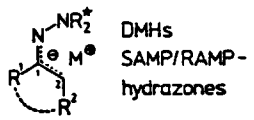
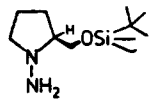
DIETER ENDERS

SUMMARY OF LECTURE

REAGENTS FOR REGIO-, DIASTEREO-, AND ENANTIOSELECTIVE ELECTROPHILIC SUBSTITUTIONS AND FOR CHROMATOGRAPHIC RESOLUTION

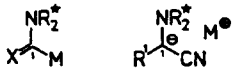


DMHs
SAMP/RAMP-hydrazones



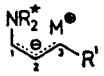
resolution reagent (HPLC)

$d^{2\bullet}$-reagents

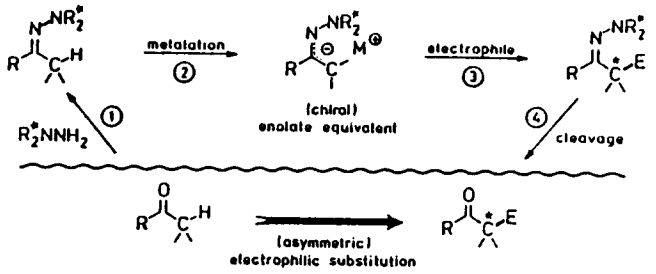


$d^{1\bullet}$-reagents

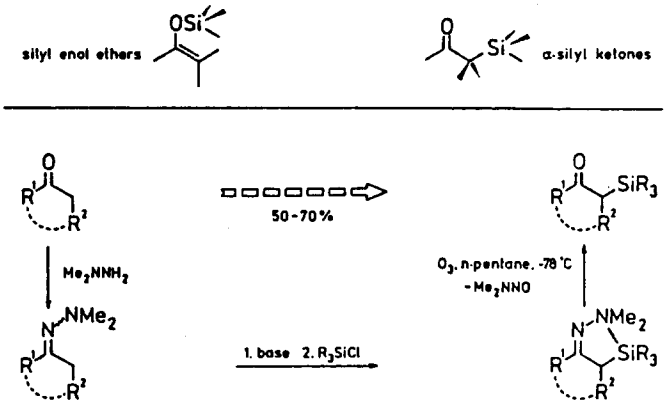
(X = O, S)



$d^{3\bullet}$-reagents



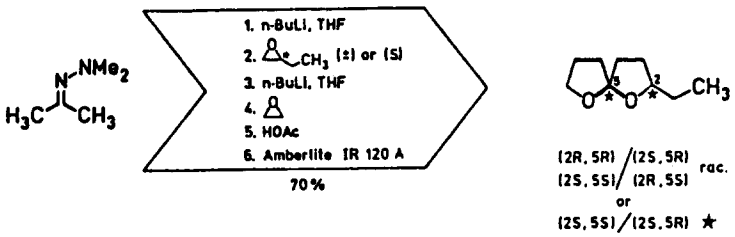
A NEW SIMPLE SYNTHESIS OF α-SILYLATED KETONES



R_3 = Me_3, Et_3, $t\text{-}BuMe_2$, Ph_3

D. ENDERS, P. WEUSTER, KAGAKU-ZOKAN (KYOTO) 99, 95 (1983)

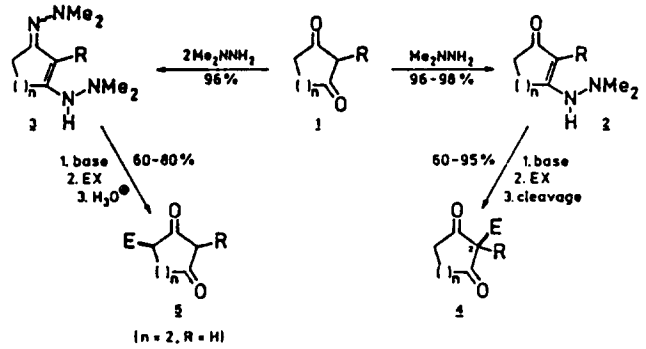
SYNTHESIS OF RAC. AND OPTICALLY ACTIVE CHALCOGRAN AGGREGATION PHEROMONE OF PITYOGENES CHALCOGRAPHUS L.



steps 1-5 in one pot, 10g scale!
rac. chalcogran biologically active in field tests (CELAMERCK, Ingelheim)

D. ENDERS, P. WEUSTER, W. DAHMEN, E. DEDERICHS, SYNTH. COMMUN. 13, 1235 (1983)

REGIOSELECTIVE ALKYLATIONS OF CYCLIC 1.3-DIKETONES VIA METALATED MONO- AND BIS-DIMETHYLHYDRAZONES (DMHs)

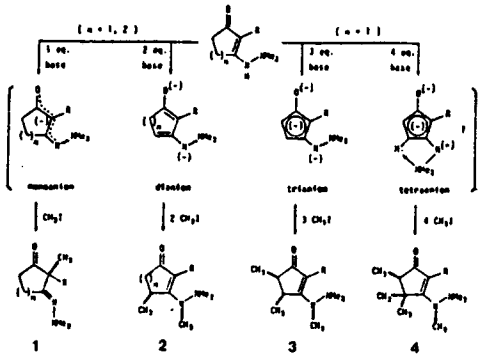


EX = CH_3I, C_2H_5I, $BrCH_2C{\equiv}CH$, $BrCH_2COOC_2H_5$, $BrCH_2-\overset{Br}{C}=CH_2$, $C_6H_5CH_2Br$,

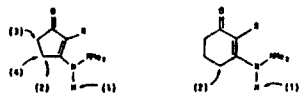
ICH_2CH_2CH (dioxolane) etc.

D.ENDERS, A.S.DEMIR, KAGAKU-ZOKAN (KYOTO) 99, 95 (1983)

REGIOSELEKTIVE ALKYLATIONS OF CYCLIC 1.3 - DIKETONES VIA POLYMETALATED DMH - DERIVATIVES



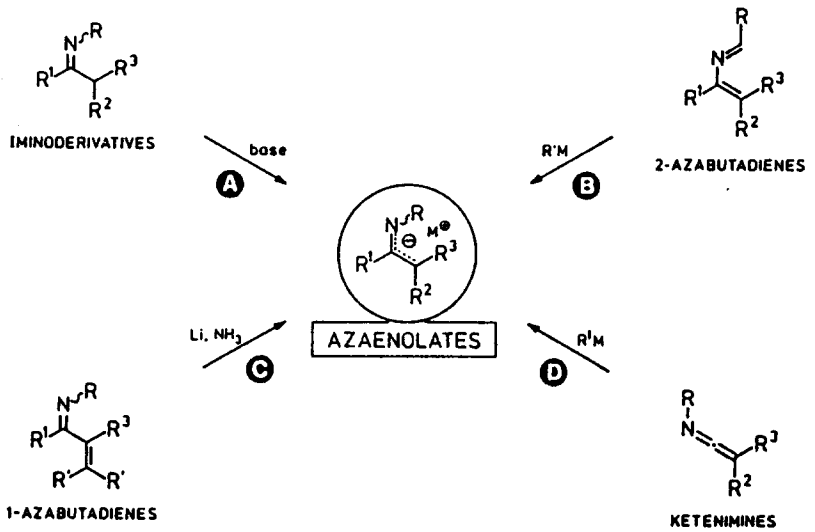
SEQUENCE OF DEPROTONATION



YIELDS: 1,2,3 (85 - 95%)
HYDROLYSIS TO 1.3-DIONES (75 - 85%)

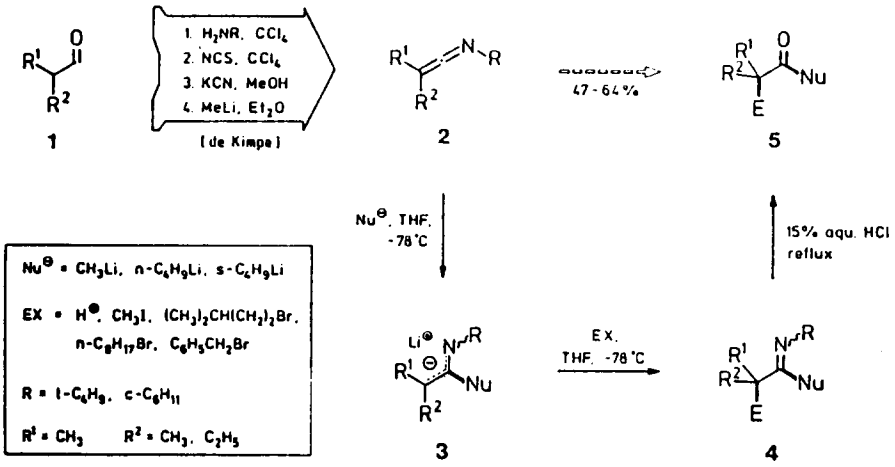
D.ENDERS, A.S.DEMIR, KAGAKU - ZOKAN (KYOTO) 99, 95 (1983)

REGIOSELECTIVE GENERATION OF AZAENOLATES

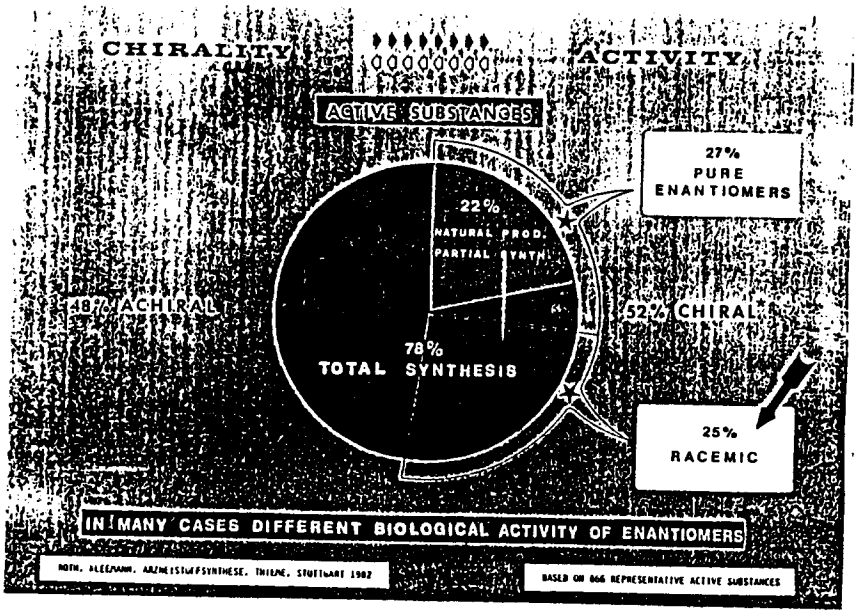


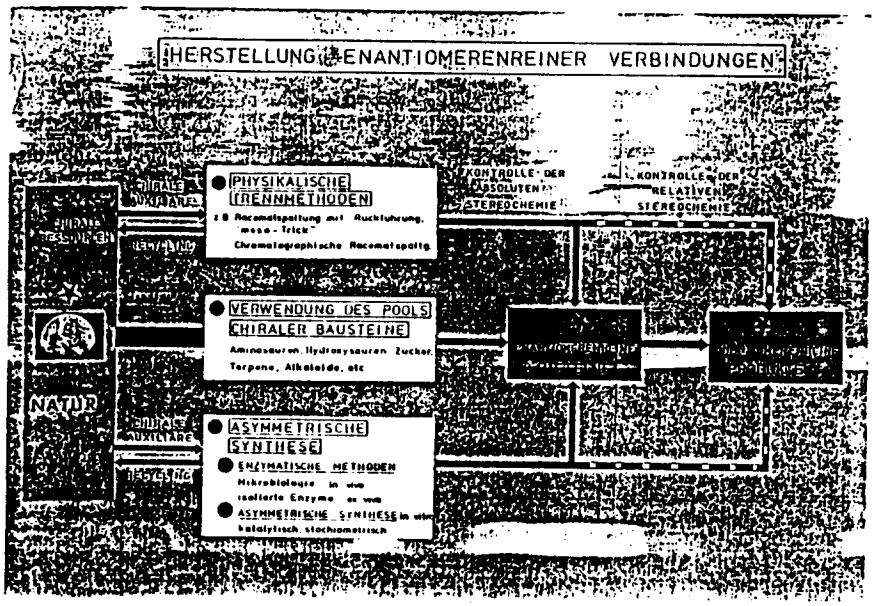
A VERY FLEXIBLE, REGIOSELECTIVE SYNTHESIS OF ACYCLIC KETONES

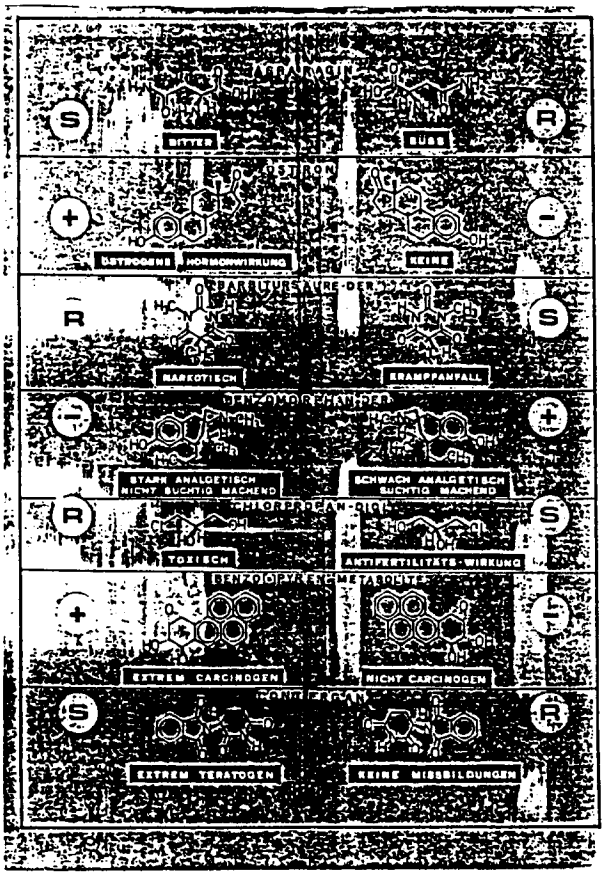
GENERATION OF AZAENOLATES BY NUCLEOPHILIC ADDITION OF ORGANOLITHIUMS TO KETENIMINES

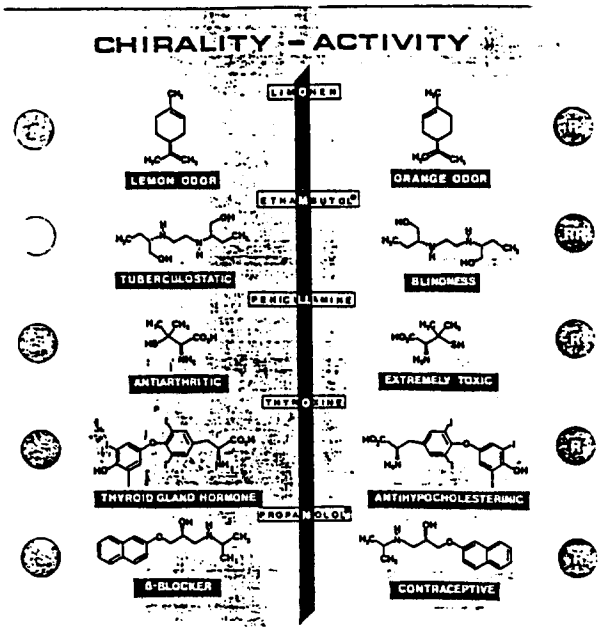


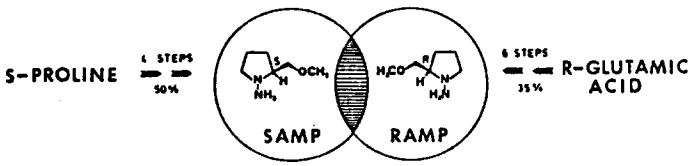
D. ENDERS, H. H. SPELTHANN, unpublished



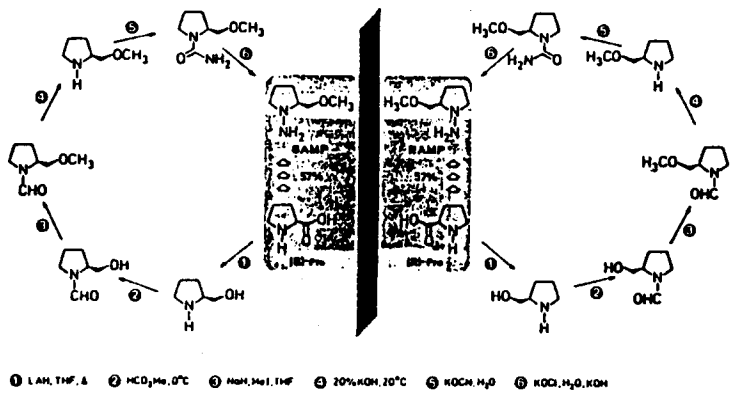






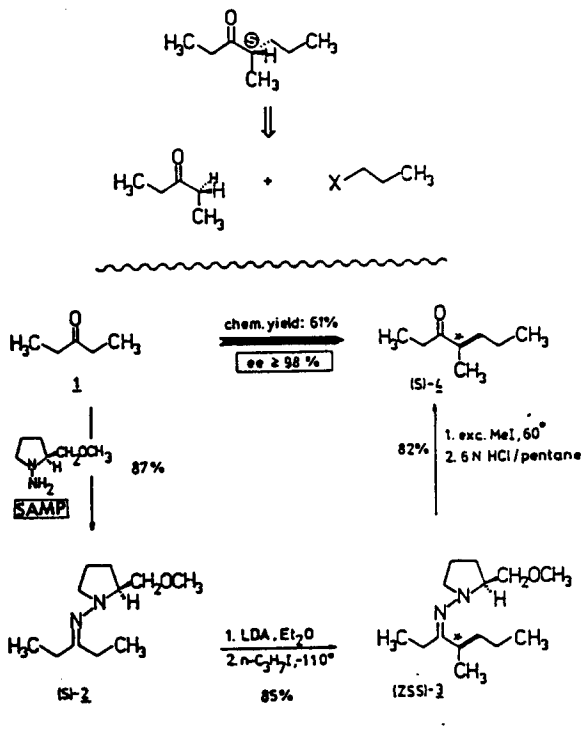


NITROSAMINE FREE, LARGE SCALE PREPARATION OF SAMP AND RAMP VIA HOFMANN DEGRADATION



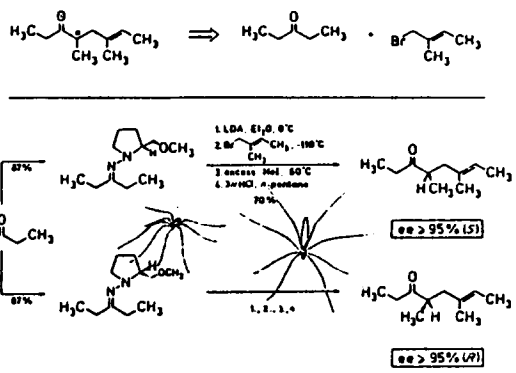
D. ENDERS, P. FEY, H. KIPPHARDT, OPPI 17.1 (1985)

Enantioselective Synthesis of (S)-(+)-4-Methyl-3-heptanone. Alarm Pheromone of the leaf-cutting ant atta texana

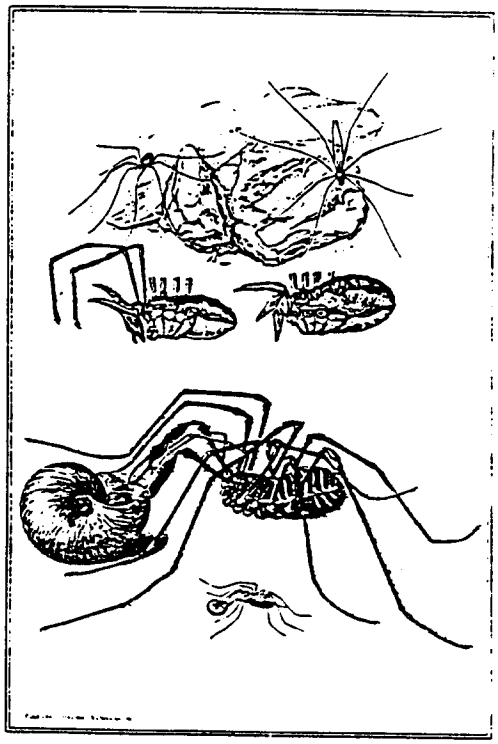


D. ENDERS, H. EICHENAUER, ANGEW. CHEM. 91, 425 (1979)

ASYMMETRIC SYNTHESIS OF BOTH ENANTIOMERS OF (E)-4,6-DIMETHYL-6-OCTENE-3-ONE — DEFENSIVE SUBSTANCE OF "DADDY LONGLEGS" LEIOBUNUM VITTATUM AND L.CALCAR (OPILIONIDS)



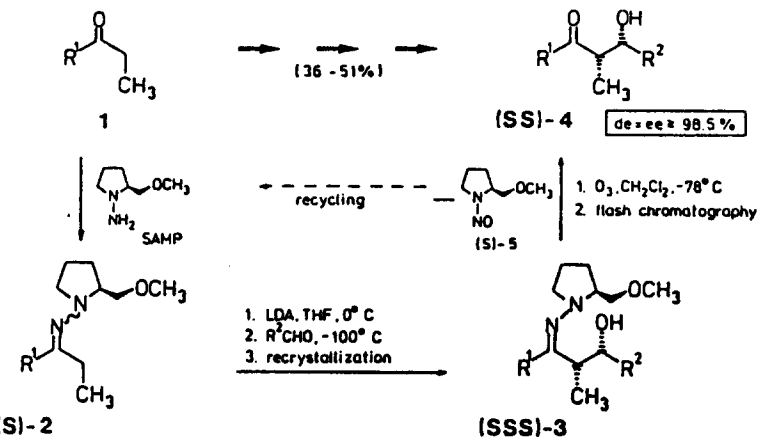
D.ENDERS, U.BAUS, LIEBIGS ANN CHEM. (1983), 1439



SYNTHETIC APPLICATIONS OF THE SAMP/RAMP-HYDRAZONE METHOD

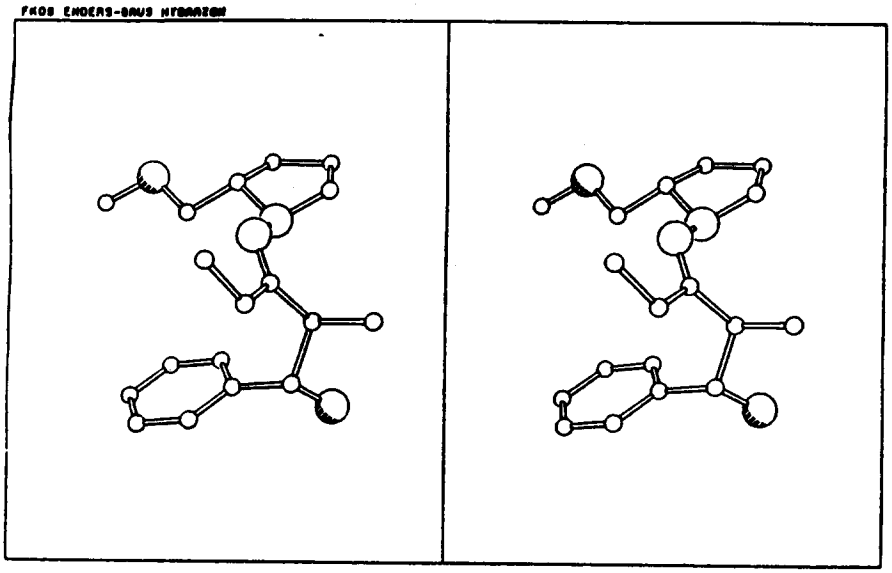
1. BESTMANN et al. 1981 unpublished — PHEROMONES — ee ≥ 95%
2. NICOLAOU et al. J. Am. Chem. Soc. 103, 6967, 6969 (1981). — IONOPHORE ANTIBIOTIC X 14547 A — de = 95%, ee = 82%
3. PENNANEN Acta Chem. Scand. B 35, 555 (1981). — SESQUITERPENE — ee = 89%
4. MORI et al. Tetrahedron 38, 3705 (1982) — PHEROMONE (cigarette beetle) — as active as natural pheromone, ee ≥ 99%

SYN- DIASTEREO- AND ENANTIOSELECTIVE ALDOL REACTIONS VIA SAMP/RAMP-HYDRAZONES. PREPARATION OF DIASTEREO- AND ENANTIOMERICALLY PURE SYN- β-KETOLS

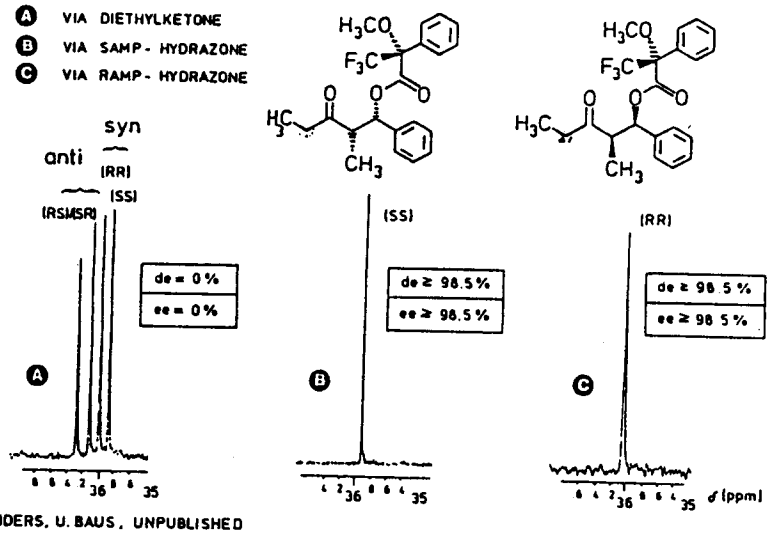


D.ENDERS, U.BAUS, K.A.M.KREMER, ANGEW. CHEM.

FROM ENDERS-BAUS HYDRAZONE

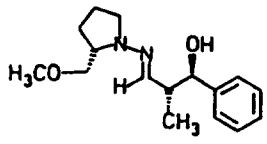


DETERMINATION OF PERCENT DE AND EE OF α-SUBSTITUTED β-KETOLS BY ^{13}C NMR SPECTROSCOPY OF THEIR MTPA-ESTERS



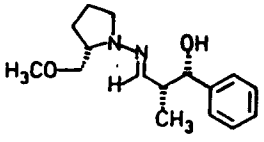
D. ENDERS, U. BAUS, UNPUBLISHED

FFECT OF GEGENION ON THE DIASTEREOSELECTIVITY OF THE ALDOL-REACTION OF PROPANAL-SAMP-HYDRAZONE AND BENZALDEHYDE



Li — de = 60% (anti)

MgBr — de = 0%

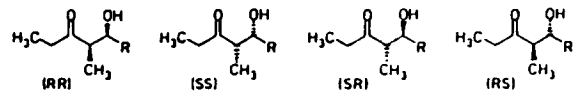


TiO^iPr_3 — de = 84% (syn)

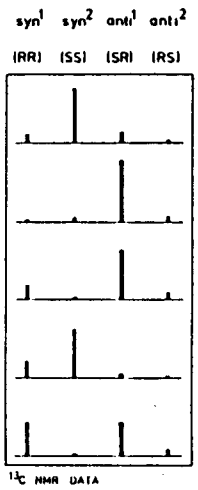
solvent: THF

D.Enders, U.Baus, unpublished results

EFFECTS OF GEGENION AND SOLVENT ON THE DIASTEREO- AND ENANTIO-SELECTIVITY OF ALDOL REACTIONS VIA SAMP-HYDRAZONES

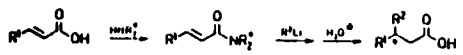


R = C_6H_5	Li	de = 66 % (syn)	ee = 74 %
solvent : THF	MgBr	de = 80 % (anti)	ee = 82 %
R = C_2H_5	Li	de = 55 % (anti)	ee = 74 %
solvent : THF	SnCl	de = 82 % (syn)	ee = 52 %
solvent: pentane	Li	de = 0 %	ee (syn) = 87 % ee (anti) = 70 %

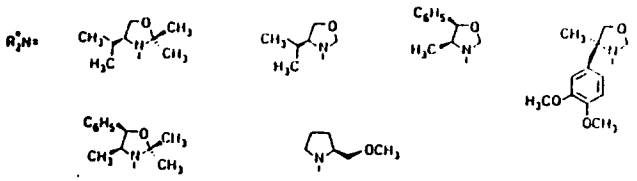


D. ENDERS, U. BAUS, UNPUBLISHED RESULTS

ASYMMETRIC SYNTHESIS OF β-SUBSTITUTED CARBOXYLIC ACIDS



good overall chem. yields — ee = 6-39%



K. PAPADOPOULOS, diploma work, Bonn 1981

MICHAEL – ADDITION

ARTHUR MICHAEL

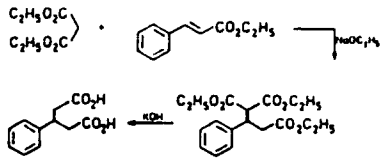
*1853 BUFFALO, NEW YORK, USA
†1942

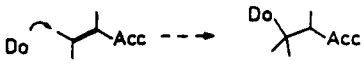
studied at Heidelberg, Berlin, Paris

teached at
Tufts College, Boston
Clark University, Worcester
Harvard University, Cambridge

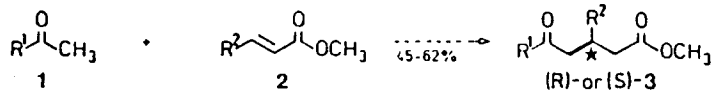
1883/84 Kommenos, Claisen, Crismer first observations

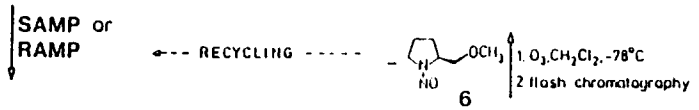
1887 A. Michael, J. prakt. Chem. 35, 349 (1887)

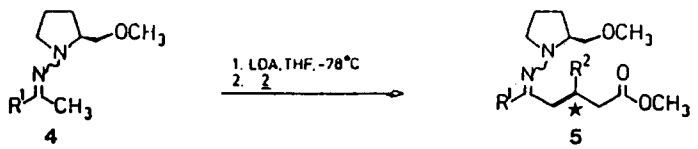




ASYMMETRIC SYNTHESIS OF δ-KETOESTERS VIA SAMP/RAMP-HYDRAZONE-MICHAEL-ADDITIONS TO α,β-UNSATURATED ESTERS VIRTUALLY COMPLETE 1,6-ASYMMETRIC INDUCTION !





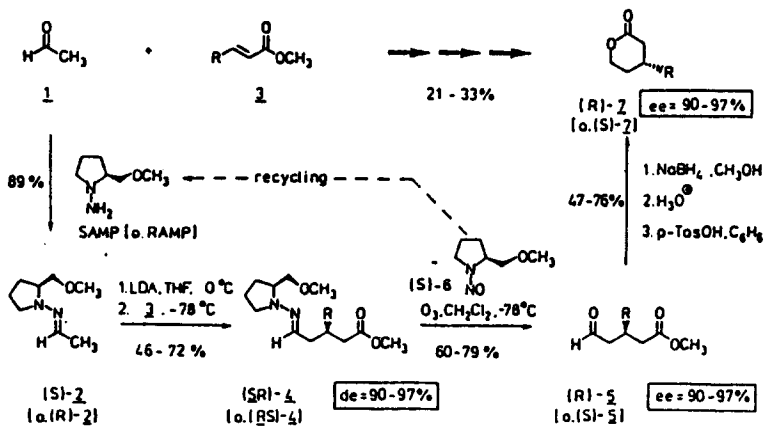


R¹ = Me, Et, n-Pr, i-Pr, n-Pent, n-Hex, Ph; R² = Me, Ph (12 examples)

D. Enders, K. Papadopoulos, Tetrahedron Lett. 24 (1983) 4967

Enantioselective Synthesis of 3-substituted 5-Oxopentanoates and δ-Lactones

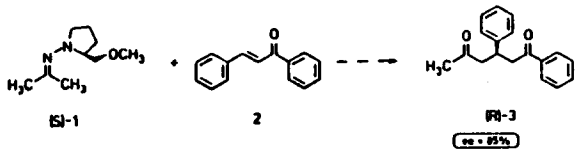
Asymmetric Michael-Addition of Acetaldehyde to Enoates via the SAMP-/RAMP-Hydrazone Method

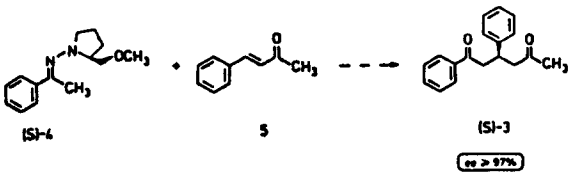


D. Enders, B. Rendenbach, unpublished results

ASYMMETRIC SYNTHESIS OF 1,5-DIKETONES VIA SAMP-HYDRAZONES

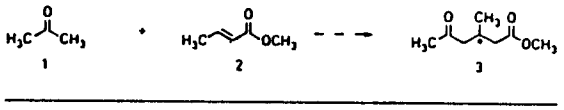
OPPOSITE ENANTIOSELECTIVITY THROUGH SYNTHON CONTROL

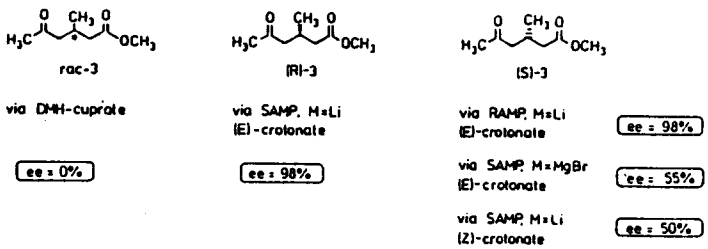




D. ENDERS, K. PAPADOPOULOS, unpublished results

CHANGE OF OVERALL ENANTIOSELECTIVITY



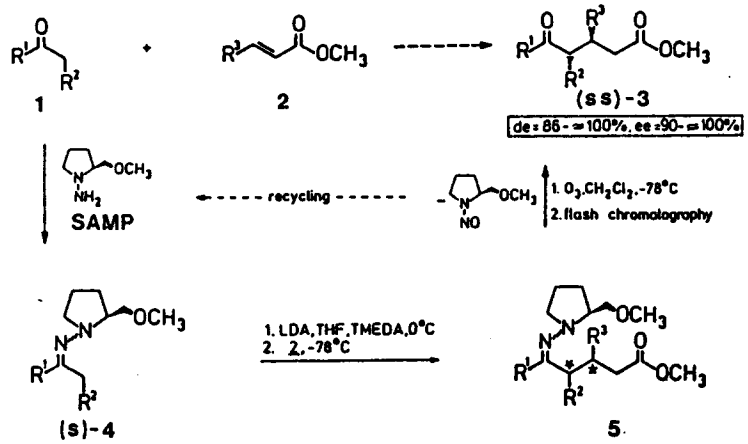


D. ENDERS, K. PAPADOPOULOS, unpublished results

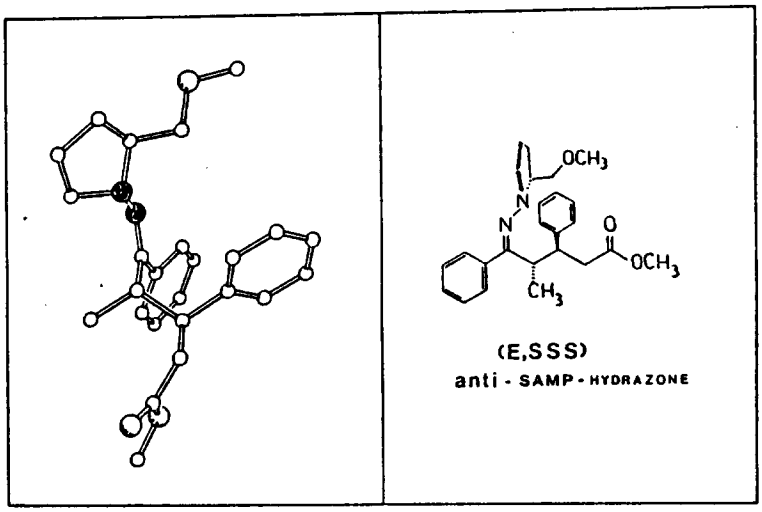
ASYMMETRIC MICHAEL-ADDITIONS VIA SAMP/RAMP-HYDRAZONES

ANTI-DIASTEREO-AND ENANTIOSELECTIVE SYNTHESIS

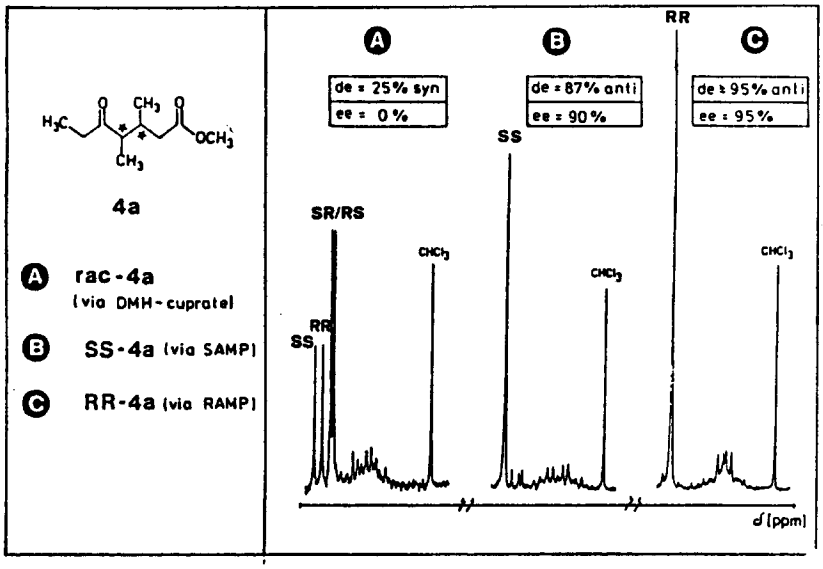
OF β,γ-DISUBSTITUTED δ-KETOESTERS



D. ENDERS, K. PAPADOPOULOS, Tetrahedron Lett. 27, (1986)



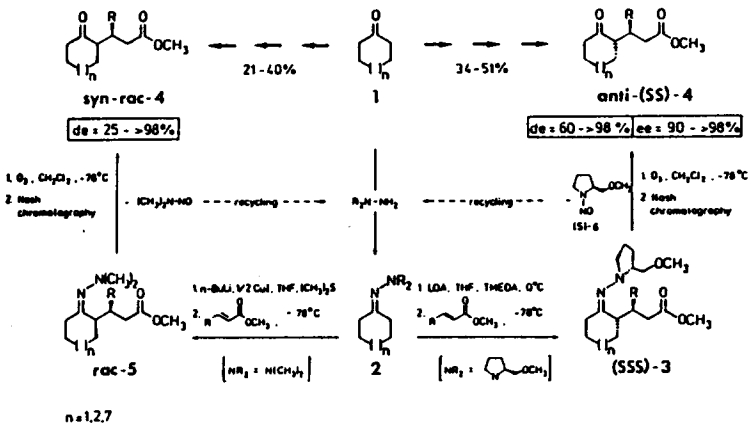
(E,SSS)
anti - SAMP - HYDRAZONE



DETERMINATION OF % EE AND DE BY NMR SHIFT EXPERIMENTS(ESTER METHOXY SINGLET, $Eu(HFC)_3$)

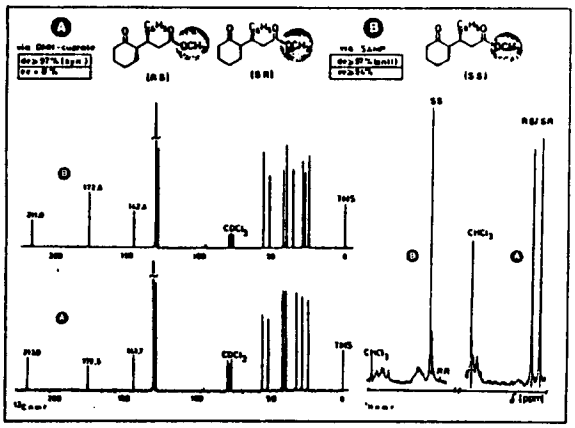
ASYMMETRIC MICHAEL-ADDITIONS OF CYCLIC KETONES TO ENOATES VIA THEIR SAMP-HYDRAZONES

METAL CONTROLLED REVERSAL OF SYN/ANTI-DIASTEREOSELECTIVITY



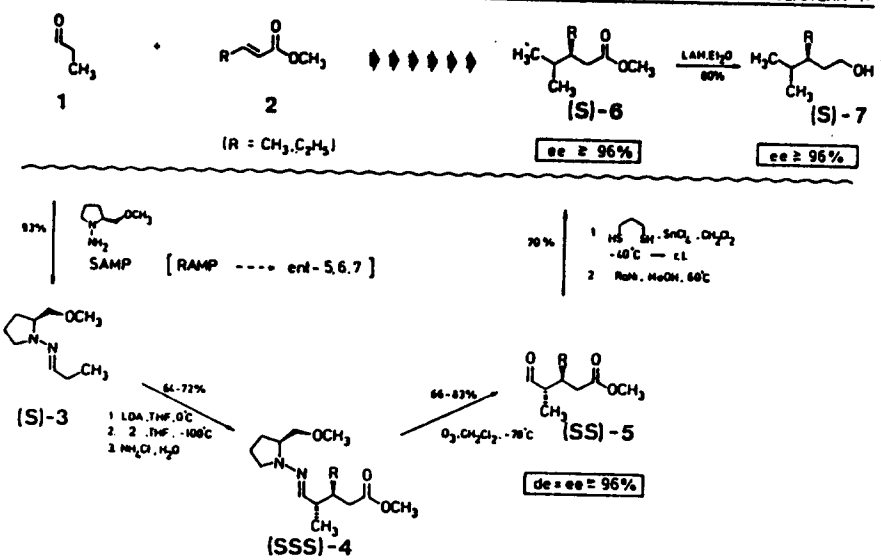
D.ENDERS, K.PAPADOPOULOS, unpublished results

DETERMINATION OF %DE AND %EE BY ^{13}C- AND ^{1}H NMR SPECTROSCOPY



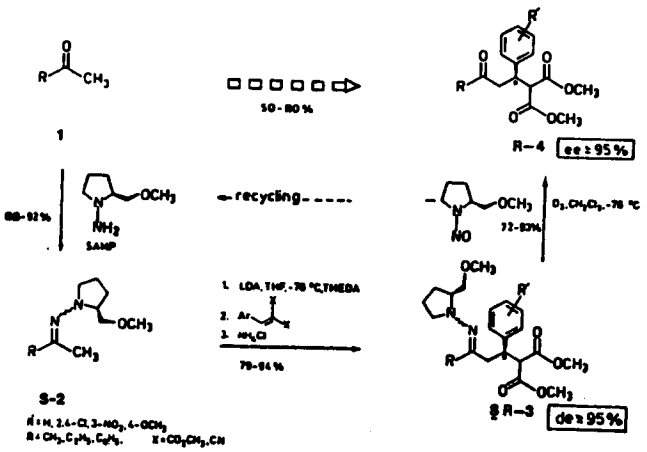
ASYMMETRIC MICHAEL ADDITIONS VIA SAMP-/RAMP-HYDRAZONES

ENANTIOSELECTIVE SYNTHESIS OF THE PHEROMONES OF THE SMALL FOREST ANT FORMICA POLYCTENA IF

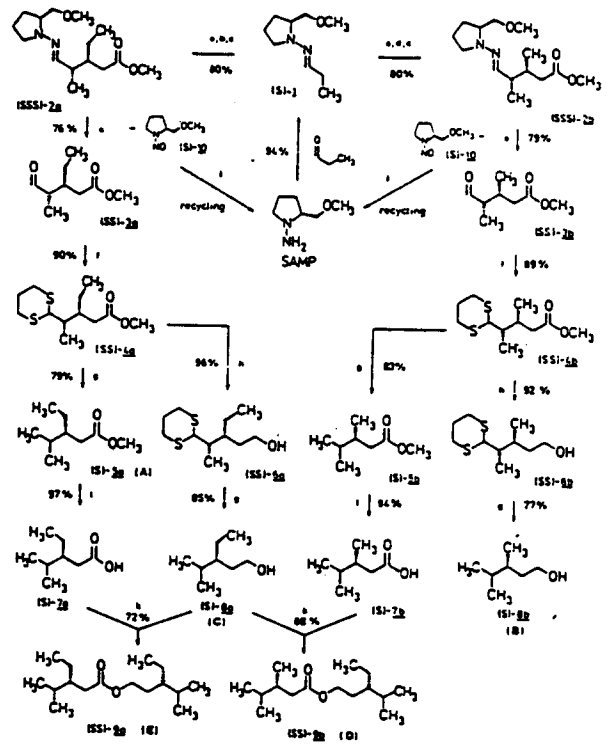


D. ENDERS, B. RENDENBACH, K. PAPADOPOULOS, TETRAHEDRON 42, 2235(1986)

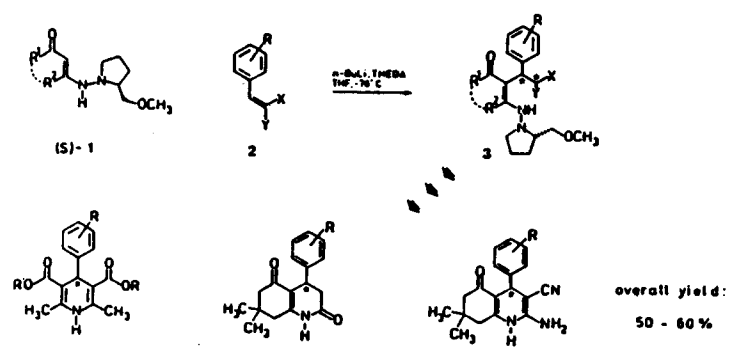
ENANTIOSELECTIVE MICHAEL-ADDITIONS OF ACYCLIC KETONES TO KNOEVENAGEL DERIVATIVES VIA SAMP-HYDRAZONES



D. ENDERS, A.S. DEMIR, unpublished results



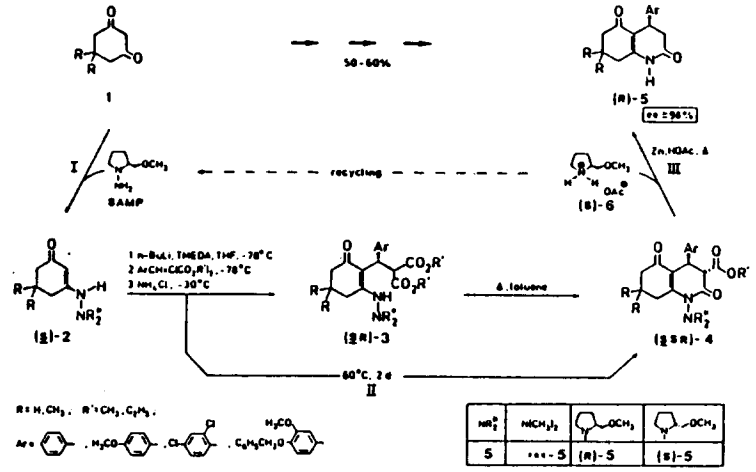
ENANTIOSELECTIVE SYNTHESIS OF DIHYDROPYRIDINE- AND -PYRIDONE -HETEROCYCLES



DIHYDROPYRIDINES	TETRAHYDRO-QUINOLIN-DIONES	TETRAHYDRO-QUINOLIN-ONES
"calcium antagonists"		
[X = COOR, Y = $COCH_3$]	[X = Y = COOR]	[X = Y = CN]
ee = 40 - 73 %	ee ≥ 98%	ee ≥ 98 %

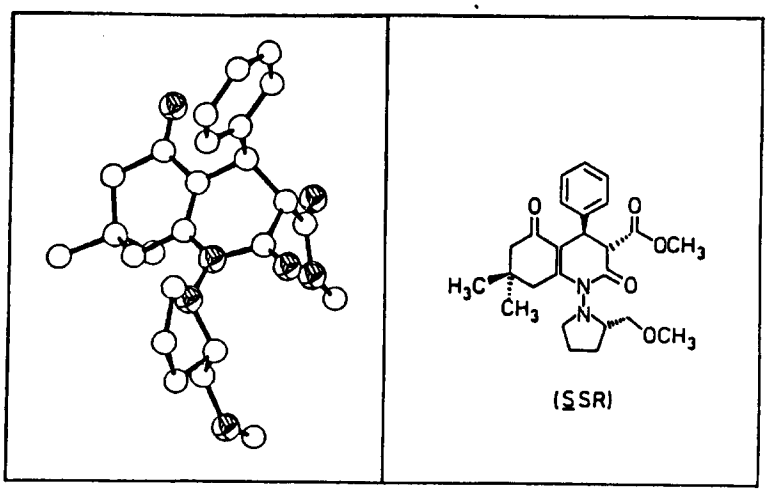
D. ENDERS, A.S. DEMIR, UNPUBLISHED

ENANTIOSELECTIVE SYNTHESIS OF SUBSTITUTED TETRAHYDROQUINOLINE-2,5-DIONES
ASYMMETRIC MICHAEL-ADDITION / LACTAMIZATION VIA SAMP-/RAMP-HYDRAZONES



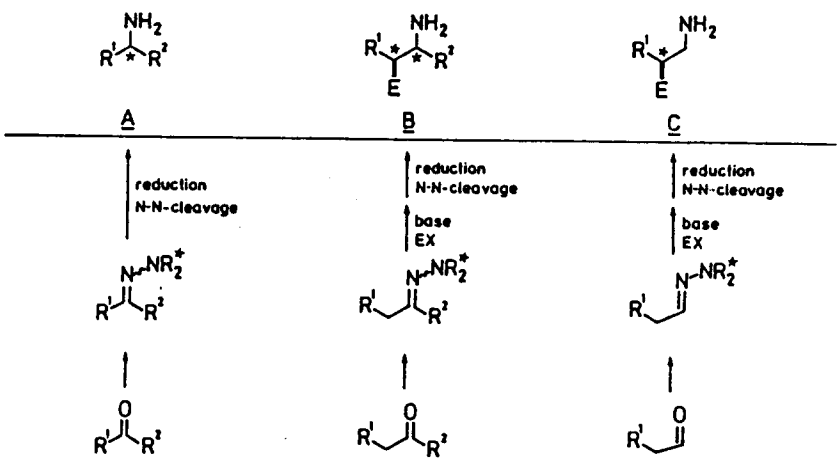
B. ENDERS, A. S. DEMIR, unpublished results

DETERMINATION OF ABSOLUTE CONFIGURATION BY X-RAY ANALYSIS

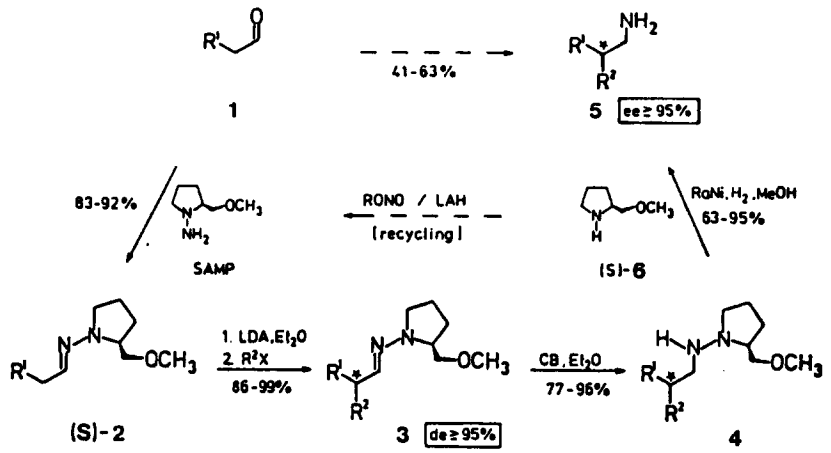


D. ENDERS, A.S. DEMIR, H. PUFF, S. FRANKEN

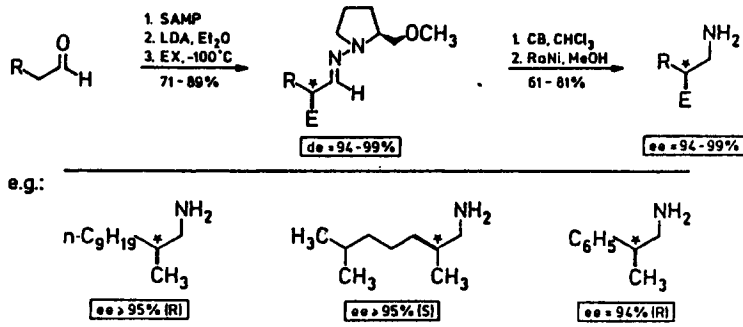
ASYMMETRIC SYNTHESIS OF α- AND/OR β-CHIRAL PRIM. AMINES VIA SAMP-HYDRAZONES



ENANTIOSELECTIVE SYNTHESIS OF β-SUBSTITUTED PRIMARY AMINES
α-ALKYLATION/REDUCTIVE AMINATION OF ALDEHYDES VIA SAMP-HYDRAZONES

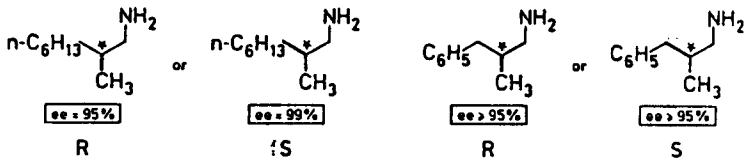


D.ENDERS, H.SCHUBERT, ANGEW. CHEM. 96, 368 (1984)



e.g.:

OPPOSITE ENANTIOSELECTIVITY BY SYNTHON CONTROL

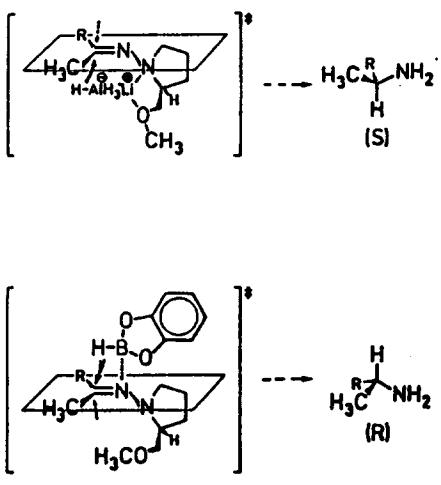


D.ENDERS, H.SCHUBERT, ANGEW. CHEM. 96, 368 (1984)

BOTH ENANTIOMERS BY SIMPLE CHANGE OF REDUCING AGENT - ENHANCEMENT OF % ee BY DEPROTONATION / PROTONATION TRICK

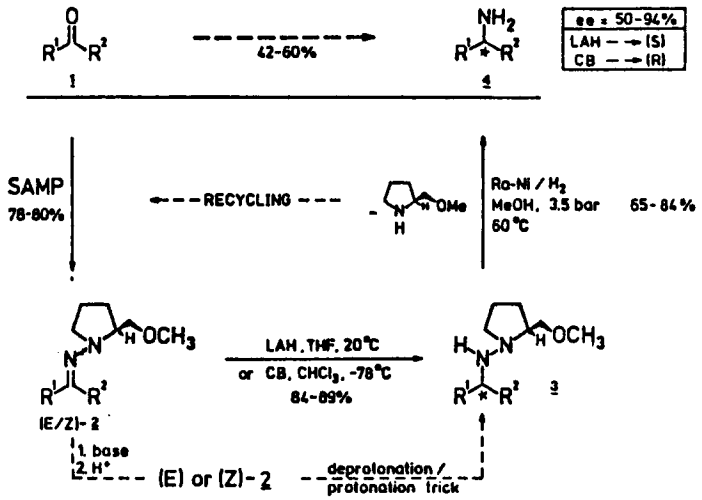
R^*NH_2	(E/Z) ratio	ee [%] LAH	ee [%] CB
$C_6H_5CH(NH_2)CH_3$	≈ 8:1	70 (S)	60 (R)
	(E)		81* (R)
$t\text{-}C_4H_9CH(NH_2)CH_3$	(E) only	90 (S)	88 (R)
$C_6H_5CH(NH_2)CH_3$	≈ 3:1	50 (S)	35 (R)

*deprotonation / protonation-trick was used



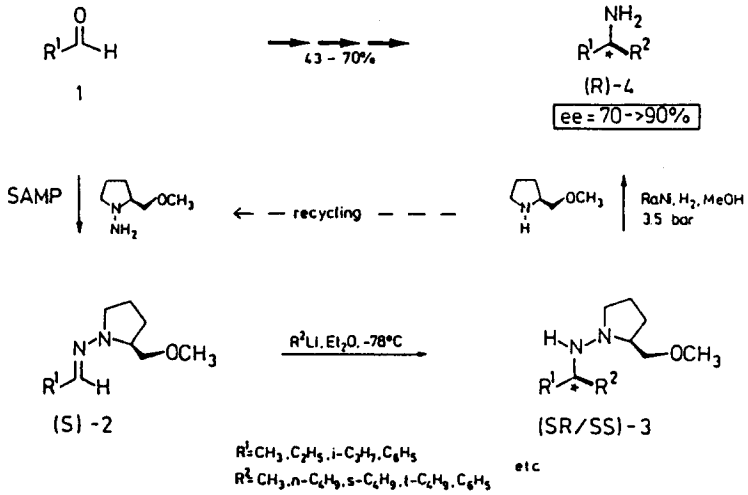
D.ENDERS, H.SCHUBERT, unpublished

ASYMMETRIC REDUCTIVE AMINATION VIA SAMP-HYDRAZONES



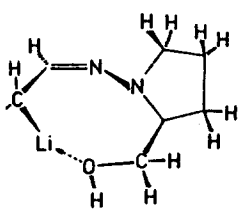
D. ENDERS, H. SCHUBERT, unpublished

ASYMMETRIC SYNTHESIS OF PRIMARY AMINES VIA NUCLEOPHILIC ADDITION OF RLi TO ALDEHYDE-SAMP/RAMP-HYDRAZONES



D. ENDERS, H. SCHUBERT, ANGEW. CHEM.

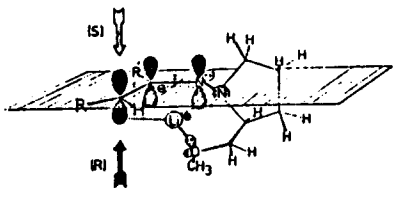
MNDO-CALCULATIONS OF THE STRUCTURE OF LITHIATED HYDRAZONES (with Li-parametrization)



α-lithio-hydrazone

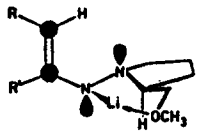
(46000 sec COMPUTERTIME)

ΔH_f° -47.1
RE 0.0
[kcal/mol]



π-1-azaallyl$^\ominus$-Li$^\oplus$-contact species

RE ≈2.5
[kcal/mol]



lithio-enehydrazinate ("Meyers-view")

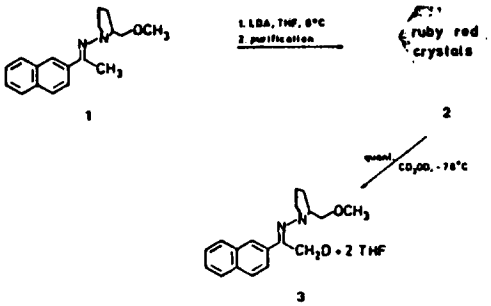
ΔH_f° -21.5
RE 25.6
[kcal/mol]

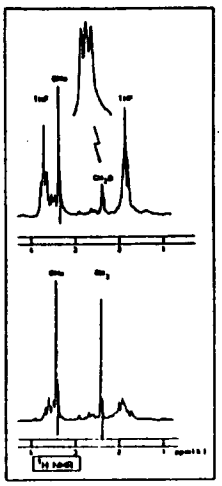
estimated:
intramolecular chelation energy
≈ 6 kcal/mol
dimerization < solvation energy
→ monomers in solution

SCHLEYER, ANDRADE, unpublished

STRUCTURE OF LITHIATED 2-ACETYL-NAPHTHALENE-SAMP-HYDRAZONE

(CRYOSCOPY, ^{1}H NMR)





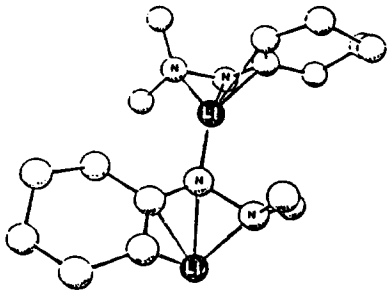
CRYOSCOPY

freezing-point depression of THF-solution of 2

⟹ MONOMER · 2 THF

D. ENDERS, K. A. M. KREMER (Bonn), D. SEEBACH, J. HANSEN (ETH Zurich)

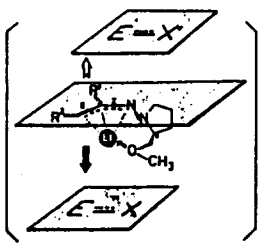
MOLECULAR STRUCTURE OF THE ASYMMETRIC UNIT OF LITHIATED CYCLOHEXANONE N,N-DIMETHYLHYDRAZONE POLYMER



D. B. COLLUM CORNELL, private communication

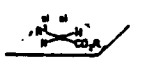
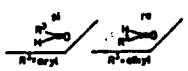
POSTULATED MECHANISM OF ELECTROPHILIC SUBSTITUTIONS VIA LITHIATED SAMP-HYDRAZONES

S_E2'-FRONT (METALLO RETENTIVE)

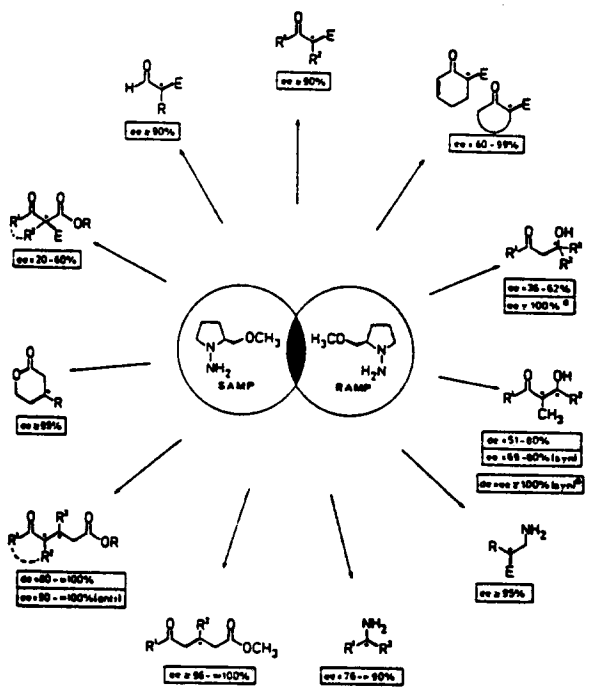


S_E2'-BACK (METALLO INVERSIVE) UNFAVOURED - low selectivity -

S_E2'-FRONT (METALLO RETENTIVE) FAVOURED - high selectivity -

α-ALKYLATIONS	MICHAEL-ADDITIONS	ALDOL REACTIONS
(in Et_2O)	(in THF or THF/TMEDA)	(in THF)
E⁺=X = RHal, R-SO$_2$Me, etc.	E⁺=X = $R^2CH{=}CHCO_2R$, $R^2CH{=}CCO_2R_2$	E⁺=X = R^2CHO
		
excellent diastereoface differentiation	excellent diastereoface and enantioface differentiation	medium - high diastereo- and enantioface differentiation

ASYMMETRIC SYNTHESES VIA SAMP-/RAMP-HYDRAZONES



[a] After crystallization

THE SAMP-/RAMP-HYDRAZONE METHODOLOGY

☆ SIMPLICITY

BOTH ENANTIOMERS, SAMP (ALDR. CA. 95) AND RAMP (ALDR. CA. 120) COMMERCIALLY AVAILABLE

INEXPENSIVE LARGE SCALE PREPARATIONS BASED ON GLUTAMIC ACID OR PROLINE (ORG. SYNTH. PROCEDURE)

RECYCLING OF AUXILIARY POSSIBLE

USUALLY 3-STEP PROCESS (HYDRAZONE FORMATION - α-REACTION - CLEAVAGE)

☆ GENERAL APPLICABILITY

ASYMMETRIC α-ALKYLATIONS OF ALDEHYDES, KETONES, ETC.

ASYMMETRIC ALDOL REACTIONS OF KETONES

ASYMMETRIC MICHAEL ADDITIONS OF KETOESTERS, LACTONES, HETEROCYCLES

ASYMMETRIC REDUCTIVE OR ALKYLATIVE AMINATIONS OF α- AND/OR β-SUBST. AMINES

DIELS - ALDER ? ANNELATIONS ? CONDENSATIONS ?

RESOLUTION OF ALDEHYDES AND KETONES (SASP METHOD)

☆ HIGH DIASTEREO- AND ENANTIOSELECTIVITIES

GENERALLY >90 % de, IN MANY CASES VIRTUALLY ENANTIOMERICALLY PURE (>99 % ee)

GOOD OVERALL CHEMICAL YIELDS

☆ ABSOLUTE CONFIGURATION PREDICTABLE - BOTH ENANTIOMERS AT WILL

AUXILIARY CONTROL (SAMP AND RAMP)

STEREOCONTROL (SAMP ONLY)

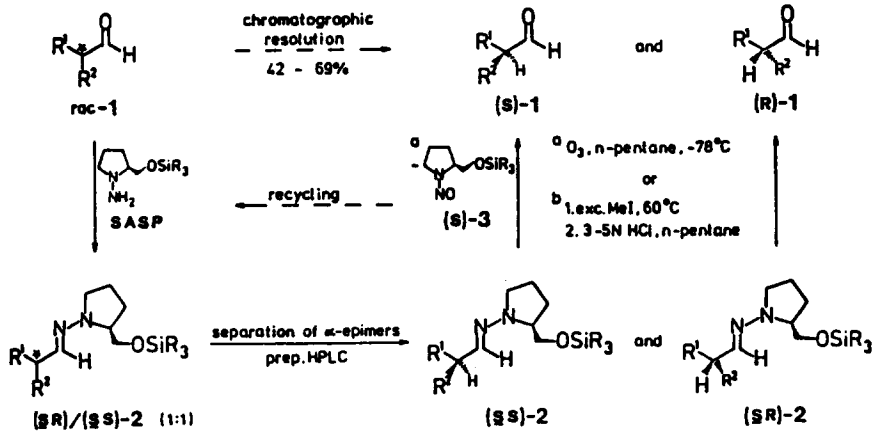
☆ EASY, QUICK AND ACCURATE DETERMINATION OF ASYMMETRIC INDUCTION

HPLC - ^{13}C NMR - ^{1}H NMR (LIS)

☆ INSENSITIVE TO PREEXISTING CHIRALITY?

☆ IMPORTANCE AND VERSATILITY OF CARBONYL COMPOUNDS AND AMINES IN CHEMISTRY

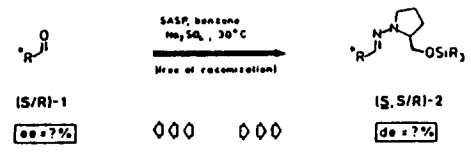
CHROMATOGRAPHIC RESOLUTION (HPLC) OF ALDEHYDES VIA SASP-HYDRAZONES

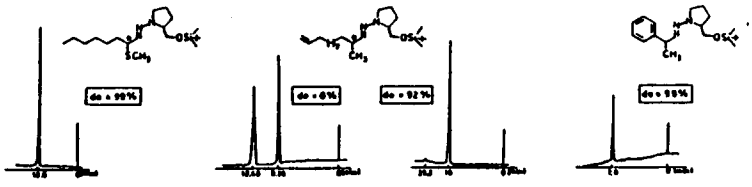


R_3 = t-BuMe$_2$, t-BuPh$_2$

D. ENDERS, W. MIES CHEM. COMMUN. 1984, 1221

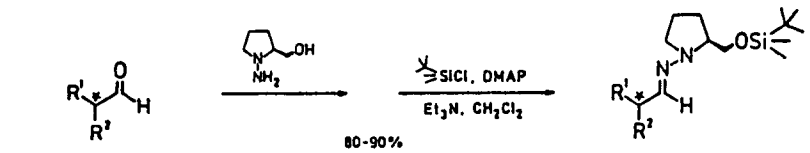
ACCURATE DETERMINATION OF ENANTIOMERIC PURITY OF ALDEHYDES VIA THEIR EPIMERIC SASP-HYDRAZONES BY HPLC





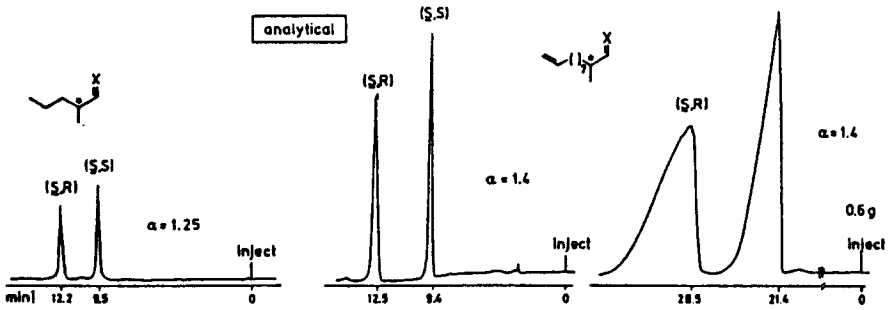
D. ENDERS, W. MIES, J.C.S. Chem Commun 1984, 1221.

CHROMATOGRAPHIC RESOLUTION OF ALDEHYDES

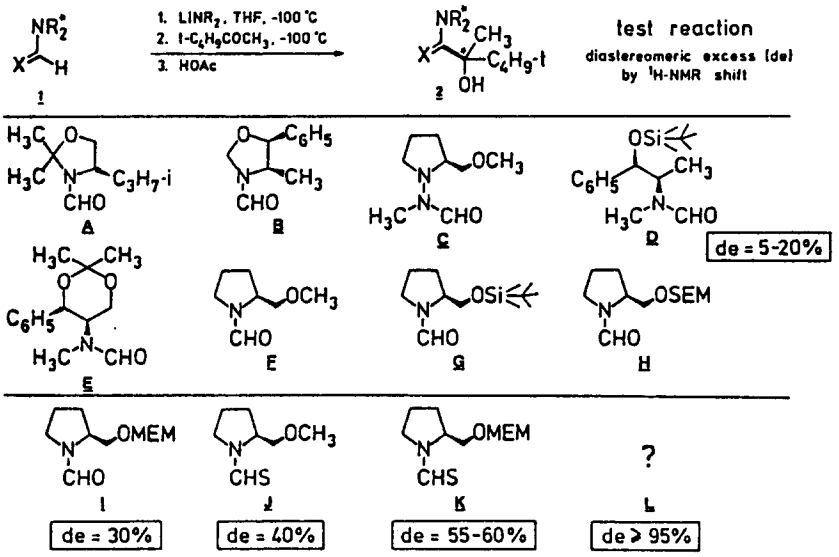


racemic (S,S)/(S,R) = 1:1

lumn: Zorbax-Sil
obile phase: p.e.-THF-Et2O (100 : 0.6 : 0.4)
essure: 35-55 bar



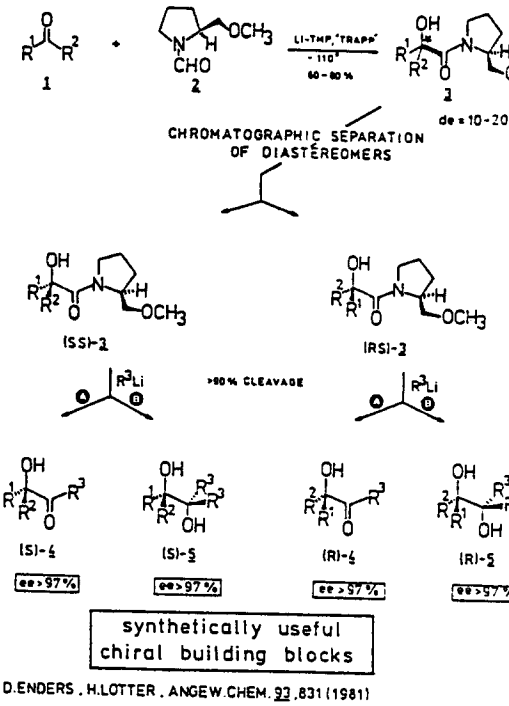
CHIRAL d¹-REAGENTS — VARIATION OF CHIRAL AUXILIARY



D.ENDERS, H.LOTTER, unpublished

CHIRAL d¹-REAGENTS*

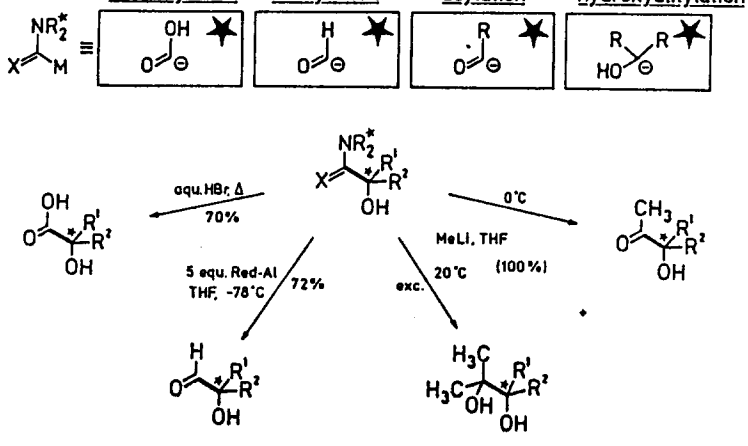
Synthesis of Enantiomerically Pure (R)- and (S)-α-Hydroxyketones and vic. Dioles



D.ENDERS, H.LOTTER, ANGEW.CHEM. 93, 831 (1981)

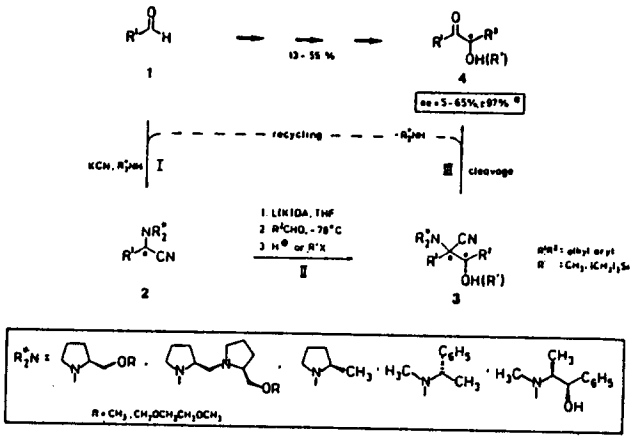
NUCLEOPHILIC ASYMMETRIC

carboxylation formylation acylation hydroxyalkylation



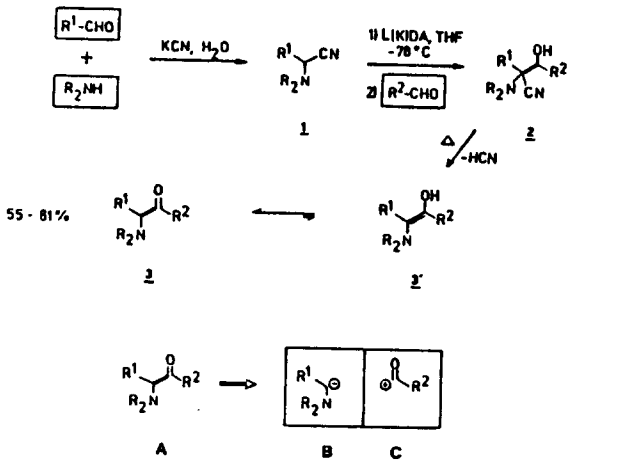
D.ENDERS, H.LOTTER, Angew. Chem. 93, 831 (1981) and unpublished results

ASYMMETRIC NUCLEOPHILIC ACYLATION VIA METALATED CHIRAL AMINONITRILES ENANTIOSELECTIVE SYNTHESIS OF α-HYDROXYKETONES



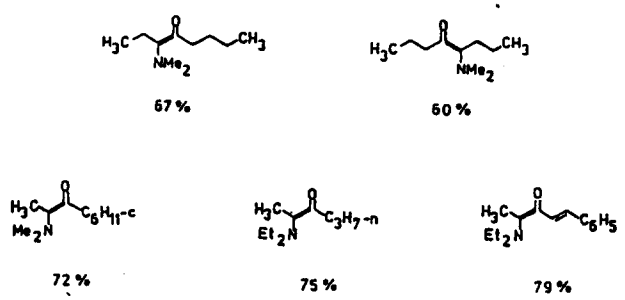
D.Enders, H.Lotter, H.Heigrat, J.-P.Hazaleyrat, Z.Welvart, Nouv. J.Chim. 5, 787 (1981)

C-C - CONNECTIVE SYNTHESIS OF α-DIALKYLAMINO - KETONES FROM ALDEHYDES AND SEC.-AMINES



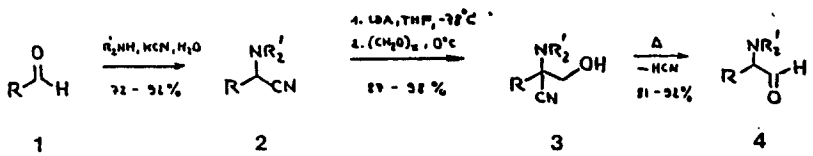
D. ENDERS, H. LOTTER THL 23, 639 (1982)

REGIOISOMERICALLY PURE α-AMINOKETONES BY SYNTHON CONTROL

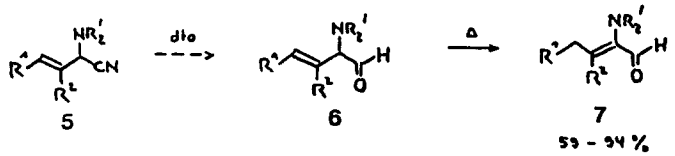


D. ENDERS, H. LOTTER, THL 23, 639 (1982)

C-C CONNECTIVE SYNTHESIS OF α-DIALKYLAMINO-ALDEHYDES AND ENAMINO-ALDEHYDES



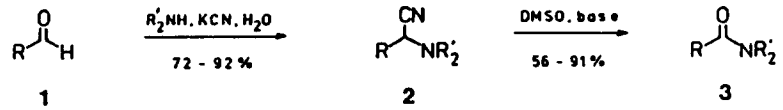
R = alkyl, aryl, heteroaryl ; NR_2' = NMe_2, NEt_2, ,

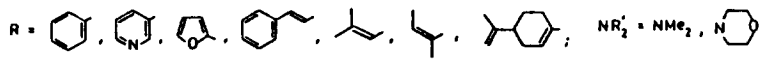


D. ENDERS, A.S. AMAYA, unpublished

DMSO MEDIATED OXIDATIVE DECYANATION OF AMINONITRILES

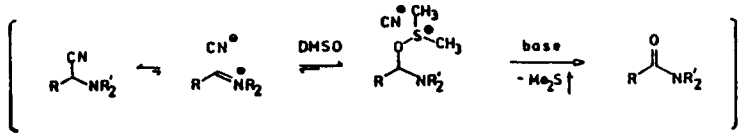
A MILD AND EFFICIENT OXIDATION OF ALDEHYDES TO NN-DIALKYLAMIDES





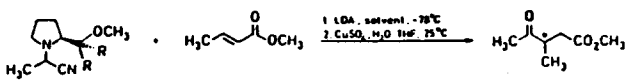
BASE = t-BuOK or KOH or Et_3N ($AgNO_3$)

POSTULATED MECHANISM:



D. ENDERS, A.S. AMAYA, unpublished

EFFECT OF SOLVENT, TEMPERATURE AND ADDITIVES



solvent, additives	ee(%)
Et_2O	43 (S)
THF	29 (R)
toluene	25 (R)
Et_2O, 2eq HMPA	27 (R)
Et_2O, 2eq TMEDA	31 (S)
pentane, 2eq Et_2O	33 (S)
pentane, 2eq HMPA	18 (R)
THF, pentane (1:1), 2eq PBC_4H_9	42 (S)

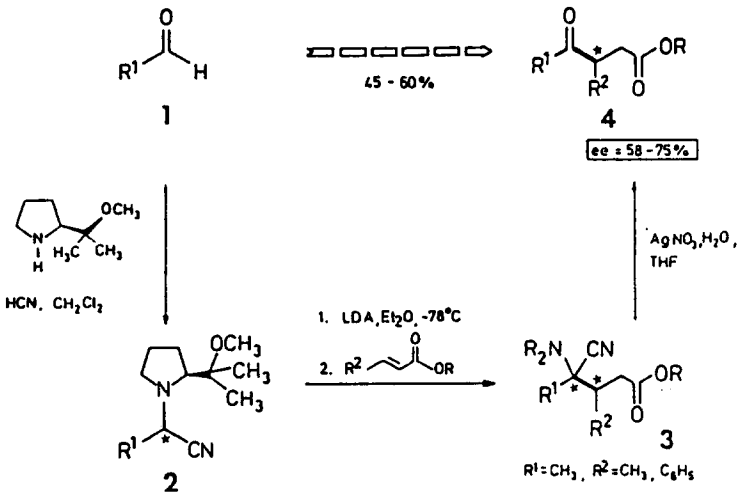
R = H

temperature (°C)	ee(%)
-10	49
-78	74
-110	83

R = CH_3

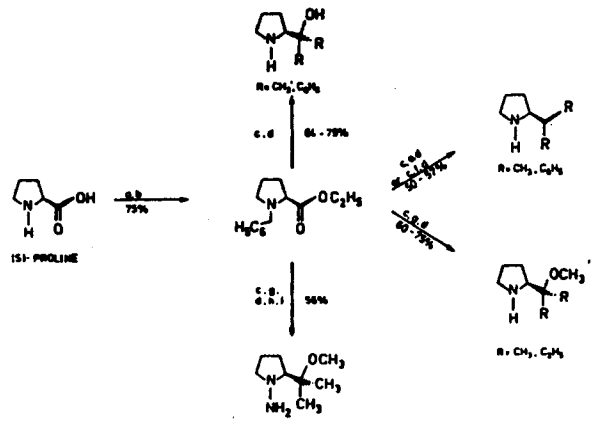
D. ENDERS, H. KIPPHARDT, unpublished results

ASYMMETRIC NUCLEOPHILIC ACYLATION VIA CHIRAL AMINONITRILE
ENANTIOSELECTIVE SYNTHESIS OF γ-KETOESTERS BY ASYMMETRIC MICHAEL-ADDITION



D. ENDERS, H. KIPPHARDT, unpublished results

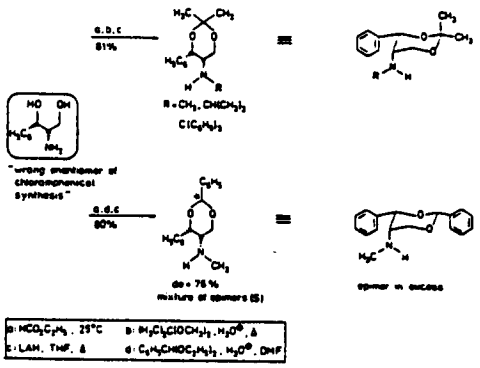
PREPARATION OF NEW CHIRAL AUXILIARIES BASED ON (S)-PROLINE



a: $SOCl_2$, EtOH; b: DCC, $C_6H_5CH_2OH$; c: RLi, Et_2O; d: H_2, Pd/C 10%, EtOH; e: Li, NH_3; f: $SOCl_2$, NEt_3, THF; g: NaH, CH_3I, THF; h: 1-C_4H_9NO, THF; i: LAH, THF

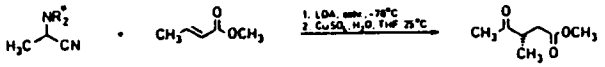
D. ENDERS, H. KIPPHARDT, unpublished results

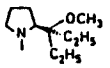
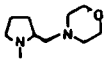
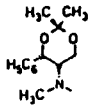
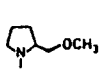
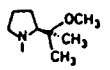
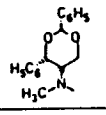
CHIRAL AUXILIARIES BASED ON (1S, 2S)-1-PHENYL-2-AMINO-1,3-PROPANDIOL



D. ENDERS, H. KIPPHARDT, unpublished results

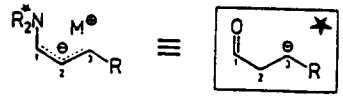
VARIATION OF CHIRAL AUXILIARIES



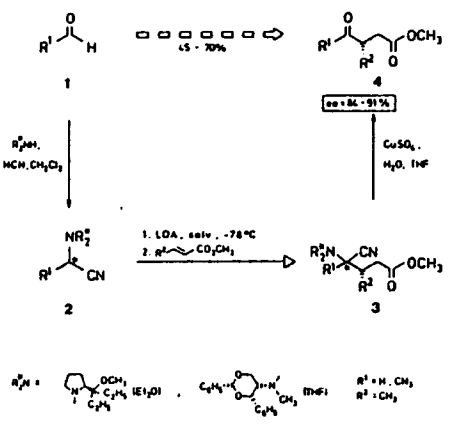
NR_2^*	solvent	ee (%)	NR_2^*	solvent	ee (%)
	THF	~5		Et_2O	90
	THF	~5		THF	65
	Et_2O	43			
	Et_2O	74		THF	91

D. ENDERS, H. KIPPHARDT, unpublished results

CHIRAL d^3-REAGENTS* (CHIRAL HOMOENOLATE EQUIVALENTS)

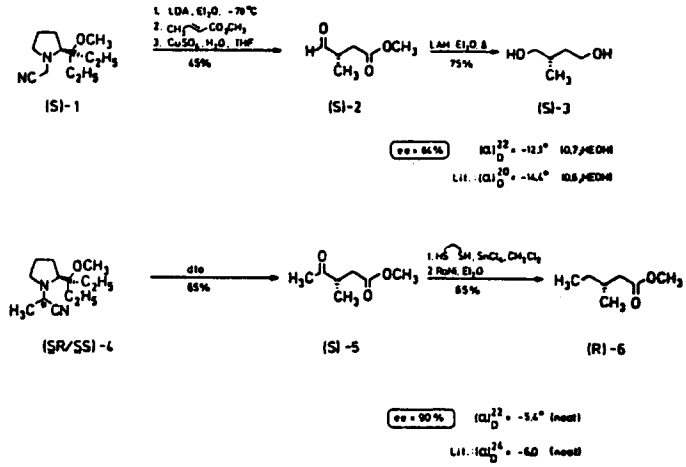


ASYMMETRIC NUCLEOPHILIC ACYLATION VIA CHIRAL AMINONITRILES. ENANTIOSELECTIVE SYNTHESIS OF γ-OXOESTERS. ASYMMETRIC MICHAEL-ADDITION



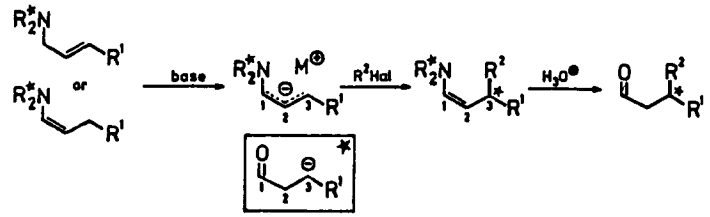
D. ENDERS, H. KIPPHARDT, unpublished results

DETERMINATION OF ABSOLUTE CONFIGURATION OF THE γ-OXOESTERS

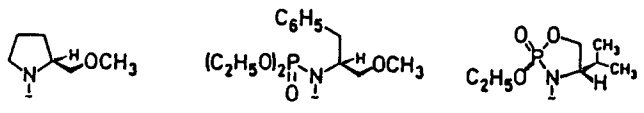


D. ENDERS, H. KIPPHARDT, unpublished results

CHIRAL HOMOENOLATE EQUIVALENTS
ASYMMETRIC SYNTHESIS OF β-CHIRAL ALDEHYDES



chiral auxiliaries NR_2^*

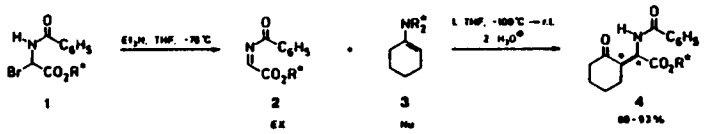


total c.y. = 20-66%	total c.y. = 65%	total c.y. = 10%
R^1=C_6H_5: ee = 50-80%; R^1=alkyl: ee = 85-95%	ee = 23-43%	ee = 38%

H. AHLBRECHT, G. BONNET, D. ENDERS, G. ZIMMERMANN, TETRAHEDRON LETT. 21, 3175 (1980)

DIASTEREO- AND ENANTIOSELECTIVE SYNTHESIS OF γ-OXO-α-AMINOACID DERIVATIVES

COMPLETE ASYMMETRIC INDUCTION THROUGH DOUBLE STEREODIFFERENTIATION IN THE REACTION OF ENAMINES WITH ACYLAMINOACETATES



1 → 2 (EE) + 3 (Nu) → 4 (80-93%)

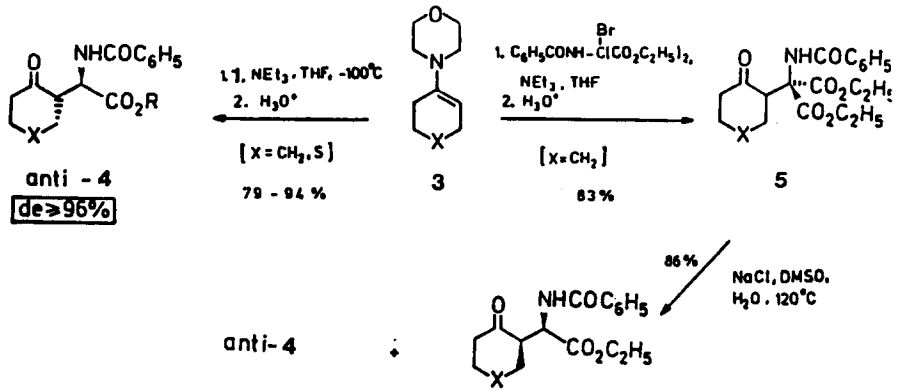
ELECTROPHILE (EX)	NUCLEOPHILE (Nu)	de [%]	ee* [%]	
achiral (R = CH_3, C_2H_5, c-C_6H_{11})	achiral	≥ 98	0	
chiral (R^M = (+)-menthyl)	achiral	≥ 98	24	
chiral (R^M = (+)-8-phenylmenthyl)	achiral	≥ 98	67	
achiral (R = CH_3)	chiral	≥ 98	85	
chiral (R^M = (-)-menthyl)	chiral	≥ 98	45	mismatched
chiral (R^M = (+)-menthyl)	chiral	≥ 99.9	≥ 99.9	matched !

* supposing the chiral auxiliary is removed

DOUBLE ASYMMETRIC INDUCTION

R. KOBER, K. PAPADOPOULOS, W. MILTZ, H. REUTER, H. PUFF, D. ENDERS, W. STEGLICH, Tetrahedron 41, 4933 (1985)

SYNTHESIS OF PURE SYN- AND ANTI-ISOMERS(racemic)[a]

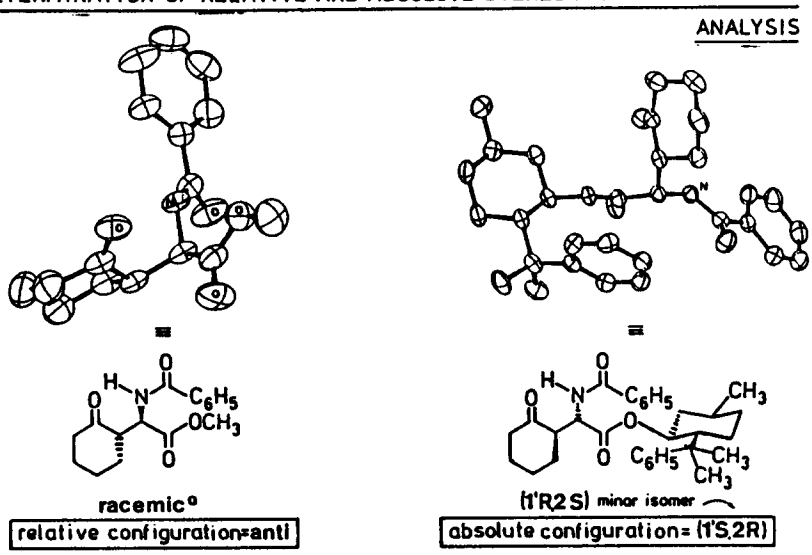


44% of pure syn-4 by fractional crystallization

[a] ONLY ONE ENANTIOMER SHOWN

D. ENDERS, W. STEGLICH ET AL. TETRAHEDRON 41, (1985)

DETERMINATION OF RELATIVE AND ABSOLUTE STEREOCHEMISTRY BY X-RAY ANALYSIS



racemic[a]

relative configuration=anti

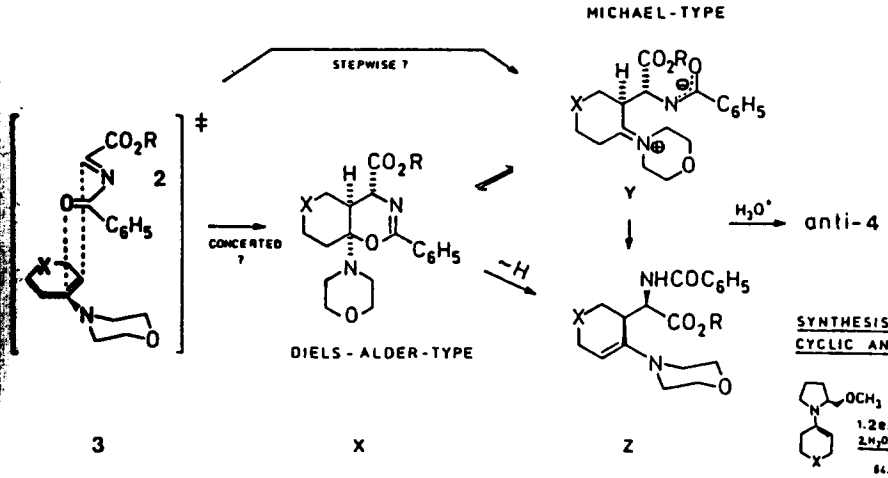
(1'R,2S) minor isomer

absolute configuration = (1'S,2R)

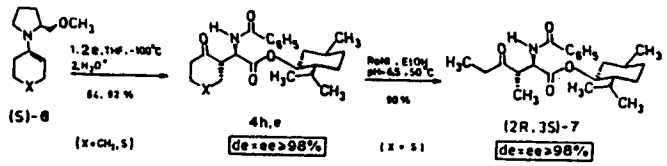
* only one enantiomer shown

R. KOBER, K. PAPADOPOULOS, W. MILTZ, H. REUTER, H. PUFF, D. ENDERS, W. STEGLICH, Tetrahedron 41, (1985)

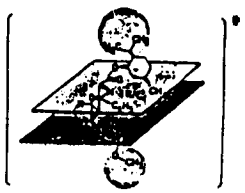
PROPOSED MECHANISM FOR THE ANTI-DIASTEREOSELECTIVITY



SYNTHESIS OF DIASTEREOMERICALLY AND ENANTIOMERICALLY PURE CYCLIC AND ACYCLIC γ-OXO-α-AMINOACID DERIVATIVES

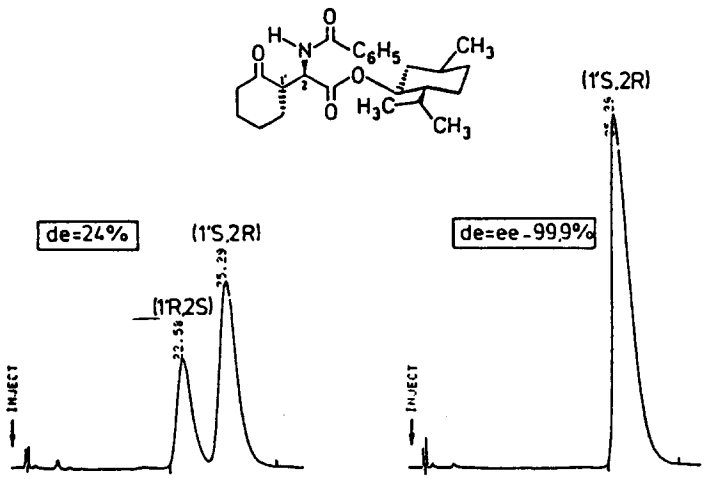


DIELS-ALDER TYPE TRANSITIONSTATE

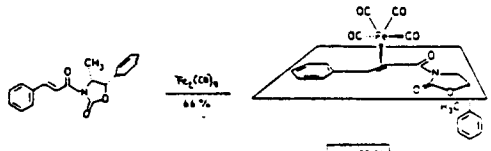


matched case of the double asymmetric induction

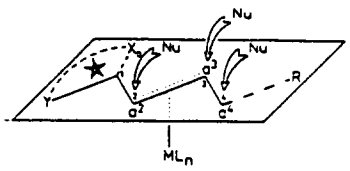
PROOF OF VIRTUALLY COMPLETE ASYMMETRIC INDUCTION BY ANALYTICAL HPLC

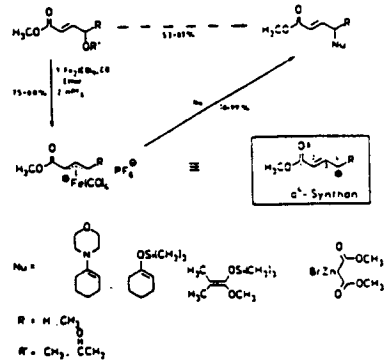


R. KOBER, K. PAPADOPOULOS, W. MILTZ, H. REUTER, H. PUFF, D. ENDERS, W. STEGLICH, Tetrahedron 41, (1985)



de ≥ 95 %





D. Enders, P. Fey, unpublished results