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ASYMMETRIC PALLADIUM-ASSISTED ALKYLATION OF OLEFINS

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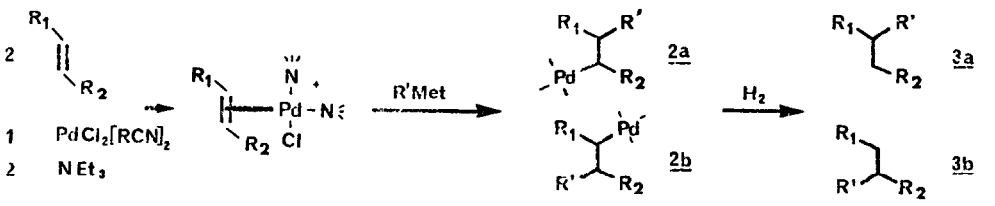
Summary Palladium-promoted alkylation of some alkenes using chiral sulfoxide-containing carbanion as nucleophiles or using optically active N,N-dimethyl-α--phenylethylamine as ligand together with a non-chiral stabilized carbanion as nucleophile results in an asymmetric induction of 10-40%.

Palladium-assisted nucleophilic additions to olefins are well known and of particular interest in organic synthesis.[1,2] During work on transition-metal assisted asymmetric synthesis[3] we became interested in the possibility of inducing asymmetry in the nucleophilic addition of stabilized carbanions to π-olefinpalladium complexes. Asymmetric induction has previously been observed in the palladium-catalyzed cyclization of 2-allylphenol[4] and in the nucleophilic addition of stabilized carbanion to π-allylpalladium complexes.[5]

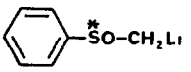
In the preceeding communication we have shown that an asymmetric induction was obtained in the palladium-promoted oxyamination of olefins.[6] We now report some results from palladium-promoted asymmetric alkylation of olefins.

The general accepted route for palladium-assisted alkylation is shown in Scheme 1.

Scheme 1.



Reductive cleavage (by H_2 or $NaBH_4$) of the palladium-carbon bond in the intermediate σ-complexes 2a and 2b gives the products 3a and 3b together with palladium black. When R_1 and R_2 are not H, the final products 3a and 3b bear an asymmetric carbon. In these reactions, chirality may be introduced by the use of a chiral ligand on the metal,[4-6] by the use of a chiral nucleophile or by the use of a chiral ligand together with a chiral nucleophile[6]. In this work we have investigated the first two approaches As chiral nucleophiles, we have used the sulfoxide-containing carbanions 4 (racemic) or 5 (optically pure).[7] As chiral ligands, we have used optically pure (-)S N,N-dimethyl-α-phenylethylamine 6, and (+) α-(1-Naphthyl) ethylamine 7.



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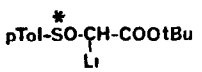

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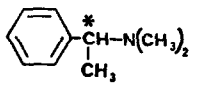
The results from asymmetric alkylation of some olefins are given in Table 1. In entries 1,2 and 4, the amount of asymmetric induction obtained is determined from the diastereomeric ratios of the crude mixtures of products, (8a + 8b), (9a + 9b) and 10, using 250 MHz ^{1}H NMR The regioselectivity is determined simultaneously from ratios between the methyl-triplets (compounds a) and the methyl doublets (compounds b). The optical purity of compound 8a could not be determined by NMR because of too many triplet-like methyl signals in the spectrum. In entry 5 the regioselectivity is determined on the crude mixture 11a + 11b, but the optical purity of 11b was indirectly determined by desulfurization (Raney Ni/etOH) to the ester 11c followed by 90 MHz ^{1}H NMR analysis using Eu(hfc)$_3$. The esters obtained from entries 6 , 7 and 9 were analysed using Eu(hfc)$_3$ and 90 MHz ^{1}H NMR.



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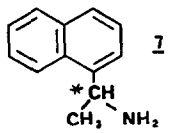

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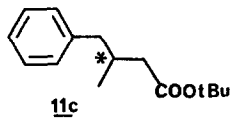
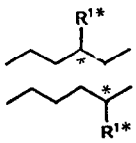
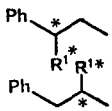
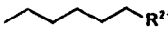
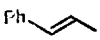
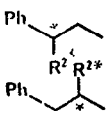
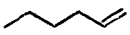
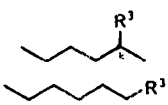
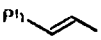
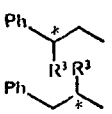
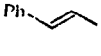
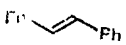


11c

A few features should be noted. The inversion of regioselectivity between run 2 and runs 5, and 7 may be related to the "size" of the anion The asymmetric inductions obtained in entries 1 and 2 (20 to 40%) are larger than those obtained during addition of the very similar methyl-p-tolyl sulfoxide to aldehydes (0% in the case of benzaldehyde)[8] But the asymmetric induction obtained in run 5 (20%) is poor compared to the asymmetric induction obtained during addition of the same anion to benzaldehyde (91%).[8] It must be pointed out that in those entries (1 to 5) the reactive π-complexes are chiral and racemic. The reactions are, therefore, kinetic resolutions, unless the exchange between the enantiomers is rapid enough compared to the rate of nucleophilic addition (Curtin-Hammet principle).

Table 1 Asymmetric Palladium-assisted alkylation of olefins

Runs	Olefins	Nucleophile R^n [a]	Ligand	Products			Ratio a/b %	Asymmetric induction %
1		4	NEt_3		a b	8	90 10	30
2		4	NEt_3		a b	9	85 15	40 20
3		4	NEt_3	no reaction				
4		5	NEt_3			10		20
5		5	NEt_3		a b	11	36 64	20
6		$NaCH(CO_2Et)_2$	6		a b	12	60 40	32
7		$NaCH(CO_2Et)_2$	6		a b	13	37 63	17 10
8		$NaCH(CO_2Et)_2$	7	no reaction				
9		$LiCH(CO_2Et)_2$	6			14		0
10		$NaCH(CO_2Et)_2$	6	no reaction				
11		$NaCH(CO_2Et)_2$	6	no reaction				

a $R^{1*} = CH_2\overset{*}{S}OPh$, $R^{2*} = CH(\overset{*}{S}OPh)CO_2tBu$, $R^3 = CH(CO_2Et)_2$

When the chirality is introduced by the way of a chiral ligand, it appears that asymmetric induction depends upon the nature of the olefin (30% for 1-hexene, 0% for *trans*-2-butene). It must be pointed out that in those cases (runs 6,7, 9) where the π-complexes are diastereomeric mixtures, the asymmetric induction will depend upon the diastereomeric ratio, provided the rate constants for nucleophilic addition are the same for the two isomers

The following procedure has been used for the alkylations 4 mmol of $PdCl_2(C_6H_5CN)_2$ and 8 mmol of the olefin were stirred 10 min at 0°C (runs 2, 3, 4, 5, 7, 8, 9) or 10 min at 20°C (runs 1 and 6) under argon in 40 ml of anhydrous THF The mixture was then cooled to -78°C, 8 mmol of amine was added dropwise through a syringe over a period of 10 min The temperature was allowed to increase to -50°C and the carbanion (6 mmol) was added dropwise through a syringe over a period of 10 min. After the mixture was stirred for 2 hrs at -50°C, the flask was flushed with H_2 and the cold bath removed The product mixture 3a + 3b was isolated by column chromatography[9] and analyzed.

The chemical yields have not yet been optimized and are still low ,between 20 and 35% , but the asymmetric inductions thus far obtained (Table 1) are encouraging.

Attempts to increase the asymmetric induction by using a "more disymmetric" amine as ligand together with chiral nucleophile are under investigation

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