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New Methods and Reagents in Organic Synthesis. 17.[1] Trimethylsilyldiazomethane($TMSCHN_2$) as a Stable and Safe Substitute for Hazardous Diazomethane. Its Application to the Arndt–Eistert Synthesis[2]

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Although diazomethane is used in the Arndt–Eistert synthesis, it is both highly toxic and also explosive, and hence should be very carefully handled. In place of this hazardous diazomethane, stable and safe trimethylsilyldiazomethane ($TMSCHN_2$) was found to be very useful for the Arndt–Eistert synthesis. $TMSCHN_2$ was easily acylated with a carboxylic acid chloride in tetrahydrofuran–acetonitrile, and thermal treatment of the acylated product in benzyl alcohol and 2,4,6-trimethylpyridine smoothly gave the benzyl ester of a homologated acid. Nucleophiles other than benzyl alcohol could also be used. $TMSCHN_2$ may also be able to replace diazomethane in other areas of chemistry.

Keywords——trimethylsilyldiazomethane; Arndt–Eistert synthesis; Wolff rearrangement; acylation; carboxylic acid; benzyl alcohol; diazomethane

Diazomethane is a well-known reagent in organic synthesis, and its use for synthetic purposes has been well explored.[3] However, it is notorious because of its highly toxic, thermally labile, and potentially explosive nature. Hence reactions using diazomethane should be very carefully carried out on a small scale, and its industrial use has not been possible.

It is already known that an α-hetero atom containing a d-orbital, such as silicon, sulfur, or phosphorus, stabilizes a diazomethyl function to heat owing to a $p\pi$–$d\pi$ resonance between carbon and the adjacent hetero atom. Thus, with a few exceptions, silyldiazomethanes,[4] sulfonyldiazomethanes,[5,6] or phosphoryldiazomethanes[5,7] are thermally stable and non-explosive derivatives of diazomethane. Although their chemical properties have been studied to some extent, only a few reports have dealt with their synthetic uses.

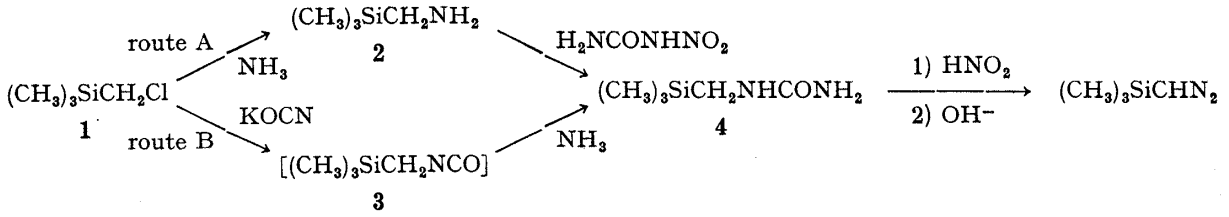


Chart 1

We now report the synthetic utility of stabilized diazomethane analogs. Our attention was first directed to the synthetic use of trimethylsilyldiazomethane ($TMSCHN_2$, $(CH_3)_3SiCHN_2$). Its practical synthesis and some investigations of its physical and chemical properties were ingeniously carried out by Seyferth and co-workers in 1968.[8] Although some different preparations of $TMSCHN_2$ have been reported,[9] we repeated Seyferth's method[8] shown as route A in Chart 1 since it seemed to be the method of choice. However, we found that the amination of chloromethyltrimethylsilane (**1**) afforded trimethylsilylmethylamine(**2**) in low yield.[10] Thus, we devised route B, in which **1** was allowed to react with potassium cyanate, followed by treatment with ammonia. The resulting urea **4** was nitrosated and then hydrolyzed according to Seyferth's method[8] to give a mixture of $TMSCHN_2$ and hexamethyl-

disiloxane in a ratio of *ca.* 7: 3. We used this mixture for the reaction below because their separation was not as easy as reported,[8] and hexamethyldisiloxane seemed to have no influence on the reaction.

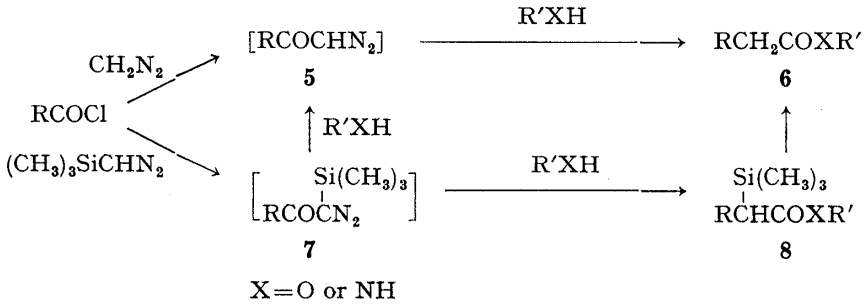
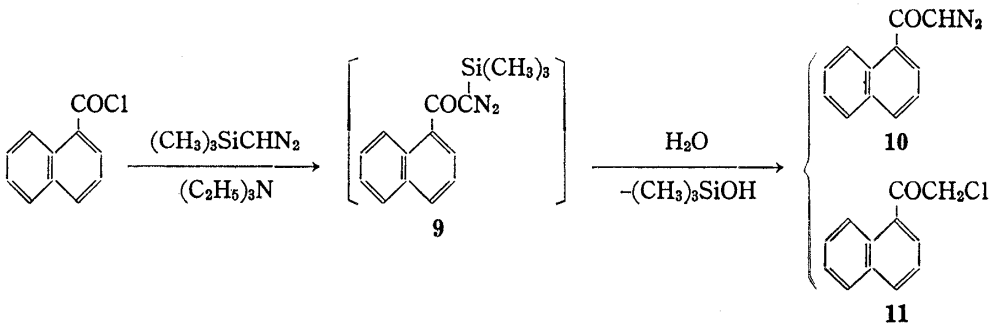


Chart 2

As our first application of $TMSCHN_2$ to organic synthesis, we chose the Arndt–Eistert synthesis,[11] which is one of the most important and useful applications of diazomethane to organic synthesis. As is well known, the Arndt–Eistert synthesis involves reaction of a carboxylic acid chloride with diazomethane followed by the Wolff rearrangement of the resulting diazoketone **5** in the presence of a suitable nucleophile, giving a carboxylic acid derivative of the next higher homolog **6**. We hoped that the replacement of hazardous diazomethane with safe and stable $TMSCHN_2$ in the Arndt–Eistert synthesis would first give a trimethylsilyldiazoketone **7**. The diazoketone **7** would be transformed to the homologous acid derivative **6** *via* **5**, which would be produced by the action of a nucleophile on **7**. Alternatively, the Wolff rearrangement of **7** would give an α-trimethylsilylated homologous acid derivative **8**, which would furnish **6** on a suitable aqueous treatment, as shown in Chart 2.

In fact, treatment of 1-naphthoyl chloride with $TMSCHN_2$ in the presence of triethylamine followed by aqueous work-up gave 1-(diazoacetyl)naphthalene(**10**) accompanied with a trace amount of 1-(chloroacetyl)naphthalene(**11**). The results are summarized in Table I. Tetrahydrofuran as well as acetonitrile seemed to be the solvent of choice.

TABLE I.

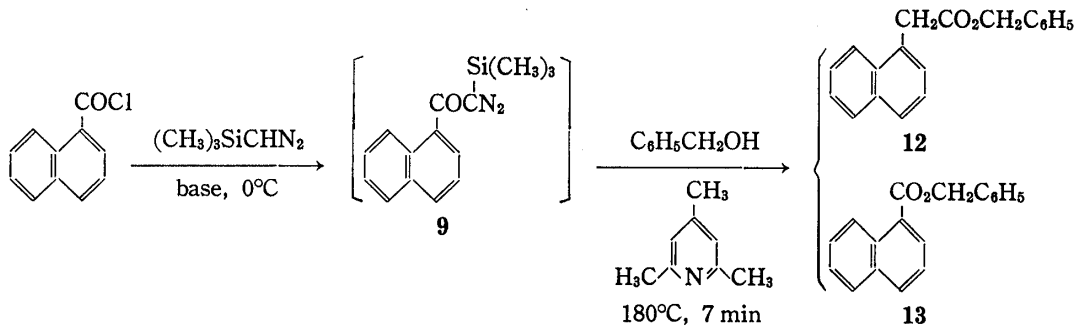


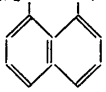
Reaction solvent	Reaction conditions		Yield (%)	
	Temp. (°C)	Time (h)	**10**	**11**
Diethyl ether	0	96	28	Trace
Tetrahydrofuran	0	96	74	Trace
Tetrahydrofuran	Room temp.	46	56	5.3
Dimethoxyethane	0	72	71	Trace
Acetonitrile	0	24	74	Trace
Benzene	0	96	61	Trace

Intermediacy of the α-trimethylsilyldiazoketone **9** in the reaction was proved by the infrared spectrum of the crude diazoketone, which showed absorptions at 1250 and 840 cm^{-1} due to the Si–CH_3 group in addition to the bands at 2080 (N_2) and 1615 cm^{-1} (CO). No absorption at about 1050 cm^{-1} due to the Si–O bond was observed. Treatment of **9** with benzyl alcohol in benzene at room temperature for 1 hour afforded a compound whose infrared spectrum was identical with that of **10**.

Next, we investigated a one-pot conversion of 1-naphthoyl chloride to benzyl 1-naphthylacetate (**12**) in the Arndt–Eistert manner. Acylation of $TMSCHN_2$ was carried out as described above, and the crude acylated product was heated in a mixture of benzyl alcohol and 2,4,6-trimethylpyridine at 180°C for 7 minutes.[12] As shown in Table II, the main product was benzyl 1-naphthylacetate (**12**), and benzyl 1-naphthoate (**13**), derived from 1-naphthoyl chloride by the action of benzyl alcohol, was also obtained in a small quantity.

Table II.



Acylation			Yield (%)	
Solvent	Base	Time (h)	**12**	**13**
Tetrahydrofuran	$(C_2H_5)_3N$	96	68	18
Acetonitrile	$(C_2H_5)_3N$	24	68	Trace
Tetrahydrofuran–acetonitrile (1 : 1)	$(C_2H_5)_3N$	30	78	7
Tetrahydrofuran–acetonitrile (1 : 1)	$(CH_3)_2N$ $N(CH_3)_2$ 	24	82	Trace

Various other aromatic acid chlorides efficiently reacted with $TMSCHN_2$ in the presence of triethylamine at 0°C during 24—48 hours in tetrahydrofuran–acetonitrile (1 : 1). Although acylation of $TMSCHN_2$ with aliphatic and alicyclic acid chlorides afforded a complicated mixture of products under the same reaction conditions, the use of 2 equivalents of $TMSCHN_2$ without triethylamine allowed the reaction to proceed smoothly. The crude acylated products easily underwent the Wolff rearrangement in the presence of benzyl alcohol and 2,4,6-trimethylpyridine at 180°C for 7 minutes to give the benzyl esters of the homologated acids, as shown in Table III. The Wolff rearrangement of the acylated product derived from N-benzyloxycarbonyl-L-proline proceeded with retention of configuration.[13]

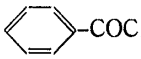
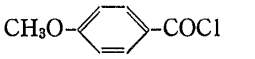
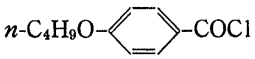
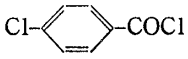
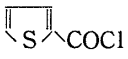
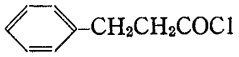
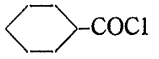
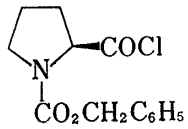
Finally, the Arndt–Eistert synthesis using nucleophiles other than benzyl alcohol was investigated briefly. As summarized in Table IV, the diazoketone **9** derived from 1-naphthoyl chloride smoothly underwent the Wolff rearrangement in the presence of ethanol, *tert*-butyl alcohol, or phenol to give esters of 1-naphthylacetic acid. The Wolff rearrangement of **9** in the presence of aniline afforded 1-naphthylacetanilide in good yield.

Although optimum conditions for this modified Arndt–Eistert synthesis have yet to be established, the above experimental results reveal that reasonable overall yields can be obtained

using $TMSCHN_2$. If $TMSCHN_2$ is used in place of diazomethane for the Arndt–Eistert synthesis, it is not necessary that "one should wear heavy gloves and goggles and work behind a safety screen or a hood door with safety glass, ..., ground joints and sharp surfaces should be avoided. Thus all glass tubes should be carefully fire-polished, connections should be made with rubber stoppers, ..."[14] Since $TMSCHN_2$ is

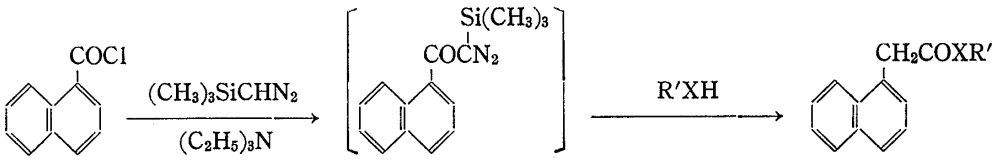
Table III.

$$RCOCl \xrightarrow[\text{ii) } C_6H_5CH_2OH]{\text{i) } (CH_3)_3SiCHN_2} RCH_2CO_2CH_2C_6H_5$$

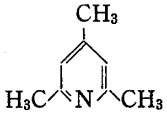
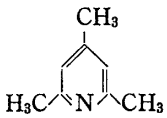
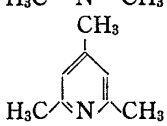
RCOCl	$TMSCHN_2$ (equiv.)	Reaction time for acylation (h)	Yield (%) of $RCH_2CO_2CH_2C_6H_5$
	1.25	24	63
	1.5	48	60
	2	48	76
	1.25	24	66
	1.5	48	64
	2.2	4	72
	2.2	6	59
	2.2	5	77[a]

a) Based on N-benzyloxycarbonyl-L-proline.

Table IV.



9

R'XH	Reaction conditions for rearrangement: Additive	Temp. (°C)	Time	Yield (%)
C_2H_5OH		105—110	24 h	66
tert-C_4H_9OH		105—110	24 h	69
C_6H_5OH		100—105	16 h	50
$C_6H_5NH_2$	—	180—185	7 min	80

both non-explosive and non-mutagenic,[15] it can be used for industrial purposes without any hazard in contrast to diazomethane. Furthermore, since $TMSCHN_2$ exists as a stable liquid at room temperature, it is very easily managed for stoichiometric use.[16]

$TMSCHN_2$ may replace diazomethane and create added flexibility in both organic synthesis and other areas of chemistry. Additional experiments are under way to determine the full potential of this reagent.[17–19]

Experimental

^1H-Nuclear magnetic resonance (NMR) spectra were recorded on a JEOL JNM-MH-100 spectrometer with tetramethylsilane as an internal standard. Infrared (IR) spectra were obtained using a JASCO IRA-2 spectrometer. Optical rotations were measured with a JASCO DIP-140 unit. All melting points are uncorrected. Silica gel (Silic AR CC-7 special, Mallinckrodt), and alumina (activated, Wako Pure Chemical Industries, Ltd.) were used for column chromatography. Preparative layer chromatography (PLC) was carried out on plates (20 cm × 20 cm, 2 mm thick) precoated with silica gel $60F_{254}$ (Merck). Tetrahydrofuran (THF) and diethyl ether were dried by distillation from lithium aluminum hydride prior to use. Acetonitrile was dried by distillation from phosphorus pentoxide.

All esters obtained by the modified Arndt–Eistert synthesis were hydrolyzed with alkali to give known acids, which were identified by spectroscopic comparison with authentic samples.

N-(Trimethylsilylmethyl)urea (4)——A mixture of potassium cyanate (33.1 g, 90% purity, 367 mmol), chloromethyltrimethylsilane (30 g, 245 mmol) and tetraethylammonium iodide (2.9 g, 11.3 mmol) in dimethylformamide (240 ml) was heated to 100—105°C within 20 min. The mixture was stirred at the same temperature for 40 min and then cooled to 0°C. Ammonia gas was bubbled into the mixture at 0—15°C for 1 h. The inorganic salt was removed by filtration, and washed with benzene. The filtrate and washings were combined, and concentrated *in vacuo*. Water was added to the residue and the mixture was extracted with benzene–ethyl acetate (1: 1). The extract was washed with water and saturated aqueous sodium chloride, and dried over magnesium sulfate. The solvent was evaporated, and the residue was recrystallized from benzene to give **4** (21.6 g, 60%) as colorless needles, mp 114—116°C (lit.,[8] mp 113—114°C). IR ν_{max}^{Nujol} cm^{-1}: 3420, 3350, and 3220 (NH), 1650 (C=O), 1250 and 860 ($SiCH_3$).

Trimethylsilyldiazomethane (TMSCHN$_2$)——$TMSCHN_2$ was prepared from the urea **4** by nitrosation followed by hydrolysis according to Seyferth's method.[8] NMR analysis of the product showed that it was a mixture of $TMSCHN_2$ and hexamethyldisiloxane (*ca.* 7: 3). NMR of $TMSCHN_2$ (δ in benzene): −0.01 (s, CH_3), 2.23 (s, CHN_2). NMR of hexamethyldisiloxane (δ in benzene): 0.11 (s, CH_3). This mixture was used for the Arndt–Eistert synthesis.

1-(Diazoacetyl)naphthalene (10)——General procedure: To a mixture of $TMSCHN_2$ (3 mmol) and triethylamine (303 mg, 3 mmol) in an organic solvent (10 ml) was added dropwise 1-naphthoyl chloride (458 mg, 2.4 mmol) at 0°C. The mixture was stirred at 0°C for 24—96 h, then evaporated *in vacuo*. Saturated aqueous sodium bicarbonate was added to the residue and the mixture was extracted with diethyl ether. The ethereal extracts were washed with water and saturated aqueous sodium chloride, and dried over sodium sulfate. Evaporation of the solvent gave a yellow oil, which was purified by alumina column chromatography with benzene. The first fraction to be eluted contained 1-(chloroacetyl)naphthalene (**11**). IR ν_{max}^{Film} cm^{-1}: 1695 (C=O). NMR (δ in $CDCl_3$): 4.80 (2H, s, CH_2Cl), 7.40—8.76 (7H, m, aromatic H).

The second fraction to be eluted contained 1-(diazoacetyl)naphthalene (**10**). IR ν_{max}^{Nujol} cm^{-1}: 2110 (N_2), 1613 (C=O). NMR (δ in $CDCl_3$): 5.72 (1H, s, CHN_2), 7.36—8.64 (7H, m, aromatic H). Recrystallization from benzene–hexane gave yellow prisms, mp 52—53°C (lit.[20] mp 54—55°C).

The reaction conditions and yields are shown in Table I.

Benzyl 1-Naphthylacetate (12)——General procedure: To a mixture of $TMSCHN_2$ (3 mmol) and triethylamine (303 mg, 3 mmol) in an organic solvent (10 ml) was added dropwise 1-naphthoyl chloride (458 mg, 2.4 mmol) at 0°C. The mixture was stirred at 0°C for 24—96 h, and evaporated *in vacuo*. Benzyl alcohol (2 ml) and 2,4,6-trimethylpyridine (2 ml) were added to the residue and the mixture was stirred at 180—185°C for 7 min. Benzene was added, and the mixture was successively washed with 10% aqueous citric acid, water, and saturated aqueous sodium chloride. After the mixture had been dried over magnesium sulfate, the solvent and excess benzyl alcohol were evaporated *in vacuo*. The residual oil was purified by silica gel column chromatography with benzene–hexane–diethyl ether (10: 20: 1). The first fraction to be eluted contained benzyl 1-naphthoate (**13**). IR ν_{max}^{Film} cm^{-1}: 1705 (C=O). NMR (δ in $CDCl_3$): 5.48 (2H, s, OCH_2), 7.24—9.08 (12H, m, aromatic H).

The second fraction to be eluted contained benzyl 1-naphthylacetate (**12**). IR ν_{max}^{Film} cm^{-1}: 1730 (C=O). NMR (δ in $CDCl_3$): 4.12 (2H, s, CH_2CO), 5.13 (2H, s, OCH_2), 7.16—8.17 (12H, m, aromatic H).

The reaction conditions and yields are shown in Table II.

Benzyl Arylacetates——General procedure: To a mixture of $TMSCHN_2$ (3—4.8 mmol) and triethylamine (3 mmol) in tetrahydrofuran (THF)–acetonitrile (1: 1, 10 ml) was added dropwise a carboxylic acid

chloride (2.4 mmol) at 0°C. The mixture was stirred at 0°C for 24—48 h, then evaporated *in vacuo*. Benzyl alcohol (2 ml) and 2,4,6-trimethylpyridine (2 ml) were added to the residue. The mixture was stirred at 180—185°C for 7 min, and then worked up as usual. The crude product was purified by silica gel column chromatography or PLC to give a corresponding benzyl arylacetate. The reaction conditions in each case are shown in Table III.

Benzyl Phenylacetate——Prepared from $TMSCHN_2$ (3 mmol), benzoyl chloride (337 mg, 2.4 mmol), and triethylamine (303 mg, 3 mmol). A pale yellow oil (335 mg, 63%), purified by silica gel column chromatography with benzene–hexane–diethyl ether (10: 10: 1). IR ν_{max}^{Film} cm^{-1}: 1738 (C=O). NMR (δ in $CDCl_3$): 3.64 (2H, s, CH_2CO), 5.12 (2H, s, CH_2O), 6.80—7.28 (10H, m, aromatic H).

Benzyl 4-Methoxyphenylacetate——Prepared from $TMSCHN_2$ (3.6 mmol), 4-methoxybenzoyl chloride (410 mg, 2.4 mmol) and triethylamine (303 mg, 3 mmol). A pale yellow oil (370 mg, 60%), purified by silica gel column chromatography with benzene–hexane–diethyl ether (1: 1: 1). IR ν_{max}^{Film} cm^{-1}: 1725 (C=O). NMR (δ in $CDCl_3$): 3.60 (2H, s, CH_2CO), 3.76 (3H, s, OCH_3), 5.12 (2H, s, OCH_2), 6.80—7.28 (9H, m, aromatic H).

Benzyl 4-*n*-Butoxyphenylacetate——Prepared from $TMSCHN_2$ (4.8 mmol), 4-*n*-butoxybenzoyl chloride (510 mg, 2.4 mmol), and triethylamine (303 mg, 3 mmol). A pale yellow oil (543 mg, 76%), purified by silica gel column chromatography with benzene–hexane–chloroform (1: 1: 1). IR ν_{max}^{Film} cm^{-1}: 1735 (C=O). NMR (δ in $CDCl_3$): 0.96 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 1.16—1.88 (4H, m, $C\underline{H}_2C\underline{H}_2CH_3$), 3.60 (2H, s, CH_2CO), 3.92 (2H, t, J=7 Hz, $OC\underline{H}_2CH_2$), 5.10 (2H, s, CO_2CH_2), 6.80—7.28 (9H, m, aromatic H).

Benzyl 4-Chlorophenylacetate——Prepared from $TMSCHN_2$ (3 mmol), 4-chlorobenzoyl chloride (420 mg, 2.4 mmol), and triethylamine (303 mg, 3 mmol). A pale yellow oil (413 mg, 66%), purified by PLC (benzene–hexane–diethyl ether=10: 10:1). IR ν_{max}^{Film} cm^{-1}: 1735 (C=O). NMR (δ in $CDCl_3$): 3.60 (2H, s, CH_2CO), 5.12 (2H, s, OCH_2), 7.20 (4H, s, aromatic H), 7.28 (5H, s, aromatic H).

Benzyl Thiophene-2-acetate——Prepared from $TMSCHN_2$ (3.6 mmol), thiophene-2-carbonyl chloride (352 mg, 2.4 mmol), and triethylamine (303 mg, 3 mmol). A pale yellow oil (359 mg, 64%), purified by PLC (benzene–hexane–chloroform=1: 1: 1). IR ν_{max}^{Film} cm^{-1}: 1735 (C=O). NMR (δ in $CDCl_3$): 3.88 (2H, s, CH_2CO), 5.16 (2H, s, OCH_2), 6.88—7.28 (3H, m, thienyl), 7.32 (5H, s, phenyl H).

Benzyl 4-Phenylbutyrate——To a solution of $TMSCHN_2$ (5.3 mmol) in THF–acetonitrile (1: 1, 10 ml) was added dropwise 3-phenylpropionyl chloride (405 mg, 2.4 mmol) at 0°C. The mixture was stirred at 0°C for 4 h, then evaporated *in vacuo*. Benzyl alcohol (2 ml) and 2,4,6-trimethylpyridine (2 ml) were added to the residue. The mixture was stirred at 180—185°C for 7 min, and then worked up as usual. The crude product was purified by silica gel column chromatography with benzene–hexane–diethyl ether (20: 20: 1) to give benzyl 4-phenylbutyrate (442 mg, 72%) as a pale yellow oil. IR ν_{max}^{Film} cm^{-1}: 1730 (C=O). NMR (δ in $CDCl_3$): 1.92 (2H, q, J=8 Hz, $CH_2C\underline{H}_2CH_2$), 2.36 (2H, t, J=8 Hz, CH_2CO), 2.64 (2H, t, J=8 Hz, CH_2-$C\underline{H}_2Ph$), 5.12 (2H, s, OCH_2), 7.04—7.36 (10H, m, aromatic H).

Benzyl Cyclohexylacetate——Prepared from $TMSCHN_2$ (5.3 mmol) and cyclohexylcarbonyl chloride (352 mg, 2.4 mmol) as described for the preparation of benzyl 4-phenylbutyrate. A pale yellow oil (326 mg, 59%), purified by PLC (benzene–hexane–diethyl ether=20: 20: 1). IR ν_{max}^{Film} cm^{-1}: 1735 (C=O). NMR (δ in $CDCl_3$): 0.72—2.04 (11H, m, cyclohexyl H), 2.24 (2H, d, J=8 Hz, CH_2CO), 5.12 (2H, s, OCH_2), 7.34 (5H, s, aromatic H).

Benzyl (*S*)-1-Benzyloxycarbonylpyrrolidine-2-acetate——To a mixture of 1-benzyloxycarbonyl-L-proline (598 mg, 2.4 mmol) and dimethylformamide (1 drop) in methylene chloride (4 ml) was added dropwise oxalyl chloride (0.3 ml, 3.6 mmol) at 0°C. The mixture was stirred at 0°C for 15 min, and at room temperature for 1 h, and was then evaporated *in vacuo*. The residue was dissolved in THF–acetonitrile (1: 1, 10 ml), and $TMSCHN_2$ (5.3 mmol) was added at 0°C. The mixture was stirred at 0°C for 5 h, then evaporated *in vacuo*. Benzyl alcohol (2 ml) and 2,4,6-trimethylpyridine (2 ml) were added to the residue. The mixture was stirred at 180—185°C for 7 min, and then worked up as usual. The crude product was purified by PLC (benzene–chloroform–diethyl ether=2: 2: 1) to give benzyl (*S*)-1-benzyloxycarbonylpyrrolidine-2-acetate (656 mg, 77%) as a pale yellow oil. IR ν_{max}^{Film} cm^{-1}: 1725 (C=O), 1695 (C=O). NMR (δ in $CDCl_3$): 1.60—2.38 (4H, m, CH_2CH_2), 2.50—2.98 (2H, m, CH_2CO), 3.24—3.56 (2H, m, NCH_2), 4.08—4.36 (1H, m, NCH), 5.08 (2H, s, OCH_2), 5.12 (2H, s, OCH_2), 7.32 (10H, s, aromatic H).

(*S*)-1-Benzyloxycarbonylpyrrolidine-2-acetic Acid——A mixture of benzyl (*S*)-1-benzyloxycarbonylpyrrolidine-2-acetate (466 mg, 1.32 mmol) and potassium carbonate (630 mg, 4.6 mmol) in methanol (15 ml) and water (0.7 ml) was heated under reflux for 6 h, then evaporated *in vacuo*. The residue was made acidic with 10% aqueous hydrochloric acid and extracted with ethyl acetate. The extract was washed with water, dried over magnesium sulfate, and evaporated. The residual solid was recrystallized from diisopropyl ether to give (*S*)-1-benzyloxycarbonylpyrrolidine-2-acetic acid (215 mg, 62%) as colorless prisms, mp 76—77°C (lit.[13] mp 74.5—75.5°C). IR ν_{max}^{Nujol} cm^{-1}: 1725 (C=O), 1660 (C=O). NMR (δ in $CDCl_3$): 1.60—2.16 (4H, m, CH_2CH_2), 2.24—3.20 (2H, m, CH_2CO), 3.48 (2H, t, J=7 Hz, NCH_2), 4.12—4.44 (1H, m, NCH), 5.14 (2H, s, OCH_2), 7.36 (5H, s, aromatic H), 10.4 (1H, broad s, CO_2H). $[\alpha]_D^{25}=-34.02°$ (c=1.0, CH_3CO_2H) (lit.[13] $[\alpha]_D=-35.3°$ (c=1.0, CH_3CO_2H)).

Ethyl 1-Naphthylacetate——To a mixture of $TMSCHN_2$ (3 mmol) and triethylamine (303 mg, 3 mmol) in THF–acetonitrile (1: 1, 10 ml) was added dropwise 1-naphthoyl chloride (458 mg, 2.4 mmol) at 0°C.

The mixture was stirred at 0°C for 30 h, then evaporated *in vacuo*. Ethyl alcohol (2 ml) and 2,4,6-trimethylpyridine (2 ml) were added to the residue. The mixture was stirred at 105—110°C for 24 h, and then worked up as usual. The crude product was purified by PLC (benzene–hexane–diethyl ether=10: 10: 1) to give ethyl 1-naphthylacetate (340 mg, 66%) as a pale yellow oil. IR ν_{max}^{Film} cm^{-1}: 1725 (C=O). NMR (δ in $CDCl_3$): 1.20 (3H, t, J=7 Hz, CH_2CH_3), 4.04 (2H, s, CH_2CO), 4.14 (2H, q, J=7 Hz, CH_2CH_3), 7.32—8.12 (7H, m, aromatic H).

***tert*-Butyl 1-Naphthylacetate**——To the crude acylated product prepared from 1-naphthoyl chloride (458 mg, 2.4 mmol) as described for the preparation of ethyl 1-naphthylacetate were added *tert*-butyl alcohol (2 ml) and 2,4,6-trimethylpyridine (2 ml). The mixture was stirred at 105—110°C for 24 h, and then worked up as usual. The crude product was purified by PLC (benzene–hexane–diethyl ether=20: 20: 1) to give *tert*-butyl 1-naphthylacetate (401 mg, 69%) as a pale yellow oil. IR ν_{max}^{Film} cm^{-1}: 1730 (C=O). NMR (δ in $CDCl_3$): 1.40 (9H, s, $CH_3\times3$), 3.96 (2H, s, CH_2CO), 7.32—8.16 (7H, m, aromatic H).

Phenyl 1-Naphthylacetate——To the crude acylated product prepared from 1-naphthoyl chloride (550 mg, 2.88 mmol) as described above were added phenol (2.5 ml) and 2,4,6-trimethylpyridine (2.5 ml). The mixture was stirred at 100—105°C for 16 h. Benzene was added, and the mixture was washed successively with 10% aqueous citric acid, water, 5% aqueous sodium hydroxide, water, and saturated aqueous sodium chloride. After the mixture had been dried over magnesium sulfate, the solvent was evaporated. The residual oil was purified by PLC (benzene–hexane–diethyl ether=20: 20: 1) to give phenyl 1-naphthylacetate (376 mg, 50%) as a pale yellow oil. IR ν_{max}^{Film} cm^{-1}: 1750 (C=O). NMR (δ in $CDCl_3$): 4.28 (2H, s, CH_2CO), 6.96—8.16 (12H, m, aromatic H).

1-Naphthylacetanilide——To the crude acylated product prepared from 1-naphthoyl chloride (458 mg, 2.4 mmol) as described above was added aniline (4 ml). The mixture was stirred at 180—185°C for 7 min, and then worked up as usual. The crude product was purified by PLC (chloroform) to give 1-naphthylacetanilide (499 mg, 80%), which was recrystallized from benzene–hexane to afford colorless needles, mp 156—157°C. IR ν_{max}^{Nujol} cm^{-1}: 3290 (NH), 1660 (C=O). NMR (δ in $CDCl_3$): 4.16 (2H, s, CH_2CO), 6.88—8.16 (12H, m, aromatic H). *Anal.* Calcd for $C_{18}H_{15}NO$: C, 82.73; H, 5.79; N, 5.36. Found: C, 82.78; H, 5.61; N, 5.09.

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References and Notes

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