Asymmetric Nucleophilic Acylation with Metalated Amino Nitriles: Diastereo- and Enantioselective Synthesis of 2-Substituted 3-Aroylcyclohexanones via Tandem Michael Addition/α-Alkylation

Dieter Enders,* Jochen Kirchhoff, Dietrich Mannes, Gerhard Raabe

Institut für Organische Chemie, Rheinisch-Westfälische Technische Hochschule, Professor-Pirlet-Straße 1, D-52074 Aachen, Germany

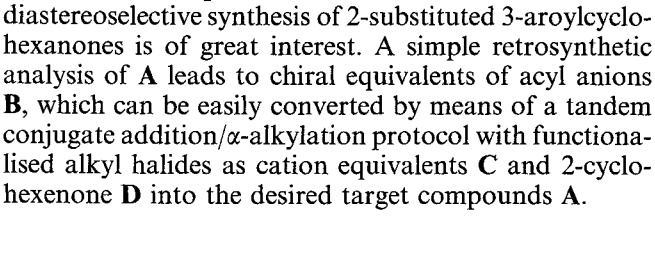
Fax +49(241)8888127; E-mail Gk010ZO@DACTH11

Received 18 January 1995

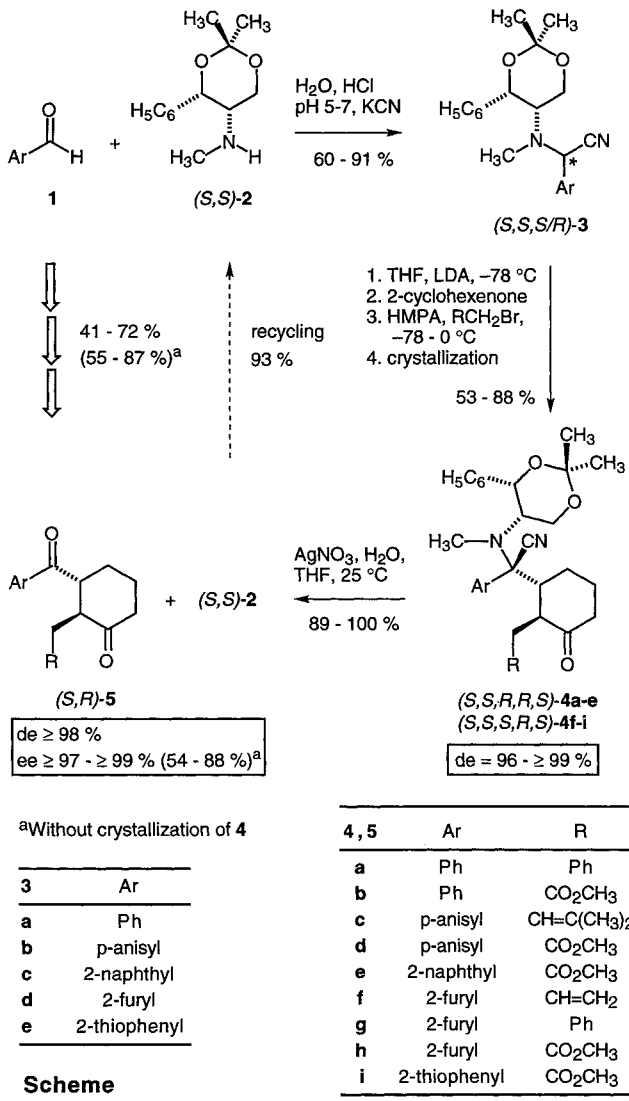
Dedicated to Professor R.R. Schmidt on the occasion of his 60th birthday.

Tandem conjugate addition/α-alkylation of lithiated chiral α-amino nitriles **3** and alkyl bromides to 2-cyclohexenone afforded 2-substituted 3-aroylcyclohexanones **5** of high diastereo- and enantiomeric purity (de ≥ 98%, ee ≥ 97 – ≥ 99%) and in good overall yields. The absolute configuration of the new stereogenic centres was determined by X-ray structure analysis of the Michael adduct **4c**.

Functionalized cyclic 1,4-diketones of type **A** have been shown to be useful building blocks for the construction of bicyclic ketones,[1] which are typical structural features of many natural products.[2] Therefore, an enantio- and diastereoselective synthesis of 2-substituted 3-aroylcyclohexanones is of great interest. A simple retrosynthetic analysis of **A** leads to chiral equivalents of acyl anions **B**, which can be easily converted by means of a tandem conjugate addition/α-alkylation protocol with functionalised alkyl halides as cation equivalents **C** and 2-cyclohexenone **D** into the desired target compounds **A**.



As efficient and synthetically useful equivalents of synthons **B** enantiopure metalated α-amino nitriles **E** were chosen. Their great importance as masked acyl anion equivalents[3] of carbonyl compounds in Umpolung reactions with various electrophiles has already been described in many publications.[4] Through conjugate addition to α,β-unsaturated esters,[5] ketones[6] and cyanides,[7] 1,4-dicarbonyl compounds are available. In some cases tandem Michael additions of lithiated amino nitriles to cyclic enones[8] have also been reported. The use of chiral α-amino nitriles in asymmetric conjugate addition reactions, resulting in the enantioselective synthesis of 3-substituted 4-oxo esters[9] and 3-substituted 1,4-diketones[10] has been described previously by our group. As a further extension of this methodology, we now wish to report the synthesis of 2-substituted 3-aroylcyclohexanones of very high diastereo- and enantiomeric purity by an asymmetric one-pot tandem Michael addition/α-alkylation of lithiated chiral α-amino nitriles and alkyl bromides with 2-cyclohexenone (Scheme).



aWithout crystallization of **4**

3	Ar
a	Ph
b	p-anisyl
c	2-naphthyl
d	2-furyl
e	2-thiophenyl

4,5	Ar	R
a	Ph	Ph
b	Ph	CO_2CH_3
c	p-anisyl	$CH{=}C(CH_3)_2$
d	p-anisyl	CO_2CH_3
e	2-naphthyl	CO_2CH_3
f	2-furyl	$CH{=}CH_2$
g	2-furyl	Ph
h	2-furyl	CO_2CH_3
i	2-thiophenyl	CO_2CH_3

Scheme

The α-amino nitriles (*S,S,S/R*)-**3** were obtained in high yields by treatment of aromatic aldehydes **1** with the enantiomerically pure secondary amine (*S,S*)-**2**[9,11] and potassium cyanide in water (pH 5–7). Upon deprotonation with lithium diisopropylamide, reaction with 2-cyclohexenone in THF at – 78 °C and addition of six equivalents of HMPA (THF:HMPA = 85:15) the intermediate enolate was trapped with alkyl bromides to form the crude tandem Michael adducts **4**, which in turn could be crystallized into the diastereomerically pure amino nitriles (*S,S,R,R,S*)-**4a–e** or (*S,S,S,R,S*)-**4f–i**, respectively (Table 1). It could be shown that nearly complete alkylation took place with activated alkyl halides in the

Table 1. Amino Nitrile Adducts **4** Prepared by Tandem Michael Addition/α-Alkylation

Product	Ar	R	Yield (%)	mp[a] (°C)	$[\alpha]_D^{RT}$ (*c*, $CHCl_3$)	de[b] (%)
(*S,S,R,R,S*)-**4a**	Ph	Ph	53	134	−5.2 (0.98)	≥98
(*S,S,R,R,S*)-**4b**	Ph	CO_2CH_3	85	138	−20.7 (1.05)	96
(*S,S,R,R,S*)-**4c**	*p*-anisyl	$CH{=}C(CH_3)_2$	64	140	−47.9 (1.00)	≥99
(*S,S,R,R,S*)-**4d**	*p*-anisyl	CO_2CH_3	79	164	−63.3 (1.06)	≥96
(*S,S,R,R,S*)-**4e**	2-naphthyl	CO_2CH_3	83	141	−108.0 (0.95)	≥98
(*S,S,S,R,S*)-**4f**	2-furyl	$CH{=}CH_2$	79	127	−11.0 (1.09)	≥98
(*S,S,S,R,S*)-**4g**	2-furyl	Ph	88	147	−8.5 (0.95)	≥98
(*S,S,S,R,S*)-**4h**	2-furyl	CO_2CH_3	88	154	−8.4 (1.02)	≥98
(*S,S,S,R,S*)-**4i**	2-thioph.	CO_2CH_3	85	131	+30.9 (1.00)	≥99

[a] Uncorrected, measured on a Büchi apparatus.
[b] Determined by ^1H and ^{13}C NMR spectroscopy (two hours acquisition time).

Table 2. 2-Substituted 3-Aroylcyclohexanones **5**

Product	Ar	R	Yield[a,b] (%)	mp[c] (°C)	$[\alpha]_D^{RT}$ (*c*, $CHCl_3$)	ee[b] (%)
(*S,R*)-**5a**	Ph	Ph	47 (70)	56	+54.0 (0.99)	≥98 (77)[d]
(*S,R*)-**5b**	Ph	CO_2CH_3	81 (98)	oil	−10.4 (1.03)	98 (78)[e]
(*S,R*)-**5c**	*p*-anisyl	$CH{=}C(CH_3)_2$	62 (84)	oil	+52.6 (0.97)	≥98 (80)[f]
(*S,R*)-**5d**	*p*-anisyl	CO_2CH_3	79 (96)	oil	+13.7 (1.04)	≥99 (84)[e]
(*S,R*)-**5e**	2-naphthyl	CO_2CH_3	79 (90)	oil	+32.2 (1.05)	≥99 (61)[e]
(*S,R*)-**5f**	2-furyl	$CH{=}CH_2$	79 (90)	93	+68.2 (1.05)	≥97 (82)[f]
(*S,R*)-**5g**	2-furyl	Ph	84 (91)	114	+85.3 (0.97)	≥98 (88)[d]
(*S,R*)-**5h**	2-furyl	CO_2CH_3	86 (94)	51	+15.6 (1.03)	99 (80)[e]
(*S,R*)-**5i**	2-thioph.	CO_2CH_3	85 (91)	70	−11.2 (1.00)	≥98 (54)[e]

[a] Yield of product **5** based on amino nitrile **3**.
[b] Values in brackets refer to syntheses without crystallization of **4**.
[c] Uncorrected, measured on a Büchi apparatus.
[d] Indirectly determined by ^1H and ^{13}C NMR spectroscopy as de values of the adducts **4**.
[e] Determined by ^1H NMR shift experiments with (*R*)-(−)-(9-anthryl)-2,2,2-trifluorethanol.
[f] Determined by ^1H NMR shift experiments with $Eu(hfc)_3$.

presence of a large excess of HMPA. Unactivated alkyl halides and other cosolvents gave only low conversions, so that crystallization proved impossible.

Upon treatment of the diastereomerically enriched adducts **4** with aqueous $AgNO_3$ solution[12] the *trans*-2-substituted 3-aroylcyclohexanones (*S,R*)-**5** were obtained by amino nitrile cleavage in good to very good overall yields and with very high diastereomeric and enantiomeric purity. Lower enantiomeric excesses but higher yields were obtained by cleavage of the crude adducts **4** (Table 2).

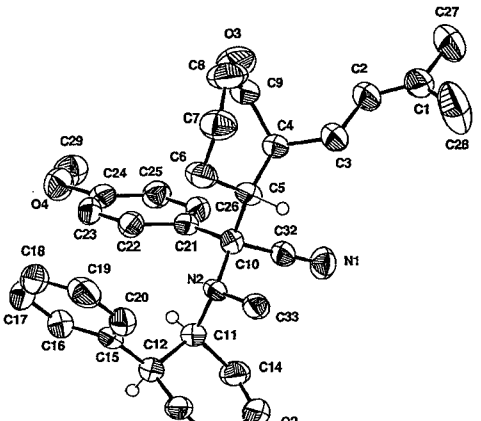
The chiral auxiliary (*S,S*)-**2** could be recovered in 93% yield by extraction from the alkaline aqueous phase.[9,11] In two cases (**4e** and **4i**) even higher amounts of diastereomerically pure adduct were crystallized than was thought possible from the crude products. This very surprising result can be explained by a second order asymmetric transformation.[13] As proposed, all stereoisomers can be converted to the most thermodynamically stable one by equilibration in polar solvents through immonium cyanide[14] and enol ene–immonium cyanide intermediates. Thermodynamically controlled crystallization of one diastereomer can then push the equilibrium towards the most stable diastereomer. According to this proposed explanation the epimerization of diastereomerically pure (*S,S,R,R,S*)-**4c** in $CDCl_3$ to mainly (*S,S,S,R,S*)-**4c**, with inverted amino nitrile centre, could be detected by NMR spectroscopy after a few days.[13]

The enantiomeric excesses of **5** were mainly determined by ^1H NMR shift experiments. The ee values of the methyl esters (**5b,d,e,h,i**) were measured by addition of the chiral cosolvent (*R*)-(−)-(9-anthryl)-2,2,2-trifluoroethanol causing a shift of the methoxy singlets. Compounds containing a double bond (**5c,f**) showed a large shift of the aromatic proton signals in the presence of $Eu(hfc)_3$. In all these cases the ee values of **5** were identical to the de values of **4**, checked by ^1H NMR (300 MHz) and ^{13}C NMR spectroscopy (75 MHz, two hours acquisition time). Therefore, it can be concluded that the cleavage to the 1,4-diketones proceeds without epimerization in analogy to the amino nitrile cleavage to form optically active 4-oxo esters.[11] According to these results, the ee values of **5a** and **5g** are based on the de values of the corresponding adducts **4**.

The relative *trans* configuration of the 2,3-disubstituted cyclohexanones **5** could be determined easily by ^1H NMR spectroscopy through the *trans*-diaxial coupling constants (10.4–11.8 Hz) of the protons at the stereogenic

carbon centres. This result was confirmed by NOE experiments on compound **5j** (Ar = *p*-anisyl, R = $CH=CH_2$, ee = 82%).

The absolute configuration of the new stereogenic centres given is based on an X-ray structure analysis of crystalline adduct **4c** (attempts to determine the absolute configuration employing Flack's method[23] met with failure; the assignment is therefore based on the known topology of the atoms C^{11} and C^{12} of the auxiliary, Figure) and the proposal of a uniform reaction mechanism.[15]



Figure

In summary, a very efficient, highly diastereo- and enantioselective synthesis of 2-substituted 3-aroylcyclohexanones **5** via conjugate addition of metalated amino nitriles to 2-cyclohexenone and subsequent α-alkylation has been developed. The title compounds are synthetically useful building blocks, which can be converted into functionalized bicyclic ketones,[1] characteristic structural features of many natural products. Preliminary investigations on related asymmetric tandem Michael addition/α-aldol reactions with cyclic Michael acceptors show that the procedure has an even broader scope of applications.[16]

All reagents were of commercial quality from freshly opened containers or distilled before use. The chiral auxiliary (*S,S*)-**2** was prepared according to the literature procedure.[9,11] THF was freshly distilled from potassium–benzophenone. Analytical TLC plates (silica gel 60 F_{254}) and silica gel 60 (230–400 mesh) were purchased from Merck, Darmstadt. BuLi (1.6 N in hexane) was purchased from Aldrich. All melting points (Büchi apparatus, system Dr. Tottoli) are uncorrected. Optical rotation values were measured using a Perkin-Elmer P 241 polarimeter. Microanalyses were obtained with a Heraeus CHN-O-RAPID element analyser. Mass spectra were recorded on a Varian MAT 212 (70 eV, 1 mA) spectrometer with DEI ionisation. IR spectra were obtained using a Perkin-Elmer FT 1750 spectrometer. The ^1H and ^{13}C NMR spectra were measured on a Varian VXR 300 (300 and 75 MHz) or Varian UNITY 500 (500 and 125 MHz). In the case of the amino nitriles **3a–e** the data of both epimers are given.

Amino Nitriles 3; General Procedure:

(4*S*,5*S*)-(+)-2,2-Dimethyl-5-methylamino-4-phenyl-1,3-dioxan[11] [(*S,S*)-**2**] (33.2 g, 0.15 mol) was diluted in water (150 mL) and 1 N HCl solution was added to reach pH 5–7. After addition of KCN (9.8 g, 0.15 mol) and the aldehyde (0.15 mol), pure or dissolved in methanol at 0°C the reaction mixture was stirred 18 to 72 h at r.t. The aqueous solution was decanted from the precipited crude product and extracted three times with Et_2O. The crude precipitate was dissolved in the ether phases, washed with brine and dried ($MgSO_4$). After evaporation of the solvent the crude product was recrystallized from EtOH.

(4S,5S,R/S)-(+)-[N-(2,2-Dimethyl-4-phenyl-1,2-dioxan-5-yl)-N-methylamino]phenylacetonitrile **[(*S,S,R/S*)-3a]**:[17]

According to the general procedure (*S,S*)-**2** was reacted with KCN and benzaldehyde (15.9 g). Yield: 44.4 g (88%); colourless needles; mp 87°C; $[\alpha]_D^{23} = +116.0$ ($c = 1.02$, $CHCl_3$); de = 82%.

IR (KBr): ν = 3065, 3040, 2990, 2950, 2860, 2805 (m, NCH_3), 2225 (w, C≡N), 1600, 1500, 1465, 1380, 1240, 1200 (s, COC), 1150, 1135, 1080, 1050 (s, COC), 1005, 855, 790, 765, 740, 700 cm^{-1}.

MS (70 eV): *m/z* (%) = 336 (0.4, $M^{+\cdot}$), 172 (99), 171 (88), 144 (13), 132 (100), 131 (44), 116 (45), 105 (10), 91 (31), 77 (15), 43 (18), 42 (15).

^1H NMR (300 MHz, $CDCl_3$): δ = 1.58 [s, 6H, $C(CH_3)_2$]/1.53 (s, 3H, CCH_3), 1.56 (s, 3H, CCH_3), 2.27/2.40 (s, 3H, NCH_3), 2.85/2.95 (td, 1H, *J* = 3.4, 1.3, C*H*N), 4.21/4.33 (dd, 1H, *J* = 13.1, 3.0, CH_2O), 4.63/4.56 (dd, 1H, *J* = 13.1, 1.3, CH_2O), 5.27/5.25 (d, 1H, *J* = 3.7, C*H*O), 5.65/4.52 (s, 1H, C*H*C≡N), 6.70–7.40 (m, 10H, CH_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.5/18.8 (CH_3), 29.7/29.4 (CH_3), 37.6/33.4 (NCH_3), 57.2/60.8 (*C*HN), 57.7/62.8 (*C*C≡N), 59.1/60.3 (CH_2O), 73.5/74.6 (*C*HO), 99.3/99.0 (*O*CO), 117.9/117.6 (*C*≡N), 125.5–128.1/125.7–128.3 ($C^t_{arom.}$), 134.0 ($C^q_{arom.}$), 139.1/140.1 ($C^q_{arom.}$).

$C_{21}H_{24}N_2O_2$ (336.4) calc. C 74.97, H 7.19, N 8.33. found: C 75.17, H 7.17, N 8.44.

(4S,5S,R/S)-(+)-[N-(2,2-Dimethyl-4-phenyl-1,2-dioxan-5-yl)-N-methylamino](4'-methoxyphenyl)acetonitrile **[(*S,S,S/R*)-3b]**:[17]

According to the general procedure (*S,S*)-**2** was treated with KCN and 4-methoxybenzaldehyde (20.4 g). Yield: 50.1 g (91%); colourless needles; mp 130°C; $[\alpha]_D^{23} = +105.8$ ($c = 0.98$, $CHCl_3$); de = 88%.

IR (KBr): ν = 3075, 3050, 2990, 2950, 2850, 2840 (m, OCH_3), 2805 (m, NCH_3), 2220 (w, C≡N), 1610, 1510, 1460, 1415, 1380, 1275, 1255, 1200 (s, COC), 1160, 1120, 1080, 1045 (s, COC), 1000, 860, 790, 775, 740, 705 cm^{-1}.

MS (70 eV): *m/z* (%) = 336 (0.1, $M^{+\cdot}$), 202 (46), 201 (31), 197 (4), 162 (15), 146 (100), 91 (8), 43 (7), 42 (7).

^1H NMR (300 MHz, $CDCl_3$): δ = 1.52/1.56 (s, 3H, CCH_3), 1.55/1.57 (s, 3H, CCH_3), 2.39/2.28 (s, 3H, NCH_3), 2.89/2.83 (td, 1H, *J* = 3.4, 1.4, C*H*N), 3.72/3.72 (s, 3H, OCH_3), 4.32/4.19 (dd, 1H, *J* = 13.2, 3.4, CH_2O), 4.43/5.53 (s, 1H, C*H*C≡N), 4.54/4.61 (dd, 1H, *J* = 13.2, 1.4, CH_2O), 5.23/5.25 (d, 1H, *J* = 3.4, C*H*O), 6.58–6.73 (m, 4H, $CH_{arom.}$), 7.26–7.40 (m, 5H, $CH_{arom.}$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.8/18.5 (CH_3), 29.5/29.7 (CH_3), 33.1/37.5 (NCH_3), 55.2 (OCH_3), 60.2/59.1 (CH_2O), 60.6/57.2 (*C*HN), 62.3/57.0 (*C*C≡N), 74.6/73.6 (*C*HO), 99.0/99.3 (*O*CO), 113.6/113.4 ($C^t_{arom.}$), 117.8/118.1 (*C*≡N), 125.8/125.6 ($C^t_{arom.}$), 126.02 ($C^q_{arom.}$), 126.9–128.5 ($C^t_{arom.}$), 140.2/139.2 ($C^q_{arom.}$), 159.6/159.3 ($C^q_{arom.}$).

$C_{22}H_{26}N_2O_3$ (366.5) calc. C 72.10, H 7.15, N 7.65. found: C 72,15, H 7.11, N 7.61.

(4S,5S,R/S)-(+)-[N-(2,2-Dimethyl-4-phenyl-1,2-dioxan-5-yl)-N-methylamino](2'naphthyl)acetonitrile **[(*S,S,R/S*)-3c]**:[18]

According to the general procedure (*S,S*)-**2** (4.2 g, 20 mmol) was treated with KCN (1.3 g, 20 mmol) and 2-naphthaldehyde (3.2 g, 20 mmol). Yield: 4.7 g (61%); colourless solid; mp 169°C; $[\alpha]_D^{25} = +126.8$ ($c = 0.97$, $CHCl_3$); de = 94%.

IR (KBr): ν = 3061, 3030, 2994, 2949, 2873, 2804 (m, NCH_3), 2224 (w, C≡N), 1600, 1500, 1452, 1381, 1360, 1338, 1239, 1201 (s, COC), 1160, 1124, 1083, 1045 (s, COC), 1003, 852, 838, 796, 765, 740, 703 cm^{-1}.

Table 3. Spectroscopic Data of the Tandem Michael/α-Alkylation Adducts (*S,S,R,R,S*)-**4a–e** and (*S,S,S,R,S*)-**4f–i**[a]

Product	IR (KBr) ν (cm^{-1})	^1H NMR (C_6D_6/TMS) δ (ppm), J (Hz)	^{13}C NMR (C_6D_6/TMS) δ (ppm)	MS (70 eV) m/z (%)
4a	3063, 3029, 2991, 2942, 2868, 2820, 2212, 1712, 1604, 1451, 1383, 1200, 1122, 1021, 851, 762, 746, 702	0.77–1.08 (m, 2H, CH_2CH_2CH), 1.14 (s, 3H, CCH_3), 1.10–1.36 (m, 2H, CH_2CH_2CH), 1.47 (m, 1H, $CH_2C{=}O$), 1.51 (s, 3H, CCH_3), 1.83 (dm, J = 15.1, 1H, $CH_2C{=}O$), 2.27 (ddd, J = 9.7, 8.9, 4.0, 1H, $CH^{ax}C{=}O$), 2.44 (td, J = 8.9, 4.0, 1H, $CH^{ax}CC{\equiv}N$), 2.44 (td, J = 4.0, 1.7, 1H, CHN), 2.96 (s, 3H, NCH_3), 3.09 (dd, J = 13.4, 9.7, 1H, CH_2Ph), 3.25 (dd, J = 13.4, 4.0, 1H, CH_2Ph), 3.45 (dd, J = 13.1, 4.0, 1H, CH_2O), 4.54 (d, J = 4.0, 1H, OCHPh), 4.95 (dd, 13.1, 1.7, 1H, CH_2O), 6.91–7.28 (m, 15H, CH_{arom})	19.0 (CCH_3), 22.3 (CH_2CH_2), 23.4 (CH_2CH_2), 29.4 (CCH_3), 35.7 (NCH_3), 37.2 (CH_2Ph), 39.5 ($CH_2C{=}O$), 48.2 (CHCC≡N), 54.7, 54.8 (CHC=O, CHN), 58.9 (CH_2O), 72.0 (CC≡N), 76.1 (OCHPh), 99.2 (OCO), 121.4 (C≡N), 126.5–129.7 (C^t_{arom}), 134.2, 140.0, 140.0 (C^q_{arom}), 208.3 (C=O)	495 ($M^{+\bullet}$ − HCN, 2), 404 (42), 267 (19), 240 (33), 183 (10), 171 (62), 146 (17), 133 (42), 105 (37), 91 (61), 77 (25), 57 (26), 44 (48), 42 (100)
4b	3058, 2993, 2947, 2867, 2821, 2211, 1744, 1712, 1451, 1382, 1207, 1170, 1116, 1024, 852, 763, 750, 708	0.76 (m, 1H, CH_2CH_2CH), 1.08 (m, 1H, CH_2CH_2CH), 1.13 (s, 3H, CCH_3), 1.25–1.45 (m, 2H, CH_2CH_2CH), 1.50 (s, 3H, CCH_3), 1.60 (ddd, J = 11.4, 7.4, 3.7, 1H, $CH^{ax}C{=}O$), 1.61 (m, 1H, $CH_2C{=}O$), 2.13 (dm, J = 14.4, 1H, $CH_2C{=}O$), 2.42 (td, J = 3.7, 1.7, 1H, CHN), 2.61 (td, J = 11.4, 2.7, 1H, $CH^{ax}CC{\equiv}N$), 2.91 (s, 3H, NCH_3), 3.06 (dd, J = 17.5, 7.4, 1H, $CH_2CO_2CH_3$), 3.15 (dd, J = 17.5, 3.7, 1H, $CH_2CO_2CH_3$), 3.41 (s, 3H, $COOCH_3$), 3.45 (dd, J = 13.1, 4.0, 1H, CH_2O), 4.54 (d, J = 3.7, 1H, OCHPh), 4.91 (dd, J = 13.1, 1.7, 1H, CH_2O), 6.94–7.28 (m, 10H, CH_{arom})	19.1 (CCH_3), 23.3 (CH_2CH_2), 24.7 (CH_2CH_2), 29.3 (CCH_3), 32.2 ($CH_2CO_2CH_3$), 35.5 (NCH_3), 40.8 ($CH_2C{=}O$), 47.5 (CHCC≡N), 50.1 (CHC=O), 51.3 ($COOCH_3$), 55.1 (CHN), 58.8 (CH_2O), 71.0 (CC≡N), 76.0 (OCHPh), 99.2 (OCO), 121.7 (C≡N), 127.5–129.2 (C^t_{arom}), 133.9, 140.0 (C^q_{arom}), 172.3 ($COOCH_3$), 207.5 (C=O)	504 ($M^{+\bullet}$, 1), 340 (37), 288 (10), 267 (15), 252 (16), 171 (100), 146 (17), 105 (9), 91 (12), 57 (11), 42 (48)
4c	3070, 2993, 2957, 2860, 2811, 2213, 1713, 1611, 1512, 1452, 1380, 1257, 1198, 1119, 1022, 951, 849, 754, 705	0.92 (dddd, J = 14.3, 11.2, 10.0, 4.4, 1H, $CH_2CH^{ax}_2CH$), 1.18 (s, 3H, $CC^{trans}H_3$), 1.15–1.27 (m, 2H, CH_2CH_2CH), 1.45 (m, 1H, $CH_2CH^{eq}_2CH$), 1.48 (m, 1H, $CH^{ax}_2C{=}O$), 1.52 (s, 3H, $CC^{cis}H_3$), 1.63 (d, J = 1.0, 3H, ${=}CC^{E}H_3$), 1.64 (d, J = 1.0, 3H, $={=}CC^{Z}CH_3$), 1.93 (dddd, J = 16.3, 6.6, 4.3, 1.2, 1H, $CH^{eq}_2C{=}O$), 2.17 (dt, J = 10.0, 5.6, 1H, $CH^{ax}C{=}O$), 2.46 (m, 1H, $CH_2C{=}$), 2.51 (td, J = 10.1, 5.5, 1H, $CH^{ax}CC{\equiv}N$), 2.59 (td, J = 4.0, 1.8, 1H, $CH^{eq}N$), 2.64 (m, 1H, $CH_2C{=}$), 3.04 (s, 3H, NCH_3), 3.28 (s, 3H, OCH_3), 3.57 (dd, J = 13.3, 4.0, 1H, CH^{ax}_2O), 4.61 (d, J = 4.0, 1H, $OCH^{ax}Ph$), 5.01 (dd, J = 13.3, 1.8, 1H, CH^{eq}_2O), 5.12 (tm, J = 7.2, 1H, $={=}CH$), 6.59 (m, 2H, CH_{arom}), 5.3–8.6 (m, 2H, CH_{arom}), 7.15–7.25 (m, 5H, CH_{arom})	18.1 ($={=}CC^{Z}H_3$), 19.1 ($CC^{trans}H_3$), 21.5 (CH_2CH_2), 22.3 (CH_2CH_2), 25.9 ($={=}CC^{E}H_3$), 29.4 ($CC^{cis}H_3$), 31.7 ($CH_2C{=}$), 35.7 (NCH_3), 38.2 ($CH_2C{=}O$), 47.3 (CHCC≡N), 52.5 (CHC=O), 54.7 (CHN), 54.8 (OCH_3), 58.9 (CH_2O), 72.1 (CC≡N), 76.2 (OCHPh), 99.2 (OCO), 113.9 (C^t_{arom}), 121.5 (C≡N), 121.7 (CH=C), 126.0 ($C^q_{arom}CN$), 127.5–130.5 (C^t_{arom}), 133.7 (C=CH), 139.9 (C^q_{arom}), 160.3 ($C^q_{arom}OCH_3$), 209.2 (C=O)	530 ($M^{+\bullet}$, 1), 434 (100), 365 (12), 310 (16), 270 (13), 244 (10), 201 (15), 133 (46), 124 (52), 114 (12), 109 (10), 105 (39), 91 (15), 83 (20), 77 (17), 72 (12), 69 (15), 57 (22), 42 (52)
4d	3000, 2946, 2865, 2217, 1739, 1713, 1609, 1512, 1382, 1369, 1256, 1202, 1171, 1119, 1013, 837, 747, 720	0.78 (m, 1H, CH_2CH_2CH), 1.09 (m, 1H, CH_2CH_2CH), 1.16 (s, 3H, CCH_3), 1.26–1.49 (m, 2H, CH_2CH_2CH), 1.50 (s, 3H, CCH_3), 1.62 (dm, J = 14.4, 1H, $CH_2C{=}O$), 1.72 (ddd, J = 11.4, 7.7, 3.7, 1H, $CH^{ax}C{=}O$), 2.15 (dm, J = 14.5, 1H, CHC=O), 2.53 (td, J = 4.0, 2.0, 1H, CHN), 2.61 (td, J = 11.4, 2.4, 1H, $CH^{ax}CC{\equiv}N$), 2.91 (s, 3H, NCH_3), 3.09 (dd, J = 17.1, 7.7, 1H, $CH_2CO_2CH_3$), 3.21 (dd, J = 17.1, 3.7, 1H, $CH_2CO_2CH_3$), 3.30 (s, 3H, $C_{arom}OCH_3$), 3.42 (s, 3H, $COOCH_3$), 3.54 (dd, J = 13.1, 4.0, 1H, CH_2O), 4.59 (d, J = 4.0, 1H, OCHPh), 4.95 (dd, J = 13.1, 2.0, 1H, CH_2O), 6.6 (m_{broad}, 2H, CH_{arom}), 5.5–8.0 (m, 2H, CH_{arom}), 7.16 (m, 5H, CH_{arom})	19.2 (CCH_3), 23.4 (CH_2CH_2), 24.8 (CH_2CH_2), 29.2 (CCH_3), 32.3 ($CH_2CO_2CH_3$), 35.5 (NCH_3), 40.9 ($CH_2C{=}O$), 47.5 (CHCC≡N), 50.3 (CHC=O), 51.3 ($COOCH_3$), 54.9 ($C_{arom}OCH_3$), 55.1 (CHN), 58.8 (CH_2O), 70.4 (CC≡N), 76.0 (OCHPh), 99.3 (OCO), 113.8 (C^t_{arom}), 122.0 (C≡N), 125.7 ($C^q_{arom}CN$), 127.5–130.1 (C^t_{arom}), 140.0, C^q_{arom}), 160.4 ($C^q_{arom}OCH_3$), 172.4 ($COOCH_3$), 207.7 (C=O)	507 ($M^{+\bullet}$ − HCN, 9), 434 (33), 370 (41), 365 (14), 318 (33), 314 (26), 282 (100), 270 (18), 242 (17), 236 (21), 201 (66), 185 (22), 133 (31), 105 (30), 91 (22), 83 (25), 77 (16), 57 (19), 44 (25), 42 (67)
4e[b]	3040, 2991, 2938, 2865, 2214, 1743, 1709, 1453, 1435, 1381, 1196, 1172, 1118, 1011, 878, 853, 835, 767, 746, 702	1.08 (m, 1H, CH_2CH_2CH), 1.37 (s, 3H, CCH_3), 1.50 (m, 1H, CH_2CH_2CH), 1.51 (s, 3H, CCH_3), 1.55 (ddd, J = 12.0, 6.1, 3.7, 1H, $CH^{ax}C{=}O$), 1.78–2.02 (m, 3H, $CH_2CH_2CH_2C{=}O$), 2.35 (m, 1H, $CH_2C{=}O$), 2.71 (m, 1H, CHN), 2.75 (tm, J = 11.9, 1H, $CH^{ax}CC{\equiv}N$), 2.83 (dd, J = 17.8, 6.0, 1H, $CH_2CO_2CH_3$), 2.90 (dd, J = 17.8, 4.4, 1H, $CH_2CO_2CH_3$), 3.02 (s, 3H, NCH_3), 3.58 (s, 3H, $COOCH_3$), 3.84 (dd, J = 13.4, 4.4, 1H, CH_2O), 4.72 (dd, J = 13.4, 2.4, 1H, CH_2O), 4.89 (d, J = 4.4, 1H, OCHPh), 6.2 (m_{wide}, 1H, CH_{arom}), 7.29–7.90 (m, 10H, CH_{arom}), 8.1 (m_{broad}, 1H, CH_{arom})	19.4 (CCH_3), 23.4 (CH_2CH_2), 24.8 (CH_2CH_2), 28.7 (CCH_3), 31.7 ($CH_2CO_2CH_3$), 35.4 (NCH_3), 40.8 ($CH_2C{=}O$), 47.5 (CHCC≡N), 49.7 (CHC=O), 51.6 ($COOCH_3$), 55.3 (CHN), 58.6 (CH_2O), 70.9 (CC≡N), 75.7 (OCHPh), 99.5 (OCO), 121.4 (C≡N), 125.2–128.5 (C^t_{arom}), 130.5, 132.6, 133.3, 139.1 (C^q_{arom}), 172.4 ($COOCH_3$), 209.3 (C=O)	527 ($M^{+\bullet}$ − HCN, 23), 390 (19), 338 (64), 335 (20), 307 (29), 302 (23), 290 (39), 266 (47), 233 (29), 222 (62), 191 (34), 168 (25), 105 (29), 91 (29), 77 (21), 42 (100)
4f	3120, 3075, 2992, 2959, 2866, 2816, 2218, 1709, 1637, 1499, 1452, 1383, 1239, 1201, 1173, 1126,	0.98–1.20 (m, 3H, CH_2CH_2), 1.16 (s, 3H, CCH_3), 1.37 (m, 1H, CH_2CH_2), 1.50 (s, 3H, CCH_3), 1.68 (m, 1H, $CH_2C{=}O$), 1.92–2.05 (m, 2H, $CH_2C(O)CH$), 2.27 (m, 1H, CHCC≡N), 2.30 (m, 1H, CHN), 2.39 (ddm, J = 14.1, 6.7, 1H, $CH_2C{=}$), 2.48 (ddm, J = 14.1, 6.0, 1H, $CH_2C{=}$), 2.72 (s, 3H, NCH_3), 3.61 (dd, J = 13.1, 4.4, 1H, CH_2O), 4.60 (dd, 13.1, 2.7, 1H, CH_2O), 4.75 (d, J = 4.4, 1H, OCHPh), 4.94 (dm, J = 10.2, 1H, $={=}CH_2$), 4.97 (dm,	19.5 (CCH_3), 22.3, 22.5 (CH_2CH_2CH), 28.9 (CCH_3), 34.7 (NCH_3), 35.6 ($CH_2C{=}$), 39.1 ($CH_2C{=}O$), 47.5 (CHCC≡N), 52.6 (CHC=O), 55.7 (CHN), 59.1 (CH_2O), 67.4 (CC≡N), 74.1 (OCHPh), 99.4 (OCO), 111.0, 113.6 (C^t_{fur}), 117.1 ($={=}CH_2$), 119.8	462 ($M^{+\bullet}$, 1), 394 (24), 325 (16), 298 (39), 270 (60), 242 (11), 230 (18), 217 (19), 215 (10), 161 (100), 133 (15), 117 (10), 105 (14), 96 (23), 91 (15), 83

Table 3. (continued)

Product	IR (KBr) ν (cm^{-1})	^1H NMR (C_6D_6/TMS) δ (ppm), J (Hz)	^{13}C NMR (C_6D_6/TMS) δ (ppm)	MS (70 eV) m/z (%)
	1084, 1030, 972, 914, 854, 763, 744, 701	J = 17.1, 1H, =CH$_2$), 5.77 (ddt, J = 17.1, 10.1, 7.1, 1H, CH=CH$_2$), 5.98 (dd, J = 3.4, 1.7, 1H, CH$_{fur}$), 6.36 (dd, J = 3.4, 0.7, 1H, CH$_{fur}$), 6.94 (dd, J = 1.7, 0.7, 1H, CH$_{fur}$), 7.15–7.32 (m, 5H, CH$_{arom}$)	(C≡N), 126.8, 126.9, 127.5 (C^t_{arom}), 136.2 (HC=CH$_2$), 139.9 (C^q_{arom}), 143.3 (C^t_{fur}), 148.2 (C^q_{fur}), 208.5 (C=O)	(18), 77 (13), 57 (24), 42 (67)
4g	3113, 3031, 2994, 2960, 2904, 2869, 2820, 2217, 1712, 1605, 1495, 1452, 1384, 1201, 1125, 1082, 1022, 853, 833, 751, 740, 702	0.90–1.09 (m, 2H, CH$_2$CH$_2$CH), 1.14 (s, 3H, CCH$_3$), 1.16, 1.36 (m, 2H, CH$_2$CH$_2$CH), 1.50 (s, 3H, CCH$_3$), 1.56 (ddd, J = 14.8, 11.1, 6.7, 1H, CH$_2$C=O), 1.94 (ddd, J = 14.8, 5.4, 3.7, 1H, CH$_2$C=O), 2.21–2.36 (m, 3H, CHC=O, CHCC≡N, CHN), 2.67 (s, 3H, NCH$_3$), 3.01 (dd, J = 13.4, 9.4, 1H, CH$_2$Ph), 3.11 (dd, J = 13.4, 4.7, 1H, CH$_2$Ph), 3.60 (dd, J = 13.1, 4.4, 1H, CH$_2$O), 4.60 (dd, J = 13.1, 2.4, 1H, CH$_2$O), 4.73 (d, J = 4.4, 1H, OCHPh), 5.95 (dd, J = 3.4, 1.7, 1H, CH$_{fur}$), 6.34 (dd, J = 3.4, 0.7, 1H, CH$_{fur}$), 6.92 (dd, J = 1.7, 0.7, 1H, CH$_{fur}$), 6.97–7.30 (m, 10H, CH$_{arom}$)	19.5 (CCH$_3$), 23.1, 23.1 (CH$_2$CH$_2$), 28.9 (CCH$_3$), 34.7 (NCH$_3$), 36.8 (CH$_2$Ph), 39.8 (CH$_2$C=O), 48.3 (CHCC≡N), 55.0, 55.7 (CHC=O, CHN), 59.1 (CH$_2$O), 67.0 (CC≡N), 74.1 (OCHPh), 99.4 (OCO), 111.0, 113.7 (C^t_{fur}), 119.8 (C≡N), 126.4–129.7 (C^t_{arom}), 140.0, 140.1 (C^q_{arom}), 143.3 (C^t_{fur}), 148.2 (C^q_{fur}), 208.2 (C=O)	512 ($M^{+\bullet}$, 1), 394 (21), 348 (22), 325 (11), 267 (62), 257 (30), 230 (23), 161 (100), 146 (27), 133 (16), 117 (10), 105 (16), 91 (71), 83 (14), 77 (13), 57 (38), 55 (11), 42 (79)
4h	3125, 3000, 2951, 2880, 2815, 2219, 1737, 1707, 1500, 1454, 1385, 1259, 1200, 1125, 1035, 851, 778, 744, 699	0.88–1.15 (m, 2H, CH$_2$CH$_2$), 1.15 (s, 3H, CCH$_3$), 1.25 (dm, J = 14.1, 1H, CH$_2$C=O), 1.36 (m, 1H, CH$_2$CH$_2$CH), 1.49 (s, 3H, CCH$_3$), 1.65 (td, J = 13.4, 6.4, 1H, CH$_2$CH$_2$CH), 1.96 (ddd, J = 11.4, 7.7, 4.4, 1H, CH^{ax}C=O), 2.14 (dm, J = 14.1, 1H, CH$_2$C=O), 2.25 (m, 1H CHN), 2.28 (td, J = 11.4, 3.4, 1H CH^{ax}CC≡N), 2.64 (s, 3H, NCH$_3$), 2.95 (dd, J = 16.8, 7.7, 1H, CH$_2$CO$_2$CH$_3$), 3.02 (dd, J = 16.8, 4.4, 1H, CH$_2$CO$_2$CH$_3$), 3.38 (s, 3H, COOCH$_3$), 3.59 (dd, J = 13.1, 4.4, 1H, CH$_2$O), 4.61 (dd, J = 13.1, 2.4, 1H, CH$_2$O), 4.74 (d, J = 4.4, 1H, OCHPh), 5.95 (dd, J = 3.4, 1.7, 1H, CH$_{fur}$), 6.24 (m, 1H, CH$_{fur}$), 6.98 (dd, J = 1.7, 0.7, 1H, CH$_{fur}$), 7.15–7.29 (m, 5H, CH$_{arom}$)	19.5 (CCH$_3$), 24.1, 24.8 (CH$_2$CH$_2$), 28.8 (CCH$_3$), 32.0 (CH$_2$CO$_2$CH$_3$), 34.6 (NCH$_3$), 41.0 (CH$_2$C=O), 47.8 (CHCC≡N), 50.1 (CHC=O), 51.3 (COOCH$_3$), 55.9 (CHN), 59.1 (CH$_2$O), 65.7 (CC≡N), 74.1 (OCHPh), 99.4 (OCO), 110.9, 113.0 (C^t_{fur}), 120.0 (C≡N), 126.8, 126.9, 127.6 (C^t_{arom}), 139.9 (C^q_{arom}), 143.7 (C^t_{fur}), 148.0 (C^q_{fur}), 172.4 (COOCH$_3$), 207.6 (C=O)	479 ($M^{+\bullet}-CH_3$, 2), 330 (51), 325 (8), 242 (26), 200 (7), 161 (100), 137 (8), 133 (12), 117 (8), 105 (12), 91 (16), 83 (12), 81 (9), 77 (12), 72 (9), 55 (14), 42 (88)
4i	3122, 3002, 2945, 2865, 2819, 2214, 1735, 1708, 1438, 1384, 1261, 1200, 1169, 1119, 1082, 1024, 851, 746, 701	0.98–1.11 (m, 2H, CH$_2$CH$_2$), 1.14 (s, 3H, CCH$_3$), 1.25–1.43 (m, 2H, CH$_2$CH$_2$), 1.48 (s, 3H, CCH$_3$), 1.63 (m, 1H, CH$_2$C=O), 2.05 (m, 1H, CHC=O), 2.17 (dm, J = 14.4, 1H, CH$_2$C=O), 2.52 (td, J = 11.4, 2.8, 1H, CH^{ax}CC≡N), 2.63 (td, J = 4.7, 2.7, 1H, CHN), 2.73 (s, 3H, NCH$_3$), 3.02 (m, 2H, CH$_2$CO$_2$CH$_3$), 3.37 (s, 3H, COOCH$_3$), 3.57 (dd, J = 13.1, 4.4, 1H, CH$_2$O), 4.68 (d, J = 4.7, 1H, OCHPh), 4.70 (dm, J = 13.1, 1H, CH$_2$O), 6.57 (dd, J = 5.0, 3.7, 1H, CH$_{thioph}$), 6.89 (dd, J = 5.0, 1.0, 1H, CH$_{thioph}$), 7.16–7.30 (m, 6H, CH$_{arom}$)	19.7 (CCH$_3$), 23.7, 24.4 (CH$_2$CH$_2$), 28.6 (CCH$_3$), 31.9 (CH$_2$CO$_2$CH$_3$), 35.2 (NCH$_3$), 41.0 (CH$_2$C=O), 47.6 (CHCC≡N), 50.1 (CHC=O), 51.3 (COOCH$_3$), 55.4 (CHN), 58.7 (CH$_2$O), 67.5 (CC≡N), 74.6 (OCHPh), 99.5 (OCO), 121.1 (C≡N), 126.9–129.9 (C^t_{arom}), 136.4, 139.8 (C^q_{arom}), 172.4 (COOCH$_3$), 207.4 (C=O)	495 ($M^{+\bullet}-CH_3$, 1), 346 (60), 273 (17), 258 (70), 230 (10), 216 (11), 177 (100), 133 (10), 105 (14), 91 (14), 83 (18), 82 (10), 72 (13), 57 (12), 55 (16), 42 (62)

[a] Satisfactory microanalyses obtained for **4a–i**: C ± 0.34, H ± 0.26, N ± 0.29%.
[b] NMR spectrum determined in $CDCl_3$/TMS.

Table 4. Spectroscopic Data of the 2-Substituted 3-Aroylcyclohexanones (*S,R*)-**5** prepared by Tandem Michael Addition/α-Alkylation[a]

Product	IR (KBr) ν (cm^{-1})	^1H NMR ($CDCl_3$/TMS) δ (ppm), J (Hz)	^{13}C NMR ($CDCl_3$/TMS) δ (ppm)	MS (70 eV) m/z (%)
5a	3030, 2955, 2924, 2858, 1709, 1673, 1598, 1451, 1267, 1229, 1003, 913, 723, 706, 696, 509	1.68–1.86 (m, 2H, CH$_2$CH$_2$), 1.99–2.14 (m, 2H, CH$_2$CH$_2$), 2.31–2.50 (m, 2H, CH$_2$CO), 2.68 (dd, J = 13.8, 3.0, 1H, CH$_2$Ph), 2.96 (dd, J = 13.8, 8.4, 1H, CH$_2$Ph), 3.32 (dddd, J = 10.4, 8.4, 3.3, 1.0, 1H, CH^{ax}COCH$_2$), 3.62 (td, J = 10.4, 3.7, 1H, CH^{ax}COPh), 7.08–7.2 (m, 5H, CH$_{arom}$), 7.43 (tm, J = 7.5, 2H, CH$_{arom}$), 7.55 (tt, J = 7.4, 1.3, 1H, CH$_{arom}$), 7.83 (dm, J = 7.4, 2H, CH$_{arom}$)	25.9 (CH$_2$CH$_2$CH), 29.7 (CH$_2$CH$_2$CH), 33.2 (CH$_2$Ph), 41.4 (CH$_2$CO), 50.2 (CHCOPh), 53.1 (CHCOCH$_2$), 126.0–133.4 (C^t_{arom}), 136.1, 140.3 (C^q_{arom}), 200.7 (COPh), 211.1 (CH$_2$CO)	292 ($M^{+\bullet}$, 4), 187 (100), 146 (29), 105 (37), 91 (15), 77 (27), 51 (8)
5b	3064, 2951, 2867, 1738, 1714, 1681, 1597, 1449, 1269, 1224, 1164, 1003, 907, 703	1.71–1.97 (m, 2H, CH$_2$CH$_2$), 2.10–2.24 (m, 2H, CH$_2$CH$_2$), 2.37 (dd, J = 16.8, 4.0, 1H, CH$_2$CO$_2$CH$_3$), 2.46 (dd, J = 16.8, 7.4, 1H, CH$_2$COOCH$_3$), 2.50 (m, 2H, CH$_2$CO), 3.41 (ddd, J = 11.4, 7.1, 4.0, 1.0, 1H, CH^{ax}COCH$_2$), 3.61 (s, 3H, OCH$_3$), 3.94 (td, J = 11.4, 3.7, 1H, CH^{ax}COPh), 7.50 (tm, J = 7.4, 2H, CH$_{arom}$), 7.61 (tt, J = 6.7, 1.4, 1H, CH$_{arom}$), 7.98 (dm, J = 7.1, 2H, CH$_{arom}$)	26.0 (CH$_2$CH$_2$CH), 30.3 (CH$_2$CH$_2$CH), 31.8 (CH$_2$COOCH$_3$), 41.0 (CH$_2$CO), 47.7 (CHCOPh), 49.6 (CHCOCH$_2$), 51.5 (OCH$_3$), 128.4–133.7 (C^t_{arom}), 135.9 (C^q_{arom}), 172.5 (COOCH$_3$), 200.7 (COPh), 210.2 (CHCO)	274 ($M^{+\bullet}$, 21), 243 (5), 169 (17), 137 (11), 105 (100), 77 (20)

Table 4. (continued)

Product	IR (KBr) ν (cm^{-1})	^1H NMR ($CDCl_3$/TMS) δ (ppm), J (Hz)	^{13}C NMR ($CDCl_3$/TMS) δ (ppm)	MS (70 eV) m/z (%)
5c	2936, 2863, 1709, 1671, 1600, 1576, 1511, 1449, 1422, 1272, 1172, 1031, 842	1.29 (s, 3H, $=CCH_3$), 1.50 (d, J = 1.0, 3H, $=CCH_3$), 1.70–1.89 (m, 2H, CH_2CH_2), 1.93–2.29 (m, 4H, CH_2CH_2, $CH_2C=$), 2.44 (m, 2H, CH_2CO), 3.04 (ddd, J = 10.8, 5.7, 5.0, 1H, $CH^{ax}COCH_2$), 3.62 (td, J = 10.8, 4.0, 1H, $CH^{ax}COC_{arom}$), 3.88 (s, 3H, OCH_3), 5.03 (tm, J = 7.4, 1H, $HC=$), 6.94 (dm, J = 9.1, 2H, CH_{arom}), 7.92 (dm, J = 9.1, 2H, CH_{arom})	17.4 (CCH_3), 25.7 (CCH_3), 25.9, 26.2 (CH_2CH_2CH, $CH_2C=$), 29.8 (CH_2CH_2CH), 41.4 (CH_2CO), 49.2 ($CHCOC_{arom}$), 51.5 ($CHCOCH_2$), 55.5 (OCH_3), 113.9 (C^t_{arom}), 122.2 ($HC=$), 129.2 (C^q_{arom}), 130.6 (C^t_{arom}), 133.2 ($HC=C$), 163.7 (C^q_{arom}), 199.4 (COC_{arom}), 212.1 (CH_2CO)	300 ($M^{+\bullet}$, 41), 176 (45), 165 (84), 163 (15), 147 (38), 145 (33), 135 (100), 107 (26), 92 (15), 77 (31), 55 (15), 41 (29)
5d	2951, 2866, 1738, 1713, 1672, 1600, 1575, 1512, 1438, 1262, 1235, 1172, 1028, 908, 843	1.72–1.96 (m, 2H, CH_2CH_2), 2.05–2.24 (m, 2H, CH_2CH_2), 2.34 (dd, J = 16.8, 4.0, 1H, $CH_2CO_2CH_3$), 2.43 (dd, J = 16.8, 7.4, 1H, CH_2COOCH_3), 2.49 (m, 2H, CH_2CO), 3.40 (ddd, J = 11.4, 7.4, 4.0, 1H, $CH^{ax}COCH_2$), 3.61 (s, 3H, $COOCH_3$), 3.87 (td, J = 11.4, 3.7, 1H, $CH^{ax}COC_{arom}$), 3.89 (s, 3H, OCH_3), 6.97 (dm, J = 8.7, 2H, CH_{arom}), 7.96 (dm, J = 9.1, 2H, CH_{arom})	26.0 (CH_2CH_2CH), 30.4 (CH_2CH_2CH), 31.8 (CH_2COOCH_3), 41.1 (CH_2CO), 47.8 ($CHCOC_{arom}$), 49.3 ($CHCOCH_2$), 51.5 ($COOCH_3$), 55.6 (OCH_3), 114.1 (C^t_{arom}), 128.2 (C^q_{arom}), 130.8 (C^t_{arom}), 164.1, C^q_{arom}), 172.5 ($COOCH_3$), 198.7 (COC_{arom}), 210.5 (CH_2CO)	304 ($M^{+\bullet}$, 6), 169 (5), 137 (4), 135 (100), 107 (8), 92 (10), 77 (19), 55 (7), 41 (12)
5e	3023, 2951, 1737, 1713, 1674, 1628, 1437, 1281, 1222, 1185, 911, 829, 759, 476	1.76–2.02 (m, 2H, CH_2CH_2), 2.10–2.27 (m, 2H, CH_2CH_2), 2.42 (dd, J = 16.8, 4.0, 1H, CH_2COCH_3), 2.51 (dd, J = 16.8, 7.1, 1H, CH_2COOCH_3), 2.41–2.61 (m, 2H, CH_2CO), 3.46 (ddd, J = 11.4, 7.1, 4.0, 1.0, $CH^{ax}COCH_2$), 3.60 (s, 3H, OCH_3), 4.11 (td, J = 11.4, 3.4, 1H, $CH^{ax}COC_{arom}$), 7.59 (m, 2H, CH_{arom}), 7.85–8.06 (m, 4H, CH_{arom}), 8.49 (s, 1H, CH_{arom})	26.0 (CH_2CH_2CH), 30.4 (CH_2CH_2CH), 31.8 (CH_2COOCH_3), 41.1 (CH_2CO), 47.8 ($CHCOC_{arom}$), 49.6 ($CHCOCH_2$), 51.6 (OCH_3), 124.0, 127.0–130.2 (C^t_{arom}), 132.5, 133.3, 135.8 (C^q_{arom}), 172.5 ($COOCH_3$), 200.2 (COC_{arom}), 210.3 (CH_2CO)	324 ($M^{+\bullet}$, 27), 169 (5),***5 (100), 137 (4), 127 (24), 77 (4), 55 (5), 41 (6)
5f	3148, 3077, 2938, 2857, 1705, 1661, 1563, 1468, 1402, 1277, 1167, 1002, 918, 891, 780, 594	1.71–1.94 (m, 2H, CH_2CH_2), 2.02–2.21 (m, 2H, CH_2CH_2), 2.75 (m, 2H, $CH_2C=$), 2.45 (m, 2H, CH_2CO), 3.03 (ddd, J = 11.1, 5.4, 5.0, 1H, $CH^{ax}COCH_2$), 3.47 (td, J = 11.1, 4.0, 1H, $CH^{ax}COC_{arom}$), 4.82 (dm, J = 17.1, 1H, $=CH_2$), 4.87 (dm, J = 10.1, 1H, $=CH_2$), 5.74 (ddt, J = 17.1, 10.1, 7.1, 1H, $HC=CH_2$), 6.58 (dd, J = 3.7, 1.7, 1H, CH_{arom}), 7.25 (dd, J = 3.7, 0.7, 1H, CH_{arom}), 7.64 (dd, J = 1.7, 0.7, 1H, CH_{arom})	25.9 (CH_2CH_2CH), 29.5 (CH_2CH_2CH), 31.9 ($CH_2C=$), 41.4 (CH_2CO), 50.2, 50.4 ($CHCOC_{arom}$, $CHCOCH_2$), 112.6 (C^t_{arom}), 116.8 ($=CH_2$), 118.1 (C^t_{arom}), 136.0 ($HC=CH_2$), 147.1 (C^t_{arom}), 152.2, C^q_{arom}), 189.4 (COC_{arom}), 210.9 (CH_2CO)	232 ($M^{+\bullet}$, 63), 137 (94), 136 (72), 123 (88), 122 (47), 119 (24), 110 (31), 107 (49), 95 (100), 91 (21), 81 (17), 79 (20), 67 (34), 55 (36), 41 (35), 39 (40)
5g	3126, 2934, 2862, 1713, 1661, 1466, 1399, 1277, 1169, 1053, 1009, 934, 786, 720, 698, 503	1.68–1.93 (m, 2H, CH_2CH_2), 2.03–2.17 (m, 2H, CH_2CH_2), 2.31–2.50 (m, 2H, CH_2CO), 2.61 (dd, J = 13.8, 3.4, 1H, CH_2Ph), 2.98 (dd, J = 13.8, 8.1, 1H, CH_2Ph), 3.27 (dddd, J = 10.7, 8.1, 3.4, 0.7, 1H, $CH^{ax}COCH_2$), 3.41 (td, J = 10.7, 3.7, 1H, $CH^{ax}COC_{arom}$), 6.53 (dd, J = 3.7, 1H, CH_{arom}), 7.07–7.18 (m, 6H, CH_{arom}), 7.58 (dd, J = 1.7, 0.7, 1H, CH_{arom})	26.1 (CH_2CH_2CH), 29.6 (CH_2CH_2CH), 33.2 (CH_2Ph), 41.6 (CH_2CO), 51.3 ($CHCOPh$), 52.7 ($CHCOCH_2$), 112.6, 118.1, 126.0–129.5 (C^t_{arom}), 140.3 (C^q_{arom}), 146.9 (C^t_{arom}), 152.1 (C^q_{arom}), 189.4 (COC_{arom}), 210.8 (CH_2CO)	282 ($M^{+\bullet}$, 21), 187 (100), 136 (63), 109 (25), 107 (35), 95 (30), 91 (37), 81 (25), 65 (11), 55 (11), 39 (19)
5h	3133, 2960, 2866, 1737, 1710, 1663, 1564, 1435, 1400, 1214, 1165, 1000, 934, 893, 777, 593	1.76–1.96 (m, 2H, CH_2CH_2), 2.08–2.26 (m, 2H, CH_2CH_2), 2.34 (dd, J = 16.8, 3.7, 1H, $CH_2CO_2CH_3$), 2.46 (dd, J = 16.8, 7.4, 1H, CH_2COOCH_3), 2.50 (m, 2H, CH_2CO), 3.34 (ddd, J = 11.8, 7.4, 3.7, 1.0, 1H, $CH^{ax}COCH_2$), 3.63 (s, 3H, OCH_3), 3.65 (td, J = 11.8, 3.7, 1H, $CH^{ax}COC_{arom}$), 6.60 (dd, J = 3.7, 1.7, 1H, CH_{arom}), 7.30 (dd, J = 3.7, 0.7, 1H, CH_{arom}), 7.67 (dd, J = 1.7, 0.7, 1H, CH_{arom})	25.9 (CH_2CH_2CH), 29.8 (CH_2CH_2CH), 31.8 (CH_2COOCH_3), 41.0 (CH_2CO), 47.2 ($CHCOC_{arom}$), 50.4 ($CHCOCH_2$), 51.6 (OCH_3), 112.7, 118.7, 147.4 (C^t_{arom}), 152.0 (C^q_{arom}), 172.3 ($COOCH_3$), 188.9 (COC_{arom}), 209.9 ($CHCO$)	264 ($M^{+\bullet}$, 22), 232 (18), 204 (17), 169 (29), 137 (76), 123 (18), 110 (33), 109 (32), 95 (100), 81 (21), 67 (14), 55 (17), 39 (28)
5i	3094, 2949, 2867, 1733, 1707, 1653, 1520, 1417, 1327, 1271, 1223, 1160, 986, 834, 806, 728	1.77–2.05 (m, 2H, CH_2CH_2), 2.12–2.25 (m, 2H, CH_2CH_2), 2.38 (dd, J = 16.8, 4.1, 1H, $CH_2CO_2CH_3$), 2.46 (dd, J = 16.8, 7.1, 1H, CH_2COOCH_3), 2.50 (m, 2H, CH_2CO), 3.35 (ddd, J = 11.5, 7.1, 4.1, 1.0, 1H, $CH^{ax}COCH_2$), 3.62 (s, 3H, OCH_3), 3.73 (td, J = 11.5, 3.3, 1H, $CH^{ax}COC_{arom}$), 7.18 (dd, J = 5.0, 3.7, 1H, CH_{arom}), 7.74 (dd, J = 5.0, 1.4, 1H, CH_{arom}), 7.78 (dd, J = 3.7, 1.5, 1H, CH_{arom})	25.9 (CH_2CH_2CH), 30.5 (CH_2CH_2CH), 31.7 (CH_2COOCH_3), 41.0 (CH_2CO), 47.7 ($CHCOC_{arom}$), 51.4 ($CHCOCH_2$), 51.6 (OCH_3), 128.5, 132.6, 135.2 (C^t_{arom}), 143.5 (C^q_{arom}), 172.3 ($COOCH_3$), 193.0 (COC_{arom}), 209.8 ($CHCO$)	280 ($M^{+\bullet}$, 9), 169 (16), 137 (29), 126 (7), 111 (100), 109 (11), 83 (6), 81 (9), 67 (6), 55 (8), 41 (9), 39 (21)

[a] Satisfactory microanalyses obtained for **5e**: C −0.41, H −0.41%. For Compounds **5a–d**, **f–i**: C ±0.40, H ±0.22%.

MS (70 eV): m/z (%) = 386 (0.1, $M^{+\cdot}$), 222 (59), 221 (8), 194 (6), 182 (91), 181 (53), 166 (100), 154 (6), 140 (15), 139 (15), 117 (9), 105 (7), 91 15), 77 (10), 56 (7), 42 (36).

^1H NMR (500 MHz, $CDCl_3$): δ = 1.52/1.56 (s, 3H, CCH_3), 1.55/1.60 (s, 3H, CCH_3), 2.41/2.27 (s, 3H, NCH_3), 2.90/2.86 (tm, 1H, J = 3.4, CHN), 4.31/4.18 (dd, 1H, J = 13.1/12.8, 3.4, CH_2O), 4.61/5.82 (s, 1H, $CHC\equiv N$), 4.59/4.64 (dd, 1H, J = 13.2/12.8, 1.8, CHO), 5.24/5.27 (d, 1H, J = 3.4, CHO), 6.49/6.70 (dd, 1H, J = 8.6, 1.8, $CH_{arom.}$), 7.39–7.49/7.30–7.37 (m, 8H, $CH_{arom.}$), 7.54/7.52 (d, 1H, J = 8.6, $CH_{arom.}$), 7.71/7.63 (m, 2H, $CH_{arom.}$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.8/18.4 (CH_3), 29.5/29.7 (CH_3), 33.4/37.5 (NCH_3), 60.2/59.1 (CH_2O), 61.0/57.3 (CHN), 63.0/57.7 ($CC\equiv N$), 74.6/73.4 (CHO), 99.0/99.4 (OCO), 117.6/117.9 ($C\equiv N$), 124.7–128.3 ($C^t_{arom.}$), 131.5 ($C^q_{arom.}$), 132.8/132.5 ($C^q_{arom.}$), 133.1/132.9 ($C^q_{arom.}$), 140.3/139.2 ($C^q_{arom.}$).

$C_{25}H_{26}N_2O_2$ (386.5) calc. C 77.69, H 6.78, N 7.25. found: C 77.36, H 6.63, N 7.25.

*(4S,5S,R/S)-(+)-[N-(2,2-Dimethyl-4-phenyl-1,2-dioxan-5-yl)-N-methylamino](2'-furyl)acetonitrile [(**S,S,R/S**)-**3d**)]:*[17]

According to the general procedure (*S,S*)-**2** was reacted with KCN and furfural (14.4 g). Yield: 40.1 g (82%); light yellow crystals; mp 108°C; $[\alpha]_D^{23}$ = +119.5 (*c* = 1.10, $CHCl_3$); de = 87%.

IR (KBr): ν = 3150, 3130, 3070, 3030, 2990, 2940, 2880, 2810 (m, NCH_3), 2230 (w, C≡N), 1610, 1500, 1470, 1385, 1240, 1205 (s, COC), 1155, 1120, 1080, 1050 (s, COC), 1015, 855, 800, 760, 745, 695 cm^{-1}.

MS (70 eV): *m/z* (%) = 326 (0.2, $M^{+\cdot}$), 162 (100), 157 (9), 134 (24), 133 (36), 119 (18), 106 (62), 94 (11), 91 (14), 81 (22), 77 (9), 57 (26), 32 (21), 42 (22).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.58 [s, 6H, $C(CH_3)_2$]/1.54 (s, 3H, CCH_3), 1.55 (s, 3H, CCH_3), 2.38/2.40 (s, 3H, NCH_3), 2.80/2.89 (td, 1H, *J* = 3.4, 1.3, CHN), 4.22/4.23 (dd, 1H, *J* = 13.1, 3.4, CH_2O), 4.54 (dd, 1H, *J* = 13.1, 1.3, CH_2O), 5.22/5.19 (d, 1H, *J* = 3.5, CHO), 5.67/4.91 (s, 1H, $CHC\equiv N$), 5.83/6.09 (m, 1H, $CH_{fur.}$), 6.20/6.27 (dd, 1H, *J* = 3.4, 2.0, $CH_{fur.}$), 7.21–7.35 (m, 6H, $CH_{arom.}$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.5/18.8 (CH_3), 29.6/29.4 (CH_3), 37.9/35.7 (NCH_3), 52.6 ($CC\equiv N$), 57.3 (CHN), 59.4/59.0 (CH_2O), 73.9/74.3 (CHO), 99.4 (OCO), 108.8/109.4 ($C^t_{fur.}$), 110.3/110.5 ($C^t_{fur.}$), 116.3 ($C\equiv N$), 125.7/126.1 ($C^t_{arom.}$), 127.0/127.2 ($C^t_{arom.}$), 127.9/128.1 ($C^t_{arom.}$), 138.9 ($C^q_{arom.}$), 142.7/143.0 ($C^t_{fur.}$), 147.8 ($C^q_{fur.}$).

$C_{19}H_{22}N_2O_3$ (326.4) calc. C 69.91, H 6.78, N 8.58. found C 69.60, H 6.52, N 8.58.

*(4S,5S,R/S)-(+)-[N-(2,2-Dimethyl-4-phenyl-1,2-dioxan-5-yl)-N-methylamino](2'-thiophenyl)acetonitrile [(**S,S,R/S**)-**3e**]:*[17]

According to the general procedure (*S,S*)-**2** was treated with KCN and 2-thiophenaldehyde (16.8 g). Yield: 37.1 g (72%); colourless solid; mp 106°C; $[\alpha]_D^{23}$ = +116.2 (*c* = 1.00, $CHCl_3$); de = 69%.

IR (KBr): ν = 3120, 3090, 3030, 2990, 2940, 2870, 2810 (m, NCH_3), 2230 (w, C≡N), 1605, 1500, 1440, 1380, 1240, 1200 (s, COC), 1155, 1125, 1080, 1045 (s, COC), 1000, 850, 800, 760, 740, 700 cm^{-1}.

MS (70 eV): *m/z* (%) = 342 (0.2, $M^{+\cdot}$), 327 (25), 178 (100), 163 (6), 145 (24), 137 (25), 122 (48), 97 (12), 91 (7), 42 (24).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.59 [s, 6H, $C(CH_3)_2$]/1.55 (s, 3H, CCH_3), 1.56 (s, 3H, CCH_3), 2.27/2.47 (s, 3H, NCH_3), 2.90/2.94 (m, 1H, CHN), 4.21/4.31 (dm, 1H, *J* = 13.1, CH_2O), 4.57/4.47 (dm, 1H, *J* = 13.1, CH_2O), 5.30/5.23 (m, 1H, CHO), 5.91/4.78 (s, 1H, $CHC\equiv N$), 6.80/6.83 (m, 1H, $CH_{thioph.}$), 6.94 (m, 1H, $CH_{thioph.}$), 7.09/7.16 (m, 1H, $CH_{thioph.}$), 7.26–7.42 (m, 5H, $CH_{arom.}$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.4/18.8 (CH_3), 29.7/29.4 (CH_3), 37.2/33.9 (NCH_3), 53.6/58.2 ($CC\equiv N$), 57.7/60.4 (CHN), 59.1/60.8 (CH_2O), 73.3/74.2 (CHO), 99.4/99.2 (OCO), 117.3/117.0 ($C\equiv N$), 125.4–128.3 ($C^t_{arom.}$), 138.7/138.9 ($C^q_{arom.}$), 140.5/139.5 ($C^q_{arom.}$).

$C_{19}H_{22}N_2O_2S$ (342.5) calc. C 66.63, H 6.47, M 8.18. found C 66.42, H 6.52, N 8.13.

Tandem Michael Adducts 4; General Procedure:

A solution of (*S,S,S/R*)-**3** (10 mmol) in THF (40 mL) was treated with a solution of LDA (11 mmol) in THF (10 mL) at −78°C. After 1 h 2-cyclohexenone (0.96 g, 10 mmol) was added. Upon stirring for 2 h HMPA/THF (22 mL, 1:1) was added by a syringe pump over a period of 30 min. The mixture was treated with the alkyl halide (11 mmol) and allowed to warm up to 0°C overnight. After hydrolysis with saturated NH_4Cl solution the aqueous phase was extracted with Et_2O, the combined organic layers were washed with water and then dried ($MgSO_4$). After evaporation the crude adducts are crystallized from Et_2O/light petroleum bp 40–80°C (0.1–10:1) or THF/Et_2O (1:1, **4d**) at r.t.

Cyclohexanones 5; General Procedure:

The crude or the crystallized tandem Michael/α-alkylation adducts were dissolved in THF (20 mL) and treated with 2 equiv. $AgNO_3$ (2 N aqueous solution). The reaction was monitored by TLC. After stirring overnight, the precipitate was filtered and washed with Et_2O and H_2O. The aqueous phase was extracted with Et_2O and the combined organic layers were washed with brine and dried ($MgSO_4$). Purification by flash chromatography (silica gel, Et_2O/light petroleum, 0.5–2:1) gave analytically pure products.

X-ray Structure Determination of (*S,S,R,R,S*)-4c:

The obtained crystals of the tandem Michael/α-alkylation product **4c** were of sufficient quality. The compound crystallizes in orthorhombic space group $P2_12_12_1$ (19), a = 11.3150(9), b = 13.570(1), c = 19.4991(5) Å. At Z = 4, V = 2994.0 Å^3 and M_r = 530.7 the calculated density is ϱ_{cal} = 1.177 gcm^{-3}, while the total number of electrons per unit cell amounts to F(000) = 1144. $\sin\Theta/\lambda_{max}$ = 0.620 for solution and refinement. The structure was solved by direct methods employing the XTAL3.2 package of crystallographic programs,[19] using GENSIN[20] to generate structure invariant relationships and GENTAN[21] for the general tangent phasing procedure. A total number of 7074 reflections was collected in the range +h+k+l (plus Friedel mates) at 20°C on an ENRAF-NONIUS CAD4 diffractometer. R_{av} = 0.00914. Graphite-monochrombated CuK_α radiation (λ = 1.54179 Å), μ = 5.76 cm^{-1}, no absorption correction. 2927 reflections with $I > 2\sigma(I)$ were used in the final full matrix least-squares refinement process of 353 variables terminating at R = 0.047 (R_w = 0.041, w = $1/\sigma^2$(F)) and a final shift/error smaller than 0.004. Residual electron density ϱ = −0.3/0.2 eÅ^{-3}, Zachariasen parameter[24] r* = 5855. Most hydrogen positions could be located in a difference Fourier map, and remaining H atoms were calculated in idealized positions. All hydrogen positions were subjected to several cycles of isotopic refinement but were excluded from the final refinement steps.

Further details of the X-ray structure determination may be obtained through the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, Eggenstein-Leopoldshafen 2, on quoting the depository number CSD-58824, the authors and the bibliographical data.

This work was supported by the Deutsche Forschungsgemeinschaft (Leibniz prize) and the Fonds der Chemischen Industrie. We thank Boehringer Mannheim GmbH for providing us with "L-Acetonamin" und Bayer AG, BASF AG, Degussa AG and Hoechst AG for donation of chemicals. G.R. thanks Prof. S.R. Hall for his hospitility during his stay at the University of Western Australia, Perth.

(1) Roux, M.-C.; Wartski, L.; Nierlich, M.; Vigner, D.; Lance, M. *Tetrahedron* **1994**, *50*, 8845.
(2) For example see: Heathcock, C.H.; Graham, S.L.; Pirrung, M.C.; Plavac, F.; White, C.T. in *Total Synthesis of Natural Products*, Vol. 5, Apsimon, S. (Ed.); Wiley: New York, 1983.
(3) Seebach, D. *Angew. Chem.* **1979**, *91*, 259; *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 239.
Ager, D.J. in *Umpoled Synthons*, Hase, T.A. (Ed.); Wiley: New York, 1987.
Hebert, E.; Chauffaille, J.; Welvart, Z. *J. Chem. Soc., Perkin Trans. 2* **1982**, 1645.
Jonczyk, A.; Lipiak, D.; Stepniewski, P. Zdrojewski, T. *Bull. Soc. Chim. Belg.* **1988**, *97*, 165.
Jonczyk, A.; Zdrojewski, T. *Synthesis* **1990**, 224.
(4) For a review see: Albright, J.D. *Tetrahedron* **1983**, *39*, 3207.
Enders, D. in *Current Trends in Organic Synthesis*, Nozaki, H. (Ed.); Pergamon: Oxford, 1983; p 151.
Chang, C.-J.; Fang, J.-M.; Liao, L.-F. *J. Org. Chem.* **1993**, *58*, 1754.
Guillaume, D.; Brumbousquet, M.; Aitken, D.J.; Husson, H.P. *Bull. Soc. Chim. Fr.* **1994**, *131*, 391.

(5) Schick, H.; Theil, F.; Jablokoff, H.; Schwarz, S. *Z. Chem.* **1981**, *21*, 68.
Albright, J.D.; McEvoy; F.J.; Morgan, D.B. *J. Heterocycl. Chem.* **1978**, *15*, 881.
Albright, J.D.; McEvoy, F.J.; Morgan, D.B. *J. Org. Chem.* **1979**, *44*, 4597.
(6) Taylor, H.M.; Hauser, C.R. *J. Am. Chem. Soc.* **1960**, *82*, 1790.
Leete, E. *J. Org. Chem.* **1976**, *41*, 3438.
Ahlbrecht, H.; Kompter, H.-M. *Synthesis* **1983**, 645.
Zervos, M.; Wartski, L. *Tetrahedron Lett.* **1984**, *25*, 4641.
Zervos, M.; Wartski, L.; Seyden-Penne, J. *Tetrahedron* **1986**, *42*, 4963.
(7) Leete, E.; Chedekel, M.R.; Bodem, G.B. *J. Org. Chem.* **1972**, *37*, 4465.
(8) Roux, M.-C.; Seyden-Penne, J.; Wartski, L.; Posner, G.H.; Nierlich, M.; Vigner, D.; Lance, M. *J. Org. Chem.* **1993**, *58*, 3969.
(9) Enders, D.; Gerdes, P.; Kipphardt, H. *Angew. Chem.* **1990**, *102*, 226; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 179.
(10) Enders, D.; Mannes, D.; Raabe, G. *Synlett* **1992**, 837.
(11) Lotter, H. Dissertation, Universität Bonn 1985.
(12) Treatment with aqueous $CuSO_4$ solution gave lower yields and sometimes incomplete cleavage.
(13) See also:
Weinges, K.; Brune, G.; Droste, H. *Liebigs Ann. Chem.* **1980**, 212.
Weinges, K.; Blackholm, H. *Chem. Ber.* **1980**, *113*, 3098.
Inaba, T.; Fuijata, M.; Ogura, K. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 3427.
(14) Overman, L.E.; Ricca, D.J. in *Comprehensive Organic Synthesis*, Vol. 2, Trost, B.M.; Fleming, I. (Eds.); Pergamon: London, 1991.
(15) Raabe, G.; Zobel, E.; Fleischhauer, J.; Gerdes, P.; Mannes, D.; Müller, E.; Enders, D. *Z. Naturforsch.* **1991**, *46a*, 275.
(16) Enders, D.; Kirchhoff, J. unpublished results.
(17) Gerdes, P. Dissertation, Technical University of Aachen 1989.
(18) Mannes, D. Dissertation, Technical University of Aachen 1992.
(19) Hall, S.R.; Flack, H.D.; Stewart, J.M. *Xtal3.2 Reference Manual*; Universities of Western Australia, Geneva, and Maryland, Lamb, Perth: 1992.
(20) Subramanian, V.; Hall, S.R. "*GENSIN*" in *Xtal3.2 Reference Manual*; (1992). Hall, S.R.; Flack, H.D. and Stewart, J.M. (Eds.) Universities of Western Australia, Geneva, and Maryland, Lamb, Perth: 1992; p 131.
(21) Hall, S.R. "GENTAN" in *Xtal3.2 Reference Manual*; Hall, S.R.; Flack, H.D. and Stewart, J.M. Eds. Universities of Western Australia, Geneva, and Maryland, Lamb, Perth: 1992; p 139.
(22) Johnson, C.K. *"Ortep"*; Oak Ridge National Laboratory. ORNL-Report 3794, Oak Ridge, Tennesse: 1970.
(23) Flack, H.D. *Acta Cryst.* **1983**, *A 39*, 876.
(24) Larson, A.C. in *The Inclusion of Secondary Extinction in Least-Squares Refinement of Crystal Structures*; Crystallographic Computing Ahmed, F.R.; Hall, S.R.; Huber, C.P. (Eds.) Munksgaard: Copenhagen, 1969; p 291.