Stereoselective Reactions of Phthalimido-Substituted Radicals Derived from (±)-Threonine: a Comparison with Reactions of *N*-Phthaloyliminium Ions

by **Aleksandar Stojanovic** and **Philippe Renaud***

Institut de Chimie Organique, Université de Fribourg, Pérolles, CH-1700 Fribourg

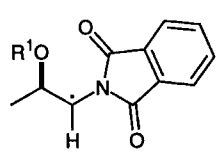
and **Kurt Schenk**

Institut de Cristallographie, Université de Lausanne, BSP, CH-1015 Lausanne

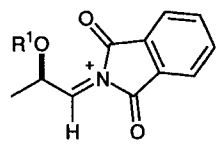
Stereoselective reactions of phthalimido-substituted radicals derived from (±)-threonine with different radical traps are reported (*Scheme 3*, *Table 1*). A strong influence of the nature of the radical trap on the stereoselectivity was noticed. Small nucleophilic radical traps gave preferentially the *syn* products. The observed selectivities are explained with the $A^{1,3}$ strain model and depend on steric and electronic effects (*Fig. 2*). Reactions with electrophilic radical traps such as diphenyl diselenide gave the *anti* diastereoisomers with moderate stereocontrol, presumably due to stereoelectronic effects. The same stereochemical outcome, *i.e.*, preferential formation of the *anti* products, was observed for the reactions of the related *N*-phthaloyliminium ion (*Scheme 5*, *Table 2*). The stereochemistry of the ionic reaction is rationalized by a *Felkin-Anh* model (*Fig. 3*).

Introduction. – Recent studies on the stereochemical outcome of radical reactions have demonstrated that several models previously developed for ionic reactions can be applied to this class of reactions [1]. Examination of 1,2-asymmetric induction allows, *e.g.*, to draw parallels between carbonyl-substituted radicals and enolates [2] as well as *O*-substituted radicals and ketones or aldehydes [3]. 1-Amino-substituted radicals are interesting intermediates in the synthesis of N-containing compounds of biological interest such as alkaloids, unusual amino acids, and peptides [4]. Recently, we have reported that the addition of electrophilic alkyl radicals to cyclic and acyclic enamines produces 1-amino-substituted radicals which undergo a highly stereoselective reduction within tin hydride to provide tertiary amines [5][6]. The observed diastereoselectivities in the acyclic systems were explained with a model minimizing allylic 1,3-strain ($A^{1,3}$ strain) in analogy to the related allylic systems [7]. Primary amines are accessible by using particular enamines prepared from piperidinone [8]. In this account, we describe a study of the reactions of (phthaloylamino)-substituted radicals of type **A** which should allow $A^{1,3}$-strain-based stereocontrol and a facile deprotection. A comparison of the stereoselectivity with the related *N*-phthaloyliminium ions of type **B** is made. Astonishing differences between the two systems have been found and will be discussed[1]).

[1]) For a preliminary communication, see [9]. For a related work on phthalimido-substituted radicals, see [10].



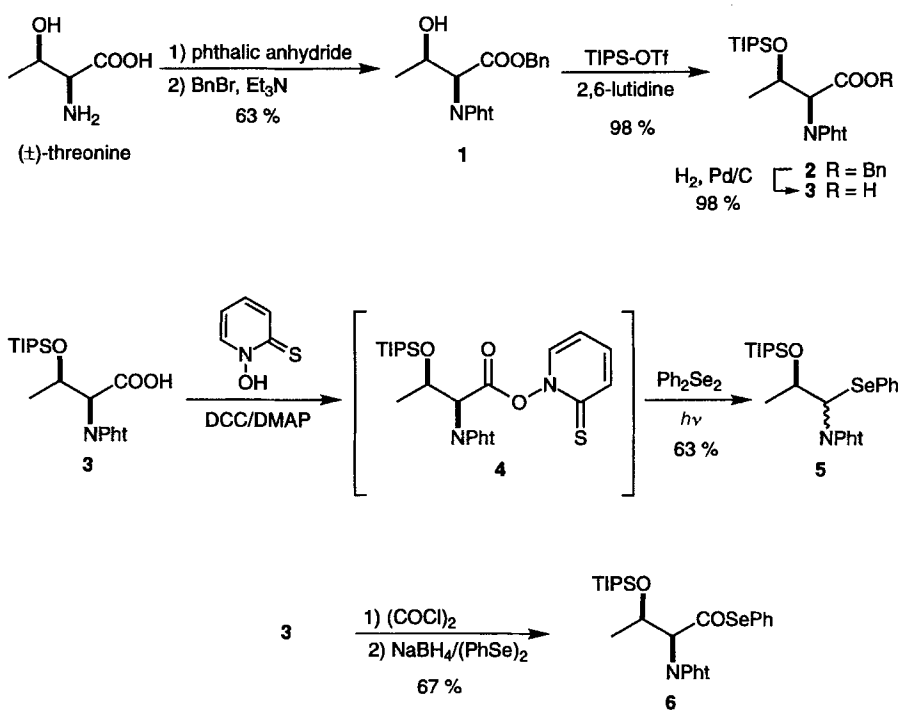
A



B

Results. – *Preparation of Radical Precursors.* The *N*-phthaloylated, *O*-silylated aminohydroxycarboxylic acid **3** was prepared in four steps (62% overall yield) from (±)-threonine according to *Scheme 1.* Treatment of the free amino acid with phthalic anhydride gave *N*-phthaloylthreonine which was then esterified to its benzyl ester **1** with $BnBr/Et_3N$ (63% overall yield). Silylation of **1** with triisopropylsilyl trifluoromethanesulfonate ($(i\text{-}Pr)_3SiOTf$) and 2,6-dimethylpyridine followed by catalytic hydrogenation of benzyl ester **2** gave acid **3** in nearly quantitative yield. Treatment of **3** with 1-hydroxypyridin-2(1*H*)-thione/dicyclohexylcarbodiimide (DCC)/4-(dimethylamino)pyridine (DMAP) gave the *Barton* ester **4** [11]. This unstable compound could not be stored and was immediately used for radical reactions without purification. The *Barton* ester **4** was transformed into the more convenient N,Se-acetal radical precursor **5** by sun lamp irradiation in the presence of diphenyl diselenide in 63% yield. A third radical precursor,

Scheme 1

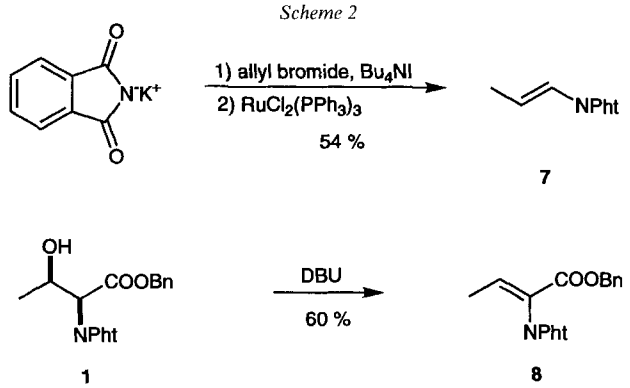


Pht = phthaloyl, Bn = $PhCH_2$, TIPS = $(i\text{-}Pr)_3Si$

the stable seleno ester **6** was also prepared by treatment of carboxylic acid **3** with oxalyl chloride followed by $NaBH_4/(PhSe)_2$ (67% yield)[2]).

We were also interested in the addition of alkyl radicals to enamides. For this purpose, we prepared the enamides **7** and **8** according to *Scheme 2*. Allylation of the potassium salt of phthalimide and subsequent isomerization of the allylic double bond gave **7** in 54% yield [14]. The aminodidehydro-acid derivative **8** was obtained in 60% yield from **1** upon treatment with DBU (1,8-diazabicyclo[5.4.0]undec-7-ene).

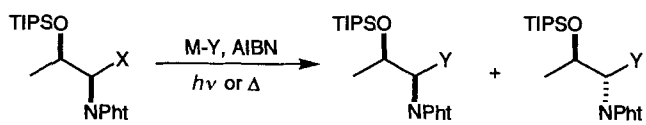
Scheme 2



Pht = phthaloyl, Bn = $PhCH_2$

Radical Reactions. The results of the radical reactions of precursors **4**–**6** are summarized in *Table 1* (see also *Scheme 3*). The nature of the radical trap has a dramatic influence on the diastereoselectivity. Irradiation of the *Barton* ester **4** with a 300-W sun lamp at 10° gave the pyridylthio derivative **9** as *syn* isomer in 79% ds (*Entry 1*). The selectivity was reversed when the intermediate radical was trapped with $(PhSe)_2$, and the N,Se-acetal *anti*-**5** was obtained in 70% ds (*Entry 2*). Deuteration of **5** and **6** with Bu_3SnD/AIBN (2,2′-azobis[isobutyronitrile]) gave preferentially the *syn*-**10** (85% ds, *Entries 3* and *4*; see below for the undeuterated analogue **12**)[3]). The allylation reaction

Scheme 3



syn *anti*

4 X = $COOC_5H_4NS$
5 X = SePh
6 X = COSePh

5 Y = SePh
9 Y = SPy
10 Y = D
11 Y = $CH_2C(COOMe)=CH_2$
12 Y = H

TIPS = $(i\text{-}Pr)_3Si$, Pht = phthaloyl

[2]) We have recently reported the use of seleno esters derived from *N*-protected α-amino acids for the preparation of 1-amido-substituted radical [12]. For a related work, see [13].

[3]) A slightly higher selectivity (90% ds) was observed by *Giese* using $(t\text{-Bu})Ph_2Si$ instead of a $(i\text{-}Pr)_3Si$ as protecting group, see [10].

Table 1. *Radical Reactions of Precusors* **4–6** *According to* Scheme 3

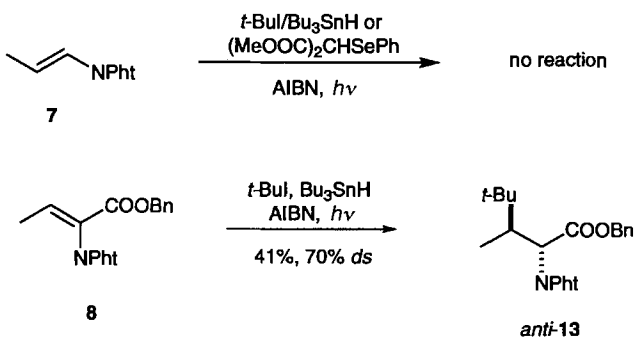
Entry	Precursor	Radical trap (M–Y)	Product	Yield [%]	*syn/anti*[a])
1	**4**[b])	–	**9**	65	79:21
2	**4**[b])	$(PhSe)_2$	**5**	63	30:70
3	**5**[b])	Bu_3SnD	**10**	73	85:15
4	**6**[b])	Bu_3SnD	**10**	80	85:15
5	**5**[b])	$CH_2=C(COOMe)CH_2SnBu_3$	**11**	84	38:62[c])
6	**6**[d])	$CH_2=C(COOMe)CH_2SnBu_3$	**11**	65	50:50

[a]) *syn/anti* refers to the arrangements of the groups $(i\text{-}Pr)_3SiO$ and PhtN. [b]) Irradiation with 300-W sun lamp at 10°. [c]) The configuration was not established, but comparison of the ^{1}H-NMR spectra of **11** with those of compound **20** suggests a relative *anti* configuration for the major isomer. [d]) Heated at reflux in benzene.

of **5** and **6** with methyl 2-[(tributylstannyl)methyl]prop-2-enoate gave **11** with almost no control of stereoselectivity (62 and 50% ds, *Entries 5* and *6*). The absence of diastereoselectivity in the last entry is explained by the higher reaction temperature.

Next, the addition of alkyl radicals to enamides **7** and **8** was investigated (*Scheme 4*). The strong electron-withdrawing effect of the phthaloyl group at the N-atom was expected to make possible the addition of simple nucleophilic alkyl radicals to the enamide double bond. However, no product was observed when **7** was reacted with *tert*-butyl iodide/Bu_3SnH/AIBN. Reaction with dimethyl (phenylseleno)malonate under PhSe-group transfer conditions also gave no addition product. Addition of the *tert*-butyl radical to the aminodidehydro acid derivative **8** was successful, and *anti*-**13** was obtained in 41% yield and 70% ds.

Scheme 4

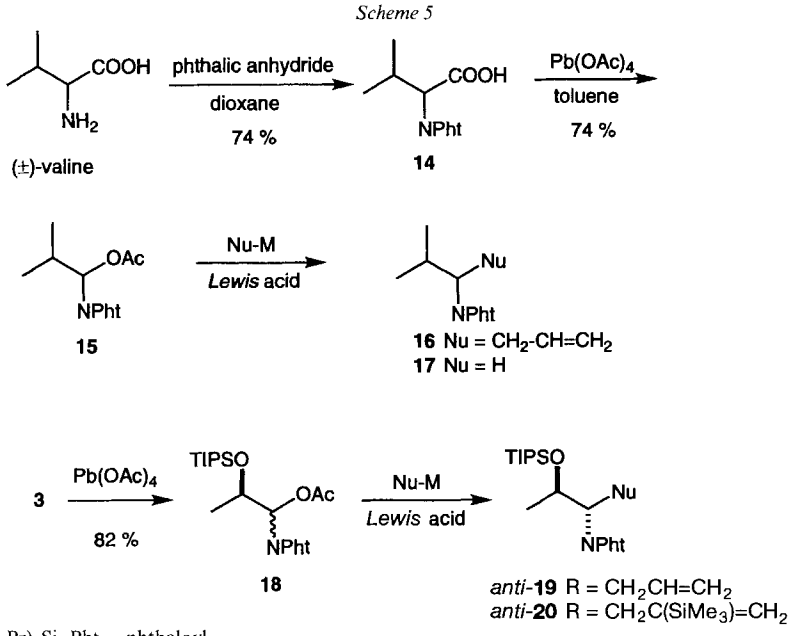


Pht = phthaloyl, Bn = $PhCH_2$

Reactions of N-*Phthaloyliminium Ions*. In a preliminary study, we have optimized the conditions for the *Lewis*-acid-promoted reactions of the phthaloyliminium ion generated from N,O-acetal **15** (prepared from (±)-valine *via* **14** according to *Scheme 5*). Reactions with allyltrimethylsilane in the presence of 1.1 equiv. of *Lewis* acid ($BF_3 \cdot OEt_2$ or $TiCl_4$) gave **16** in moderate yields (*Table 2*, *Entries 1* and *2*). Reduction with Et_3SiH of the intermediate phthaloyliminium ion generated with $BF_3 \cdot OEt_2$ provided the phthalimide **17** in 85% yield (*Table 2*, *Entry 3*).

The N,O-acetal **18** was prepared from **3** by oxidative decarboxylation with lead tetraacetate (*Scheme 5*). The allylation of **18** with allyltrimethylsilane required 5 equiv. of $BF_3 \cdot OEt_2$ in refluxing $CHCl_3$ to take place. The allylated compound *anti*-**19** was isolated in 89% ds and 67% yield (*Table 2, Entry 4*). Milder reaction conditions were found by using trimethylsilyl triflate (2.0 equiv.) in refluxing CH_2Cl_2 (*Table 2, Entry 5*). However, the best results were obtained with 2.1 equiv. of $EtAlCl_2$ at $-78°$ to room temperature (74% yield, 89% ds, *Table 2, Entry 6*). The stereoselectivity of the reaction is neither influenced by the nature of the *Lewis* acid nor by the reaction temperature. However, the nature of the nucleophile is important; reaction of **18** with trimethyl-{1-[(tributylstannyl)methyl]ethenyl}silane (*Table 2, Entry 7*) gave *anti*-**20** with a lower selectivity (71% ds).

Scheme 5



TIPS = $(i\text{-}Pr)_3Si$, Pht = phthaloyl

Table 2. *Reactions of* **15** *and* **19** *with Nucleophiles/*Lewis *Acids According to* Scheme 5

Entry	N,O-Acetal	*Lewis* acid (equiv.)	Nu-M	Product	*T* [°C]	Yield [%] (*syn*/*anti*[a])
1	**15**	$BF_3 \cdot OEt_2$ (2.0)	$CH_2{=}CHCH_2SiMe_3$	**16**	−78 to r.t.	45
2	**15**	$TiCl_4$ (1.1)	$CH_2{=}CHCH_2SiMe_3$	**16**	−78 to r.t.	30
3	**15**	$BF_3 \cdot OEt_2$ (3.0)	$Et_3Si\text{-}H$	**17**	0 to r.t.	85
4	**18**	$BF_3 \cdot OEt_2$ (5.0)	$CH_2{=}CHCH_2SiMe_3$	*anti*-**19**	61	67 (11:89)
5	**18**	Me_3SiOTf (2.1)	$CH_2{=}CHCH_2SiMe_3$	*anti*-**19**	40	50 (11:89)
6	**18**	$EtAlCl_2$ (2.0)	$CH_2{=}CHCH_2SiMe_3$	*anti*-**19**	−78 to r.t.	74 (11:89)
7	**18**	$EtAlCl_2$ (2.0)	$CH_2{=}C(SiMe_3)CH_2SnBu_3$	*anti*-**20**	−78 to r.t.	60 (29:71)

[a]) *syn*/*anti* refers to the arrangements of the groups $(i\text{-}Pr)_3SiO$ and PhtN.

Determination of the Relative Configurations. The two diastereoisomers of the N,Se-acetal **5** were separated by flash chromatography and were crystalline. The *anti* configuration of the major isomer was established by X-ray crystal-structure analysis (*Fig. 1*).

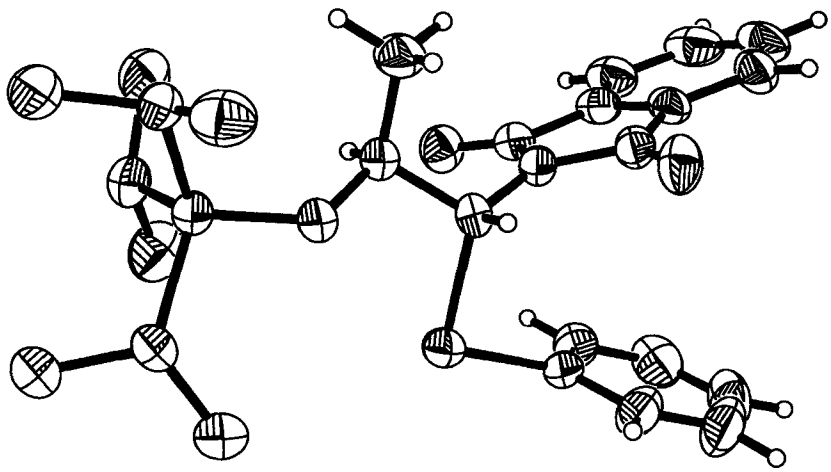
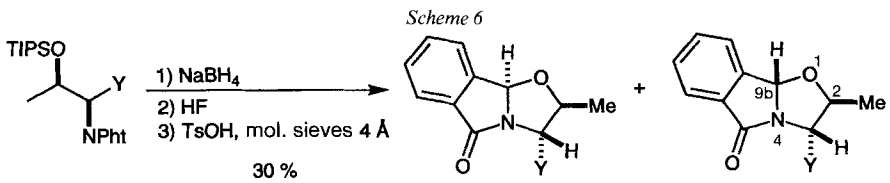


Fig. 1. *X-Ray crystal-structure analysis of* anti-**5**

The relative configuration of the N,S-acetal **9** was established by comparison of ^{1}H- and ^{13}C-NMR spectra of **9** and **5**. The spectra of the major isomer of **9** strongly resemble the spectra of *syn*-**5** (minor isomer).

The *syn* relative configuration of the major deuterated compound **10**[4]) was established by converting it to the cyclic derivative **21a**/**21b** by reduction with $NaBH_4$, removal of the $(i\text{-}Pr)_3Si$ group with HF, and treatment of the crude diol with *p*-toluenesulfonic acid (TsOH; *Scheme 6*). The diastereoisomers **21a** and **21b** (2:1 ratio) were separated by flash chromatography. For the NMR study, compounds **22a**/**22b**, the undeuterated analogs of **21a**/**21b**, were prepared from **12** according to the same procedure. The attribution of the ^{1}H-NMR signals was possible by NOESY experiments on the major diastereoisomer **22a** (1.36 (Me–C(2)); 3.39 (H–C(3) *trans* to H–C(2)); 3.56

Scheme 6



syn-**10** Y = D
12 Y = H

21a Y = D
22a Y = H

2:1

21b Y = D
22b Y = H

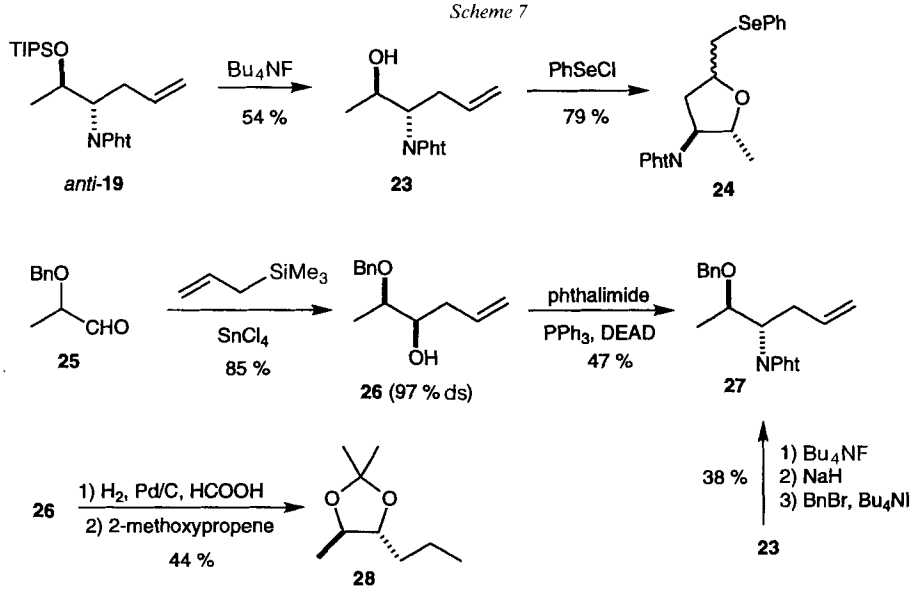
TIPS = $(i\text{-}Pr)_3Si$, Pht = phthaloyl

[4]) The reaction was run with a *syn*/*anti* 85:15 mixture of diastereoisomers. For convenience, only the major *syn* isomer is shown.

(H–C(3) *cis* to H–C(2)); 4.70–4.61 (H–C(2)); 5.86 ppm (H–C(9b) *cis* to H–C(2)). Based on this analysis, the relative configuration of **21a** was attributed confirming the *syn* configuration of **10** (major isomer).

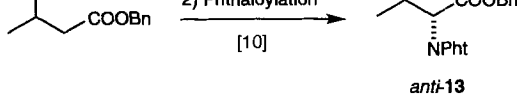
Determination of the relative configuration of benzyl ester **13** was possible by comparing its ^{1}H- and ^{13}C-NMR spectra with literature data [10][5]). Our first attempt to determine the relative configuration of **19** relies on its conversion into **24** by desilylation and treatment of alcohol **23** with PhSeCl (*Scheme 7*). Cyclized product **24** was obtained as an inseparable 1:1 mixture of diastereoisomers whose relative configuration could not be assessed by NOE analysis. Furthermore, elimination of the newly formed asymmetric center by an oxidation-elimination procedure was not possible. Therefore, we decided to perform a chemical correlation with a product of known configuration. For this purpose, phthalimide **27** was prepared in four steps starting from 2-(benzyloxy)propanal (**25**) according to *Scheme 7*. Allylation of **25** with allyltrimethylsilane/$SnCl_4$ **26** in good yield (85%) and 97% ds [16]. The *syn* configuration of **26** was assigned after transformation into the known *trans*-disubstituted dioxolane **28** [17]. NOE Measurements on **28** con-

Scheme 7



TIPS = $(i\text{-Pr})_3$Si, Pht = phthaloyl, Bn = $PhCH_2$

[5]) Indeed, the same major product *anti*-**13** was obtained by a diastereoselective azidation of the enolate derived from benzyl 3-(*tert*-butyl)butanoate followed by reduction and *N*-phthaloylation. The relative configuration has not been proven but can be deduced from the well-established $A^{1,3}$ strain stereocontrol of enolate alkylation [15].



firmed that **26** is *syn* configurated in accordance with [16]. Finally, **26** (*syn*) was transformed into **27** (*anti*) *via* a *Mitsunobu* reaction [18]. An identical sample of **27** was prepared by benzylation of phthalimide **23** (major isomer). This result confirms that the major isomer of **19** is *anti*-configurated[6]).

The relative *anti* configuration of **20** (major isomer) was determined by comparison of the ^{1}H- and ^{13}C-NMR spectra of the major and the minor isomer with those of **19**.

Discussion. – *Radical Reactions.* Reaction of the radical **29** generated from the precursors **4**–**6** gives *syn* products when the radical trap is the *Barton* ester **4** and Bu_3SnD. A possible rationalization of these results can be given by considering the ground-state conformation of the reactive intermediate. We assume that the radical lies in a conformation which minimizes $A^{1,3}$ strain interactions, and attack is occurring *anti* to the bulky $(i\text{-Pr})_3SiO$ group (*Fig. 2*, model **C**)[7]). This reaction topicity is also certainly favored by a stereoelectronic effect; indeed, the reaction is occurring *anti* to the adjacent C–O bond. This effect is reinforced by the nucleophilic character of the radical traps[8]). On the other

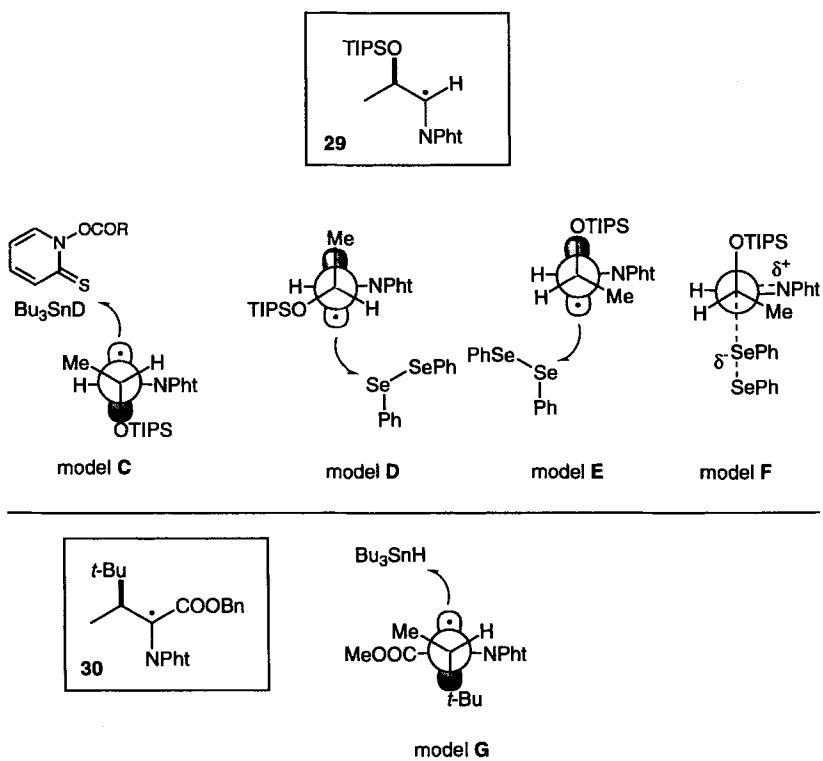


Fig. 2. *Models for the stereochemistry of the radical reactions.* TIPS = $(i\text{-Pr})_3Si$, Pht = phthaloyl.

[6]) The relative configuration of **20** was erroneously assigned in the preliminary communication [9].

[7]) A similar model was proposed for a phthalimido-substituted radical [10] and for *N*-alkyl-*N*-(acylamino)-substituted radicals [6].

[8]) For a discussion of stereoelectronic effects in radical reactions, see [1b] and [19].

hand, trapping of the radical intermediate with diphenyl diselenide, an electrophilic radical trap, provided preferentially the *anti* isomer. This may partially be explained by a stereoelectronic effect (attack is occurring *anti* to the Me group in a conformation which minimizes $A^{1,3}$ strain (*Fig. 2*, model **D**)[9]) or by a *Felkin-Anh* model (*Fig. 2*, model **E**). This last model is expected to be favored by bulky radical traps[10])[11]) and also by the transition-state polarization (model **F**) which resembles the iminium ion (see discussion below).

The stereoselectivity observed in the radical addition to the aminodidehydro-acid derivative **8** can be explained by the model **G** (*Fig. 2*). The conformation of the radical intermediate **30** is governed by $A^{1,3}$ strain. As expected from steric considerations[12]), the minimization of the $A^{1,3}$ strain with the phthalimido group prevails over the ester group.

N-Phthaloyliminium-Ion Reactions. The stereoselectivities of the reactions of the N-phthaloyliminium ion **31** (from **18**) reported in *Table 2* are best explained by a *Felkin-Anh* model (model **H**, *Fig. 3*). Interestingly, a similar model has been already proposed for reactions of a related *N*-(ethoxycarbonyl)iminium ion [21].

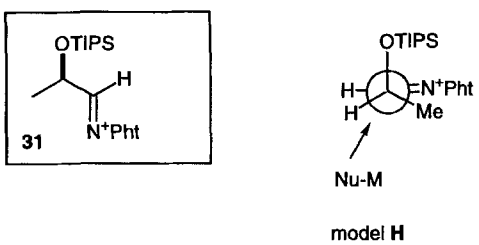
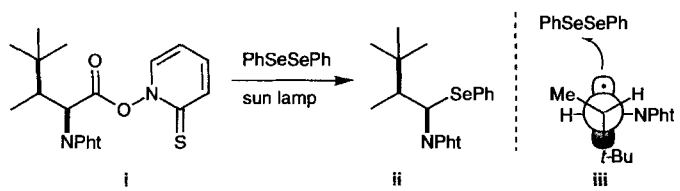


Fig. 3. *Stereochemical model for the reactions of the* N-*phthaloyliminium ion* **31**. TIPS = $(i\text{-Pr})_3Si$, Pht = phthaloyl.

Conclusion. – The phthaloyl group is a useful protective and activating group for amino-substituted radicals and iminium ions. The stereochemical outcome of radical reactions depends strongly on the radical trap used. Nucleophilic traps give, as expected, products predicted by the $A^{1,3}$-strain model and steric considerations. However, reactions with diphenyl diselenide, an electrophilic radical trap, yield products of opposite relative configuration. The same inverted stereochemistry is observed during the reaction

[9]) *Giese* and coworkers [10] have reported a $A^{1,3}$-strain stereocontrol for the conversion of the *Barton* ester **i** to the N,Se-acetal **ii**. In this case, both steric and electronic factors favor the transition state **iii**.



[10]) For a discussion of a related competition between $A^{1,3}$-strain and *Felkin-Anh* stereocontrol, see [20].

[11]) It is reasonable to assume that diphenyl diselenide and methyl 2-[(tributylstannyl)methyl]prop-2-enoate are larger than tributyltin deuteride and the thiocarbonyl group of the *Barton* ester **4**.

[12]) The two carbonyl groups of the phthalimido substitutent are pointing toward the radical center.

of the *N*-phthaloyliminium ion with nucleophiles. In this last case, it has been rationalized with a transition state analogous to the *Felkin-Anh* model. The similarity of the transition-state polarization may partially explain this analogy. This point is certainly of importance for other comparisons between radical and ionic reactions. For instance, the excellent convergence of ester radicals and ester enolates [2] is certainly favored by the analogous polarization of the transition states.

We are very grateful to the *Swiss National Science Foundation* (project No. 20-44'234.95) for funding and to *Ciba-Geigy AG*, Marly, for performing microanalyses.

Experimental Part

General. THF was freshly distilled from K under N_2, CH_2Cl_2, DMF, and benzene from CaH_2 under N_2 and toluene from Na under N_2. Methyl 2-[(tributylstannyl)methyl]prop-2-enoate [22] and trimethyl{1-[(tributylstannyl)methyl]ethenyl}silane [23] were prepared according to the literature procedure. Bu_3SnD was obtained by reduction of Bu_3SnCl with $LiAlD_4$ [24]. The 1-hydroxypyridin-2(1*H*)-thione was obtained by extraction of its sodium salt in Et_2O with 3M aq. HCl soln. Irradiations were conducted using a sun lamp *Osram Ultra-Vitalux 300 W*. The diastereoselectivities were determined by ^{1}H-NMR after filtration through a short silica-gel column if not otherwise stated. Flash column chromatography (FC) and filtration: *Merck* silica gel *60* (70–230 mesh). TLC: *Merck* silica gel *60* F_{254} anal. plates; detection either with UV, I_2, or by spraying with a soln. of phosphomolybdic acid (25 g), $Ce(SO_4)_2 \cdot 4\,H_2O$ (10 g), conc. H_2SO_4 soln. (60 ml), and H_2O (940 ml) with subsequent heating. HPLC: *Waters-600-E* controller, *Waters-486* detector and *Waters-Nova-Pak-Silica* 3.9 × 150-mm column. M.p.: not corrected; *Reichert Thermovar Kofler* hot stage apparatus. IR Spectra: *Perkin-Elmer 16PC* and *Mattson Unicam 5000*; in cm^{-1}. NMR Spectra: *Varian Gemini 200* (^{1}H 200 MHz, ^{13}C 50.3 MHz), *Bruker AM 360* (^{1}H 360 MHz), *Bruker Avance DRX-500* (^{1}H 500 MHz); δ(H) in ppm rel. to $CDCl_3$ (= 7.26 ppm) and δ(C) in ppm rel. to $CDCl_3$ (= 77.0 ppm); unless otherwise stated, $CDCl_3$ solns.; ^{13}C multiplicities by APT sequence; coupling constants *J* in Hz; NOE: irradiated signal → affected signal (%). MS: *Vacuum Generators Micromass VG 70/70E DS 11-250*; EI (70 eV), CI (CH_4 gas); *m/z* (re. %); FAB: matrix 3-nitrobenzyl alcohol (NBA), Xe bombardment (8 kV, 1 mA).

N-*Phthaloylthreonine.* A mixture of (±)-threonine (50.0 g, 0.42 mol) and phthalic anhydride (74.6 g, 0.50 mol) in dioxane (250 ml) was heated under reflux for 16 h. After evaporation, the residue was treated with H_2O (300 ml) and left to crystallize in an ice-bath. The solid was filtered, washed with H_2O and dried under vacuum. Recrystallization (AcOEt/hexane) gave *N*-phthaloylthreonine (88.3 g, 84%). M.p. 122–123° [25]: 122–123°). ^{1}H-NMR (200 MHz): 7.92–7.74 (*m*, 4 arom. H); 5.08 (br. *s*, NH_2); 4.45 (*d*, *J* = 4.9, CHN); 4.80–6.68 (*m*, CHO); 1.31 (*d*, *J* = 7.6, Me).

Benzyl 3-Hydroxy-2-(phthaloylamino)butanoate (= *Benzyl 1,3-Dihydro-α-(1-hydroxyethyl)-1,3-dioxo-2H-isoindole-2-acetate*; **1**). A mixture of *N*-phthaloylthreonine (49.8 g, 0.20 mol), benzyl bromide (36.0 ml, 0.30 mol), and Et_3N (42.0 ml, 0.30 mol) was heated under reflux for 8 h. The mixture was diluted with H_2O, the org. layer washed with 3M HCl, H_2O, and sat. brine, dried ($MgSO_4$), and evaporated, and the residue recrystallized (AcOEt/hexane): **1** (51.2 g, 75%). White solid. M.p. 103–105°. IR (KBr): 3406, 3015, 2940, 1740. ^{1}H-NMR (360 MHz): 7.92–7.75 (*m*, 4 arom. H); 7.34–7.32 (*m*, 5 arom. H); 5.25 ('*d*', *A* of *AB*, J_{AB} = 12.2, 1 H, PhCH_2); 5.21 ('*d*', *B* of *AB*, J_{AB} = 12.5, 1 H, PhCH_2); 5.03 (*d*, *J* = 3.1, CHN); 4.75–4.64 (*m*, CHO); 1.22 (*d*, *J* = 6.5, Me). ^{13}C-NMR (50.3 MHz): 168.73 (*s*); 167.72 (*s*); 135.11 (*s*); 134.56 (*d*); 131.68 (*s*); 128.55 (*d*); 128.38 (*d*); 128.15 (*d*); 67.78 (*t*); 66.72 (*d*); 59.44 (*d*); 20.24 (*q*). FAB-MS: 340 ([*M* + 1]$^+$), 250, 204, 136, 91. Anal. calc. for $C_{19}H_{17}NO_3$ (339.35): C 67.25, H 5.05, N 4.13; found: C 67.06, H 5.10, N 4.13.

Benzyl 2-(Phthaloylamino)-3-[(triisopropylsilyl)oxy]butanoate (= *Benzyl 1,3-Dihydro-1,3-dioxo-α-{1-[(triisopropylsilyl)oxy]ethyl}-2H-isoindole-2-acetate*; **2**). Freshly distilled 2,6-dimethylpyridine (from CaH_2; 5.80 ml, 50.0 mmol) was added under N_2 to a soln. of **1** (6.79 g, 20.0 mmol) in dry CH_2Cl_2 (20 ml). The mixture was cooled to 0°, and (i-Pr)$_3$SiOTf (7.00 ml, 26.0 mmol) was added dropwise. The mixture was kept for 30 min at 0° until the reaction was complete (TLC monitoring) and then poured into H_2O. The org. layer was washed with 1M HCl and H_2O, dried ($MgSO_4$), and evaporated. FC (AcOEt/hexane 1:5) provided **2** (9.78 g, 98%). Colorless oil. Crystallization from MeOH/H_2O gave a white solid. M.p. 63–64°. IR (KBr): 2945, 2867, 1745, 1720, 1466, 1395, 1272, 1216. ^{1}H-NMR (200 MHz): 7.87–7.69 (*m*, 4 arom. H); 7.27 (*s*, 5 arom. H); 5.18 (*s*, PhCH_2); 4.81–7.72 (*m*, CHO); 4.74 (*d*, *J* = 5.6, CHN); 1.48 (*d*, *J* = 5.6, Me); 1.22–0.89 (*m*, 21H, (i-Pr)$_3$Si). ^{13}C-NMR (50.3 MHz):

167.79 (*s*); 167.46 (*s*); 135.25 (*s*); 133.97 (*d*); 132.04 (*s*); 128.49 (*d*); 128.44 (*d*); 128.21 (*d*); 128.11 (*d*); 123.28 (*d*); 67.18 (*t*); 66.31 (*d*); 58.28 (*d*); 23.07 (*d*); 17.91 (*q*); 12.77 (*q*). FAB-MS: 496 (M^+), 452, 360, 318, 157, 115, 92. Anal. calc. for $C_{28}H_{39}NO_5Si$ (495.69): C 67.85, H 7.52, N 2.83; found: C 67.65, H 7.59, N 2.80.

2-{Phthaloylamino}-3-[(triisopropylsilyl)oxy]butanoic Acid (= *1,3-Dihydro-1,3-dioxo-α-{1-[(triisopropylsilyl)oxy]ethyl}-2H-isoindole-2-acetic Acid*; **3**). Benzyl ester **2** (1.75 g, 43.8 mmol) was dissolved in EtOH (100 ml) and hydrogenated (1 atm) overnight over 10% Pd/C (2 g). The soln. was filtered through *Celite*, the cake extracted with EtOH, and the solvent evaporated. The resulting oil was dried under high vacuum: **3** (17.4 g, 98%). White solid. M.p. 107–108°. IR (KBr): 2944, 2870, 2618, 1781, 1760, 1720, 1464, 1380. ^{1}H-NMR (360 MHz): 7.87–7.72 (*m*, 4 arom. H); 4.88 (*d*, J = 7.0, CHN); 4.61 (*quint.*, J = 6.4, CHO); 1.49 (*d*, J = 6.1, Me); 1.04–0.96 (*m*, 21 H, (i-Pr)$_3$Si). ^{13}C-NMR (50.3 MHz): 169.75 (*s*); 167.49 (*s*); 133.91 (*d*); 132.11 (*s*); 123.26 (*d*); 66.67 (*d*); 57.86 (*d*); 22.85 (*d*); 17.88 (*q*); 12.69 (*q*). CI-MS: 406 (100, M^+), 362 (55), 344 (6), 260 (5), 232 (18). Anal. calc. for $C_{21}H_{31}NO_5Si$ (405.57): C 62.19, H 7.70, N 3.45; found: C 62.26, H 7.58, N 3.38.

1-{{2-{Phthaloylamino}-3-[(triisopropylsilyl)oxy]butanooyl}oxy}pyridine-2(1H)-thione (= *1-{{2-[(1,3-Dihydro-1,3-dioxo-2H-isoindol-2-yl)amino]-3-[(triisopropylsilyl)oxy]butanoyl}oxy}pyridine-2(1H)-thione*; **4**). To a soln. of **3** (4.06 g, 10.0 mmol), DCC (2.68 g, 13.0 mmol), and DMAP (1.81 g, 12.0 mmol) in dry THF (140 ml), a soln. of 1-hydroxypyridin-2(1*H*)-thione (1.51 g, 12.0 mmol) in dry THF (10 ml) was added at 0° under N_2 in the dark. After stirring for 6 h at 0°, a yellow soln. of the *Barton* ester **4** was obtained and used directly for radical reactions.

2-[1-(Phenylseleno)-2-[(triisopropylsilyl)oxy]propyl]-1H-isoindole-1,3(2H)-dione (**5**). A soln. of diphenyl diselenide (3.43 g, 11.0 mmol) in dry THF (50 ml) was added to a crude soln. of *Barton* ester **4** (see above; 10 mmol). The mixture was irradiated with a 300-W sun lamp at 10° for 30 min. After completion of the reaction, the precipitate of dicyclohexylurea was filtered off, the filtrate diluted with Et_2O (500 ml), washed with 1M HCl and H_2O, dried ($MgSO_4$), and evaporated, and the crude product submitted to FC (AcOEt/hexane 1:5): **5** (3.24 g, 63%), separable 70:30 *anti*/*syn* mixture of diastereoisomers. Yellow solid. M.p. 76–77° (*anti*); 80–85° (*syn*). IR (KBr): 3071, 2943, 2442, 2392, 2249, 1774, 1719, 1390. ^{1}H-NMR (360 MHz): *anti*: 7.74–7.63 (*m*, 4 arom. H); 7.53–7.48 (*m*, 2 arom. H); 7.09–7.04 (*m*, 3 arom. H); 5.66 (*d*, J = 8.6, CHN); 4.95 (*dq*, J = 8.5, 6.1, CHO); 1.24 (*d*, J = 6.1, Me); 1.13 (*s*, 21 H, (i-Pr)$_3$Si); *syn*: 7.82–7.66 (*m*, 4 arom. H); 7.60–7.55 (*m*, 2 arom. H); 7.22–7.19 (*m*, 3 arom. H); 5.39 (*d*, J = 9.7, CHN); 4.86 (*dq*, J = 9.7, 6.0, CHO); 1.49 (*d*, J = 6.0, Me); 0.86 (*m*, 21 H, (i-Pr)$_3$Si). ^{13}C-NMR (50.3 MHz): *anti*: 167.02 (*s*); 136.14 (*d*); 133.96 (*d*); 131.53 (*s*); 128.69 (*d*); 128.70 (*s*); 127.96 (*d*); 123.09 (*s*); 69.87 (*d*); 58.08 (*d*); 21.51 (*d*); 18.20 (*q*); 12.84 (*q*); *syn*: 167.23 (*s*); 134.95 (*d*); 133.94 (*d*); 132.00 (*s*); 129.38 (*s*); 129.19 (*d*); 128.07 (*d*); 123.16 (*d*); 69.51 (*d*); 58.99 (*d*); 22.52 (*d*); 17.94 (*q*); 12.73 (*q*). CI-MS (*syn*/*anti*): 516 (3, M^+), 502 (5), 476 (25), 474 (100), 360 (95), 344 (13), 318 (15). Anal. calc. for $C_{26}H_{35}NO_3SeSi$ (516.62; *syn*/*anti*): C 60.45, H 6.83, N 2.71; found: C 60.47, H 6.84, N 2.73.

Phenyl 2-{Phthaloylamino}-3-[(triisopropylsilyl)oxy]butaneselenoate (= *Phenyl 1,3-dihydro-1,3-dioxo-α-{1-[(triisopropylsilyl)oxy]ethyl}-2H-isoindole-2-ethaneselenoate*; **6**). Oxalyl chloride (1.03 ml, 12.0 mmol) was added dropwise at 0° under N_2 to a soln. of **3** (811 mg, 2.00 mmol) and DMF (1 drop) in dry CH_2Cl_2 (6 ml). The soln. was stirred at 0° for 30 min and left at r.t. for another 30 min. After evaporation, the crude acyl chloride was dissolved in dry THF (4 ml). This soln. was added dropwise at 0° to a soln. of Na[PhSeB(OEt)$_3$] freshly prepared from $NaBH_4$ (83 mg, 2.20 mmol) and diphenyl diselenide (344 mg, 1.10 mmol) in EtOH (2 ml) [26]. The mixture was stirred for 30 min at 0° and the soln. filtered through *Celite* with Et_2O (30 ml). The filtrate was washed with H_2O and brine, dried ($MgSO_4$), and evaporated. FC (AcOEt/hexane 1:10, then 1:7) of the residue provided **6** (730 mg, 67%). White solid. M.p. 65–68°. IR (film): 2946, 2868, 1777, 1726, 1467, 1383, 1149. ^{1}H-NMR (360 MHz): 7.95–7.76 (*m*, 4 arom. H); 7.50–7.33 (*m*, 5 arom. H); 4.87–4.79 (*m*, CHO, CHN); 1.50 (*d*, J = 5.5, Me); 0.92–0.83 (*m*, 21 H, (i-Pr)$_3$Si). ^{13}C-NMR (50.3 MHz): 165.50 (*s*); 167.29 (*s*); 135.96 (*d*); 134.29 (*d*); 131.99 (*s*); 129.23 (*d*); 128.97 (*d*); 125.36 (*s*); 123.55 (*d*); 67.90 (*d*); 65.96 (*d*); 23.02 (*q*); 17.82 (*q*); 12.79 (*q*). CI-MS: 546 (21, $[M + 1]^+$), 545 (7, M^+), 502 (42), 390 (30), 344 (100), 201 (39), 157 (33). Anal. calc. for $C_{27}H_{35}NO_4SeSi$ (544.63): C 59.55, H 6.48, N 2.57; found: C 59.43, H 6.56, N 2.64.

2-[(E)-Prop-1-enyl]-1H-isoindole-1,3(2H)-dione (**7**) [14]. Allyl bromide (10.0 ml, 0.12 mol) was added dropwise at r.t. to a suspension of potassium phthalimide (20.0 g, 0.11 mol) and BuNI (1.58 g, 4.30 mmol) in DMF (55 ml). The mixture was stirred for 20 h, and then H_2O (250 ml) was added. The precipitate was isolated by filtration, dried, and recrystallized from AcOEt to give 2-(prop-2-enyl)-1*H*-isoindol-1,3(2*H*)-dione (12.8 g, 60%). White solid. M.p. 69–70° ([14]: 70°). ^{1}H-NMR (200 MHz): 7.90–7.69 (*m*, 4 arom. H); 6.00–5.78 (*m*, *H*C = CH$_2$); 5.31–5.12 (*m*, CH=C*H*$_2$); 4.29 (*dm*, J = 6.7, CH$_2$).

Under N_2, 2-(prop-2-enyl)-1*H*-isoindole-1,3(2*H*)-dione (5.00 g, 25.0 mmol) and [$RuCl_2(PPh_3)_3$] (240 mg, 0.25 mmol) were heated for 13 h at 150°. The product, a yellow solid, was dissolved in benzene, the soln. filtered through a short column of silica gel, the filtrate evaporated and the residue recrystallized from hexane: **7** (3.00 g,

60%). M.p. 149–150° ([14]: 150°). ^{1}H-NMR (200 MHz): 7.88–7.65 (*m*, 4 arom. H); 6.55 (*m*, 2 H, C*H*=C*H*); 1.85 (*d*, *J* = 7.6, Me).

Benzyl (Z)-2-(Phthaloylamino)but-2-enoate (= *Benzyl (Z)-α-Ethylidene-1,3-dihydro-1,3-dioxo 2H-isoindole-2-acetate*; **8**). A mixture of **1** (339 mg, 1.00 mmol) and DBU (0.18 ml, 1.20 mmol) in dry THF (3 ml) was heated under reflux for 2 h. After cooling, Et_2O (10 ml) was added, the org. layer washed with 1M HCl, H_2O, and brine, dried ($MgSO_4$), and evaporated, and the residue purified by FC (AcOEt/hexane 1:3) and recrystallized from MeOH: **8** (198 mg, 62%). White solid. M.p. 94–95°. IR (KBr): 3055, 2992, 2917, 1896, 1765, 1408, 1370, 1265, 1134. ^{1}H-NMR (360 MHz): 7.94–7.75 (*m*, 4 arom. H); 7.43 (*q*, *J* = 7.2, C=CH); 7.35–7.30 (*m*, 5 arom. H); 5.22 (*s*, CH_2O); 1.84 (*d*, *J* = 7.0, Me). ^{13}C-NMR (50.3 MHz): 167.00 (*s*); 162.00 (*s*); I143.37 (*d*); 135.57 (*s*); 134.34 (*d*); 128.55 (*d*); 128.27 (*d*); 128.05 (*d*); 127.95 (*d*); 123.86 (*d*); 123.64 (*s*); 67.34 (*t*); 14.45 (*q*). EI-MS: 321 (1, M^+), 215 (79), 187 (30), 186 (33), 169 (23), 132 (26), 104 (52), 91 (100), 65 (18). Anal. calc. for $C_{19}H_{15}NO_4$ (321.34): C 71.02, H 4.71, N 4.36; found: C 70.80, H 4.86, N 4.25.

(±)- and (1)-2-{1-[(Pyridin-2-ylthio)-2[(triisopropylsilyl)oxy]propyl}-1H-isoindole-1,3(2H)-dione (**9**). A crude soln. of **4** (see above; 1.0 mmol) was irradiated with a 300-W sun lamp at 10° for 30 min. The precipitated dicyclohexylurea was filtered off, the solvents were removed, and the residue was purified by FC (AcOEt/hexane 1:3): **9** (311 mg, 65%), 79:21 diastereoisomer mixture. M.p. 88–93°. IR (KBr): 3058, 2941, 2866, 1774, 1720, 1577, 1466, 1387, 883. ^{1}H-NMR (360 MHz, 79:21 mixture): 8.51–8.47 (*m*, 1 Py H, major); 8.42–8.38 (*m*, 1 Py H, minor); 7.90–7.65 (*m*, 4 arom. H); 7.49 (*m*, 1 Py H); 7.18 (*m*, 1 Py H); 6.99 (*ddd*, *J* = 7.3, 5.0, 1.1, 1 Py H, major); 6.95 (*ddd*, *J* = 7.3, 4.9, 0.9, 1 Py H, minor); 6.60 (*d*, *J* = 7.3, CHN, minor); 6.56 (*d*, *J* = 9.5, CHN, major); 4.73 (*dq*, *J* = 9.5, 6.1, CHO, major); 4.72–4.63 (*m*, Me, minor); 1.48 (*d*, *J* = 6.1, Me); 1.32 (*d*, *J* = 6.1, Me, minor); 1.10–1.00 (*m*, 21 H, (i-Pr)$_3$Si, minor); 0.92–0.82 (*m*, 21 H, (i-Pr)$_3$Si, major). ^{13}C-NMR (50.3 MHz, major): 167.43 (*s*); 149.60 (*s*); 136.27 (*d*); 133.90 (*d*); 132.00 (*s*); 123.39 (*d*); 123.20 (*d*); 120.15 (*d*); 69.50 (*d*); 58.82 (*d*); 21.59 (*d*); 18.00 (*q*); 12.85 (*q*). Comparison of ^{1}H- and ^{13}C-NMR of **9** with those of **5**: major = *syn*, minor = *anti*. CI-MS: 471 (100, M^+), 427 (74), 360 (20), 324 (8), 297 (18), 188 (9), 41 (39). Anal. calc. for $C_{25}H_{34}N_2O_3SSi$ (470.70): C 63.79, H 7.28, N 5.95; found: C 63.87, H 7.52, N 5.80.

(±)- and (1)-2-{2-[(Triisopropylsilyl)oxy](1-$^2H_1$)propyl}-1H-isoindole-1,3(2H)-dione (**10**). a) *From* **5**: A degassed soln. of **5** (258 mg, 0.50 mmol), Bu_3SnD (292 mg, 1.00 mmol) and AIBN (16 mg, 0.10 mmol) in dry benzene (4 ml) was irradiated at 10° with a 300-W sun lamp under N_2. After 1 h, the mixture was evaporated, the residue dissolved in CH_2Cl_2, a sat. aq. KF soln. added, and the mixture stirred for 1 h at r.t. Then the aq. phase was extracted with CH_2Cl_2 (3×), the combined org. phase washed with H_2O, dried ($MgSO_4$), and evaporated, and the residue submitted to FC (AcOEt/hexane 1:10): **10** (132 mg, 73%), 85:15 *syn*/*anti* mixture.

b) *From* **6**: As described above, with **6** (120 mg, 0.22 mmol), Bu_3SnD (97 mg, 0.33 mmol), AIBN (5 mg, 0.05 mmol), and benzene (2 ml): **10** (64 mg, 80%), 85:15 *syn*/*anti* mixture. White solid. M.p. 51–54°. IR (KBr): 2943, 2867, 2316, 2184, 1774, 1712, 1465, 1403 1116. ^{1}H-NMR (360 MHz): 7.86–7.69 (*m*, 4 arom. H); 4.32 (*quint.*, *J* = 6.1, CHO); 3.74 (*d*, *J* = 6.1, CHD, *syn*); 3.60 (*dm*, *J* = 7.0, CHD, *anti*); 1.20 (*d*, *J* = 6.1, Me); 1.05 (*s*, 21 H, (i-Pr)$_3$Si). ^{13}C-NMR (50.3 MHz): 168.36 (*s*); 133.86 (*d*); 132.26 (*s*); 123.16 (*d*); 66.10 (*t*); 45.27 (*t*); 21.89 (*d*); 18.00 (*q*); 12.51 (*q*). CI-MS: 363 (100, M^+), 347 (23), 320 (90), 319 (100), 189 (84). Anal. calc. for $C_{20}H_{30}DNO_3Si$ (362.56): C 66.26, H 8.89, N 3.86; found: C 66.05, H 8.95, N 3.85.

(±)- and (1)-Methyl 2-{2-(Phthaloylamino)-3-[(triisopropylsilyl)oxy]butyl}acrylate (= *Methyl 1,3-Dihydro-α-methylidene-1,3-dioxo-γ-{1-[(triisopropylsilyl)oxy]ethyl}-2H-isoindole-2-butanoate*; **11**). a) *From* **5**: A degassed soln. of **5** (258 mg, 0.50 mmol), methyl 2-[(tributylstannyl)methyl]prop-2-enoate (536 mg, 1.50 mmol), and AIBN (16 mg, 0.10 mmol) in dry benzene (4 ml) was irradiated at 10° with a 300-W sun lamp under N_2 for 9 h; AIBN (5 mg) was added every 3 h. After evaporation, the residue was dissolved in CH_2Cl_2, a sat. aq. KF soln. added, and the mixture stirred for 1 h at r.t. Then the aq. layer was extracted with CH_2Cl_2 (3×), the combined org. phase washed with H_2O, dried ($MgSO_4$), and evaporated and the residue submitted to FC (AcOEt/hexane 1:10): **11** (180 mg, 78%), 62:38 diastereoisomer mixture.

b) *From* **6**: A degassed soln. of **6** (272 mg, 0.50 mmol), methyl 2-[(tributylstannyl)methyl]prop-2-enoate (389 mg, 1.00 mmol), and AIBN (16 mg, 0.10 mmol) was heated under reflux for 2 h. Then the mixture was evaporated, the residue dissolved in CH_2Cl_2, a sat. aq. KF soln. added, and the mixture stirred for 1 h at r.t. Then the aq. layer was extracted with CH_2Cl_2 (3×), the combined org. phase washed with H_2O, dried ($MgSO_4$), and evaporated, and the residue submitted to FC (AcOEt/hexane 1:10): **11** (150 mg, 65%), 1:1 diastereoisomer mixture. Colorless oil. IR ($CHCl_3$): 2947, 2868, 1774, 1710, 1394. ^{1}H-NMR (360 MHz, 62:38 mixture from *Procedure a*): 7.80–7.64 (*m*, 4 arom. H); 6.04 (*s*, 1 H of C=CH_2); 5.48 (*s*, 1 H of C=CH_2, minor); 5.43 (*s*, 1 H of C=CH_2, major); 4.60 (*dq*, *J* = 8.9, 6.1, CHO, major); 4.53 (*dq*, *J* = 8.2, 6.1, CHO, minor); 4.42–4.34 (*m*, CHN, minor); 4.38–4.28 (*m*, CHN, major); 3.68 (*s*, MeO, minor); 3.65 (*s*, MeO, major); 3.21 (*ddd*, *J* = 13.7, 3.4, 1.2, 1 H of CH_2, major); 3.11–3.00 (*m*, 1 H of CH_2); 2.80 (*ddd*, *J* = 14.0, 4.0, 0.9, 1 H of CH_2, minor); 1.37 (*d*, *J* = 6.1,

Me, minor); 1.13 (*d*, *J* = 6.1, Me, major); 1.11 (*m*, 21 H, (i-Pr)$_3$Si, major); 0.91 (*m*, 21 H, (i-Pr)$_3$Si, minor). ^{13}C-NMR (50.3 MHz, 62:38 mixture from *Procedure a*): 168.61 (*s*); 166.20 (*s*); 137.31 (*s*); 133.92 (*d*, major); 133.70 (*d*, minor); 132.10 (*s*); 127.39 (*t*); 123.18 (*d*, major); 122.93 (*d*, minor); 68.77 (*d*); 57.67 (*d*, major); 57.37 (*d*, minor); 51.88 (*q*); 31.72 (*t*, major); 30.52 (*t*, minor); 21.60 (*t*); 18.00 (*q*); 12.79 (*q*). Comparison of ^{1}H- and ^{13}C-NMR of **11** with those of **20**: major = *anti*, minor = *syn*. CI-MS: 460 (62, M^+), 416 (76), 286 (100), 254 (8), 210 (14), 159 (21), 81 (10), 41 (84). Anal. calc. for $C_{25}H_{37}NO_5Si$ (459.66): C 65.33, H 8.11, N 3.05; found: C 64.98, H 8.17, N 2.81.

*2-{2-[(Triisopropylsilyl)oxy]propyl}-1*H*-isoindole-1,3(2*H*)-dione* (**12**). As described for **10**, with **6** (932 mg, 1.71 mmol), Bu_3SnH (0.64 ml, 2.40 mmol), AIBN (39 mg, 0.24 mmol), and benzene (8 ml). FC (AcOEt/hexane 1:10) gave **12** (386 mg, 62%). ^{1}H-NMR (200 MHz): 7.88–7.67 (*m*, 4 arom. H); 4.40–4.24 (*m*, CHO); 3.75 (*dd*, *J* = 13.4, 6.3, 1 H, CH_2N); 3.62 (*dd*, *J* = 13.4, 6.7, 1 H, CH_2N); 1.20 (*d*, *J* = 6.1, Me); 1.05 (*s*, 21 H, (i-Pr)$_3$Si).

Benzyl 3,4,4-Trimethyl-2-(phthaloylamino)pentanoate (*= Benzyl 1,3-Dihydro-1,3-dioxo-α-(1,2,2-trimethylpropyl)-2*H*-isoindole-2-acetate*; **13**). A soln. of Bu_3SnH (0.32 ml, 1.20 mmol) and AIBN (16 mg, 0.1 mmol) in dry benzene (10 ml) was added to a sun lamp irradiated soln. of **8** (1.29 g, 4.00 mmol) and *t*-BuI (0.12 ml, 1.00 mmol) in dry benzene (5 ml) at 10° over 24 h (syringe pump). The solvent was evaporated, the residue dissolved in CH_2Cl_2, a sat. aq. KF soln. added, and the mixture stirred overnight at r.t. The soln. was filtered through *Celite*, the filtrate washed with H_2O and brine, the org. layer dried ($MgSO_4$) and evaporated, and the residue purified by FC (AcOEt/hexane 1:3): **13** (156 mg, 41%), 70:30 *anti*/*syn* mixture. Colorless oil. IR ($CHCl_3$): 2961, 2874, 1777, 1726, 1468, 1383, 1055. ^{1}H-NMR (360 MHz): *anti*: 7.88–7.75 (*m*, 4 arom. H); 5.19 ('*d*', *A* of *AB*, J_{AB} = 12.2, 1 H, PhCH_2); 5.16 ('*d*', *B* of *AB*, J_{AB} = 12.5, 1 H, PhCH_2); 5.10 (*d*, *J* = 4.6, CHN); 2.69 (*dq*, *J* = 7.3, 4.7, C*H*(*t*-Bu)); 0.98 (*s*, *t*-Bu); 0.97 (*d*, *J* = 7.3, Me); *syn*: 7.88–7.75 (*m*, 4 arom. H); 5.18 (*s*, PhCH_2); 5.07 (*d*, *J* = 3.6, CHN); 2.31 (*dq*, *J* = 7.3, 3.7, C*H*(*t*-Bu)); 1.19 (*d*, *J* = 7.3, Me); 0.98 (*s*, *t*-Bu). ^{13}C-NMR (50.3 MHz): *anti*: 169.53 (*s*); 168.07 (*s*); 135.46 (*s*); 134.11 (*d*); 131.89 (*d*); 128.40 (*d*); 128.28 (*d*); 128.12 (*d*); 123.44 (*d*); 67.43 (*t*); 53.31 (*d*); 42.24 (*d*); 33.44 (*s*); 27.54 (*q*); 11.82 (*q*); *syn*: 169.53 (*s*); 167.50 (*s*); 135.46 (*s*); 134.11 (*d*); 131.99 (*d*); 128.40 (*d*); 128.25 (*d*); 128.12 (*d*); 123.44 (*d*); 67.24 (*t*); 54.47 (*d*); 45.12 (*d*); 34.20 (*s*); 27.36 (*q*); 12.94 (*q*). CI-MS: 380 (23, $[M + 1]^+$), 364 (6), 272 (9), 244 (29), 188 (18), 119 (99), 41 (100). Anal. calc. for $C_{23}H_{25}NO_4$ (379.46): C 72.80, H 6.64, N 3.69; found: C 72.78, H 6.61, N 3.69.

3-Methyl-2-(phthaloylamino)butanoic Acid (*= 1,3-Dihydro-α-isopropyl-1,3-dioxo-2*H*-isoindole-2-acetic Acid*; **14**) [27]. A soln. of DL-valine (10.8 g, 0.82 mol) and phthalic anhydride (16.3 g, 0.11 mol) in dioxane (60 ml) was heated under reflux for 14 h. After evaporation, the residue was recrystallized in AcOEt/hexane: **14** (15.0 g, 74%). M.p. 101–102° ([27]: 101.5–102°). ^{1}H-NMR (200 MHz): 7.78–7.63 (*m*, 4 arom. H); 4.43 (*d*, *J* = 9.0, CHN); 2.68–2.59 (*m*, Me_2CH); 1.07 (*d*, *J* = 6.0, Me); 0.81 (*d*, *J* = 6.2, Me).

*1-(1,3-Dihydro-1,3-dioxo-2*H*-isoindole-2-yl)-2-methylpropyl Acetate* (**15**). A soln. of $Pb(OAc)_4$ (5.69 g, 12.6 mmol), in dry toluene (20 ml) was added to a suspension of **14** (2.52 g, 10.2 mmol) in dry toluene (30 ml) at r.t. under N_2. The mixture was heated under reflux for 3 h, the soln. filtered through *Celite* with Et_2O, the filtrate washed with 10% aq. $NaHCO_3$ soln., H_2O, and brine, dried ($MgSO_4$), and evaporated and the residue purified by FC (AcOEt/hexane 1:3): **15** (1.97 g, 74%). White solid. M.p. 88.5–89.5°. IR (KBr): 3064, 2979, 2938, 2882, 1777, 1722, 1431, 1365, 1236, 1027. ^{1}H-NMR (360 MHz): 7.88–7.73 (*m*, 4 arom. H); 6.22 (*d*, *J* = 10.1, CHN); 2.90 (*dsept.*, *J* = 10.4, 6.7, Me_2CH); 2.03 (*s*, MeCO); 1.08 (*d*, *J* = 6.7, Me); 0.89 (*d*, *J* = 6.7, Me). ^{13}C-NMR (50.3 MHz): 169.56 (*s*); 166.76 (*s*); 134.26 (*d*); 131.53 (*s*); 123.62 (*d*); 79.30 (*d*); 29.51 (*q*); 20.56 (*d*); 18.77 (*q*); 17.72 (*q*). CI-MS: 202 (100, $[M - OAc]^+$), 176 (14), 41 (37). Anal. calc. for $C_{14}H_{15}NO_4$ (261.28): C 64.36, H 5.79, N 5.36; found: C 64.37, H 5.82, N 5.10.

*2-(1-Isopropylbut-3-enyl)-1*H*-isoindole-1,3(2*H*)-dione* (**16**). a) *Reaction with $BF_3 \cdot OEt_2$*: A soln. of $BF_3 \cdot OEt_2$ (0.13 ml, 1.00 mmol) in dry CH_2Cl_2 (1 ml) was added at −78° to a soln. of **15** (131 mg, 0.50 mmol) and allyltrimethylsilane (0.08 ml, 1.00 mmol) in dry CH_2Cl_2 (2 ml). The mixture was allowed to warm to r.t. overnight, then diluted with more CH_2Cl_2, extracted with 10% Na_2CO_3 soln. and H_2O, and dried ($MgSO_4$). After evaporation, the residue was purified by FC (AcOEt/hexane 1:5): **16** (55 mg, 45%).

b) *Reaction with $TiCl_4$*: A soln. of $TiCl_4$ (0.06 ml, 0.55 mmol) in dry CH_2Cl_2 (0.28 ml) was added dropwise at −78° to a soln. of **15** (131 mg, 0.50 mmol) and allyltrimethylsilane (0.06 ml, 0.75 mmol) in dry CH_2Cl_2 (2 ml). The mixture was allowed to warm to r.t. overnight, and $Na_2CO_3 \cdot 10\ H_2O$ (200 mg, 0.70 mmol) was added. The heterogeneous mixture was stirred for 30 min at r.t. and the org. layer washed with H_2O, dried, ($MgSO_4$), and evaporated. FC (AcOEt/hexane 1:5) provided **16** (40 mg, 33%). Colorless oil. IR ($CHCl_3$): 2969, 2928, 1771, 1707, 1391. ^{1}H-NMR (360 MHz): 7.83–7.67 (*m*, 4 arom. H); 5.71–5.59 (*m*, C*H*=CH_2); 4.98 (*dm*, *J* = 17.3, 1 H, CH=CH_2); 4.87 (*dm*, *J* = 10.1, 1 H, CH=CH_2); 3.92 (*ddd*, *J* = 11.6, 10.1, 4.0, CHN); 2.80 (*ddd*, *J* = 14.0, 11.6, 9.1, 1 H, CH_2); 2.61–2.54 (*m*, 1 H, CH_2); 2.42 (*dsept.*, *J* = 10.1, 6.7, Me_2CH); 1.06 (*d*, *J* = 6.7, Me); 0.85 (*d*, *J* = 6.7, Me). ^{13}C-NMR (50.3 MHz): 168.67 (*s*); 135.01 (*d*); 133.69 (*d*); 131.73 (*s*); 123.00 (*d*); 117.38 (*t*); 58.11

(*d*); 34.22 (*t*); 30.33 (*d*); 20.29 (*q*); 20.14 (*q*). EI-MS: 243 (2, M^+), 202 (100), 182 (15), 160 (43), 148 (35), 130 (39), 104 (13), 76 (21), 43 (14). Anal. calc. for $C_{15}H_{17}NO_2$ (243.31): C 74.05, H 7.04, N 5.76; found: C 73.87, H 7.11, N 5.54.

*2-Isobutyl-1*H*-isoindole-1,3(2*H*)-dione* (**17**). A soln. of $BF_3 \cdot OEt_2$ (0.20 ml, 1.50 mmol) in dry CH_2Cl_2 (1 ml) was added to a soln. of **15** (131 mg, 0.50 mmol) and triethylsilane (0.24 ml, 0.50 mmol) in dry CH_2Cl_2 (3 ml) at 0°. The mixture was stirred for 6 h at r.t., diluted with CH_2Cl_2, and washed with 10% Na_2CO_3 soln. and H_2O. After drying ($MgSO_4$) and evaporation, the residue was purified by FC (AcOEt/hexane 1:4): **17** (85 mg, 85%). White solid. M.p. 93° ([28]: 90–92°). ^{1}H-NMR (200 MHz): 7.87–7.69 (*m*, 4 arom. H); 3.51 (*d*, *J* = 7.4, CH_2); 2.21–2.02 (*m*, Me_2CH); 0.94 (*d*, *J* = 6.7, 2 Me).

*(*u*)- and (*l*)-1-(1,3-Dihydro-1,3-dioxo-2*H*-isoindol-2-yl)-2-[(triisopropylsilyl)oxy]propyl Acetate* (**18**). A soln. of acid **3** (8.11 g, 20.0 mmol) in dry THF (100 ml) was added to a suspension of $Pb(OAc)_4$ (9.75 g, 22.0 mmol) in dry THF (100 ml) at r.t. under N_2. The soln. was stirred for 2 h at r.t. and filtered through *Celite* with Et_2O. Et_2O was added to the filtrate and the soln. washed with 10% $NaHCO_3$ soln., H_2O, and brine. After drying ($MgSO_4$) and evaporation. FC (AcOEt/hexane 1:3) afforded **18** (6.85 g, 82%; diastereoisomer mixture). M.p. 85–90°. IR ($CHCl_3$): 2946, 2869, 1847, 1720, 1492. ^{1}H-NMR (360 MHz): major: 7.87–7.13 (*m*, 4 arom. H); 6.30 (*d*, *J* = 8.9, CHN); 4.90 (*dq*, *J* = 8.9, 6.1, MeC*H*); 2.09 (*s*, MeCO); 1.35 (*d*, *J* = 6.1, Me); 0.92–0.85 (*m*, 21 H, (i-Pr)$_3$Si); minor: 7.87–7.13 (*m*, 4 arom. H); 6.36 (*d*, *J* = 8.9, CHN); 4.98 (*dq*, *J* = 8.9, 6.4, MeC*H*); 2.06 (*s*, MeCO); 1.14 (*d*, *J* = 6.4, Me); 0.92–0.85 (*m*, 21 H, (i-Pr)$_3$Si). ^{13}C-NMR (50.3 MHz, major): 169.16 (*s*); 166.90 (*s*); 134.18 (*d*); 131.88 (*s*); 123.48 (*d*); 77.69 (*d*); 66.59 (*d*); 20.84, 20.66 (*d* and *q*, resp.); 17.89 (*q*); 12.69 (*q*). CI-MS: 376 (8, $[M - OAc]^+$), 361 (27), 360 (27), 318 (7), 41 (46). Anal. calc. for $C_{22}H_{33}NO_5Si$ (419.60): C 62.98, H 7.93, N 3.34; found: C 63.06, H 8.05, N 3.18.

*(*u*)-2-{1-{1-[(Triisopropylsilyl)oxy]ethyl}but-3-enyl}-1*H*-isoindole-1,3(2*H*)-dione* (**19**). a) *Reaction with $BF_3 \cdot OEt_2$*: Freshly distilled $BF_3 \cdot OEt_2$ (0.32 ml, 2.50 mmol) was added dropwise at r.t. to a mixture of **18** (210 mg, 0.50 mmol), allyltrimethylsilane (0.24 ml, 1.50 mmol), and activated molecular sieves 4 Å (200 mg) in dry $CHCl_3$ (2 ml). The soln. was then heated under reflux for 24 h. CH_2Cl_2 was added, the soln. washed with 10% Na_2CO_3 soln. and H_2O, dried ($MgSO_4$), and evaporated, and the crude product filtered through a short column of silica gel (AcOEt/hexane 1:5). ^{1}H-NMR and HPLC: 85:15 *anti*/*syn* ratio. The product was purified by FC (AcOEt/hexane 1:5): **19** (110 mg, 67% based on 80% conversion).

b) *Reaction with Me_3SiOTf*: Me_3SiOTf (0.20 ml, 1.05 mmol) was added dropwise at 0° to a soln. of **18** (210 mg, 0.50 mmol) and allyltrimethylsilane (0.24 ml, 1.50 mmol) in dry CH_2Cl_2 (2 ml). The soln. was heated to reflux for 24 h and then treated according to *Procedure a*. FC (AcOEt/hexane 1:5) gave **19** (82 mg, 50% based on 76% conversion; *anti*/*syn* 89:11).

c) *Reaction with $EtAlCl_2$*: At −78°, 1M $EtAlCl_2$ in hexane (1.0 mmol, 1.0 ml) was added to a soln. of **18** (210 mg, 0.50 mmol) and allyltrimethylsilane (0.24 ml, 1.50 mmol) in CH_2Cl_2 (2 ml). The mixture was allowed to warm slowly to r.t. overnight. CH_2Cl_2 was added and the soln. treated according to *Procedure a*. FC (AcOEt/hexane 1:5) gave **19** (149 mg, 74%; *anti*/*syn* 89:11). Only the major *anti* isomer was characterized. M.p. 47–50°. IR (KBr): 3065, 2941, 2868, 1771, 1711, 1468, 1385, 1132. ^{1}H-NMR (360 MHz): 7.82–7.69 (*m*, 4 arom. H); 5.73–5.62 (*m*, C*H*=CH$_2$); 4.96 (*dd*, *J* = 17.1, 1.5, 1 H, CH=C*H*); 4.87 (*dm*, *J* = 10.3, 1 H, CH=CH$_2$); 4.58 (*dq*, *J* = 9.2, 6.1, CHO); 4.13 (*dm*, *J* = 9.4, CHN); 2.87–2.82 (*m*, CH_2); 1.13 (*d*, *J* = 6.1, Me); 1.12–1.05 (*m*, 21 H, (i-Pr)$_3$Si). ^{13}C-NMR (50.3 MHz): 168.53 (*s*); 135.19 (*d*); 133.84 (*d*); 131.84 (*s*); 123.14 (*d*); 117.50 (*t*); 68.71 (*d*); 58.39 (*d*); 33.32 (*t*); 21.45 (*d*); 18.21 (*q*); 12.86 (*q*). CI-MS: 402 (100, $[M + 1]^+$), 359 (20), 358 (74), 228 (42), 41 (13). Anal. calc. for $C_{23}H_{35}NO_3Si$ (401.63): C 68.78, H 8.78, N 3.49; found: C 68.79, H 8.74, N 3.50.

*(*u*)- and (*l*)-2-{1-{1-[(Triisopropylsilyl)oxy]ethyl}-3-(trimethylsilyl)but-3-enyl}-1*H*-isoindole-1,3(2*H*)-dione* (**20**). As described for **19** (*Procedure c*), with **18** (839 mg, 2.00 mmol), trimethyl{1-[(tributylstannyl)-methyl]ethenyl}silane (2.42 g, 6.00 mmol), and CH_2Cl_2 (5 ml). The reaction was stopped after 12 h. FC (AcOEt/hexane 1:10, then 1:7) gave **20** (575 mg, 61%; 71:29 *anti*/*syn* mixture of separable diastereoisomers). Colorless oil. IR ($CHCl_3$): 2963, 2867, 2593, 1773, 1723, 1463, 1383, 1132. ^{1}H-NMR (360 MHz): *anti*: 7.81–7.68 (*m*, 4 arom. H); 5.38–5.37 (*m*, 1 H, C=CH$_2$); 5.19 (*d*, *J* = 2.9, 1 H, C=CH$_2$); 4.86 (*dq*, *J* = 8.8, 6.0, CHO); 4.14 (*ddd*, *J* = 10.0, 8.8. 5.1, CHN); 2.98–2.95 (*m*, CH_2); 1.14–1.12 (*m*, 24 H, Me, (i-Pr)$_3$Si); 0.08 (*s*, Me_3Si); *syn*: 7.79–7.66 (*m*, 4 arom. H); 5.49 (*s*, 1 H, C=CH$_2$); 5.25 (*d*, *J* = 2.8, 1 H, C=CH$_2$); 4.47 (*dq*, *J* = 7.9, 6.1, CHO); 4.28 (*ddd*, *J* = 12.2, 7.9, 3.4, CHN); 3.09 (*dd*, *J* = 14.6, 12.2, 1 H, CH_2); 2.50 (*dm*, *J* = 14.7, 1 H, CH_2); 1.34 (*d*, *J* = 6.1, Me); 0.93 (*m*, 21 H, (i-Pr)$_3$Si); 0.08 (*s*, Me_3Si). ^{13}C-NMR (50.3 MHz): *anti*: 168.62 (*s*); 149.42 (*s*); 133.80 (*d*); 131.98 (*s*); 126.63 (*t*); 123.10 (*d*); 69.01 (*d*); 58.06 (*d*); 34.21 (*t*); 21.59 (*d*); 18.30 (*q*); 18.20 (*q*); 12.96 (*q*); −1.39 (*q*); *syn*: 168.74 (*s*); 148.47 (*s*); 133.60 (*d*); 132.09 (*s*); 126.48 (*t*); 122.83 (*d*); 69.06 (*d*); 57.61 (*d*); 32.29 (*t*); 21.65 (*d*); 18.02 (*q*); 17.99 (*q*); 12.77 (*q*); −1.39 (*q*). CI-MS: 474 (10, M^+), 459 (13), 431 (24), 300 (18), 41 (100). Anal. calc. for $C_{26}H_{43}NO_3Si_2$ (473.81): C 65.91, H 9.15, N 2.96; found: C 65.85, H 9.13, N 2.83.

3,9b-Dihydro-2-methyl(3-$^2H_1$)oxazolo[2,3-a]isoindol-5(2H)-one (**21a**/**21b**). A soln. of **10** (231 mg, 0.64 mmol; *syn*/*anti* 85:15) in MeOH (2 ml) was cooled to 0°. $NaBH_4$ (169 mg, 4.46 mmol) was added portionwise over 1 h. The mixture was stirred for 2 h at 0° and then treated with sat. NH_4Cl soln. and extracted with Et_2O (3 ×). The combined org. phase was washed with H_2O and brine, dried ($MgSO_4$), and evaporated. FC (AcOEt/hexane 1:2) gave the hemiaminal (169 mg). A 40% aq. HF soln. (0.05 ml) was added at 0° to a soln. of the hemiaminal (169 mg) in THF (3 ml). The soln. was left at r.t. for 1 h, and then Et_2O (20 ml) was added. The org. layer was washed with 10% $NaHCO_3$ soln., H_2O, and brine, dried ($MgSO_4$), and evaporated. To the residue in dry THF (3 ml), molecular sieves 4 Å (200 mg) and TsOH (10 mg) were added. The soln. was heated under reflux for 12 h, then cooled, and filtered. Et_2O (20 ml) was added to the filtrate, the soln. washed with 10% $NaHCO_3$ soln., H_2O, and brine, dried ($MgSO_4$), and evaporated, and the residue purified by FC (AcOEt/hexane 1:2): **21a** (28 mg, 23%) and **21b** (14 mg, 11%). The poor yield is caused by the volatility of **21**. ^{1}H-NMR (360 MHz): **21a**: 7.81–7.77 (*m*, 1 arom. H); 7.62–7.52 (*m*, 3 arom. H); 5.86 (*s*, OCHN); 4.70–4.61 (*m*, J = 6.2, MeC*H*); 3.56 (*d*, J = 6.6, CHD, minor); 3.39 (*d*, J = 10.5, CHD, major); 1.36 (*d*, J = 6.2, Me); **21b**: 7.81–7.77 (*m*, 1 arom. H); 7.62–7.52 (*m*, 3 arom. H); 6.03 (*s*, OCHN); 4.40–4.32 (*m*, MeC*H*); 4.25 (*d*, J = 6.2, CHD, minor); 3.00 (*d*, J = 11.2, CHD, major); 1.39 (*d*, J = 6.2, Me). ^{13}C-NMR (50.3 MHz): **21a**: 173.61 (*s*); 142.31 (*s*); 133.54 (*s*); 132.70 (*d*); 130.51 (*d*); 124.36 (*d*); 123.96 (*d*); 91.28 (*d*); 79.61 (*d*); 49.06 (*t*); 19.66 (*q*); **21b**: 173.53 (*s*); 143.72 (*s*); 133.02 (*d*); 132.91 (*s*); 130.33 (*d*); 124.32 (*d*); 123.92 (*d*); 90.18 (*d*); 77.55 (*d*); 49.77 (*t*); 19.61 (*q*). HR-EI-MS: 190.0850 ($C_{11}H_{10}DNO_2^+$; calc. 190.0851).

3,9b-Dihydro-2-methyloxazolo[2,3-a]isoindol-5(2H)-one (**22a**/**22b**). As described for **21**, with **12** (231 mg, 0.64 mmol): **22a** (27 mg, 20%) and **22b** (10 mg, 10%). ^{1}H-NMR (360 MHz): **22a**: 7.81–7.77 (*m*, 1 arom. H); 7.62–7.52 (*m*, 3 arom. H); 5.86 (*s*, OCHN); 4.70–4.61 (*m*, J = 6.2, MeC*H*); 3.56 (*dd*, J = 10.5, 6.6, 1 H, CH_2); 3.39 (*dd*, J = 10.5, 7.9, 1 H, CH_2); 1.36 (*d*, J = 6.2, Me); **22b**: 7.81–7.77 (*m*, 1 arom. H); 7.62–7.52 (*m*, 3 arom. H); 6.03 (*s*, OCHN); 4.40–4.32 (*m*, MeC*H*); 4.25 (*dd*, J = 11.5, 6.2, 1 H, CH_2); 3.00 (*dd*, J = 11.2, 7.2, 1 H, CH_2); 1.39 (*d*, J = 6.2, Me).

(u)-2-[1-(1-Hydroxyethyl)but-3-enyl]-1H-isoindole-1,3(2H)-dione (**23**). At 0°, 1M Bu_4NF in THF (8.0 ml) was added to a soln. of **19** (1.32 g, 3.29 mmol) in THF (5 ml). The mixture was left at r.t. for 24 h, diluted with Et_2O (30 ml), and washed with H_2O and brine. After drying ($MgSO_4$) and evaporation. FC (AcOEt/hexane 1:2) provided **23** (439 mg, 54%). Colorless oil. IR (film): 3465, 3079, 2977, 2931, 2361, 2251, 1771, 1720, 1390, 1118. ^{1}H-NMR (360 MHz): 7.83–7.71 (*m*, 4 arom. H); 5.70 (*dddd*, J = 17.1, 10.1, 9.1, 5.4, C*H*=CH_2); 4.98 (*dm*, J = 17.1, 1 H, CH=CH_2); 4.90 (*d*, J = 10.3, 1 H, CH=CH_2); 4.31–4.20 (*m*, CHO, CHN); 3.42 (*d*, J = 2.6, OH); 2.86–2.76 (*m*, 1 H, CH_2); 2.69–2.62 (*m*, 1 H, CH_2); 1.27 (*d*, J = 6.3, Me). ^{13}C-NMR (50.3 MHz): 168.88 (*s*); 134.55 (*d*); 134.00 (*d*); 131.50 (*s*); 123.23 (*d*); 117.70 (*t*); 68.75 (*d*); 57.47 (*d*); 31.45 (*t*); 20.69 (*q*). CI-MS: 246 (54, $[M + 1]^+$), 204 (14), 160 (15), 148 (14), 81 (17), 41 (18). Anal. calc. for $C_{14}H_{15}NO_3$ (245.28): C 68.56, H 6.16, N 5.71; found: C 68.63, H 6.21, N 5.67.

2-{(2RS,3SR)-Tetrahydro-2-methyl-5-[(phenylseleno)methyl]furan-3-yl}-1H-isoindole-1,3(2H)-dione (**24**). A soln. of PhSeCl (187 mg, 0.98 mmol) in CH_2Cl_2 (1 ml) was added at 0° to a soln. of **23** (200 mg, 0.82 mmol) in dry CH_2Cl_2 (4 ml). The mixture was stirred for 30 min at 0° and then evaporated. The residue was purified by FC: **24** (251 mg, 79%), 1:1 diastereoisomer mixture. Colorless oil. IR (film): 3058, 2972, 2930, 2361, 1774, 1711, 1383, 1108. ^{1}H-NMR (500 MHz; 1:1 mixture): 7.88–7.71 (*m*, 4 arom. H); 7.56–7.53 (*m*, 2 arom. H); 7.28–7.21 (*m*, 3 arom. H); 4.66–4.60 (*m*, $SeCH_2CH$, isomer 2); 4.54 (*dq*, J = 9.0, 6.0, MeC*H*, isomer 1); 4.27 (*dq*, J = 8.2, 6.0, MeC*H*, isomer 2); 4.42–4.37 (*m*, CHN); 4.39–4.32 (*m*, $SeCH_2CH$, isomer 1); 3.37 (*dd*, J = 12.2, 5.7, 1 H, $SeCH_2$, isomer 1); 3.19 (*dd*, J = 12.2, 8.1, 1 H, $SeCH_2$, isomer 1); 3.21–3.16 (*m*, 1 H, $SeCH_2$, isomer 2); 3.11 (*dd*, J = 12.4, 6.6, 1 H, $SeCH_2$, isomer 2); 2.72–2.53 (*m*, 1 H, CH_2CHN); 2.39 (*ddd*, J = 12.4, 8.8, 6.8, 1 H of CH_2CHN, isomer 1); 2.04 (*ddd*, J = 12.9, 11.0, 7.7, 1 H of CH_2CHN, isomer 2); 1.26 (*d*, J = 6.0, Me, isomer 2); 1.21 (*d*, J = 6.0, Me, isomer 1). ^{13}C-NMR (50.3 MHz, 1:1 mixture): 167.80 (*s*); 133.96 (*d*); 132.71, 132.63 (2*d*); 131.71 (*s*); 130.34, 129.76 (2*s*); 128.82 (*d*); 126.81 (*d*); 123.14 (*d*); 76.76 (*d*); 23.27 (*d*); 56.64, 55.69 (2*d*); 34.94, 34.18 (2*t*); 33.05, 32.78 (2*t*); 18.50 (*q*). CI-MS: 402 (100, $[M + 1]^+$), 384 (9), 244 (38), 226 (32). HR-EI-MS: 401.5320 ($C_{20}H_{19}NO_3Se^+$; calc. 401.0530).

2-(Benzyloxy)propanal (**25**) [29]. A 55% dispersion of NaH in oil (4.36 g, 0.10 mol) was added at 0° to a soln. of ethyl (*S*)-lactate (1.80 g, 0.10 mol) in dry DMF (30 ml). After 15 min stirring at 0°, benzyl bromide (17.8 ml, 0.15 mol) and Bu_4NI (3.69 g, 10.0 mmol) were added. The mixture was stirred overnight at r.t., treated with H_2O (200 ml), and extracted with Et_2O (3 × 150 ml). The org. phases were washed with H_2O and brine, dried ($MgSO_4$), and evaporated. FC (AcOEt/hexane 1:10) gave racemic ethyl 2-(benzyloxy)propanoate (12.8 g, 61%). Colorless liquid. ^{1}H-NMR (360 MHz): 7.39–7.26 (*m*, 5 arom. H); 4.70 (*A* of *AB*, J_{AB} = 11.7, 1 H, PhCH_2); 4.45 (*B* of *AB*, J_{AB} = 11.7, 1 H, PhCH_2); 4.22 (*dq*, J = 7.1, 2.3, CHO); 4.05 (*q*, J = 6.8, MeCH_2); 1.44 (*d*, J = 6.8, Me); 1.30 (*t*, J = 6.8, *Me*CH_2). ^{13}C-NMR (50.3 MHz): 173.14 (*s*); 137.65 (*s*); 128.33 (*d*); 127.88 (*d*); 127.75 (*d*); 74.07 (*d*); 71.92 (*t*); 60.70 (*t*); 18.59 (*q*); 14.15 (*q*).

To a soln. of ethyl 2-(benzyloxy)propanoate (10.4 g, 50.0 mmol) in dry Et_2O (200 ml) at $-78°$ under N_2, 1M DIBAL-H in toluene (50 ml) was added, and the soln. was stirred for 10 min at $-78°$. The mixture was treated with MeOH/H_2O 1:3 (8 ml) and warmed to r.t. The gel-like precipitate was filtered through *Celite* with Et_2O. After drying ($MgSO_4$) and evaporation, FC (AcOEt/hexane 1:5) gave **25** (6.24 g, 76%). ^{1}H-NMR (360 MHz): 9.67 (*d*, J = 1.9, CHO); 7.38–7.30 (*m*, 5 arom. H); 4.66 (*A* of *AB*, J_{AB} = 11.7, 1 H, PhCH_2); 4.60 (*B* of *AB*, J_{AB} = 11.7, 1 H, PhCH_2); 3.90 (*qd*, J = 6.8, 1.9, MeC*H*); 1.34 (*d*, J = 6.8, Me). ^{13}C-NMR (50.3 MHz): 203.26 (*d*); 134.42 (*s*); 128.60 (*d*); 128.07 (*d*); 127.92 (*d*); 79.47 (*d*); 72.03 (*t*); 15.28 (*q*).

(1)-2-(Benzyloxy)hex-5-en-3-ol (**26**) [16]. A soln. of $SnCl_4$ (1.20 ml, 10.0 mmol) in dry CH_2Cl_2 (40 ml) was cooled to $-78°$, and a soln. of **25** (1.64 g, 10.0 mmol) in dry CH_2Cl_2 (5 ml) was added over 5 min. The mixture was stirred at $-78°$ for 3 min, and allyltrimethylsilane (1.80 ml, 11.0 mmol) was added. After 15 min at $-78°$, the mixture was treated with H_2O (20 ml), the aq. phase extracted with Et_2O (3 × 20 ml), and the combined org. phase dried ($MgSO_4$) and evaporated. FC (AcOEt/hexane 1:4, then 1:3) gave **26** (1.74 g, 85%). Colorless liquid. ^{1}H-NMR (360 MHz): 7.38–7.27 (*m*, 5 arom. H); 5.94–5.82 (*m*, C*H*=CH$_2$); 5.13–5.07 (*m*, CH=CH_2); 4.68 ('*d*', *A* of *AB*, J_{AB} = 11.7, 1 H, PhCH_2); 4.45 ('*d*', *B* of *AB*, J_{AB} = 11.7, 1 H, PhCH_2); 3.57–3.51 (*m*, C*H*OH); 3.45 (*quint.*, J = 6.2, BnOC*H*); 2.55 (*s*, OH); 2.40–2.32 (*m*, 1 H, CH_2CH=CH$_2$); 2.26–2.17 (*m*, 1 H, CH_2CH=CH$_2$); 1.21 (*d*, J = 6.2, Me). ^{13}C-NMR (50.3 MHz): 138.38 (*s*); 134.81 (*d*); 128.37 (*d*); 127.72 (*d*); 127.64 (*d*); 117.02 (*t*); 77.45 (*d*); 74.20 (*d*); 70.98 (*t*); 37.51 (*t*); 15.40 (*q*).

*(u)-2-{1-[1-(Benzyloxy)ethyl]but-3-enyl}-1*H*-isoindole-1,3(2*H*)-dione* (**27**). a) *Starting from* **23**: NaH (55% dispersion in oil; 10 mg, 0.22 mmol) was added at 0° to a soln. of **23** (52 mg, 0.21 mmol) in dry THF (1 ml). After 30 min at 0°, Bu_4NI (11 mg, 0.03 mmol) and benzyl bromide (0.04 ml, 0.30 mmol) were added, and the soln. was stirred for 20 h at r.t. The mixture was treated with H_2O (5 ml) and extracted with Et_2O. After drying ($MgSO_4$) and evaporation, FC (AcOEt/hexane 1:4) gave **27** (50 mg, 71%).

b) *Starting from* **26**: A soln. of DEAD (diethyl azodicarboxylate; 0.09 ml, 0.55 mmol) in dry THF (1 ml) was added to a soln. of **26** (103 mg, 0.50 mmol), PPh_3 (144 mg, 0.55 mmol), and phthalimide (81 mg, 0.55 mmol) in dry THF (2 ml). The soln. was left 1 h at r.t., treated with brine, and extracted with Et_2O. After drying ($MgSO_4$) and evaporation, FC of the residue gave **27** (78 mg, 47%). Colorless liquid. IR (film): 2981, 2932, 1777, 1713, 1234. ^{1}H-NMR (360 MHz): 7.83–7.69 (*m*, 4 arom. H); 7.39–7.27 (*m*, 5 arom. H); 5.68 (*ddm*, J = 17.1, 10.3, C*H*=CH$_2$); 4.97 (*dm*, J = 17.1, 1 H, CH=CH_2); 4.89 (*dm*, J = 10.3, 1 H, CH=CH_2); 4.67 (*A* of *AB*, J_{AB} = 11.4, 1 H, PhCH_2); 4.55 (*B* of *AB*, J_{AB} = 11.4, 1 H, PhCH_2); 4.34–4.27 (*m*, CHN); 4.17 (*dq*, J = 9.1, 6.3, CHO); 2.87–2.82 (*m*, CH_2); 1.16 (*d*, J = 6.3, Me). ^{13}C-NMR (50.3 MHz): 168.47 (*s*); 138.41 (*s*); 134.84 (*d*); 133.90 (*d*); 131.71 (*s*); 128.37 (*d*); 127.75 (*d*); 127.60 (*d*); 123.19 (*d*); 117.62 (*t*); 75.22 (*d*); 71.48 (*t*); 55.86 (*d*); 33.29 (*t*); 16.88 (*q*). CI-MS: 336 (100, $[M+1]^+$), 318 (16), 244 (18), 228 (42), 200 (23), 188 (12), 171 (38), 119 (13), 117 (15), 91 (41). Anal. calc. for $C_{21}H_{21}NO_3$ (335.41): C 75.20, H 6.31, N 4.18; found: C 75.07, H 6.31, N 4.04.

Table 3. *Crystal Data and Structure Refinement for* anti-**5**

Crystal data		*Data Collection*	
Empirical formula	$C_{26}H_{35}NO_3SeSi$	Diffractometer used	
Formula weight	516.60	θ Rang of data collection	1.75 to 23.22°
Color	colorless	Indexes ranges	$-11 \le h \le 13$
Crystal system	monoclinic		$-15 \le k \le 17$
Space group	$P2_1/c$		$-14 \le l \le 16$
Unit cell dimensions	a = 12.4187(4) Å	Reflections collected	10261
	b = 15.6814(6) Å	Independent reflections	3870 (R_{int} = 0.0424)
	c = 14.9241(5) Å	*Refinement*	
	β = 110.6690(10)°	Refinement method	Full matrix least squares on F^2
Volume	2719.3(2) Å^3	Data/restraints/parameters	3866/0/311
Z	4	Goodness of fit on F^2	0.768
Density (calc.)	1.262 Mg/m^3	Final R indices [$I > 2s(I)$]	$R1$ = 0.0406
Absorption coefficient	1.450 mm^{-1}		$wR2$ = 0.1177
F(000)	1080	R Indices (all data)	$R1$ = 0.0759
			$wR2$ = 0.1731
		Extinction coefficient	0.0007(5)
		Largest diff. peak	0.198 eÅ^{-3}
		Largest diff. hole	−0.194 eÅ^{-3}

trans-*2,2,4-Trimethyl-5-propyl-1,3-dioxolane* (**28**) [16]. A soln. of **26** (300 mg, 1.36 mmol) and 10% Pd/C (80 mg) in EtOH/HCOOH 10:1 (14 ml) was stirred under H_2 for 16 h. The catalyst was removed by filtration through *Celite* and the cake washed with EtOH. Evaporation gave the diol (131 mg, 82%) as a colorless liquid which was used directly for the next step. A soln. of the diol and 2-methoxypropene (0.21 ml, 2.20 mmol) in dry CH_2Cl_2 (4 ml) was cooled to 0° under N_2. A cat. amount of dried TsOH was added and the soln. left at r.t. for 1 h. Then CH_2Cl_2 (25 ml) was added, the soln. washed with sat. $NaHCO_3$ soln. and H_2O, dried ($MgSO_4$), and evaporated. FC (AcOEt/hexane 1:5) gave **28** (139 mg, 54%). Colorless liquid. ^{1}H-NMR (360 MHz): 3.70 (*dq*, J = 8.3, 6.0, MeC*H*O); 3.55–3.46 (*m*, CH_2CHO); 1.51–1.48 (*m*, 4 H, CH_2CH_2); 1.39 (*s*, Me_2C); 1.24 (*d*, J = 6.0, *Me*CHO); 0.96–0.92 (*m*, *Me*CH_2). NOE (360 MH_2, $CDCl_3$): 3.70 (MeC*H*O) → 1.50 (CH_2CHO; 5.5%); 3.50 (CH_2C*H*O) → 1.24 (*Me*CH; 3.5%); 1.24 (*Me*CH) → 3.50 (CH_2C*H*O; 3.7%). ^{13}C-NMR (50.3 MHz): 82.28 (*d*); 76.82 (*d*); 53.35 (*s*); 34.46 (*t*); 27.25 (*q*); 19.28 (*t*); 17.64 (*q*); 14.14 (*q*).

X-Ray Structure Analysis of anti-**5**. Suitable crystals were obtained by slow crystallization from hexane at –20°. Exper. parameters are given in *Table 3*.

REFERENCES

[1] a) N. A. Porter, B. Giese, D. P. Curran, *Acc. Chem. Res* **1991**, *24*, 296; b) W. Smadja, *Synlett* **1994**, 1; c) D. P. Curran, N. A. Porter, B. Giese, 'Stereochemistry of Radical Reactions', VCH, Weinheim, 1995.

[2] M. Bulliard, M. Zehnder, B. Giese, *Helv. Chim. Acta* **1991**, *74*, 1600.

[3] B. Giese, W. Damm, J. Dickhaut, F. Wetterich, S. Sun, D. P. Curran, *Tetrahedron Lett.* **1991**, *32*, 6097.

[4] P. Renaud, L. Giraud, *Synthesis* **1996**, 913; C. J. Easton, *Chem. Rev.* **1997**, *97*, 53.

[5] P. Renaud, P. Björup, P.-A. Carrupt, K. Schenk, S. Schubert, *Synlett* **1992**, 211; S. Schubert, P. Renaud, P.-A. Carrupt, K. Schenk, *Helv. Chim. Acta* **1993**, *76*, 2473.

[6] D. P. Curran, G. Thoma, *J. Am. Chem. Soc.* **1992**, *114*, 4436; D. P. Curran, S. N. Sun, *Tetrahedron Lett.* **1993**, *34*, 6181; D. P. Curran, E. Eichenberger, M. Collis, M. G. Roepel, G. Thoma, *J. Am. Chem. Soc.* **1994**, *116*, 4279.

[7] B. Giese, W. Damm, R. Batra, *Chemtracts-Org. Chem.* **1994**, *7*, 355; B. Giese, M. Bulliard, J. Dickhaut, R. Halbach, C. Hassler, U. Hoffmann, B. Hinzen, M. Senn, *Synlett* **1995**, 116.

[8] P. Renaud, I. Bétrisey, *Synth. Commun.* **1995**, *25*, 3479.

[9] P. Renaud, A. Stojanovic, *Tetrahedron Lett.* **1996**, *37*, 2569.

[10] W. Damm, U. Hoffmann, L. Macko, M. Neuburger, M. Zehnder, B. Giese, *Tetrahedron* **1994**, *50*, 7029.

[11] D. H. R. Barton, Y. Hervé, P. Potier, J. Thierry, *Tetrahedron* **1987**, *43*, 4297.

[12] A. Stojanovic, P. Renaud, *Synlett* **1997**, 181.

[13] J. Quirante, C. Escolano, J. Bonjoch, *Synlett* **1997**, 179.

[14] G. Delogu, G. Faedda, S. Gladiali, *J. Organomet. Chem.* **1984**, *268*, 167.

[15] H. Kawasaki, K. Tomioka, K. Koga, *Tetrahedron Lett.* **1985**, *26*, 3031; D. J. Hart, R. Krishnamurthy, *J. Org. Chem.* **1992**, *57*, 4456.

[16] C. H. Heathcock, S.-I. Kiyooka, T. A. Blumenkopf, *J. Org. Chem.* **1984**, *49*, 4214.

[17] F. Schroeder, R. Fettkoether, U. Noldt, K. Dettner, W. A. König, W. Francke, *Liebigs Ann. Chem.* **1994**, 1211.

[18] P. G. Sammes, D. Thetford, *J. Chem. Soc., Perkin Trans. 1* **1989**, 655.

[19] D. P. Curran, L. Balas, *Synlett* **1995**, 119.

[20] M. Roth, W. Damm, B. Giese, *Tetrahedron Lett.* **1996**, *37*, 351.

[21] D. Seebach, R. Charczuk, C. Gerber, P. Renaud, H. Berner, H. Schneider, *Helv. Chim. Acta* **1989**, *72*, 401.

[22] J. E. Baldwin, R. M. Adlington, M. B. Mitchell, J. Robertson, *Tetrahedron* **1991**, *47*, 5901.

[23] P. Renaud, M. Gerster, M. Ribezzo, *Chimia* **1994**, *48*, 366.

[24] W. P. Neumann, *Synthesis* **1987**, 665.

[25] K. Vogler, P. Lanz, *Helv. Chim. Acta* **1959**, *42*, 209.

[26] K. B. Sharpless, R. F. Lauer, *J. Am. Chem. Soc.* **1973**, *95*, 2697.

[27] D. A. Hoogwater, D. N. Reinhoudt, T. S. Lie, J. J. Gunneweg, H. C. Beyerman, *Recl. Trav. Chim. Pays-Bas* **1973**, *92*, 819.

[28] G. Losse, E. Wottgen, H. Just, *J. Prakt. Chem.* **1959**, *7*, 28.

[29] Y. Ito, Y. Kobayashi, T. Kawabata, M. Takase, S. Terashima, *Tetrahedron* **1989**, *45*, 5767.

Received November 13, 1997