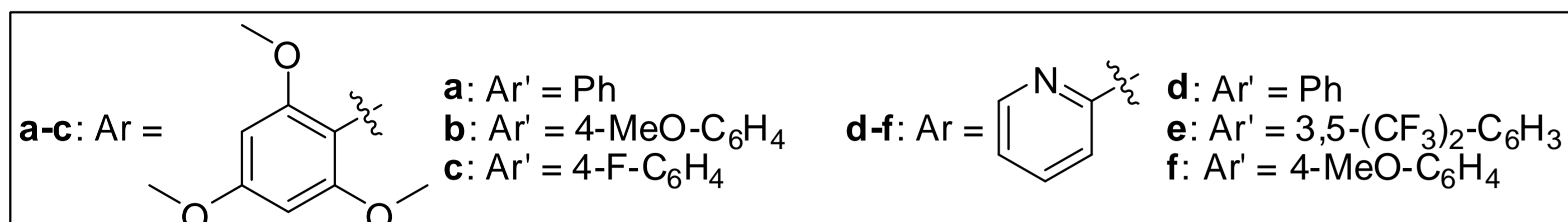
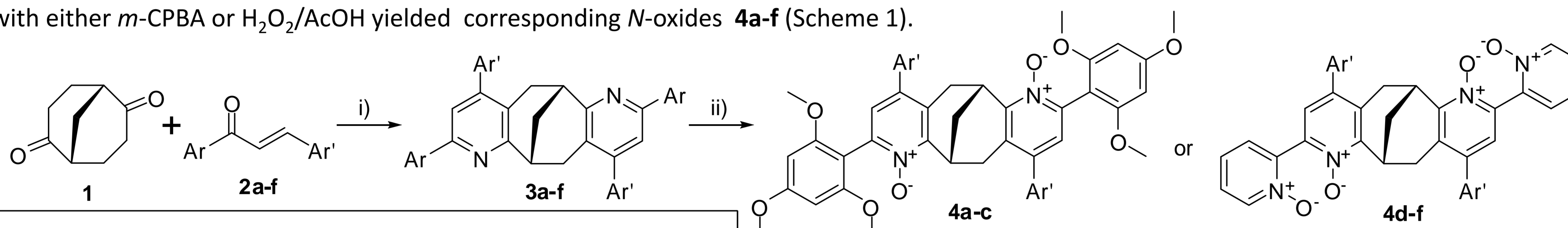


Introduction

Over the preceding decade, asymmetric organocatalysis has become one of the most rapidly developing areas in synthetic organic chemistry. In particular, activation of organosilicon reagents with chiral Lewis-basic catalysts has attracted considerable attention due to ability of silicon atom to expand its coordination sphere forming hypervalent species with enhanced reactivity [1]. Because of the high Lewis basicity, pyridine and 2,2'-bipyridine *N*-oxides proved to be efficient catalysts for activation of allyltrichlorosilanes, silyl enol ethers, chlorosilanes, etc., towards electrophilic targets [2]. Herein we present the synthesis of chiral bicyclo[3.3.1]nonane derived pyridine and 2,2'-bipyridine *N*-oxide derivatives **4a-f** and their application as Lewis-basic catalysts in asymmetric reactions of chlorosilanes.

Synthesis of chiral pyridine and 2,2'-bipyridine *N*-oxides

Synthesis of enantiomerically pure compounds was accomplished by using (+)-(1*S*,5*S*)-bicyclo[3.3.1]nonane-2,6-dione (**1**, >99% *ee*) [3]. Pyridine derivatives **3a-f** were synthesized *via* Michael reaction between 2,6-dione **1** and corresponding propenones **2a-f**, followed by cyclization of the obtained intermediate 1,5-diketones. Subsequent oxidation of **3a-f** with either *m*-CPBA or H₂O₂/AcOH yielded corresponding *N*-oxides **4a-f** (Scheme 1).

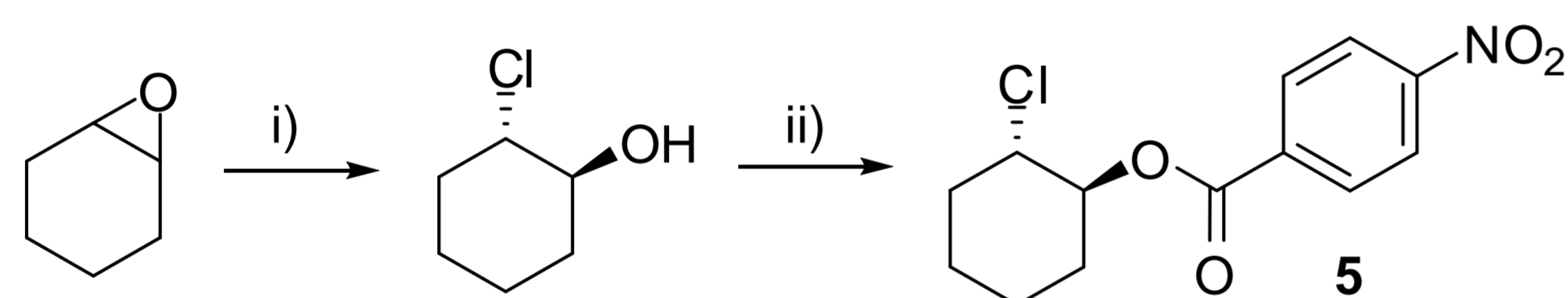


Scheme 1. i) NaH, DMF, 0 °C then NH₄OAc, AcOH, 120 °C (**a-c**, 22-48%) or NaOH, MeOH, 36 °C then NH₂OH·HCl, EtOH, Δ (**d-f**, 34-69%); ii) *m*-CPBA, K₂CO₃, DCM, 0 °C (**a-c**, 32-44%) or H₂O₂, AcOH, 76 °C (**d-f**, 55-82%).

Desymmetrization of *meso*-epoxides

Ligand screening

Lewis bases **4a-d** promoted opening of a model substrate, cyclohexene oxide, with SiCl₄ to furnish chlorohydrins in good yields (isolated as corresponding 4-nitrobenzoates **5**) and non-negligible enantioselectivities (Scheme 2).

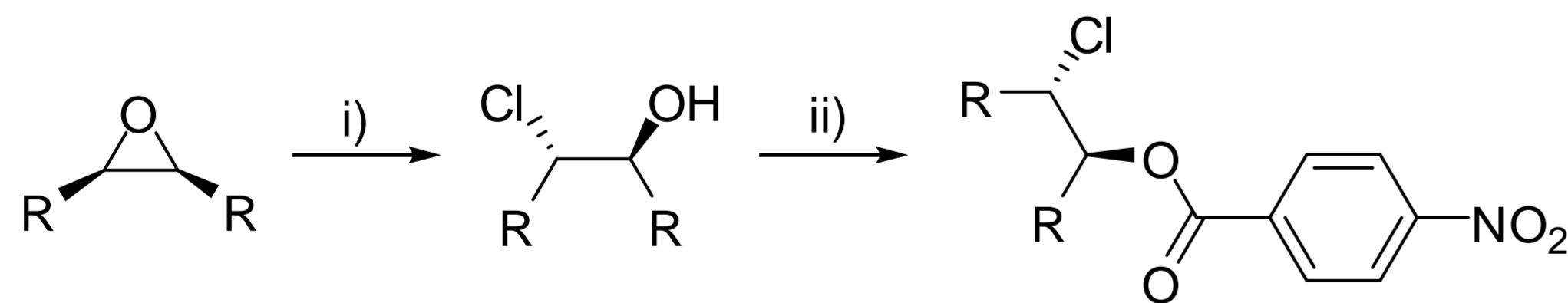


Scheme 2. i) SiCl₄, **4a-d** (10 mol%), DIPEA, DCM, -78 °C, 20 h; ii) 4-NO₂-C₆H₄COCl, DMAP, TEA, DCM.

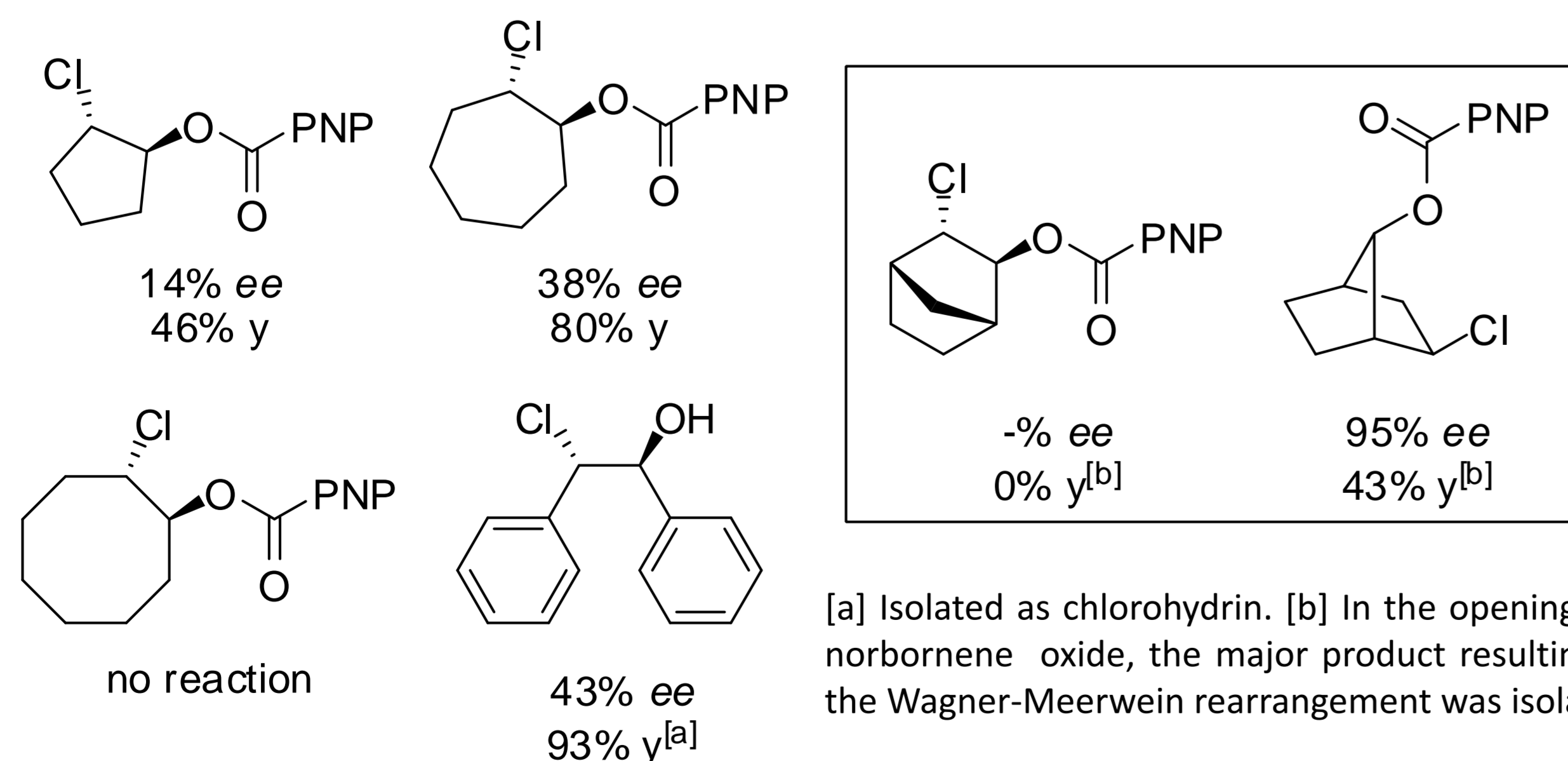
Lewis base	<i>ee</i> , % (5)	Yield, % (5)
4a	32	72
4b	18	56
4c	27	81
4d	31	85

Substrate scope

Preliminary substrate scope was explored using several other *meso*-epoxides and pyridine *N*-oxide **4a** as a catalyst (Scheme 3).



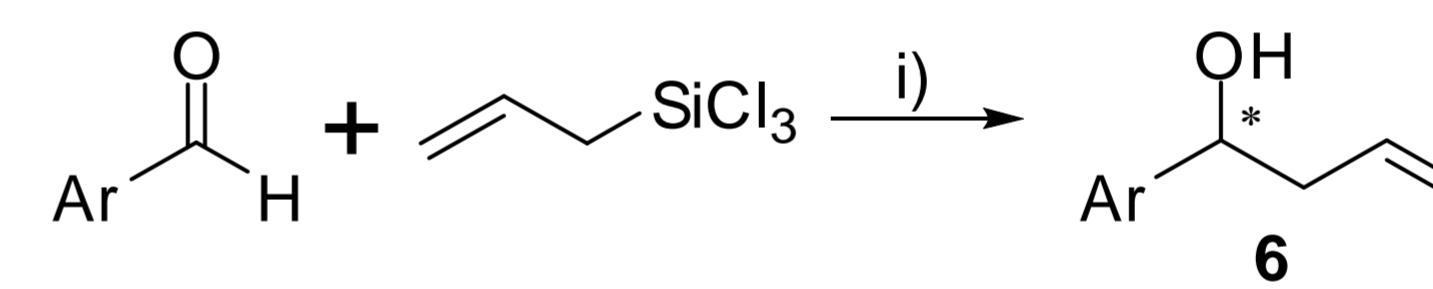
Scheme 3. i) SiCl₄, **4a** (10 mol%), DIPEA, DCM, -78 °C, 20-44 h; ii) 4-NO₂-C₆H₄COCl, DMAP, TEA, DCM.



[a] Isolated as chlorohydrin. [b] In the opening of the norbornene oxide, the major product resulting from the Wagner-Meerwein rearrangement was isolated.

Allylation of aromatic aldehydes

N-oxides **4a-f** were tested as Lewis-basic catalysts in allylation of aldehydes with allyltrichlorosilane (Scheme 4). Pyridine *N*-oxides **4a-c** were quite ineffective even at room temperature, whereas 2,2'-bipyridine *N,N'*-dioxide derivatives **4d-f** proved to be superior in terms of both stereocontrol and reactivity. Catalytic activity was retained at -40 °C and **4f** exhibited enhanced levels of asymmetric induction, furnishing corresponding homoallylic alcohols **6** in good yields and enantioselectivities up to 75%.



Scheme 4. i) **4a-f** (10 mol%), DIPEA, MeCN or DCM, 6-24 h.

Lewis base	Ar	Solvent	T, °C	<i>ee</i> , % (6)	Yield, % (6)
4a ^[a]	Ph	MeCN	r. t.	14	68
4b ^[a]	Ph	MeCN	r. t.	16	57
4d	Ph	MeCN	r. t.	20	84
4a ^[a]	Ph	DCM	r. t.	37	51
4c ^[a]	Ph	DCM	r. t.	28	20
4d	Ph	DCM	r. t.	40	69
4d	Ph	DCM	-40	55	69
4e	Ph	DCM	-40	59	67
4f	Ph	DCM	-40	63	68
4f	4-F-C ₆ H ₄	DCM	-40	55	70
4f	4-MeO-C ₆ H ₄	DCM	-40	75	73

[a] Reactions were carried out for 48h.

Conclusions

A method for the synthesis of chiral C₂-symmetric pyridine *N*-oxide and 2,2'-bipyridine *N,N'*-dioxide derivatives from enantiomerically pure bicyclo[3.3.1]nonane-2,6-dione has been developed. Lewis-basic organocatalyst **4a** exhibited moderate stereocontrol in opening of *meso*-epoxides with SiCl₄ (*ee* up to 43%), while desymmetrization of norbornene oxide yielded the Wagner-Meerwein rearrangement product in unprecedented enantioselectivity (95% *ee*). In comparison with pyridine *N*-oxides **4a-c**, 2,2'-bipyridine *N,N'*-dioxides **4d-f** were found to be superior catalysts for allylation of aldehydes with allyltrichlorosilane (*ee* up to 75% with **4f**).

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