



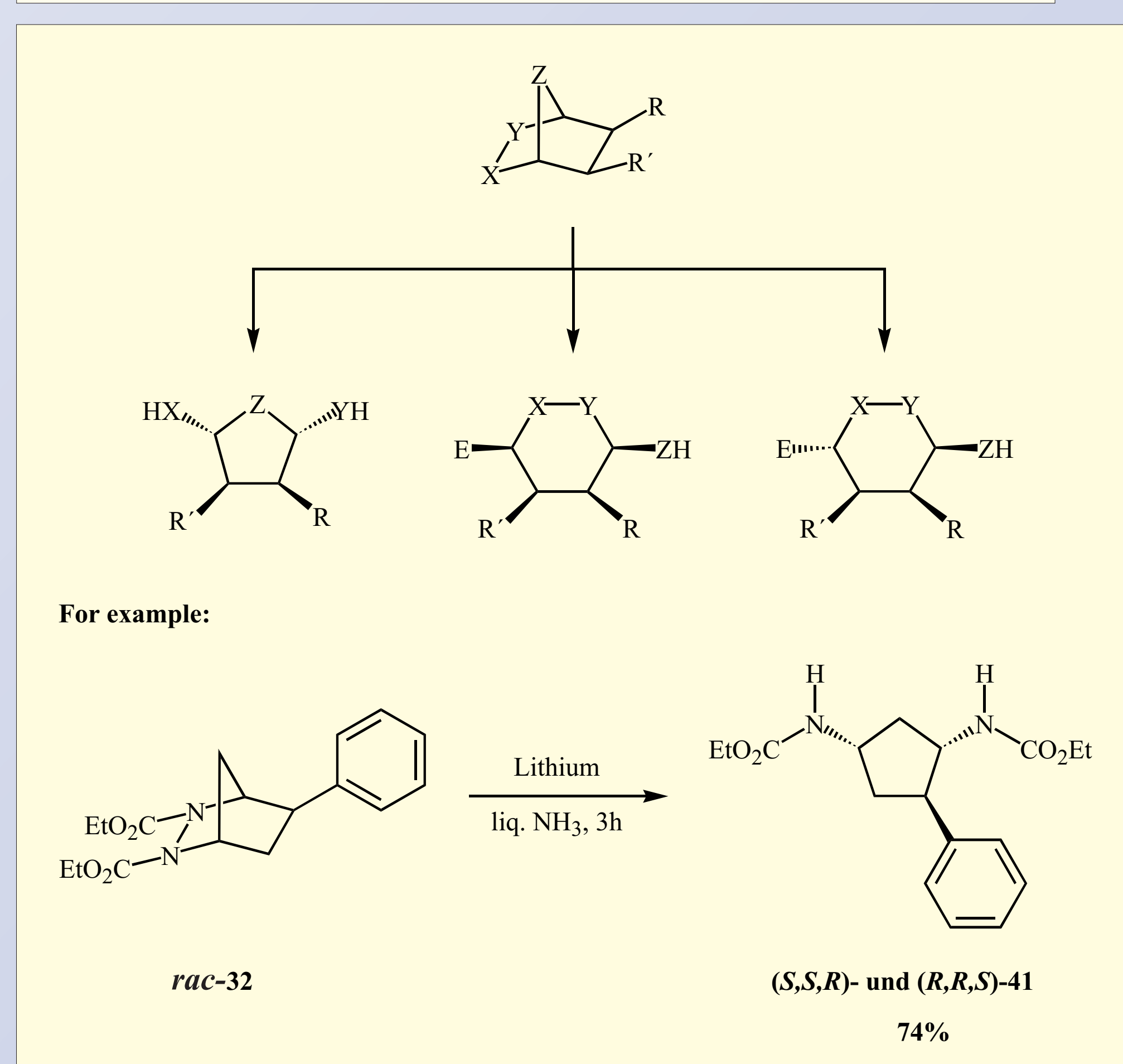
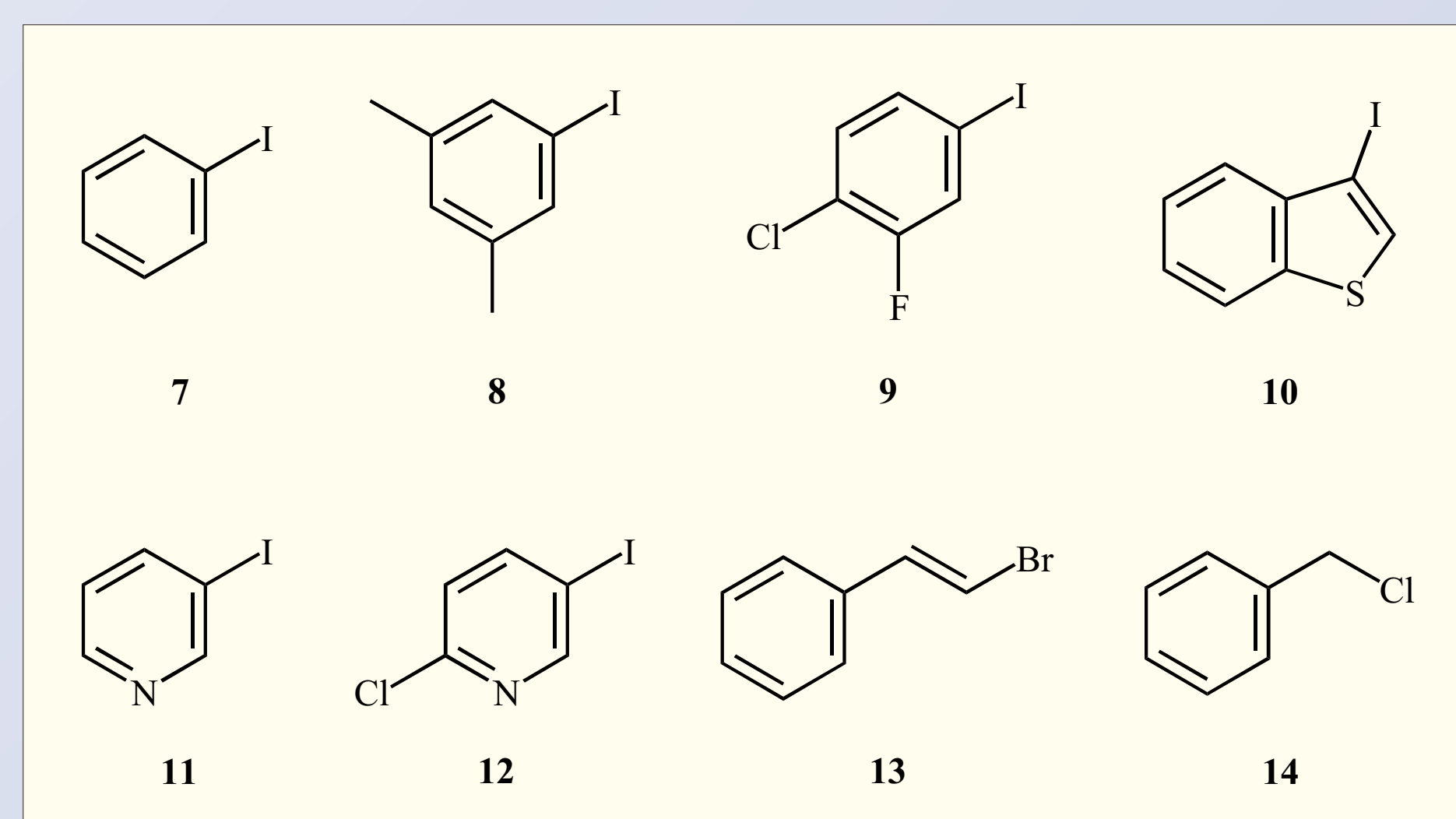
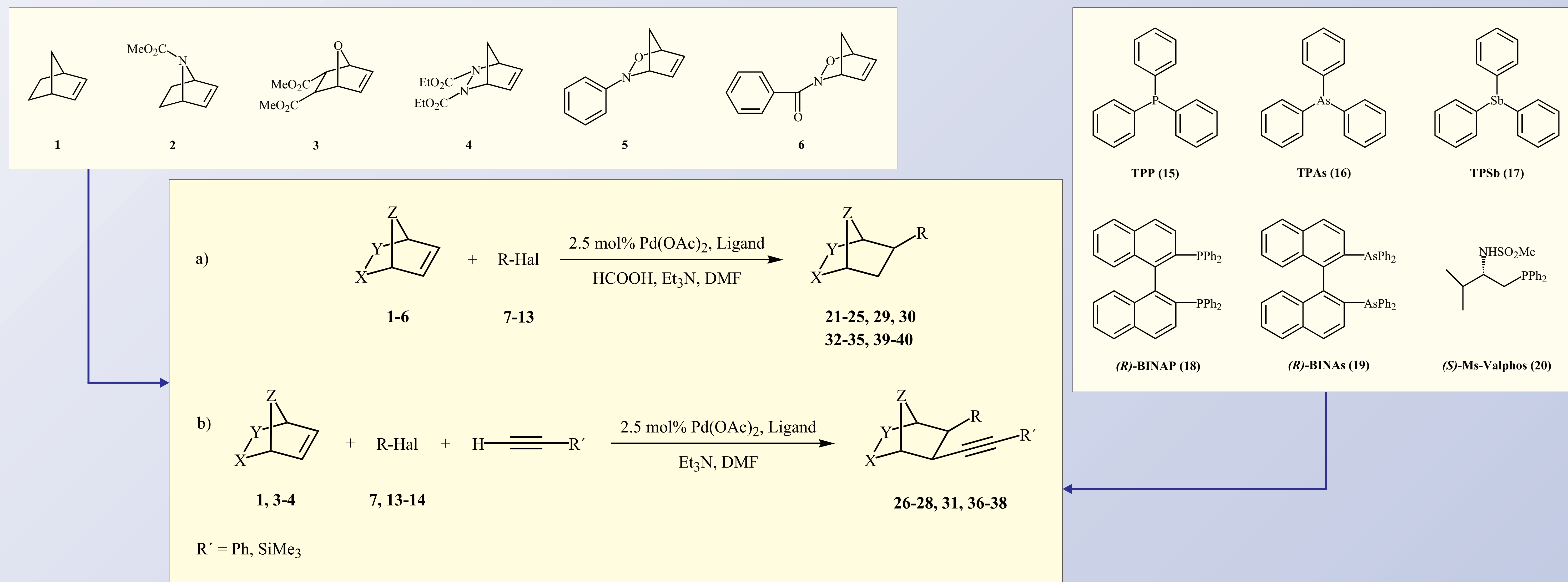
(Asymmetric) Palladium catalyzed C-C-bond formation on hetero[2.2.1]bicyclic alkenes

Jörg Storsberg and Dieter E. Kaufmann*

Technische Universität Clausthal, Institut für Organische Chemie,
Leibnizstraße 6, D-38678 Clausthal-Zellerfeld

Introduction

One of the most important class of reactions in organic synthesis are C-C-bond formations. Among them, asymmetric reactions, especially on sp^2 -carbons, recently reached more interest as an easy method to build up complex structures with defined stereochemistry from simple non-chiral precursors. Against this background, the palladium-catalyzed *Heck*-type reactions have been established as a convenient method resulting high yields and enantiomeric excesses^[1]. Aims of our work are the hydroarylations^[2] and tandem-coupling reactions^[3] on (hetero)bicyclic alkenes leading to products nearby physiologically potent mainstructures from nature. Moreover we have carried out some following chemistry using these products as precursors for cycloalkane derivatives with high stereochemical demand.



entry	alkene	arylic compound	nucleophile	T	ligand	product	c.y.	e.e.
1					16	21	99%	
2		7			20	21	55%	42%
3					19	24	84%	3%
4		8	H^\ominus			22	86%	
5		10		65°C	16	23	68%	
6		11				24	73%	
7	1	12				25	59%	
8					16	26	57%	
9		7	$\text{H-C}\equiv\text{C-Ph}$		18	26	33%	rac.
10					20	26	35%	20%
11		7	$\text{H-C}\equiv\text{C-SiMe}_3$	40°C	16	27	65%	
12		13			16	28	66%	
13			H^\ominus	65°C	16	29	81%	
14	2	12			18	29	47%	80%
15					19	29	86%	2%
16		7	H^\ominus	65°C	16	30	84%	
17	3		$\text{H-C}\equiv\text{C-Ph}$		16	31	74%	
18		7				32	77%	
19		9	H^\ominus			33	52%	
20		12				34	35%	
21	4	13		65°C	16	35	86%	
22		7	$\text{H-C}\equiv\text{C-Ph}$			36	52%	
23		13				37	18%	
24		14				38	12%	
25	5	7	H^\ominus	0°C	16	39	6%	
26	6	7	H^\ominus	65°C	16	40	38%	

Side-reactions

- Under the reductive reaction-conditions the reduction of the organic halide^[4] is a serious problem lowering the yield of the desired product. This side-reaction depends on the electronic properties of the arylic compound and can be suppressed by using **16** as a ligand. A second side-reaction is the palladium-catalyzed homo-cross-coupling^[5]. At last the ligand-scrambling-phenomenon is to mention for ligand **17** especially.
- In the case of tandem-coupling reactions the leading side-product is based on a *Sonogashira*-type reaction^[6]. The equilibrium can be affected to the side of the desired product by rising the amount of the alkene. Also homo-coupling was observed.

Summary and outlook

Based on the experiences of our working-group^[7] some (hetero)bicyclic alkenes have been proved as useful compounds in reductive *Heck*-type and also tandem-coupling reactions with a large variety of organic halides. Despite from the undesired side-reactions in most cases interesting products were obtained in good yields. The cleavage of the products of heterobicyclic alkenes on the heterobond as it is shown in the example leads to stereodefined tri- and also tetrasubstituted cycloalkane derivatives. To the best of our knowledge the *Heck*-type reaction on [2.2.1]bicyclic systems exclusively results in *exo*-configuration of the arylic moiety. In case of symmetrically substituted bicyclic compounds the number of stereochemically different products (3 stereocenters) is reduced to one pair of enantiomers [e.g. (*R,R,S*)- and (*S,S,R*)-**41**, respectively]. Studies on asymmetric palladium-catalyzed reactions are underway.

References

- [1] For reviews see: (a) R. C. Larock, *Pure and Appl. Chem.*, **1990**, 62, 653-660. (b) A. de Meijere, F. E. Meyer, *Angew. Chem.*, **1994**, 106, 2473-2506; *Angew. Chem. Int. Ed. Engl.*, **1994**, 33, 2379-2411. (c) G. T. Crisp, *Chem. Soc. Reviews*, **1998**, 27, 427-436.
- [2] (a) A. Arcadi, F. Marinelli, E. Bernocchi, S. Cacchi, G. Ortari, *J. Organomet. Chem.*, **1989**, 368, 249-256. (b) R. C. Larock, P. L. Johnson, *J. Chem. Soc., Chem. Commun.*, **1989**, 1368-1370.
- [3] (a) M. Catellani, G. P. Chiusoli, *Tetrahedron Lett.*, **1982**, 23, 4517-4520. (b) M. Catellani, B. Marmiroli, M. C. Fagnola, D. Acquotti, *J. Organomet. Chem.*, **1996**, 507, 157-162. (c) M. Catellani, E. Motti, L. Paterlini, *J. Organomet. Chem.*, **2000**, 593-594, 240-244.
- [4] Q.-Y. Chen, Y.-B. He, Z.-Y. Yang, *J. Chem. Soc., Chem. Commun.*, **1986**, 1452-1453.
- [5] Jiro Tsuji, *Palladium Reagents and Catalysts*, Wiley **1995**.
- [6] K. Nakamura, H. Okubo, M. Yamaguchi, *Synlett*, **1999**, 5, 549-550.
- [7] (a) J. C. Namyslo, D. E. Kaufmann, *Chem. Ber.*, **1997**, 130, 1327-1331. (b) A. Otten, J. C. Namyslo, M. Stoermer, D. E. Kaufmann, *Eur. J. Chem.*, **1998**, 1997-2001. (c) J. C. Namyslo, D. E. Kaufmann, *Synlett*, **1999**, 6, 804-806 and references cited therein.