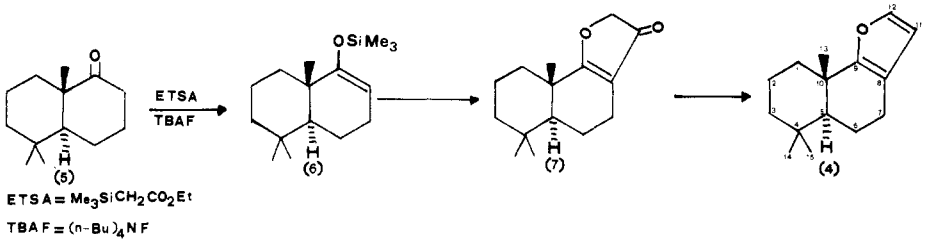
Scheme III



Synthesis of β-Furanone 2. Compound 1 (226 mg, 1 mmol) was dissolved in 8 mL of anhydrous diethyl ether, placed in a flask equipped with a dry argon inlet, and cooled at −15 °C. To the stirred solution was added 0.63 mL (1 mmol) of a 1.60 M ethereal solution of methyllithium. After 1.30 h at −15 °C, 1.5 mL of anhydrous hexamethylphosphoric triamide and 0.7 mL (8.8 mmol) of freshly distilled chloroacetyl chloride were added. The mixture was reacted 30 min at −15 °C and 1 h at room temperature.

The reaction mixture was poured into a slurry of ammonia and crushed ice, stirred for 20 min, and then extracted three times with 20 mL of diethyl ether. The combined extracts were washed with water and dried (Na_2SO_4). After evaporation at reduced pressure, 200 mg of product was obtained which was chromatographed on a Florisil (6 g) column. By elution with *n*-pentane–ethyl acetate (95:5 v/v) there was obtained 160 mg (82% yield) of pure **2**: oil; IR (liquid film) 1700, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.50 (s, 2 H, OCH_2CO), 0.95 (s, 9 H, $(CH_3)_3C$). Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.22; H, 9.28. Found: C, 74.18; H, 9.30.

Synthesis of Furan 3. In a 10-mL flask equipped with a dry argon inlet was added 40 mg (0.33 mmol) of 9-BBN to a stirred solution of 59 mg (0.30 mmol) of **2** in 6 mL of anhydrous THF at 0 °C. After 1 h at 0 °C, the cooling bath was removed and the reaction mixture left to react at room temperature for 5 h.

Methanol (0.18 mL) was added, and the solvents were evaporated under reduced pressure. The residue was dissolved in *n*-pentane, and 0.02 mL of ethanolamine was added. The mixture was filtered and the precipitate washed several times with *n*-pentane. On evaporation of the combined extracts, a crude product (56 mg) was obtained which was purified by silica gel (2 g) chromatography. Elution with *n*-pentane afforded pure **3**: 52 mg (97% yield); oil; IR (liquid film) 1505 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.30 (d, 1 H, J = 2 Hz, OCH=CH), 6.23 (d, 1 H, J = 2 Hz, OCH=CH), 0.95 (s, 9 H, $(CH_3)_3C$). Anal. Calcd for $C_{12}H_{18}O$: C, 80.90; H, 10.12. Found: C, 80.85; H, 10.15.

Synthesis of the Trimethylsilyl Enol Ether 6. In a 10-mL flask equipped with a dry argon inlet and reflux condenser was dissolved 210 mg (1.08 mmol) of **5** in 3 mL of anhydrous THF, and 173 (1.08 mg) of ethyl (trimethylsilyl)acetate was added together with a catalytic amount of tetra-*n*-butylammonium fluoride. The reaction mixture was refluxed for 4 h.

The solvent was evaporated under vacuum, and the residue, after dilution with 10 mL of water, was extracted five times with 5 mL each of diethyl ether. The organic extracts were dried over Na_2SO_4, and after evaporation at reduced pressure, 350 mg of crude product was obtained which was purified by Florisil (20 g) chromatography. By elution with pentane, 210 mg (73%) of pure **6** was obtained: oil; IR (CCl_4) 1660 cm^{-1}; ^1H NMR ($CDCl_3$; numbering of pallescensin A has been adopted) δ 4.54 (t, 1 H, J = 3.9 Hz, H_8), 2.00 (m, 2 H, H_7), 1.06 (s, 3 H, H_{13}), 0.90 (s, 3 H, H_{14} or H_{15}), 0.86 (s, 3 H, H_{14} or H_{15}), 0.17 (s, 9 H, $SiMe_3$). Anal. Calcd for $C_{16}H_{30}OSi$: C, 72.18; H, 11.28. Found: C, 72.12; H, 11.24.

Synthesis of the β-Furanone 7. The procedure described for the preparation of compound **2** was followed to synthesize the β-furanone **7**. From the compound **6** (90 mg, 0.34 mmol), after purification on a Florisil (5 g) column [*n*-pentane–ethyl acetate (95:5 vol) as eluant], was obtained pure **7**: 65 mg (81% yield); oil; IR (liquid film) 1700, 1625 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.40 (s, 2 H, H_{12}), 1.28, (s, 3 H, H_{13}), 0.96 (s, 3 H, H_{14} or H_{15}), 0.92 (s, 3 H, H_{14} or H_{15}); mass spectrum, m/e (relative intensity) 234 (M^+, 60), 123 (32), 112 (100), 111 (70), 91 (30). Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.92; H, 9.40. Found: C, 76.88; H, 9.42.

Synthesis of Pallescensin A (4). Pallescensin A (**4**) was synthesized by following the same procedure described for the preparation of compound **3**. From the β-furanone **7** (38 mg, 0.16 mmol), after purification on a silica gel (1.2 g) column with *n*-pentane as the eluant, was obtained pure pallescensin A: 34 mg (97% yield); oil; IR (liquid film) 1505 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.07 (d, 1 H, J = 2 Hz, H_{12}), 5.99 (d, 1 H, J = 2 Hz, H_{11}), 1.17 (s, 3 H, H_{13}), 0.94 (s, 3 H, H_{14} or H_{15}), 0.91 (s, 3 H, H_{14} or H_{15}); ^{13}C NMR ($CDCl_3$) δ 159.58 (s, C-9), 139.83 (d, C-12), 113.49 (s, C-8), 109.92 (d, C-11), 52.33 (d, C-5), 41.91 (t, C-7), 36.53 (s, C-10), 35.56 (t), 33.38 (q, C-13), 32.95 (s, C-4), 22.71 (t), 21.34 (2 q, C-14 and C-15), 19.54 (t), 18.60 (t); mass spectrum, m/e (relative intensity) 218 (M^+, 22), 203 (100), 147 (38), 135 (22), 69 (49). Anal. Calcd for $C_{15}H_{22}O$: C, 82.57; H, 10.09. Found: C, 82.54; H, 10.06.

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Registry No. 1, 19980-19-9; 2, 80926-07-4; 3, 80926-08-5; (±)-4, 73210-04-5; (±)-5, 65556-24-3; (±)-6, 80926-09-6; (±)-7, 80926-10-9.

Esterification of N-Protected α-Amino Acids with Alcohol/Carbodiimide/4-(Dimethylamino)-pyridine. Racemization of Aspartic and Glutamic Acid Derivatives

Madhup K. Dhaon, Richard K. Olsen,* and K. Ramasamy

Department of Chemistry and Biochemistry, Utah State University, Logan, Utah 84322

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The carboxyl group of α-amino acids is commonly protected as an alkyl ester during peptide synthesis, for which the use of methyl, ethyl, benzyl, and *tert*-butyl esters is well-documented.[1] The preparation of esters of N-protected α-amino acids is most often effected by alkylation with an alkyl halide of the triethylammonium[2] or cesium[3] salt of the corresponding carboxylate ion. Ester formation by use of carbodiimide coupling procedures has found limited application.[4]

The method of Steglich[5] and Hassner[6] is widely used for the preparation of esters of carboxylic acids, in which esterification is effected by a carbodiimide condensation catalyzed with 4-(dimethylamino)pyridine. Application[5-7] of this method has been made for esterification of a limited number of N-protected α-amino acids. Hassner and

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(3) Wang, S. S.; Gisin, B. F.; Winter, D. P.; Makofske, R.; Kulesha, I. D.; Tzongraki, C.; Meienhofer, J. *J. Org. Chem.* **1977**, *42*, 1286.

(4) Miller, A. W.; Stirling, C. J. M. *J. Chem. Soc. C* **1968**, 2612. Camble, R.; Garner, R; Young, G. T. *Ibid* **1969**, 1911. Sieber, P.; Andreatta, R.; Eisler, K.; Kamber, B.; Riniker, B.; Rink, H. In "Peptides, Proceedings of the Fifth American Peptide Symposium"; Goodman, M., Meienhofer, J., Eds.; Wiley: New York, 1977; pp 543–548.

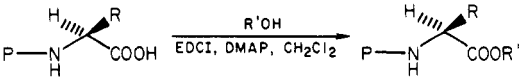
(5) Neises, B.; Steglich, W. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 552.

(6) Hassner, A.; Alexanian, V. *Tetrahedron Lett.* **1978**, 4475.

(7) Gilon, C.; Klausner, Y.; Hassner, A. *Tetrahedron Lett.* **1979**, 3811.

0022-3263/82/1947-1962$01.25/0

Table I. Preparation of Esters of N-Protected L-α-Amino Acids



entry	α-amino acid ester product	% yield of ester	mp, °C (solvent)	[α]amb D, deg (c, solvent) this study	[α]amb D, deg (c, solvent) standard
1	Z-Ala-O-t-Bu [a]	76	oil [b]	−15.8 (2.1, MeOH)	GC analysis [c]
2	Z-Val-O-t-Bu [a]	79	oil	−4.7 (2.0 MeOH)	GC analysis
3	Z-Gly-O-t-Bu [d]	78	oil		
4	Z-Pro-O-t-Bu [a]	88	44-45 [e] (ether petroleum ether)	−54.2 (2.0, EtOH)	−52.2 (2.2, EtOH)
5	Boc-Gly-OBzl	97	72-73 (n-hexane)		
6	Boc-Phe-OBzl	95	64-65 (n-hexane)	−12.8 (2, MeOH)	GC analysis
7	Boc-Val-OBzl	94	oil	−33.3 (2, MeOH)	GC analysis
8	Z-Ala-OMe [f]	96	45-46 [g] (n-hexane)	−33.9 (2, MeOH)	−35.0 (2.5, MeOH)
9	Boc-Val-OMe	96	oil	−22.7 (2, MeOH)	GC analysis
10	Boc-Ser(Bzl)-OMe	97	oil	+13.9 (0.9, $CHCl_3$)	+14.3 (1.0, $CHCl_3$)
11	Boc-Cys(Bzl)-OMe	92	oil	−34.2 (2, MeOH)	−35.0 (2, MeOH) [h]
12	Boc-Met-OMe [i]	96	oil	−34.0 (1, MeOH)	−33.6 (1, MeOH) [h]
13	Boc-Orn(Cbz)-OMe	84	oil	−10.5 (1, MeOH)	−10.6 (1, MeOH) [h]
14	Z-Ala-OTce [j]	87	oil	−9.7 (5, DMF) [j]	GC analysis
15	Z-MeAla-OTce	88	oil	−12.58 (2, DMF) [j]	GC analysis

[a] Anderson, G. W.; Callahan, F. M. *J. Am. Chem. Soc.* **1960**, *82*, 3359. [b] All oils were purified by MPLC on silica gel 60 with hexane–acetone (9:1). [c] Gas chromatographic analysis was carried out by hydrolysis (6 N HCl, 100 °C, 24 h), followed by derivatization as the *N*-trifluoroacetyl isopropyl esters and analysis on an optically active capillary column (see ref 9). [d] Tashner, V. E.; Biernat, J. F.; Rzeszotarska, B.; Wasielewski, C. *Justus Liebigs Ann. Chem.* **1961**, *646*, 123. [e] Lit. mp 44–45 °C (see ref *a*). [f] Mijoric, M. P. V.; Walker, J. *J. Org. Chem.* **1960**, *25*, 909. [g] Lit. mp 43–44 °C (see ref *f*). [h] Rotation of ester prepared by esterification of the corresponding N-protected amino acid with diazomethane in ether–methanol. [i] Dutta, A. S.; Morley, G. S. *J. Chem. Soc. C* **1971**, 2896. [j] Ciardelli, T. L.; Chakravarty, P. K.; Olsen, R. K. *J. Am. Chem. Soc.* **1978**, *100*, 7684. Optical rotations given are values obtained for corresponding hydrobromide salt.

Table II. Racemization of Boc-Asp(OBzl)-OH and Boc- or Z-Glu(OBzl)-OH upon Esterification with Alcohol/EDCI/DMAP

entry	alcohol	product	% yield [a]	method of prepn [b]	[α]D, deg obsd [c]	[α]D, deg standard	% racemization
1	t-BuOH	Boc-Asp(OBzl)-O-t-Bu	95	A	−2.9	−7.4 [d]	61
2	t-BuOH	Boc-Asp(OBzl)-O-t-Bu	90	B	−6.0	−7.4 [d]	19
3	CH_3OH	Boc-Asp(OBzl)-OMe	90	B	−6.9	−7.6 [e]	9
4	t-BuOH	Boc-Glu(OBzl)-O-t-Bu	85	A	−9.5	−20.0 [d]	52
5	t-BuOH	Boc-Glu(OBzl)-O-t-Bu	82	B	−12.0	−20.0 [d]	40
6	C_2H_5OH	Z-Glu(OBzl)-OEt	70	B	−18.6 [f]	−21.4 [g]	13
7	$PhCH_2OH$	Boc-Glu(OBzl)-OBzl	85	B	−12.5 [h]	−16.1 [i]	22

[a] Yields reported are for products purified by MPLC or by recrystallization. [b] (A) EDCI, alcohol, 0.5 equiv of DMAP, 2 h at 0 °C, overnight at room temperature; (B) EDCI, alcohol, 0.1 equiv of DMAP, 3 h at 0 °C, 3 h at room temperature. [c] Entries 1 and 2, c = 2, MeOH; entry 3, c = 1, acetone; entries 4 and 5, c = 1.7, MeOH; entries 6 and 7, c = 1, MeOH. [d] Specific rotation of compound prepared by reaction with isobutylene and acid by following the procedure of: Yang, C. C.; Merrifield, R. B. *J. Org. Chem.* **1976**, *41*, 1032. [e] Specific rotation of compound prepared by methylation with diazomethane. [f] Specific rotation of Z-Glu-OEt prepared from ester product by following sequence:

$$\text{Z-Glu(OBzl)-OEt} \xrightarrow{H_2,\ Pd/C} \text{H-Glu-OEt} \xrightarrow{\text{Z-Cl}} \text{Z-Glu-OEt}.$$

[g] Weygand, V. F.; Hunger, K., *Z. Naturforsch. B*: *Anorg. Chem., Org. Chem.* **1958**, *13B*, 50. [h] Specific rotation of Boc-Glu-OH prepared from product ester by removal of benzyl ester groups with H_2, Pd/C. [i] Schroeder, E.; Klieger, E. *Justus Liebigs Ann. Chem.* **1964**, *673*, 176.

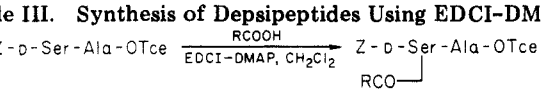
Alexanian[6] reported three examples involving α-amino acids; however, no mention was made regarding the optical integrity of the esters obtained. Neises and Steglich[5] report observing "some racemization" in the esterification of *N*-(benzyloxycarbonyl) α-amino acids with *tert*-butyl alcohol but that racemization "can be largely avoided at lower temperatures and with shorter reaction times". Racemization of the initial N-protected α-amino acid attached via an ester bond to solid-phase resins has been observed.[8] Since lack of racemization is essential if the above method is to be useful for the synthesis of esters of optically pure α-amino acids, we have determined the optical purity of several esters prepared by this method in our laboratories.

The esters (Table I) were prepared by treatment of the N-protected α-amino acid with the appropriate alcohol and 1-ethyl-3-[3-(dimethylamino)propyl]carbodiimide hydrochloride (EDCI) in methylene chloride containing 0.1 or 0.5 equiv of 4-(dimethylamino)pyridine (DMAP). Both *N*-benzyloxycarbonyl and *N*-*tert*-butyloxycarbonyl α-amino acids readily undergo esterification with *tert*-butyl alcohol, benzyl alcohol, methanol, or 2,2,2-trichloroethanol to furnish the corresponding esters in satisfactory to high yields; benzhydryl esters also can be readily prepared by this procedure. The esters listed in Table I were shown to be optically pure, though serine and cysteine (enteries 10 and 11) may be racemized to the extent of 2–3%. The optical purity of the esters prepared was determined by comparison with reported specific rotations or by analysis, following hydrolysis and derivatization, of the corresponding *N*-trifluoroacetyl isopropyl esters on an optically active gas capillary column[9] that cleanly separated the D

(8) Atherton, E.; Benoiton, N. L.; Brown, E.; Shephard, R. C.; Williams, B. J. *J. Chem. Soc., Chem. Commun.* **1981**, 336.

(9) Charles, R.; Beitler, U.; Feibush, B.; Gil-Av, E. *J. Chromatogr.* **1975**, *112*, 121.

Table III. Synthesis of Depsipeptides Using EDCI-DMAP

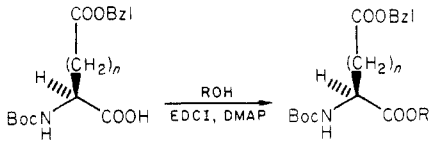


entry	RCOOH	depsipeptide (yield, %)	$[\alpha]^{amb}_D$, deg (c, solvent)	% D-Valine [b]
1	Boc-Val-OH	Z-D-Ser-Ala-OTce (80) Boc-Val	+3.2 (2, $CHCl_3$)	0
2	Boc-MeVal-OH	Z-D-Ser-Ala-OTce (90) Boc-MeVal	−47.3 (2, MeOH)	0
3	Boc-Cys(Acm)-Val-OH	Z-D-Ser-Ala-OTce (80) Boc-Cys(Acm)-Val	+0.3 (4, $CHCl_3$) [lit. [a] +6.8 (4, $CHCl_3$)]	21.5

[a] Ciardelli, T. L.; Chakravarty, P. K.; Olsen, R. K. *J. Am. Chem. Soc.* **1978**, *100*, 7684. [b] By GC analysis.

and L isomers. The majority of the esters prepared were obtained as oils that were conveniently purified by medium-pressure liquid chromatography (MPLC).[10]

We have observed, however, that esterification of the L-aspartic and L-glutamic acid derivatives Boc-Asp(OBzl)-OH (1) and Boc-Glu(OBzl)-OH (2) with various



1, $n = 1$
2, $n = 2$
3, $n = 3$

4, $n = 1$; R = *t*-Bu
5, $n = 2$; R = *t*-Bu
6, $n = 3$; R = Me

alcohols furnished the corresponding esters that had undergone moderate to extensive racemization (Table II). The degree of racemization is dependent upon the alcohol used, with the order of increased racemization being MeOH < EtOH < $PhCH_2OH$ < *t*-BuOH. Less racemization was observed if only 0.1 equiv of DMAP and a shorter reaction period were employed (compare methods A and B, Table II). No racemization was observed when the isolated *tert*-butyl esters **4** and **5** were treated under the reaction conditions for esterification, thus establishing that the product esters do not racemize.

The racemization occurring in the esterification of the above aspartic and glutamic acids appears to be due to a proximity effect of the side-chain carboxylate function. Thus, esterification of δ-benzyl N^{α}-(*tert*-butoxycarbonyl)-L-α-amino-L-adipate (**3**) furnished the corresponding methyl ester **6** that was shown to be optically pure by comparison of optical rotation with that of methyl ester **6** prepared by methylation with diazomethane. The oxygen atoms of the side-chain carboxylate functions in **1** and **2** are proximate to both the α-hydrogen or the α-carboxyl carbon by five- and six-membered-ring relationships, while for **3** a less favorable seven-ring relationship exists. Both methionine and ornithine possess side-chain functions that similarly are proximate by a five-atom disposition; these two amino acids undergo esterification without any loss of optical purity (see entries 12 and 13 in Table I). Inductive effects appear to have a minor role as serine and cysteine (entries 10 and 11) undergo racemization to a minor extent (2–3%) upon transformation to the corresponding esters. Speculation regarding the cause of the racemization observed for these aspartic and glutamic acid derivatives is interesting; however, further studies are needed to define the nature of the racemization process.

(10) Meyers, A. I.; Slade, J.; Smith, R. K.; Mihelich, E. D. *J. Org. Chem.* **1979**, *44*, 2247.

The synthesis of depsipeptides by this method has been reported.[7] Esterification of a single N-protected α-amino acid to form a depsipeptide bond occurs, using EDCI and DMAP, without racemization (Table III, entries 1 and 2). Esterification of Boc-Cys(Acm)-Val-OH with Z-D-Ser-Ala-OTce (Table III, entry 3) furnished the corresponding tetradepsipeptide in good yield. Gas capillary analysis[9] of the derivatized amino acids from hydrolysis of the tetradepsipeptide showed, however, that the valine residue was racemized to the extent of 43%. Thus, fragment coupling via formation of the depsipeptide bond by this method is not useful due to racemization of the C-terminal amino acid of the one peptide fragment.

Esters prepared by this method would require removal of the N-protecting group before use in peptide synthesis; this additional step diminishes the usefulness of the method as esters of α-amino acids are often commercially available or are routinely prepared in one step from the free amino acid. There are cases when the introduction of an unusual ester function such as the 2,2,2-trichloroethyl ester (entries 14 and 15 of Table I) or esterification in the presence of an acid-sensitive group elsewhere in the molecule would render this method of synthetic utility. The procedure does allow the preparation of *tert*-butyl and methyl esters, normally effected by acid catalysis,[1] under mild, neutral conditions and in the presence of the acid-labile *N*-*tert*-butyloxycarbonyl function.[11,12] This esterification method, being free of racemization in most cases, will be useful in many instances involving peptide synthesis and the synthesis of polyfunctional molecules and natural products.

Experimental Section

Melting points were recorded on a Thomas-Hoover capillary melting point apparatus and are uncorrected. The N-protected α-amino acids and other reagents used in this study were obtained from commercial sources. Methylene chloride was stored over 4A molecular sieves. Solvents were removed by using a rotary evaporator at reduced pressure (water aspirator). Thin-layer chromatography was performed on Quantum Industries silica gel plates (1 in. × 3 in.) developed in hexane–acetone (8:2). ^1H NMR spectra were recorded on a Varian EM-360 spectrometer in $CDCl_3$ as the solvent; all compounds prepared in this study gave consistent NMR spectra. Optical rotations were recorded on a Perkin-Elmer 241 automatic polarimeter. New compounds prepared gave satisfactory elemental analyses (C, H, and N within ±0.4%).

General Procedure of Esterification. A solution of the N-protected amino acid (2.2 mmol), 4-(dimethylamino)pyridine

(11) Preparation of Z-Ala-O-*t*-Bu ester by alkylation of the cesium salt of Z-Ala-OH with *tert*-butyl bromide gave a low yield (14%) of ester (see ref 3).

(12) The preparation of *tert*-butyl esters of the less acid labile *N*-(benzyloxycarbonyl) α-amino acids by acid-catalyzed alkylation with isobutylene has been reported by: Anderson, A. W.; Callahan, F. M. *J. Am. Chem. Soc.* **1960**, *82*, 3359.

(0.2 or 1.1 mmol), and the alcohol (2.5 mmol, except with benzyl alcohol where 2.10 mmol was used) in 8 mL of methylene chloride was cooled with stirring in an ice bath. 1-Ethyl-3-[3-(dimethylamino)propyl]carbodiimide hydrochloride (EDCI, 2.4 mmol) was added, and the reaction mixture was stirred at 0 °C for 2 h and at room temperature overnight. The solution was concentrated to dryness in vacuo, and the residue was taken up in ethyl acetate (25 mL) and water (5 mL). The organic layer was separated, washed with saturated sodium bicarbonate (2 × 15 mL) and water (2 × 15 mL), and dried (Na_2SO_4). The solvent was removed in vacuo, and the product was purified by MPLC on a column of silica gel 60 (230–400 mesh) with hexane–acetone (9:1) as the eluant.

General Procedure of Esterification by Diazomethane. The esters listed in Table I (entries 10–13) were also prepared by esterification with diazomethane. A solution of N-protected amino acid (1.2 mmol) in absolute methanol (5 mL) was cooled to 0 °C in an ice bath, and a ice cooled solution of diazomethane (2 equiv, generated from diazald) was added. The reaction mixture was kept at 0 °C for 15 min and then overnight at room temperature. The solvent was removed, and the residue was taken up in ethyl acetate (25 mL), washed with saturated sodium bicarbonate solution (2 × 10 mL) and water (2 × 10 mL), and dried (Na_2SO_4). The solvent was removed in vacuo, and the product was purified by MPLC as above. The ester products obtained were shown to be identical (NMR, TLC) with those prepared by esterification by the carbodiimide–(dimethylamino)pyridine method.

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Registry No. 1, 7536-58-5; 2, 13574-13-5; 3, 80975-50-4; 4, 80963-08-2; 5, 28812-54-6; 6, 80963-09-3; Z-Ala-OH, 1142-20-7; Z-Val-OH, 1149-26-4; Z-Gly-OH, 1138-80-3; Z-Pro-OH, 1148-11-4; Boc-Gly-OH, 4530-20-5; Boc-Phe-OH, 13734-34-4; Boc-Val-OH, 13734-41-3; Boc-Ser(Bzl)-OH, 23680-31-1; Boc-Cys(Bzl)-OH, 5068-28-0; Boc-Met-OH, 2488-15-5; Boc-Orn(Cbz)-OH, 2480-93-5; Z-MeAla-OH, 21691-41-8; Z-Ala-OBu-*t*, 50300-96-4; Z-Val-OBu-*t*, 16874-02-5; Z-Gly-O-Bu-*t*, 16881-32-6; Z-Pro-O-Bu-*t*, 16881-39-3; Boc-Gly-OBzl, 54244-69-8; Boc-Phe-OBzl, 66617-58-1; Boc-Val-OBzl, 66447-55-0; Z-Ala-OMe, 28819-05-8; Boc-Val-OMe, 58561-04-9; Boc-Ser(Bzl)-OMe, 80963-10-6; Boc-Cys(Bzl)-OMe, 55478-08-5; Boc-Met-OMe, 33900-24-2; Boc-Orn(Cbz)-OMe, 2480-95-7; Z-Ala-OTce, 67850-37-7; Z-MeAla-OTce, 80963-11-7; Z-Glu(OBzl)-OH, 5680-86-4; Boc-Asp(OBzl)-OMe, 80963-12-8; Z-Glu(OBzl)-OEt, 80963-13-9; Boc-Glu(OBzl)OBzl, 80963-14-0; Z-D-Ser-Ala-OTce, 63478-49-9; Boc-MeVal-OH, 45170-31-8; Boc-Cys(Acm)-Val-OH, 80963-15-1; Z-D-Ser(Boc-Val)-Ala-OTce, 63478-50-2; Z-D-Ser(Boc-MeVal)-Ala-OTce, 68098-67-9; Z-D-Ser[Boc-Cys(Acm)-Val]-Ala-OTce, 63478-51-3.

Reaction of 7,7,8,8-Tetracyanoquinodimethane with Cyclic Enol Ethers

Akihiro Kondo and Shouji Iwatsuki*

Department of Chemical Research for Resources, Faculty of Engineering, Mie University, Tsu 514, Japan

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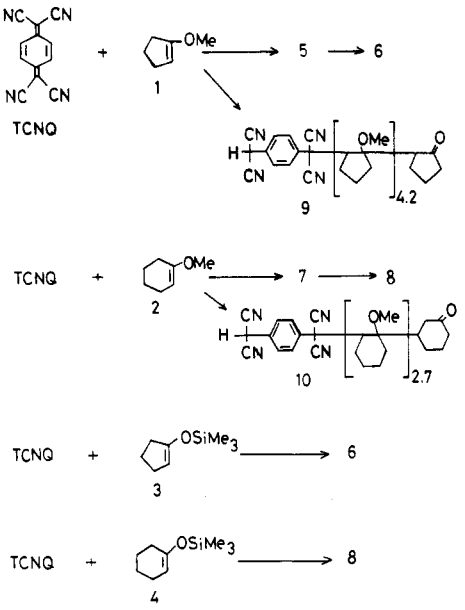
7,7,8,8-Tetracyanoquinodimethane (TCNQ)[1] is a well-known powerful π-electron acceptor. TCNQ undergoes the alternating copolymerization with styrene,[2] 2-chloroethyl vinyl ether, phenyl vinyl ether, and vinyl acetate,[3] while it causes the cationic polymerization of more powerful electron-donor monomers such as *N*-vinylcarbazole[4] and alkyl vinyl ethers.[5] For the latter reaction, Stille et al.[6] proposed that a zwitterion-type adduct is formed between TCNQ and alkyl vinyl ether and that its cationic end initiates the cationic polymerization of the alkyl vinyl ether.

Scheme I



In this paper were described the reactions of TCNQ with cyclic enol ethers such as 1-methoxy-1-cyclopentene (**1**),[7] 1-methoxy-1-cyclohexene (**2**),[7] 1-[(trimethylsilyl)oxy]-1-cyclopentene (**3**),[8] and 1-[(trimethylsilyl)oxy]-1-cyclohexene (**4**),[8] and their reaction schemes were also discussed.

Equimolar amounts of TCNQ and **1** were reacted in acetonitrile at 60 °C for 12 h. Then, the mixture was placed under reduced pressure to remove the solvent, and the solid residue obtained was found by its IR and ^1H NMR spectra to be compound **5**. The residue was chromatographed on silica gel to give a mixture of compounds **5** and **6**. Pure **5** was dissolved in aqueous ethanol with a catalytic amount of *p*-toluenesulfonic acid and was converted into **6** in quantitative yield. Comparable reaction between TCNQ and **2** gave compound **7**. On silica gel chromatography, **7** also was converted into **8**. The structures of **5**, **6**, and **8** were established by elemental analyses and IR and ^1H NMR measurements, as shown in Table I.

TCNQ and an excess amount of **1** or **2** (about 12 times the molar quantity of TCNQ) were heated at 60 °C for 48 h, and the resulting mixtures were chromatographed on silica gel to give pale yellow **9** or **10**, respectively. It was pointed out on the basis of their spectral, elemental, analysis, and molecular weight data that **9** and **10** are oligomers of **1** and **2**, respectively, with a terminal TCNQ unit and another cycloalkanone unit, conceivably derived from hydrolysis of cycloalkenyl methyl ether unit.

When equimolar amounts of TCNQ and **3** or **4** were heated in acetonitrile at 60 °C for 15 h, only one compound, **6** or **8**, was obtained, respectively, in contrast with the above-mentioned cases of **1** and **2**. Any compound

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