NH	DMF,Et_3N(1 equiv) 75°,16 hr		0
9	 (2)		A		(11) 70
10	 (3)		A		(12) 68
11	 (4)		A	12	72
12	 (5)		A		(13) 71
13	 (6)		A	 (14)  86 : 14	(15) 47
14	6	n-Pr_2NH	A	 (16) n-Pr_2N  97 : 3	(17) 52
15	 (7)		DMF,rt		0

a) All reactions were carried out on 2 mmol scale using 5 mol% $(Ph_3P)_4Pd$ and dppe under nitrogen. Satisfactory infrared, ^1H and ^{13}C NMR, and mass spectra and elemental analyses were obtained for all products. b) A: DMF, 75°, 1 hr. c) Yields determined by quantitative GLPC analysis.

in high yields from nitromethane and the corresponding aldehydes,[11] this method can complement procedures to prepare tertiary allylic amines from allylic acetates, ethers, phosphates[12,13] and halides[14].

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