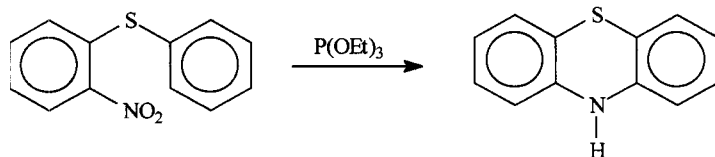
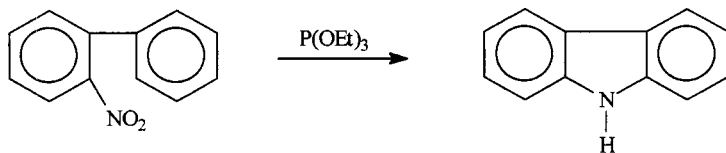
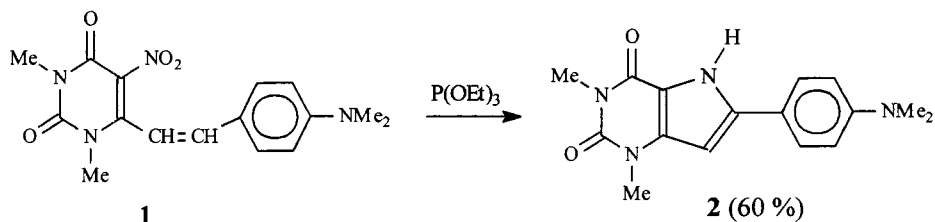


CADOGAN – CAMERON WOOD Cyclization

Synthesis of indoles, pyrroles and others N-heterocycles by cyclization of nitro compounds with trialkyl phosphite.

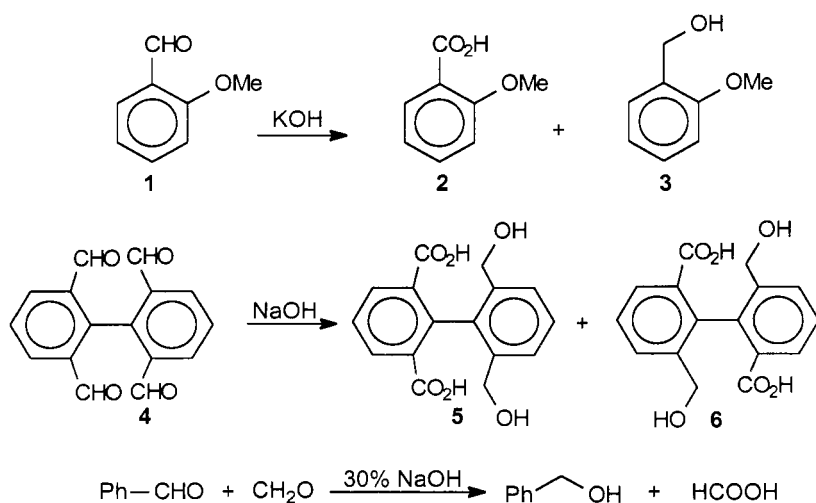


1	Cadogan, J.I.G.; Cameron-Wood, M.	<i>Proc.Chem.Soc.</i>	1962	361
2	Taylor, E. G.	<i>J.Org.Chem.</i>	1965	30 1013
3	Cadogan, J.I.G.	<i>Chem.Commun..</i>	1966	491
4	Buckl, P.	<i>Angew.Chem.Int.Ed.</i>	1969	8 120
5	Amarnath, V.	<i>Synthesis</i>	1974	840

1.3 – Dimethyl – 6 - (p-dimethylaminophenyl) - 5H - 2,4 (1H,3H) pyrrolo [3,2-d] pyrimidinedione (2).² A mixture of 1,3-dimethyl-5-nitro-6-(p-dimethylamino) styryluracil **1** (1.65 g, 5 mmol) and triethyl phosphite (5 mL, 4.85 g, 29 mmol) was refluxed under N₂ for 5.5 h. After 18 h at 20°C the volatile components were evaporated under vacuum and the residue recrystallized from DMF. Vacuum sublimation (240-250°C/0.05 mm) afforded 0.9 g of **2** (60 %), mp 310-318°C.

CANNIZZARO Oxidation - Reduction

A redox reaction between two aromatic aldehydes (or an aromatic aldehyde and formaldehyde) to a mixture of alcohol and acid (see 1st edition).



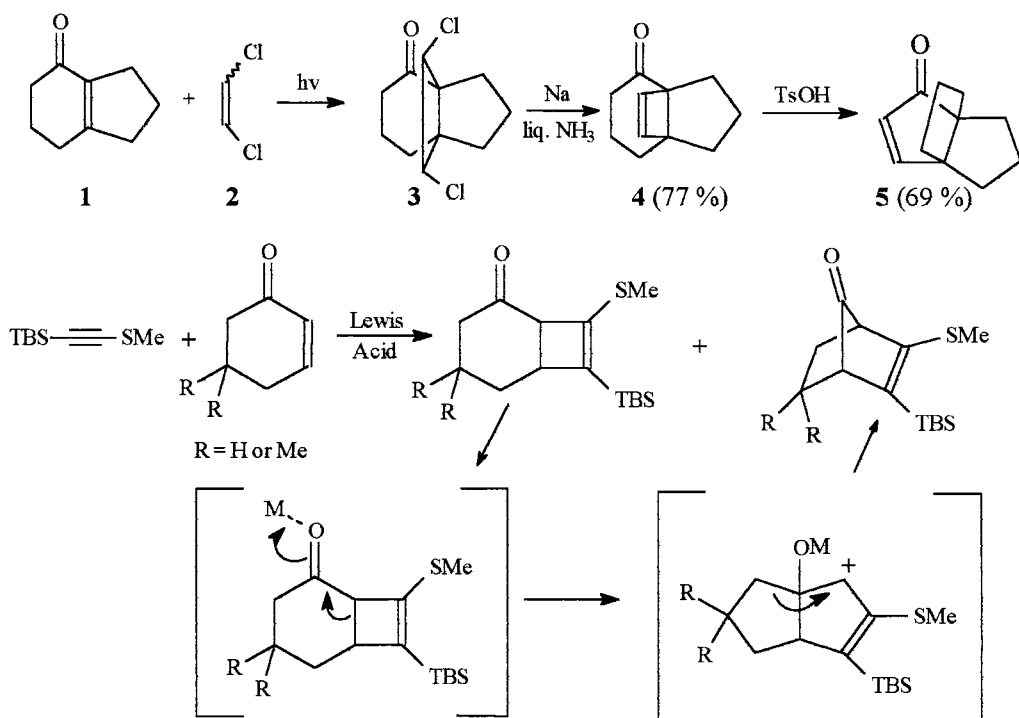
1	Wöhler, F.	<i>Liebigs Ann.</i>	1832	3	252
2	Cannizzaro, S.	<i>Liebigs Ann.</i>	1853	88	129
3	Bruce, R.A:	<i>Org.Prep.Proced.Int.</i>	1987		19
4	Geissmann, T.A.	<i>Org. React.</i>	1944	2	92
5	Moore, I.A.	<i>Org.Prep.Proced.Int.</i>	1988	20	82

o-Methoxybenzyl alcohol (3) and o-Methoxybenzoic acid (2).³ To a solution of KOH (120 g, 2 mol) in water are added o-methoxybenzaldehyde **1** (136 g, 1 mmol) under efficient stirring and external cooling with water. Stirring was maintained until a stable emulsion was obtained. After 24 h at 30°C the mixture was diluted with water and extracted with Et₂O. Evaporation of the solvent and vacuum distillation of the residue afforded 55 g of **3** (79%), bp 245-255°C. Acidification of the aqueous solution, extraction with Et₂O and evaporation of the solvent gave **2**, mp 98-99°C.

Dicarboxylic acids (5) and (6).⁵ 1,6,1',6'-Tetraformylbiphenyl **4** (25.8 g, 96.9 mmol) was dissolved in 6N NaOH (400 mL) at 25°C; The mixture warmed by the heat of reaction. After 30 min, conc HCl was added dropwise to the stirred solution until the pH of the mixture reached pH=1. The creamy colored precipitate was collected and recrystallized from water, to afford 18.7 g of **5** and **6** (64%), mp 204-206°C, tlc (EtOH) R_f (**5**)=0.56 R_f (**6**)=0.54.

CARGILL Rearrangement

Rearrangement of unsaturated ketones catalyzed by acids



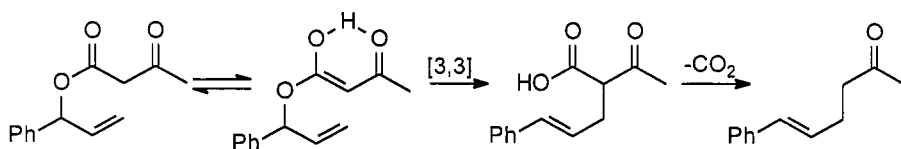
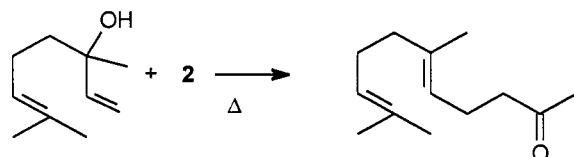
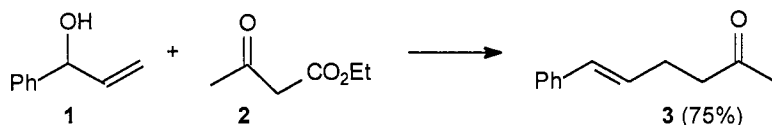
1	Cargill, R. L.	<i>Tetrahedron Lett.</i>	1967	169
2	Cargill, R. L.	<i>J.Org.Chem.</i>	1970	35 356
3	Narasaka, K.	<i>Chem.Lett.</i>	1993	621
4	Cargill, R. L.	<i>Acc.Chem.Res.</i>	1974	7 106
5	Fetizon, M.	<i>J.Chem.Soc.Chem.Comm.</i>	1975	282
6	Kakiuchi, K.	<i>J.Am.Chem.Soc.</i>	1980	111 3707

Tricyclo(4.3.2.0^{1,6})undec-10-en-2-one (4)². A solution of bicyclo [4.3.0] non-1(6) – en – 2 – one **1** (2.6 g, 19.1 mmol) and a mixture of “E” and “Z” 1,2-dichloroethylene **2** (3 ml, 7.62 g, 78 mmol) in pentane (80 mL) was irradiated (Corex) for 30 min. The residue obtained after evaporation of volatiles, was dissolved in Et₂O (100 mL) and added to dry liquid NH₃ (2,000 mL). The solution was treated with Na until a blue color was obtained. After additional 10 min stirring, NH₄Cl was added and NH₃ was evaporated. Addition of water, extraction with Et₂O followed by distillation gave 2.38 g of **4** (77 %), bp 71-73°C/0.25 Torr.

Tricyclo(3.3.3.0^{1,5})undec-3-en-2-one (5). A solution of **4** (1.92 g, 11.8 mmol) and p-TsOH.H₂O (0.8 g, 4.2 mmol) in PhH (50 mL) was refluxed for 10 min. After washing with NaHCO₃ solution and concentration, the residue after distillation afforded 1.32 g of **5** (68.7 %), bp 65°C/0.25 Torr.

C A R R O L L Rearrangement of Allyl Acetoacetic Esters

Thermal condensation of allyl alcohols with ethyl acetoacetate in the presence of a catalyst, with loss of CO₂; a one pot ester exchange-Claisen-Ireland rearrangement with loss of CO₂ (see 1st edition).

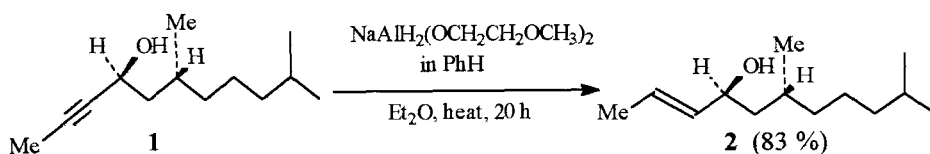


1	Carroll, M.F.	<i>J.Chem.Soc.</i>	1940	704
2	Cologne, J.	<i>Bull.Soc.Cim.Fr.</i>	1955	1312
3	Kimel, W.	<i>J.Org.Chem.</i>	1957	22 1611
4	Kimel, W.	<i>J.Org.Chem.</i>	1958	23 153
5	Stephen, W.	<i>J.Org.Chem.</i>	1984	49 722
6	Podraza, K.F.	<i>J.Heterocycl.Chem..</i>	1986	23 581
7	Enders, D.	<i>Angew.Chem.Int.Ed.</i>	1995	34 2278
8	Sorgi, K.L.	<i>Tetrahedron Lett.</i>	1995	36 3597

Cinnamylacetone (3).¹ A mixture of phenyl vinyl carbinol **1** (26.8 g, 0.2 mmol) ethyl acetoacetate **2** (35.1 g, 0.27 mmol) and KOAc (0.3 g) was heated to 220°C for 3 h and maintained at this temperature for another 3 h. 15 mL of distillate (EtOH, 0.25 mol) was collected. Washing and distillation of the residue afforded EtOAc (10 g), an alcoholic fraction (2 g) and 26 g of **3** (75%), bp 125-130°C (4 mm Hg), $\alpha_D^{20} = 1.5475$; oxime mp 87.5-89°C.

CHAN Reduction of Acetylenes

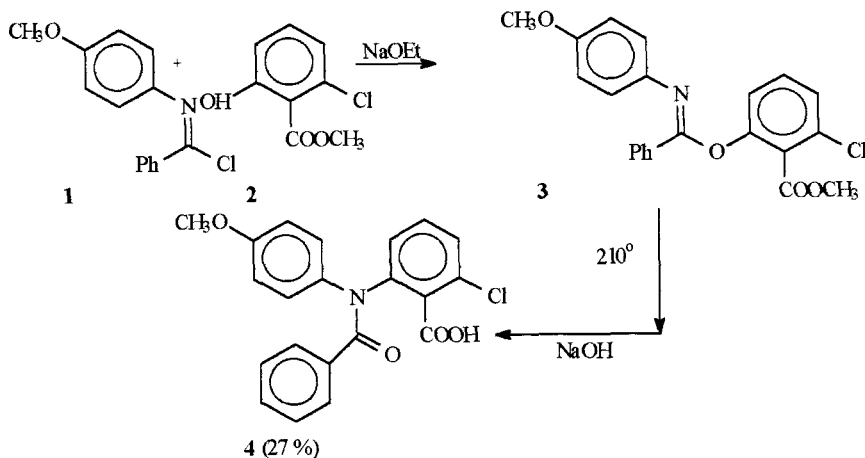
Stereospecific reduction of acetylenic alcohols to E- allylic alcohols by means of sodium bis(2-methoxyethoxy)aluminium hydride (SMEAH) (see 1st edition).



1	Chan, Ka-Kong	<i>J.Org.Chem.</i>	1976	41	62
2	Chan, Ka-Kong	<i>J.Org.Chem.</i>	1976	41	3497
3	Chan, Ka-Kong	<i>J.Org.Chem.</i>	1976	43	3435

CHAPMAN Rearrangement

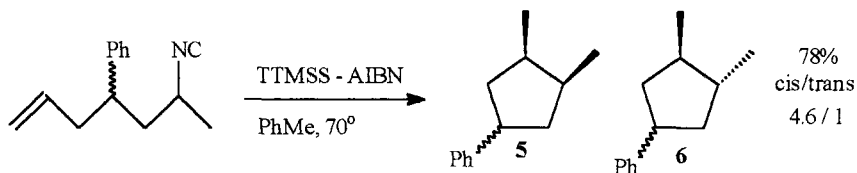
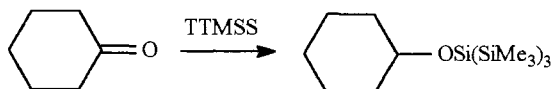
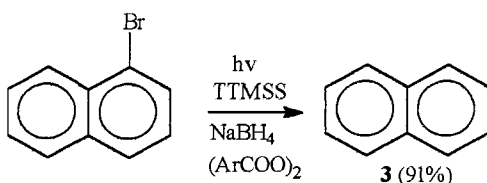
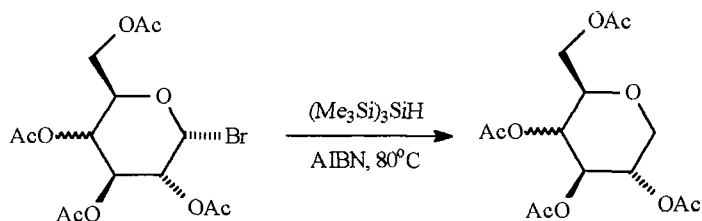
O to N aryl migration in O-aryliminoethers (see 1st edition).



1	Chapman, A.W.	<i>J.Chem.Soc.</i>	1925	127	1992
2	Dauben, W.G.	<i>J.Am.Chem.Soc.</i>	1950	72	3479
3	Crammer, F.	<i>Angew.Chem.</i>	1956	68	649
4	Roger, R.	<i>Chem.Rev.</i>	1969	69	503
5	Schulenberg, J.W.	<i>Org.React.</i>	1965	14	1

CHATGILIALOGLU Reducing agent

Tris(trimethylsilyl)silane (TTMSS) reducing agent for alkyl halides, ketones; an alternative to tributyltin hydride.



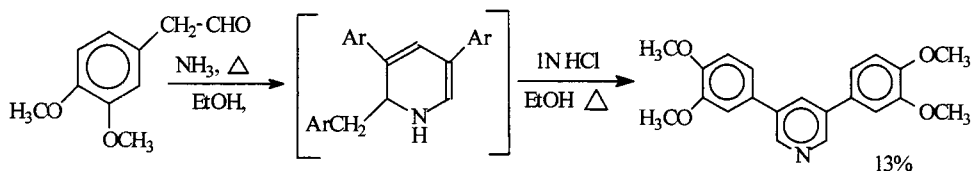
1	Chatgilialoglu, C.	<i>J.Org.Chem.</i>	1988	53	3641
2	Giese, B.	<i>Tetrahedron Lett.</i>	1989	30	681
3	Chatgilialoglu, C.	<i>J.Org.Chem.</i>	1991	56	678
4	Chatgilialoglu, C.	<i>J.Org.Chem.</i>	1989	54	2492
5	Chatgilialoglu, C.	<i>Tetrahedron Lett.</i>	1989	30	2733
6	Giese, B.	<i>Tetrahedron Lett.</i>	1990	31	6013
7	Chatgilialoglu, C.	<i>Tetrahedron</i>	1990	46	3963
8	Arya, P.	<i>J.Org.Chem.</i>	1990	55	6248

Naphthalene (3).⁵ To a solution of 1-bromonaphthalene **1** (278 mg, 1 mmol) in monoglyme (3 mL) in a quartz tube with magnetic stirrer was added NaBH₄ (1.9 g) and under Ar were added TTMSS **2** (23.8 mg, 0.1 mmol) and p-methoxybenzoyl peroxide. The reaction mixture was photolyzed at 254 nm in a Rayonet reactor. GC analysis: yield 91%.

1-Phenyl-3,4-dimethylcyclopentane (5 and 6).⁶ A solution of **4** (1.00 g, 5mmol) in PhMe (40 mL) was heated with stirring at 90°C under Ar. TTMSS and AIBN in PhMe (10 mL) was added slowly (over 3-4 h) via syringe pump. Evaporation of the solvent and chromatography (silica gel, pentane:Et₂O) afforded 78% of **5** and **6** in a ratio cis / trans 4.6 : 1.

CHICHIBABIN Pyridine synthesis

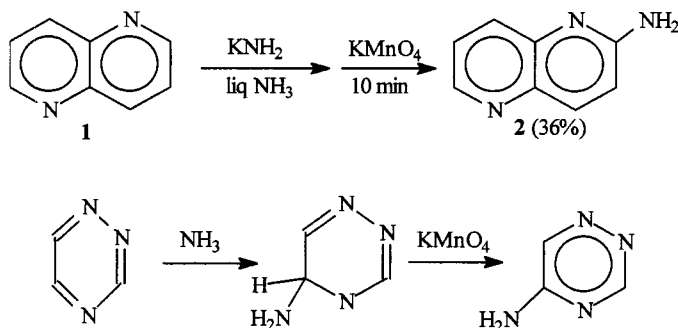
Pyridine synthesis from aromatic acetaldehydes and ammonia (see 1st edition).



1	Chichibabin, A.	<i>J.Russ.Phys.Chem.Soc.</i>	1906	37	1229
2	Eliel, E.L.	<i>J.Am.Chem.Soc.</i>	1953	75	4291
3	Sprung, M.M.	<i>Chem.Rev.</i>	1940	26	301
4	Frank, R.L.	<i>Org.Synth.Coll.</i>		IV	451
5	Mc Gill, C.K.	<i>Adv.Heterocycl.Chem.</i>	1988	44	1

CHICHIBABIN Amination

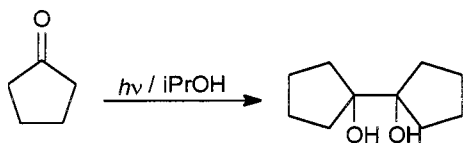
α -Amination of pyridines, quinolines and other N-heterocycles in liq. NH₃ (see 1st edition).



1	Chichibabin, A.	<i>J.Russ.Phys.Chem.Soc.</i>	1914	46	1216
2	van der Plas, H.C.	<i>J.Org.Chem.</i>	1981	46	2134
3	Bunnett, J.F.	<i>Chem.Rev.</i>	1951	49	375
4	Rykowsky, A.	<i>Synthesis</i>	1985		884
5	Leffler, M.T.	<i>Org.React.</i>	1942	1	19

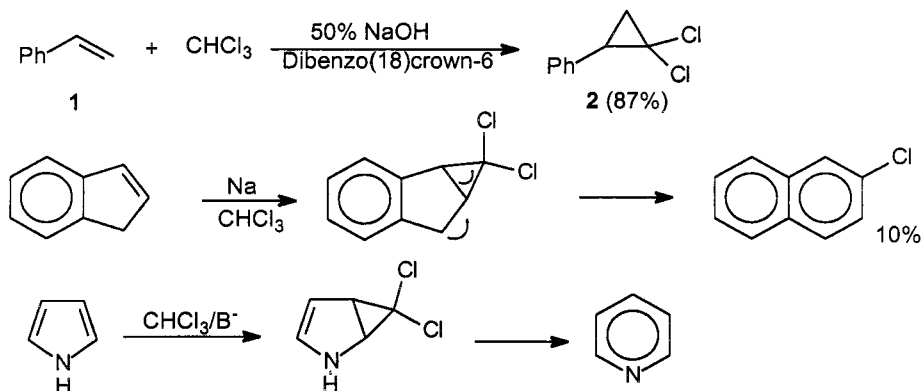
C I A M I C I A N Photocoupling

Reductive photocoupling of ketones to diols (see 1st edition).



- | | | | | | |
|---|---------------|---------------------------|-------------|----|------|
| 1 | Ciamician, G. | <i>Chem. Ber.</i> | 1900 | 33 | 2911 |
| 2 | De Mayo, P. | <i>Quart. Rev(London)</i> | 1961 | 15 | 415 |
| 3 | Goth, H. | <i>Helv. Chim. Acta</i> | 1965 | 48 | 1395 |

C I A M I C I A N - D E N N S T E D T Cyclopropanation

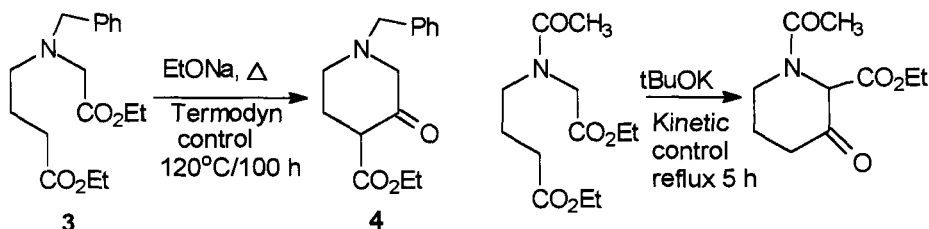
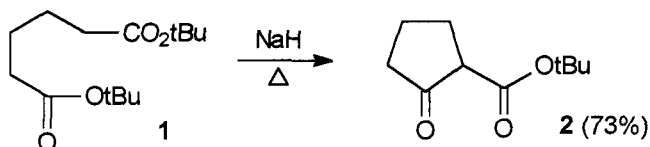
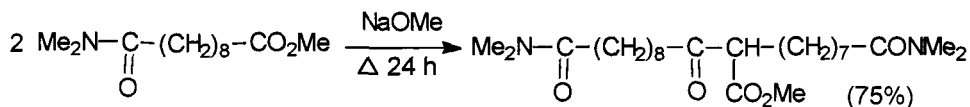
Cyclopropanation of alkenes with dichlorocarbene derived from CHCl_3 and sometimes subsequent ring enlargement of fused cyclopropanes (see 1st edition).

- | | | | | | |
|---|-----------------------------|--------------------------|-------------|----|------|
| 1 | Ciamician, G. Dennstedt, N. | <i>Chem. Ber.</i> | 1881 | 14 | 1153 |
| 2 | Parham, W.E. | <i>J. Am. Chem. Soc.</i> | 1955 | 77 | 1177 |
| 3 | Vogel, E. | <i>Angew. Chem.</i> | 1960 | 72 | 8 |
| 4 | Makosza, M. | <i>Angew. Chem. Int.</i> | 1974 | 13 | 665 |
| 5 | Skell, P.S. | <i>J. Am. Chem. Soc.</i> | 1958 | 80 | |
| 6 | Oddo, B. | <i>Gazz. Chim. Ital.</i> | 1939 | 69 | 10 |

1,1-Dichloro-2-phenylcyclopropane (2).⁴ To a solution of styrene **1** (10.4 g, 0.1 mol) in CHCl_3 (11.9 g, 0.1 mol) was added 50% NaOH followed under efficient stirring by dibenzo(18)-crown-6 (0.36 g, 1 mmol). After a mild exothermic reaction, usual work-up gave 16.25 g of **2** (87%), bp $112^\circ\text{C}/15$ torr.

CLAISEN-GEUTER-DIECKMANN Ester Condensation

Synthesis of open chain Claisen or cyclic Dieckmann β -ketoesters by aldol type condensation



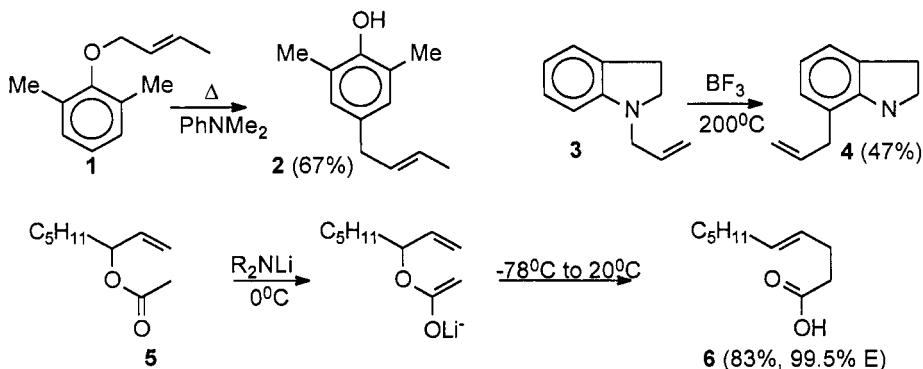
1	Geuter, A.	<i>Arch.Pharm.</i>	1863	106	97
2	Claisen, L.	<i>Chem.Ber.</i>	1887	20	651
3	Dieckmann, W.	<i>Chem.Ber.</i>	1894	27	965
4	Cohen, H.	<i>J.Org.Chem.</i>	1973	38	1425
5	Bosch, J.	<i>Tetrahedron</i>	1984	40	2505
6	Thyagarajan, B.S.	<i>Chem.Rev.</i>	1954	54	1029
7	Schaefer, J.P.	<i>Org.React.</i>	1967	15	1

2-t-Butoxycarbonylcyclopentanone 2.⁴ To a stirred suspension of NaH (24 g, 1 mol) in PhH (400 mL) under N_2 was added **1** (5.0 g, 20 mmol) and *t*-BuOH (2.0 mL) in one portion and the mixture was boiled for 30 min. Another portion of **1** (120 g, 0.465 mol) in PhH (200 mL) was added dropwise for 45 min and reflux was continued 4.5 h. The mixture was neutralized (AcOH) and water (750 mL) was added followed by extraction with Et_2O (2X500 mL). Evaporation of the solvent and distillation afforded 65.5 g of **2** (73%), bp 80-85°C/2 torr, $R_f = 0.25$ (silica gel, Et_2O :hexane 1:2).

Ethyl 1-benzyl-3-oxo-4-piperidinecarboxylate 4.⁵ A solution of **3** (25 g, 78 mmol) in dioxane (100 mL) containing EtOH (6.8 mL) was added dropwise to a suspension of NaH (2.7 g, 117 mmol) in dioxane (100 mL). After 7 h refluxing, usual work up afforded 17.5 g of **4** (80%), mp 102-104°C (Me_2CO).

CLAISEN - IRELAND Rearrangement

Rearrangement of allyl phenyl ethers to o-(or p)-allylphenols or of allyl vinyl ethers to γ,δ -unsaturated aldehydes or ketones (Claisen). Rearrangement of allyl esters as enolate anions or silyl enol ethers to γ,δ -unsaturated acids (Ireland). Also rearrangement of N-allylanilines (an aza-Cope rearrangement) (see 1st edition).



1	Claisen, L.	<i>Chem.Ber.</i>	1912	45	3517
2	Rhoades, S.L.	<i>J.Am.Chem.Soc.</i>	1955	73	5060
3	Ireland, E.	<i>J.Am.Chem.Soc.</i>	1972	94	5897
4	Daub, D.W.	<i>J.Org.Chem.</i>	1986	51	3404
5	Anderson, W.K.	<i>Synthesis</i>	1995		1287
6	Tarbell, D.S.	<i>Org.React.</i>	1944	2	1

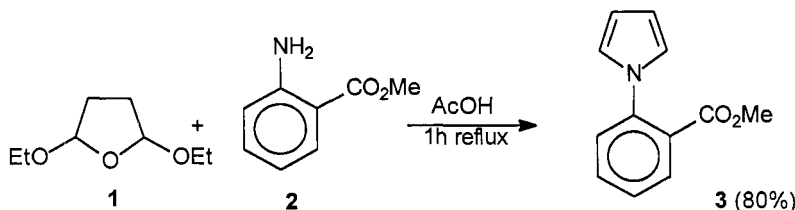
2,6-Dimethyl-4-(α -methylallyl)phenol (2).² The ether **1** (17.6 g, 0.1 mol) was heated in dimethylaniline for 3 h at reflux. After work-up are obtained 11.8 g of **2** (67%), bp 89-90°C /05 mm.

7-Allylindoline (4).⁵ N-Allylindoline **3** (9.32 g, 58.54 mmol), sulfolane (20 mL) and $\text{BF}_3 \cdot \text{OEt}_2$ (3.6 mL, 29.27 mmol, 0.5 equiv) was heated at 200-210°C under Ar. After quenching with water, extraction and chromatography of the residue (EtOAc:hexane 1:10), there are obtained 890 mg of **3** (10%) and 4.38 g of **4** (47%), $R_f = 0.47$ (EtOAc:Hexane 1:5).

4-Decenoic acid (6).³ N-Isopropylcyclohexylamine (1.7 g, 12.1 mmol) in THF (20 mL) at 0°C was treated with BuLi (5 mL, 11.1 mmol) in hexane. After 10 min **5** (1.64 g, 10 mmol) was added dropwise at -78°C. After 5 min stirring the mixture was warmed to 20°C poured into 5% NaOH (20 mL) and extracted with Et_2O . Acidification (HCl) and extraction with CH_2Cl_2 afforded 1.356 g of **6** (83%) 99.5% E.

CLAUSON - KAAS Pyrrole synthesis

Preparation of N-substituted pyrroles from 2,5-dialkoxytetrahydrofurans and primary amines.

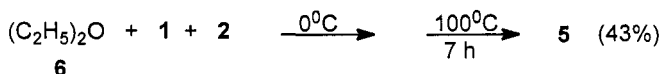
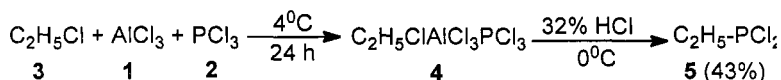


1	Clauson-Kaas, N.	<i>Acta Chem.Scand.</i>	1952	6	667
2	Josey, A.D.	<i>J.Org.Chem.</i>	1962	27	2466
3	Patterson, J.M.	<i>Synthesis</i>	1976		281

1-(2-Methoxycarbonyl)phenylpyrrole (3).² 2,5-Diethoxytetrahydrofuran **1** (95.5 g, 0.59 mol) was added to a well stirred solution of methyl antranilate **2** (90 g, 0.59 mol) in AcOH (265 mL). During the exothermic reaction, the mixture became clear deep red. The mixture was heated to reflux for 1 h and the solvent was removed in vacuum. Fractional distillation in vacuum gave 95.8 g of **3** (80%), bp 90-95°C.

CLAY - KINNEAR - PERREN Phosphonyl Chloride Synthesis

Synthesis of alkyl phosphonyl chlorides from alkyl chlorides or from ethers with PCl_3 - AlCl_3 (see 1st edition).

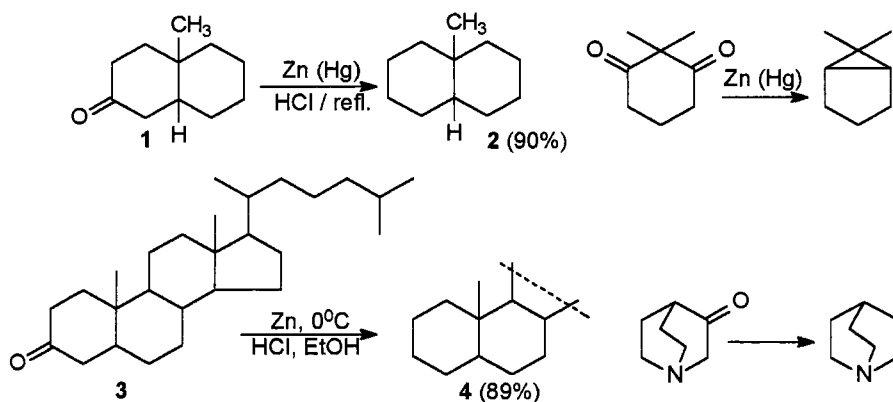


1	Clay, J.P.	<i>J.Org.Chem.</i>	1951	16	892
2	Kinnear, M.M.; Perren, E.A.	<i>J.Chem.Soc.</i>	1952		3434
3	Hamilton, C.S.	<i>Org.Synth.Coll.vol</i>		IV	950

Ethylphosphonyl dichloride (5).¹ **From diethyl ether:** Et_2O **6** (18.5 g, 0.25 mol) was added to a mixture of **1** (66.5 g, 0.5 mol) and **2** (68.5 g, 0.5 mol) at 0°C. The mixture was heated for 7 h at 100°C (sealed tube). The crystalline product was dissolved in CH_2Cl_2 and hydrolyzed with water. After filtration and distillation 28 g of **5** (43%) was isolated.

C L E M M E N S E N Reduction

Reduction of ketones or aldehydes to hydrocabons by means of zinc amalgam and acid (see 1st edition).



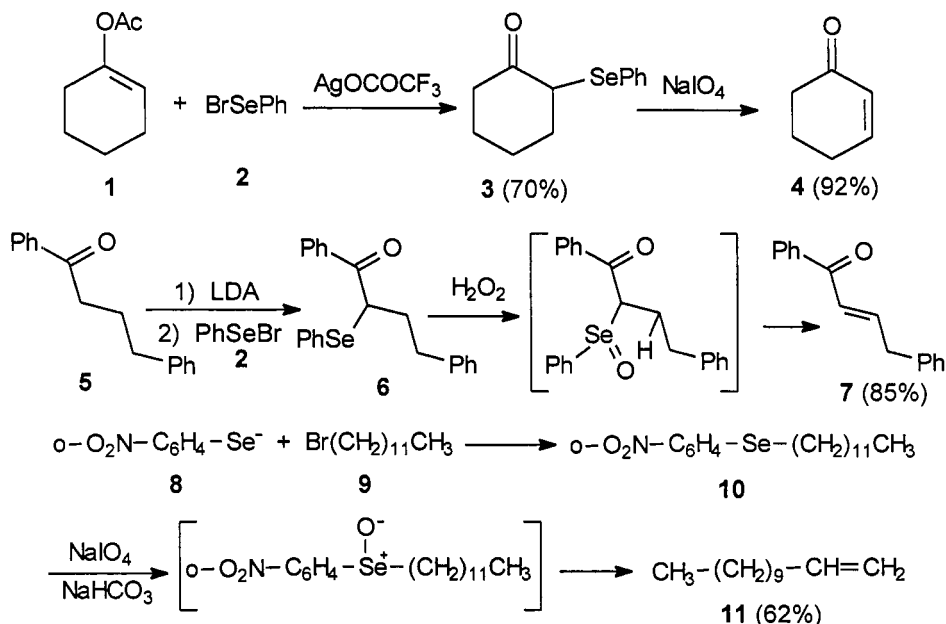
1	Clemmensen, E.	<i>Chem.Ber.</i>	1913	46	1838
2	Dauben, W.G.	<i>J.Am.Chem.Soc.</i>	1954	76	3864
3	Starschewsky, W.	<i>Angew.Chem.</i>	1959	71	726
4	Yamamura, S.	<i>Bull.Chem.Soc.Jpn.</i>	1972	45	364
5	Sanda, G.	<i>Tetrahedron Lett.</i>	1983	24	4425
6	Vedejs, E.	<i>Org.React.</i>	1975	22	401

Cis-9-Methyldecalin (2).² cis-10-Methyl-2-decalone **1** (8.0 g, 48.2 mmol) was heated under reflux with amalgamated zinc (40 g, 0:61 at g) in AcOH (35 mL) and 32% HCl (17.5 mL). Reflux was maintained for 17 h and every 2 h there was added HCl (2 mL). Water (60 mL) was added and the mixture steam distilled. Neutralization of the distillate with Na₂CO₃, extraction with pentane, evaporation of the solvent, followed by distillation from potassium afforded 6.57 g of **2** (90%), bp 91.5-92.0°C / 20 mm.

Cholestane (4).⁴ To a solution of cholestan-3-one **3** (500 mg, 1.3 mmol) in EtOH saturated with HCl gas (75 mL) at 0°C, was added active Zn powder (5.0 g) (in portions) under stirring. After being stirred for 1 h at 0°C, the reaction mixture was basified (Na₂CO₃) and extracted with Et₂O. The residue obtained after removal of the solvent, was chromatographed (silica gel, PhH) to give 431 mg of **4** (89%), mp 77.5-79°C.

CLIVE-REICH-SHARPLESS Olefination

Organoselenium compounds in synthesis of terminal olefins, unsaturated ketones



- | | | | | |
|---|-----------------|--------------------------------|------|---------|
| 1 | Clive, D.L.J. | <i>J.Chem.Soc.Chem.Commun.</i> | 1973 | 695 |
| 2 | Reich, H.J. | <i>J.Am.Chem.Soc.</i> | 1973 | 95 5813 |
| 3 | Sharpless, K.B. | <i>J.Org.Chem.</i> | 1975 | 40 947 |
| 4 | Krief, A. | <i>Bull.Soc.Chim.Fr.</i> | 1997 | 134 869 |

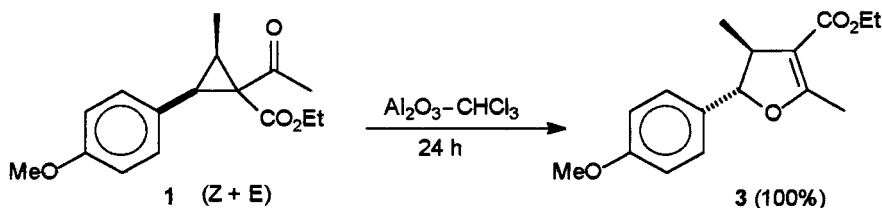
Cyclohex-2-en-1-one 4.¹ Enol acetate of cyclohexanone **1** (1 equiv) in Et₂O at 0°C in the presence of AgOCOCF₃ (1.2 equiv) and **2** (1.1 equiv) afforded after hydrolysis **3** in 70% yield. Oxidation of **3** with NaIO₄ gave **4** (92%).

Acrylophenone 7.² To a solution of LDA under N₂ in THF was added 1,4-diphenyl-1-butanone. After 10 min stirring, **2** was added dropwise at -78°C. To the solution at 0°C, H₂O₂ was added and the reaction mixture was stirred for 30 min at 20-25°C. Usual work up and chromatography afforded **7** in 85% yield.

1-Dodecene 11.³ To a solution of selenide **10** (0.2 mmol) in MeOH/THF/H₂O containing NaHCO₃ (3 equiv) at 20°C was added NaIO₄ (0.3 mmol). After 6 h the reaction mixture was evaporated in vacuum. Usual work up afforded the olefin in 72% yield.

C L O K E - W I L S O N Cyclopropylketone Rearrangement

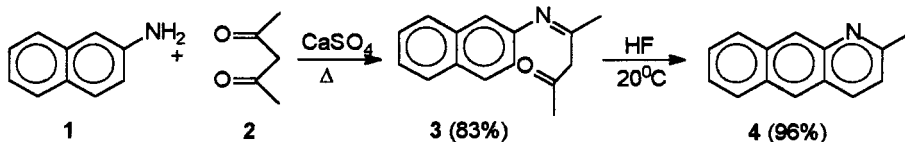
Rearrangement of cyclopropyl ketones or imines to dihydrofurans or dihydropyrroles, thermally, photochemically, or by Lewis acids (see 1st edition).



1	Cloke, J.B.	<i>J.Am.Chem.Soc.</i>	1929	51	1174
2	Wilson, C.L.	<i>J.Am.Chem.Soc.</i>	1947	69	3002
3	Alonso, M.E.	<i>J.Org.Chem.</i>	1980	45	4532
4	Hudlicky, T.	<i>Org.React.</i>	1986	33	247

C O M B E S Quinoline Synthesis

Quinoline synthesis from anilines and β -diketones (see 1st edition).

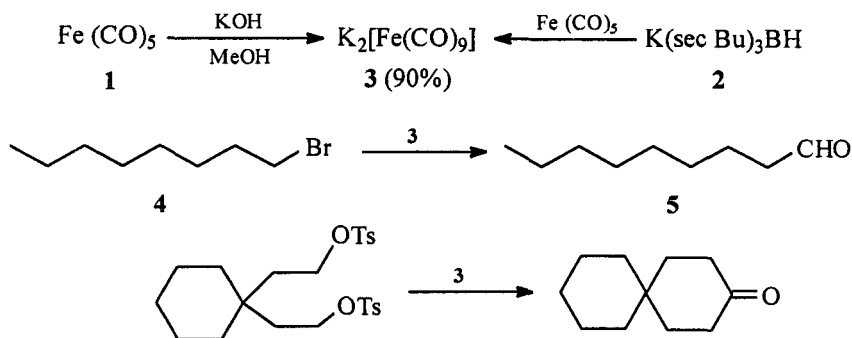


1	Combes, A.	<i>Bull.Soc.Chim.Fr.</i>	1882	49	89(2)
2	Johnson, W.S.	<i>J.Am.Chem.Soc.</i>	1944	66	210
3	Born, J.L.	<i>J.Org.Chem.</i>	1972	37	3952
4	Bergstrom, F.W.	<i>Chem.Rev.</i>	1944	35	156
5	Seifert, W.	<i>Angew.Chem.Int.Ed.</i>	1962	1	215

2,4-Dimethylbenzo(g)quinoline (4). A mixture of **3** (13.4 g, 0.059 mol) in HF (300 ml) was maintained for 24 h at 20°C . The residue obtained after removing the HF was neutralized with 10% K_2CO_3 solution, extracted with Et_2O and the solvent was evaporated to yield 11.75 g of **4** (96%), mp $91\text{-}92.5^\circ\text{C}$.

COLLMAN Carbonylation Reagent

Dipotassium or disodium iron tetracarbonyl in the synthesis of aldehydes and ketones from alkyl halides (see 1 st edition).



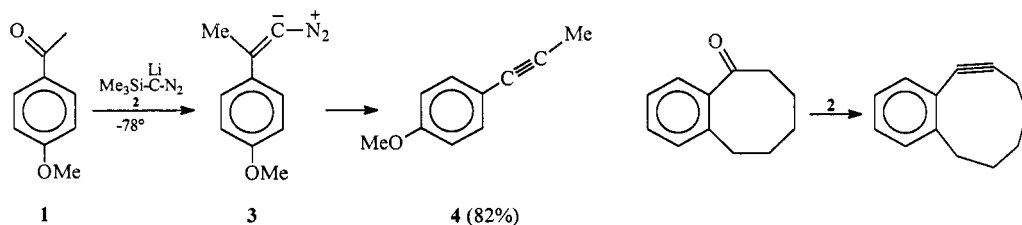
1	Collman, J.P.	<i>Acc. Chem. Res</i>	1986	1	136
2	Collman, J.P.	<i>J. Am. Chem. Soc</i>	1973	95	4089
3	Collman, J.P.	<i>Acc. Chem. Res.</i>	1975	8	342
4	Collman, J.P.	<i>J. Am. Chem. Soc.</i>	1977	99	2515
5	Glaisy, J.A.	<i>J. Am. Chem. Soc.</i>	1978	100	2545
6	Glaisy, J.A.	<i>J. Org. Chem.</i>	1978	43	2280
7	Burnett, J.J.	<i>Syn. Commun.</i>	1997	27	1473

Dipotassium iron tetracarbonyl (catalyst) 3.⁷ Fe(CO)_5 **1** (1.5 mL, 11 mmol) was syringed into a degassed sol. of KOH (1.47 g, 26 mmol) in MeOH (15 mL). After 1 h stirring at 25°C the solvent was evaporated and the residue was stirred with THF (10 mL). The new solvent was evaporated and the operation repeated to remove MeOH. Finally, the residue was extracted with THF, filtered to remove KHCO_3 to obtain a pale pink filtrate (90-95% yield).

Nonanal (5). Octyl bromide **4** (89.44 mg, 0.46 mmol), **3** (94.5 mg, 0.0384 mmol) and Et_3P (132.5 mg, 0.508 mmol) were stirred for 12 h. Glacial AcOH (200 mL) and tridecane (100 mL) (as reference standard) was added. GC analysis indicated 100% yield of **5**.

COLVIN Alkyne Synthesis

Reaction of ketones with lithium trimethylsilyldiazomethane **2** (Peterson olefination) to give after rearrangement the homologous alkynes.

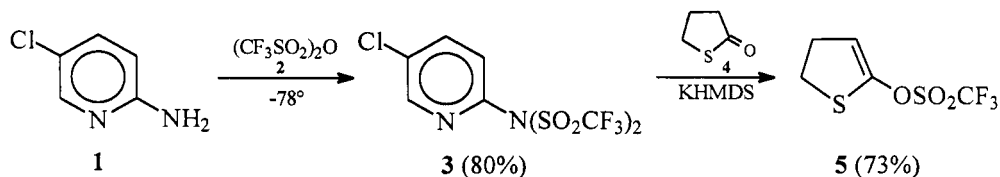


1	Colvin, E.V.	<i>J. Chem. Soc. Chem. Commun.</i>	1973	151
2	Colvin, E.V.	<i>J. Chem. Soc. Perkin Trans. I</i>	1977	869
3	Colvin, E.V.	<i>J. Chem. Soc. Chem. Commun.</i>	1992	721
4	Aoyama, T.; Shioiri, T.	<i>Tetrahedron Lett.</i>	1994	107

p-Methoxyphenylpropyne 4.⁴ To LDA in THF (8 mL) was added trimethylsilyldiazomethane **2** 1.9M in hexane (0.63 mL; 1.2 mmol) at -78°C under Ar. After 30 min **1** (150 mg; 1 mmol) in THF (2 mL) was added dropwise at -78°C . After 1 h the mixture was refluxed 3 h, quenched (H_2O) and extracted with Et_2O . Evaporation and chromatography provided 199.7 mg of **4** (82%), bp $85\text{--}88^\circ\text{C}/0.9\text{ mm}$.

COMINS Triflating Reagent

N-(5-Chloro-2-pyridyl)triflimide **3**, a reagent for introduction of the triflyl (CF_3SO_2) group.

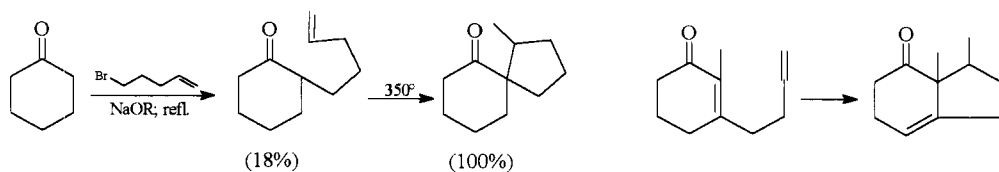


1	Comins, D.L.	<i>Tetrahedron Lett.</i>	1992	33	6299
2	O'Neil, I.A.	<i>Synlett</i>	1995		151

Enol triflate 5.² Under N_2 at -78°C γ -thio-butylolactone **4** (0.17 mL; 2 mmol) in THF (5 mL) was treated with KHMDS (4.4 mL; sol. of 0.5M in PhMe). After 1 h stirring **3** (780 mg; 2 mmol) in THF (2 mL) was added. After 3 h at -78°C , quenching (H_2O), extraction (Et_2O), evaporation and chromatography (Al_2O_3 neutral) gave 342 mg of **5** (73%).

CONIA Cyclization

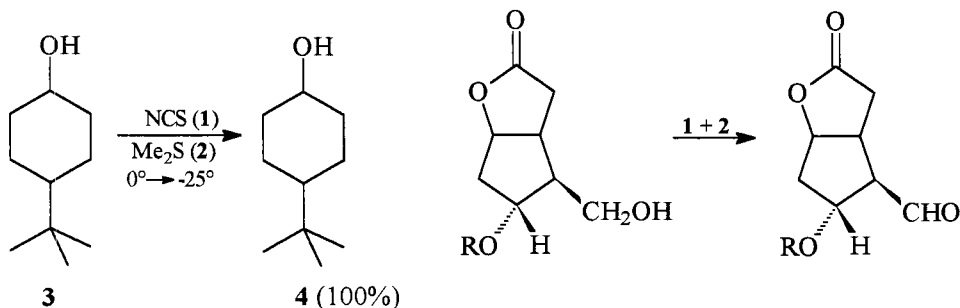
Thermal cyclization of dienones, enals, ynones, diones, ketoesters to monocyclic, spirocyclic bicyclic derivatives (ene reaction of unsaturated enol) (see 1st edition).



1	Conia, J.M.	<i>Tetrahedron Lett.</i>	1965	3305; 3319
2	Conia, J.M.	<i>Bull. Soc. Chim. Fr.</i>	1966	278; 281
3	Krapcho, A.P.	<i>Synthesis</i>	1974	416
4	Conia, J.M.	<i>Angew. Chem. Int. Ed.</i>	1975	14 473

COREY-KIM Oxidizing Reagent

Oxidation of alcohols to ketones by means of N-chlorosuccinimide (NCS) or NBS and Me₂S (see 1st edition).

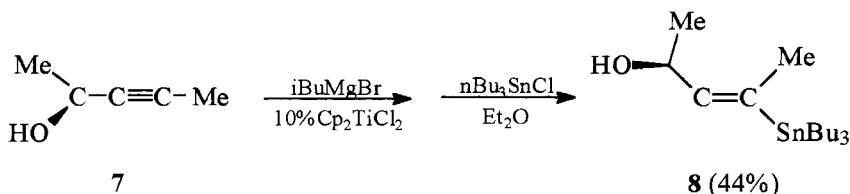
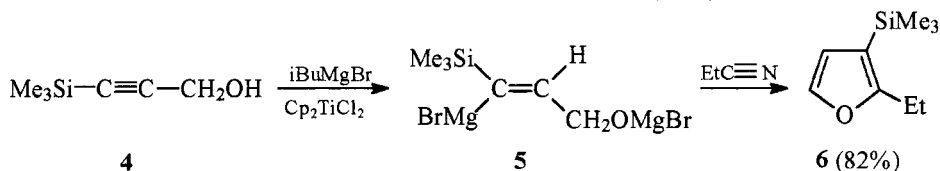
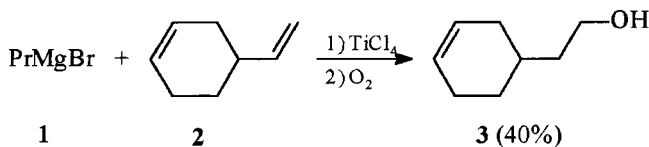


1	Corey, E.J.; Kim, C.U.	<i>J. Am. Chem. Soc.</i>	1972	94 7586
2	Corey, E.J.	<i>Tetrahedron Lett.</i>	1973	919
3	Corey, E.J.	<i>J. Org. Chem.</i>	1973	38 1223
4	Dalgard, N.K.	<i>Acta Chim. Scand.</i>	1984	38B 423
5	Jamauki, M.	<i>Chem. Lett.</i>	1989	973

Ketone 4.¹ To a stirred NCS **1** (400 mg; 3 mmol) in PhMe (10 mL) was added **2** (0.3 mL; 4.1 mmol) at 0°C under Ar; a white precipitate appeared. At -25°C **3** (312 mg; 2 mmol) in PhMe (2 mL) was added dropwise, then Et₂O (20 mL). The organic layer was washed with 1% HCl (5 mL) and twice with water (15 mL). Evaporation left 310 mg of **4** (100%), mp 44-47°C.

COOPER-FINKBEINER Hydromagnesiation

Ti catalyzed formation of Grignard reagents from olefins or acetylenes.



1	Cooper, G.D; Finkbeiner, H.L	<i>J. Org. Chem.</i>	1962	27	3395
2	Sato, F.	<i>J. Chem. Soc. Chem. Commun.</i>	1981		718
3	Sato, F.	<i>Tetrahedron Lett.</i>	1983	24	1804
4	Sato, F.	<i>J. Chem. Soc. Chem. Commun.</i>	1983		162
5	Sato, F.	<i>Tetrahedron Lett.</i>	1984	25	5063
6	Adam, W.	<i>Synthesis</i>	1994		567

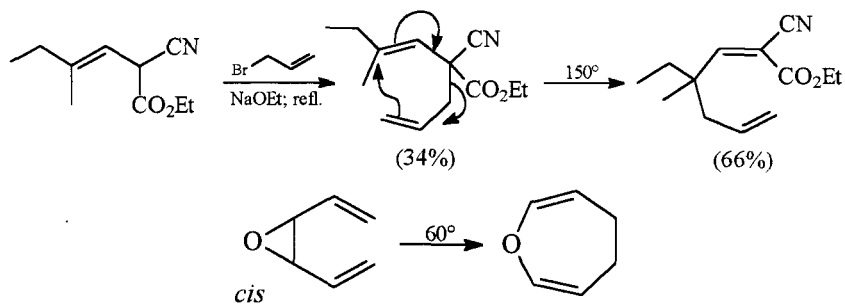
β -(Δ^3 -Cyclohexenyl)ethanol 3.¹ To **1**, from Mg 13.2 g and PrBr 61.3 g in Et₂O (150 mL) was added **2** (54 g; 0.5 mol) followed by TiCl₄ (1 mL). After 2 h reflux and heating with more TiCl₄ (0.5 mL), the mixture was oxidized with air and distilled to give 25 g of **3** (40%), bp 92-94°C.

3-Trimethylsilyl-2-ethylfuran 6.⁵ Cp₂TiCl₂ (0.12 g; 0.48 mol) was added to iBuMgBr in Et₂O (43 mL; 0.4 M) under Ar at 0°C. **4** (0.18 g; 6.8 mmol) was added and the mixture was stirred 6 h at 25°C. EtCN (0.48 g; 8.8 mmol) was added and the mixture was stirred 2 h at 25°C. Usual work up and chromatography (silica gel) afforded 0.94 g of **6** (82%).

(E)-4-(Tributylstannyl)-3-penten-2-ol 8.⁶ Cp₂TiCl₂ (1.74 g; 7 mmol) was added to iBuMgBr (2.1 equiv.) and stirred 10 min at 0°C. **7** (5.89 g; 70 mmol) was added and the mixture was stirred for 15 min at 20°C followed by reflux for 3 h. The solvent was evaporated and the residue dissolved in THF and treated with Bu₃SnCl (25.1 g; 77 mmol) at 0°C. Stirring for 1 h at 25°C and under reflux for 2 h gave after chromatography (silica gel, pentane:Et₂O) 11.6 g of **8** (44%).

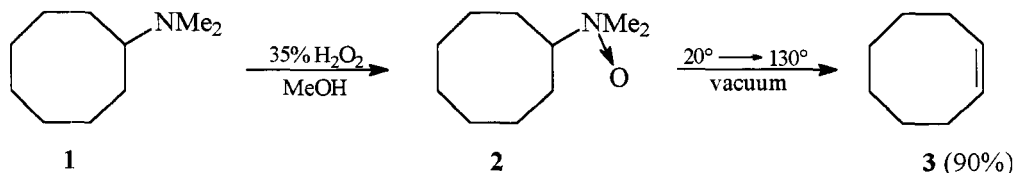
COPE Rearrangement

Thermal 3,3-sigmatropic rearrangement of 1,5-dienes (see 1st edition).



1	Cope, A.C.	<i>J. Am. Chem. Soc.</i>	1940	62	441
2	McDowell, D.W.	<i>J. Org. Chem.</i>	1986	51	183
3	Baldwin, J.E.	<i>J. Org. Chem.</i>	1987	52	676
4	Vogel, E.	<i>Liebigs Ann.</i>	1958	615	1
5	Lutz, R.P.	<i>Chem. Rev.</i>	1984	84	205
6	Blechert, S.	<i>Synthesis</i>	1989		71

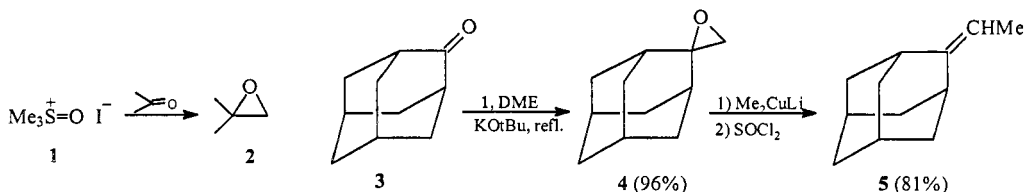
COPE - MAMLOC - WOLFENSTEIN Olefin Synthesis

Olefin formation by *syn*-elimination from tert. amine N-oxides (see 1st edition).

1	Mamloc, L.; Wolfenstein, R.	<i>Chem. Ber.</i>	1900	33	159
2	Cope, A.C.	<i>Tetrahedron Lett.</i>	1949	71	3929
3	Bluth, M.	<i>Tetrahedron Lett.</i>	1984	25	2873
4	De Puy, C.H.	<i>Chem. Rev.</i>	1960	60	448
5	Fujita, J.	<i>Synthesis</i>	1978		934
6	Cope, A.C.	<i>Org. Synth. Coll.</i>	1963	IV	612

COREY Homologative Epoxidation

Reaction of ketones with S-ylides derived from $\text{Me}_3\text{S}^+\text{I}^-$ (from DMSO+MeI) or $\text{Me}_3\text{SO}^+\text{I}^-$ to give epoxides (see 1st edition).

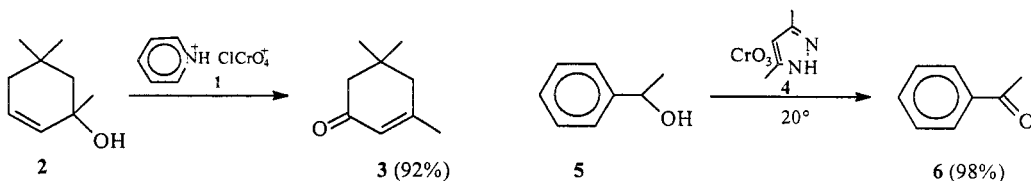


1	Corey, E.J.	<i>J. Am. Chem. Soc.</i>	1962	84	866
2	Kuhn, R.	<i>Angew. Chem.</i>	1957	68	570
3	Kuhn, R.	<i>Liebigs Ann.</i>	1958	611	117
4	Olah, G.A.	<i>Synthesis</i>	1990		887
5	Nesmeyanov, A.N.	<i>Tetrahedron</i>	1987	43	2600

2-Methyleneadamantane epoxide 4.⁴ Ketone 4 (1.5 g; 10 mmol), **1** (2.20 g; 10 mmol) and *t*-BuOK (97% 1.15 g; 10 mmol) in DME (50 mL) was refluxed with good stirring under N_2 for 8 h. Quenching (H_2O), extraction (Et_2O) and evaporation gave 1.57 g of **4** (96%), mp 176°C.

COREY Oxidizing Reagents

Pyridinium chlorochromate (PCC) **1** or CrO_3 -dimethylpyrazole **4** reagents for oxidation of alcohols to ketones or aldehydes.

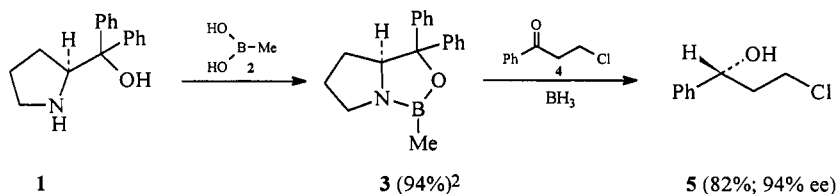


1	Corey, E.J.	<i>Tetrahedron Lett.</i>	1973		2647
2	Dauben, W.G.	<i>J. Org. Chem.</i>	1977	42	682
3	Corey, E.J.	<i>Tetrahedron Lett.</i>	1979		399
4	Luzzio, F.A.	<i>Org. Prep. Proc. Int.</i>	1988	20	559

Isophorone 3.² To a slurry of **1** (from 6M HCl, CrO_3 and pyridine at 0°C)¹ (4.30 g; 20 mmol) in CH_2Cl_2 (30 mL) was added in one portion **2** (1.40 g; 10 mmol) in CH_2Cl_2 (10 mL) at 20°C. After 3 h stirring, extraction (Et_2O), washing (5% NaOH, 5% HCl, NaHCO_3), evaporation and bulb to bulb distillation afforded 1.33 g of **3** (92%), bp 213-214°C.

COREY Enantioselective Borane Reduction

Enantioselective reduction of ketones by borane or catecholborane catalyzed by oxazaborolidine **3** (see 1st edition).

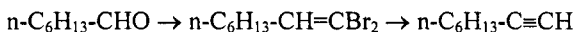
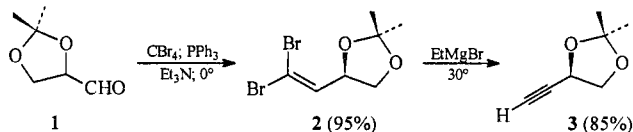


1	Corey, E.J.	<i>J. Am. Chem. Soc.</i>	1987	109	5551
2	Corey, E.J.	<i>J. Org. Chem.</i>	1988	53	2861
3	Corey, E.J.	<i>Tetrahedron Lett.</i>	1989	30	6275
4	Corey, E.J.	<i>Tetrahedron Lett.</i>	1990	31	611
5	Todd, K.J.	<i>J. Org. Chem.</i>	1991	56	763

R-(+)-3-Chloro-1-phenyl-1-propanol 5.³ β -Chloropropiophenone **4** (0.162g; 1 mmol) in THF was added to 0.6 equiv. of BH_3 and 0.1 equiv. of **3** at 0°C in THF over 20 min. After 30 min, one adds MeOH and 1.2 equiv. of HCl in Et_2O , followed by removal of the volatiles. Addition of PhMe precipitated **1**. Concentration afforded 0.162 g of **5** (99%), 94%ee, recrystallized (hexane), mp 57-58°C, $[\alpha]_D^{25} = +24^\circ$ (c=1, CHCl_3).

COREY-FUCHS Alkynes Synthesis

Chain extension of aldehydes to 1,1-dibromoalkenes followed by elimination to alkynes by means of BuLi or RMgX .

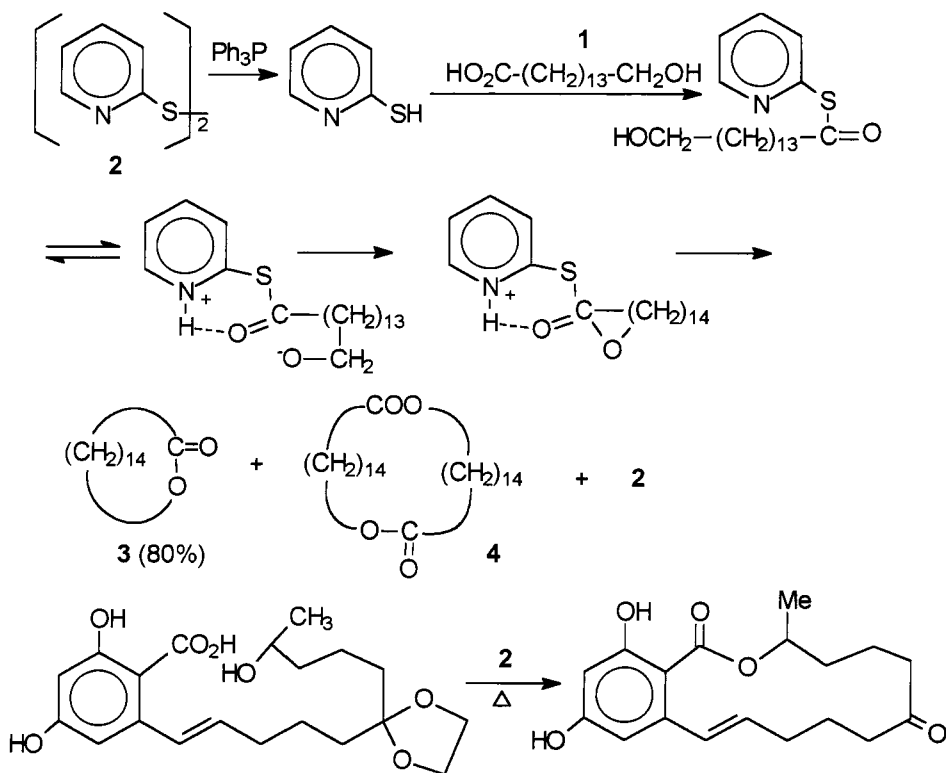


1	Corey, E.J.; Fuchs, P.L.	<i>Tetrahedron Lett.</i>	1972		3769
2	Ma, P.	<i>Synth. Commun.</i>	1995	25	3641

D-(+)-3,4-O-isopropylidenebutyne-3,4-diol 3.² To ice-cooled Ph_3P (5.19 g; 19.8 mmol) in CH_2Cl_2 (11 mL) was added CBr_4 (3.29 g; 9.9 mmol) in CH_2Cl_2 (4 mL) below 15°C. At 0°C the aldehyde **1** (1 g; 7.63 mmol) and Et_3N (1.06 mL; 7.63 mmol) in CH_2Cl_2 (1 mL) was added dropwise. After 30 min at 0°C hexane (10 mL) was added. Filtration, evaporation, dissolving the residue in hexane, filtration and concentration gave 1.96 g of **2** (95%), bp 70-72°C/0.5 mm. **2** (1.084 g; 4 mmol) in THF (2 mL) was treated with EtMgBr (1M in THF, 8 mL; 4 mmol) at 25-30°C. After 30 min quenching with solid NH_4Cl (0.53 g) afforded after vacuum distillation 0.428 g of **3** (85%), bp 70°C/735 mm, $[\alpha]_D^{25} = 33.8^\circ$ (c=1.01, CHCl_3).

COREY-NICOLAOU-GERLACH Macrolactonization

2-Pyridinethiol a reagent in the synthesis of large ring lactones.

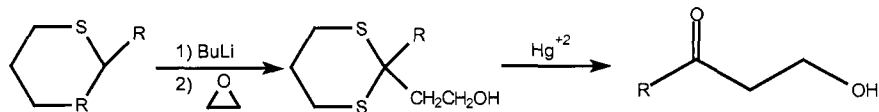
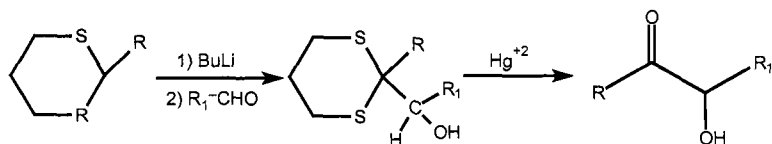
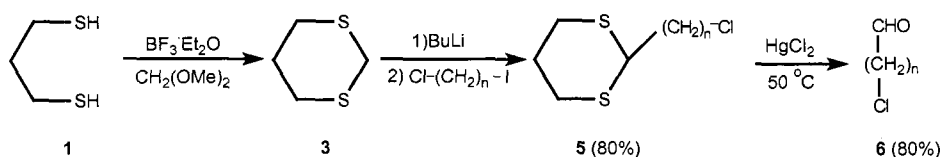


1	Corey, E.J., Nicolaou, K.C.	<i>J. Am. Chem. Soc.</i>	1974	96	5614
2	Gerlach, H.	<i>Helv. Chim. Acta</i>	1974	57	2306; 2661
3	Corey, E.J.	<i>Tetrahedron Lett.</i>	1976		3409
4	Green, A.E.	<i>J. Am. Chem. Soc.</i>	1980	102	7583
5	Nicolaou, K.C.	<i>J. Am. Chem. Soc.</i>	1997	119	3421
6	Nicolaou, K.C.	<i>Angew. Chem. Int. Ed.</i>	1998	37	2714

Lactone 3.¹ The ω -hydroxy acid 1 (129 mg, 0.5 mmol), 2,2'-dipyridyl disulfide 2 (165 mg, 0.75 mmol) and triphenyl phosphine (197 mg, 0.75 mmol) were stirred for 5 h at 25°C in xylene under Ar. The reaction mixture was diluted with xylene (10 mL) and the resulting solution was added over 15 h to xylene (200 mL) under reflux and in an Ar atmosphere. After an additional 10 h reflux (GLC 10 ft, 10% silicone SE-30 column) the solvent was removed in vacuum and the residue was purified by preparative TLC (silica gel 10% Et_2O in pentane) to furnish 96 mg of 3 (80%) and 6 mg of dilactone 4 (5%).

COREY – SEEBACH Dithiane Reagents

Dithianes as acyl anion equivalents useful for synthesis of carbonyl compounds.



1	Corey, E. J., Seebach, D.	<i>Angew. Chem. Int. Ed.</i>	1965	4	1075;1077
2	Corey, E. J., Seebach, D.	<i>J. Org. Chem.</i>	1966	31	4097
3	Corey, E. J., Seebach, D.	<i>J. Org. Chem.</i>	1968	33	300
4	Seebach, D.	<i>Synthesis</i>	1969		17
5	Seebach, D.	<i>Synthesis</i>	1977		357
6	Seebach, D.	<i>Angew. Chem. Int. Ed.</i>	1979	18	239
7	Seebach, D., Corey, E. J.	<i>Org. Synth.</i>	1970	50	487

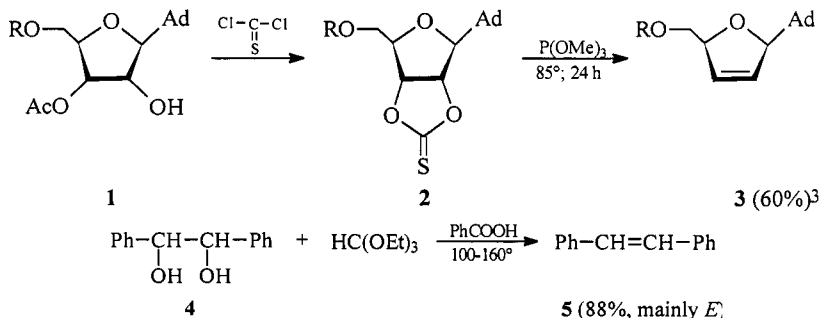
1, 3-Dithiane 3.² To a refluxing solution of $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (10 mL) in AcOH (360 mL) and CHCl_3 (600 mL) under stirring, was added a solution of 1, 3-propanedithiol **1** (150 mL, 1.5 mol) and methylal **2** (145 mL, 1.65 mol) in CHCl_3 (2.25 mL) at a constant rate over 8 h. Usual work up afforded after recrystallization from MeOH (300 mL), 130-140 g of **3** (70 %), mp 52-53 °C.

2-(ω -Chloroalkyl)-1, 3-dithiane 5. To a solution of **3** in THF at -40°C are added $n\text{-BuLi}$ (5.5 excess). Stirring was continued for 1-2 h at -25°C . To this solution an equimolar amount of neat dihalide was added under N_2 at -50°C . After 12 h at -20°C , work up afforded **5** in 60-80 % yield.

Chloro-aldehyde 6. To HgCl_2 (2.18 g, 10.3 mmol) and CaCO_3 (1.68 g, 9.8 mmol) under N_2 was added **5** (4.92 mmol) in water (2.5 mL) and MeCN (47.5 mL). After 7.5 h stirring at 50°C the mixture was concentrated to dryness. Extraction with CHCl_3 , and evaporation of the solvent afforded **6** (80%).

COREY-WINTER-EASTWOOD Olefination of Diols

Alkene synthesis from glycols via cyclic 1,2-thionocarbonates (Corey-Winter) or 1,3-dioxolanones (Eastwood) (see 1st edition).

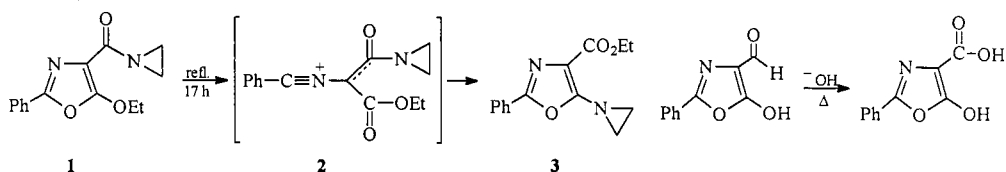


1	Corey, E.J.	<i>J. Am. Chem. Soc.</i>	1963	85	2677
2	Corey, E.J.	<i>J. Am. Chem. Soc.</i>	1965	87	934
3	Carr, R.I.	<i>Org. Prep. Proc. Int.</i>	1990	22	245
4	Eastwood, F.W.	<i>Austral. J. Chem.</i>	1964	17	1392
5	Eastwood, F.W.	<i>Austral. J. Chem.</i>	1968	21	2013
6	Eastwood, F.W.	<i>Tetrahedron Lett.</i>	1970		5223

E-Stilbene 5.⁵ **4** (10 g; 46 mmol) and ethyl orthoformate (7.2 g; 48 mmol) was heated in the presence of PhCOOH (1 g; 8.2 mmol) for 2 h at 100-105°C. More PhCOOH was added and all was heated to 160-170°C then dissolved in Et₂O, washed (aq. Na₂CO₃) and evaporated. Extraction with hexane afforded 0.1 g of Z-5 (1.2%). Evaporation gave 7.35 g of E-5 (88%), bp 74-76°C/0.2 mm.

CORN FORTH Oxazole Rearrangement

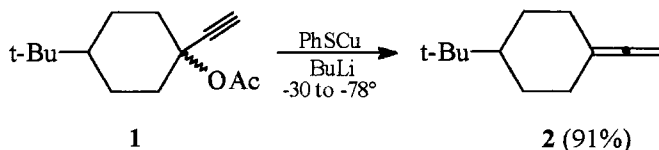
Thermal rearrangement of 4-carbonyl substituted oxazoles via nitrilium ylide **2** (see 1st edition).



1	Cornforth, J.W.	<i>The Chemistry of Penicillin</i>	1949	689	705
2	Dewar, M.J.S.	<i>J. Chem. Soc. Chem. Commun.</i>	1973		925
3	Dewar, M.J.S.	<i>J. Am. Chem. Soc.</i>	1974	96	6148
4	Dewar, M.J.S.	<i>J. Org. Chem.</i>	1975	40	1521
5	L'Abbé, G.	<i>J. Chem. Soc. Perkin I</i>	1993		2259

CRABBÉ Allene Synthesis

Synthesis of terminal allenes from propargylic acetates.

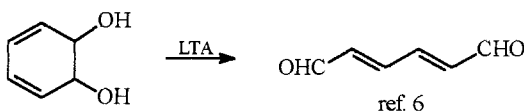
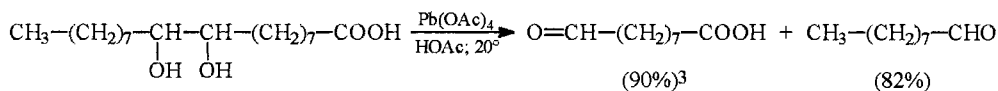


1	Crabbé, P.	<i>J. Chem. Soc. Chem. Commun.</i>	1976		183
2	Nantz, M.H.	<i>Synthesis</i>	1993		577
3	Niemstra, H.	<i>J. Org. Chem.</i>	1997	62	8862

Allene 2.² To a suspension of PhSCu (4.41 g; 25.5 mmol) in Et₂O (100 mL) at -35°C was added 2.47M BuLi in hexane (9.91 mL; 2.45 mmol). After 20 min at -30°C **2** (2.26 g; 10.2 mmol) in Et₂O (35 mL) was added dropwise at -78°C. After 1 h stirring the mixture was quenched with 2 mL of sat. NH₄Cl at a rate of 0.16 mL/min. After 6 h at -78°C and warming to 20°C, the solids were filtered. The organic phase after washing, evaporation and chromatography afforded 1.51 g of **2** (91%).

CRIEGEE Glycol Oxidation

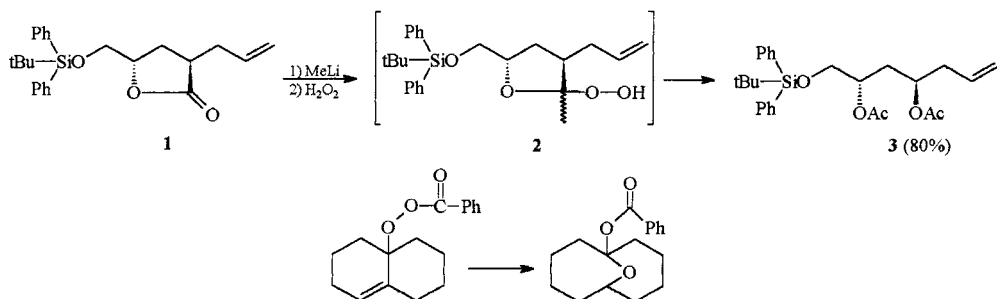
Oxidation of 1,2-glycols to two carbonyl moieties by lead tetraacetate (LTA) (see 1st edition).



1	Criegee, R.	<i>Liebigs Ann.</i>	1930	481	263
2	Criegee, R.	<i>Chem. Ber.</i>	1931	64	260
3	Chi-yi, H.	<i>J. Am. Chem. Soc.</i>	1939	61	3589
4	Criegee, R.	<i>Angew. Chem.</i>	1958	70	173
5	Michailovici, M.L.	<i>Synthesis</i>	1970		209
6	Nakajima, N.	<i>Chem. Ber.</i>	1956	89	2274

CRIEGEE Rearrangement

Rearrangement of hydroperoxides to ester ketals or 1,3-diols.



1	Criegee, R.	<i>Chem. Ber.</i>	1944	77	722
2	Criegee, R.	<i>Liebigs Ann.</i>	1948	560	127
3	Brückner, R.	<i>Synlett</i>	1993		901
4	Kishi, Y.	<i>J. Org. Chem.</i>	1994	59	5125

Triol 3.³ A solution of **1** (330 mg; 0.84 mmol) in THF (5 mL) was treated at -78°C with MeLi (1.04 mL; 1.62 mmol) in Et₂O. After 15 min a sat. solution of NaHCO₃ was added, followed by extraction with tBuOMe. After evaporation of the solvent, the residue was treated with H₂O₂ (0.3 mL of 85%) and a catalytic amount of pyridinium *p*-toluene-sulfonate in THF (4 mL). After 20 min the mixture was extracted with petroleum ether and the crude hydroperoxide **2** was dissolved in THF (3 mL). Et₃N (0.34 mL), *p*-nitrobenzenesulfonylchloride (197 mg; 0.888 mmol) were added and after 29 min the mixture was diluted with tBuOMe and washed with NaHCO₃ sol. The solvent was exchanged with THF, Et₃N (0.78 mL; 5.7 mmol), Ac₂O (0.4 mL; 4 mmol) and a catalytic amount of DMAP were added. After 2 h, work up and chromatography (silica gel, tBuOMe:petroleum ether 1:10) afforded 303 mg of **3** (80%).