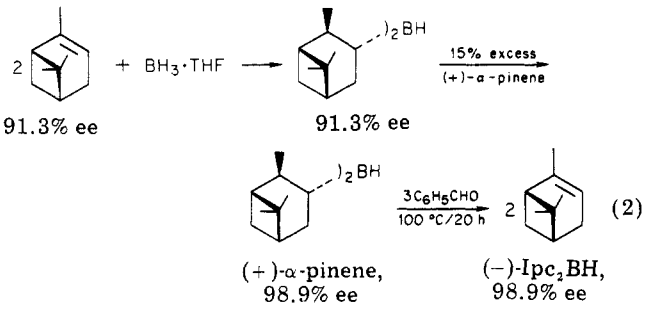
Table I. Summary of Rotations for α- and β-Pinene of High Optical Purities

compd	temp, °C	$[\alpha]^T_D$, deg (neat)	% ee[a]	ref
(+)-α-pinene	20	+51.60	100.0	14
(+)-α-pinene	20	+51.14	99.1	15
(+)-α-pinene	25	+51.0	98.9	2c
(+)-α-pinene	23	+51.0	98.9	*b*
(−)-α-pinene	20	−51.28	99.4	15
(−)-α-pinene	23	−51.1	99.0	*b*
(+)-β-pinene	25	+22.80	100.0	17
(−)-β-pinene	25	−22.70	99.6	16

[a] Percent ee of (+)- and (−)-α-pinene based on maximum rotation $[\alpha]^{20}_D$ 51.6° (neat); percent ee of (+)- and (−)-β-pinene based on maximum rotation $[\alpha]^{25}_D$ −22.8° (neat). [b] Present study.

these conditions, with the optical purity of the product α-pinene, 91.3% ee, the same as that of the α-pinene used to prepare the Ipc_2BH.

By combining the digestion procedure with this displacement procedure, we have been able to obtain (+)-α-pinene in optical purity of 98.9% from commercial (+)-α-pinene of 91.3% ee (eq 2).



(2)

In order to prepare (−)-α-pinene, the commercial (−)-β-pinene, 92% ee, is first isomerized by KAPA into (−)-α-pinene, 92% ee.[11] This material is hydroborated to form the (+)-Ipc_2BH, digested, and converted to 99% ee (−)-α-pinene.

It is desirable to summarize pertinent data for the rotations of α- and β-pinene (Table I).

Experimental Section

All operations were carried out under a nitrogen atmosphere, with ovendried glassware. GLC analyses were carried out on a Hewlett-Packard 5750 gas chromatograph with a 10 ft × 0.25 in. column packed with (a) 10% SE-30 on Chromosorb W (60–80 mesh) or (b) 10% Carbowax 20M on Chromosorb W (60–80 mesh). The ^{11}B NMR spectra were obtained on a Varian FT-80A instrument. Rotations were measured on a Rudolph Polarimeter Autopol III.

Materials. (+)-α-Pinene and (−)-β-pinene (Aldrich Chemical Co.) were distilled from a small excess of lithium aluminum hydride.

3-Aminopropylamine (APA) was distilled from a small excess of calcium hydride.

Conversion of (−)-β-Pinene to (−)-α-Pinene. In a dry 50-mL centrifuge tube fitted with a rubber septum and magnetic stirring bar was placed 1.78 mL (10 mmol) of 22.4% potassium hydride in oil. The oil was removed by washing with dry *n*-pentane (3 × 10 mL). After centrifugation, the pentane layer was removed by a double-ended needle. The residual pentane was removed under a stream of nitrogen. To the oil-free potassium hydride was rapidly added 10 mL of 3-aminopropylamine (APA). Hydrogen evolution subsided after 1.5 h, indicating that the formation of KAPA had been completed. Meanwhile, in a 500-mL round-bottom flask fitted with a septum inlet, a magnetic stirring bar, and a bent tube adaptor, connected to a mercury bubbler, was placed dry (−)-β-pinene (158.8 mL, 1 mol, $[\alpha]^{23}_D$ −21.0°, 92.1% ee, n^{20}_D 1.4782), cooled to 0 °C in an ice bath. The KAPA in APA (1 mol %) was added dropwise to the vigorously stirred β-pinene with the help of a double-ended needle. The reaction mixture, light yellow initially, turns brown after about 30 min. Aliquots (0.1 mL) were withdrawn at intervals, quenched in a vial containing ice-cold water and 0.5 mL of pentane, separated, and dried. The GLC analysis showed that the equilibration was complete after 24 h with α-pinene/β-pinene (99.4:0.6). The reaction mixture was poured into ice–water, washed with brine (2 × 50 mL), dried over anhydrous calcium chloride, and filtered, the filtrate was distilled from a small excess of lithium aluminum hydride to provide 126.5 g (93% yield) of (−)-α-pinene: bp 72 °C (46 mm); $[\alpha]^{23}_D$ −47.47° (neat); 92.0% ee.

Conversion of (−)-α-Pinene of 92% ee to (−)-α-Pinene of 99% ee. A 250-mL flask, equipped with a septum inlet, magnetic stirring bar, and a distillation condenser, connected to a receiver cooled in a dry ice–acetone bath was charged with 5.0 mL (50 mmol) of BH_3·SMe_2 and 15 mL of THF. It was cooled to 0 °C in an ice bath and 15.9 mL (100 mmol) of (−)-α-pinene, $[\alpha]^{23}_D$ −47.47° (neat), 92% ee, was added dropwise with stirring. After the contents were stirred at 0 °C for 3 h, a mixture of DMS and THF (13 mL) was removed under vacuum [0 °C (30 mm)], and the flask was brought to atmospheric pressure by flushing with nitrogen gas and charged with 18 mL of THF and 2.4 mL (15 mmol) of (−)-α-pinene. The distillation condenser was replaced by a bent tube adaptor under positive pressure of nitrogen. The flask was then stored in the cold room at 0 °C for 3 days to permit equilibration. The slurry of Ipc_2BH was transferred to a 125-mL centrifuge tube cooled in an ice bath. The upper layer containing excess α-pinene and THF was removed after centrifugation, and the solid Ipc_2BH was washed with cold (−10 °C) THF (2 × 20 mL). The solid Ipc_2BH was then transferred as a suspension in THF (15 mL) to a 100-mL flask fitted with a septum inlet, a magnetic stirring bar, and a distillation condenser connected to a mercury bubbler. The solvent was removed under reduced pressure [25 °C (2 mm), 2 h] to provide Ipc_2BH (10.86 g, 76% yield). It was then treated with benzaldehyde (11.6 mL, 114 mmol) at 25 °C. After the reaction mixture was stirred at 25 °C for 15 min, it was heated in an oil bath maintained at 100 °C for 20 h, whereby the elimination of α-pinene with the formation of tribenzyl borate [δ 18 (^{11}B NMR)] was complete. The liberated α-pinene was distilled. The distillate was stirred with a small excess of $LiAlH_4$ to remove traces of benzaldehyde and redistilled to provide α-pinene (8.3 g, 61% yield): bp 82 °C (60 mmHg); $[\alpha]^{23}_D$ −51.10° (neat); 99% ee. Alternatively, the distillate containing a mixture of α-pinene and benzaldehyde was dissolved in pentane, and the pentane solution was washed with 10% aqueous sodium bisulfite (3 × 30 mL), followed by water (30 mL). The organic layer, after drying over anhydrous magnesium sulfate, was distilled to provide pure α-pinene.

Conversion of (+)-α-Pinene of 91.3% ee to (+)-α-Pinene of 99% ee. The experimental procedure described for (−)-α-pinene is followed. (+)-α-Pinene, $[\alpha]^{23}_D$ +47.1° (neat); 91.3% ee, was used to provide (+)-α-pinene (8.15 g, 60% yield), bp 82 °C (60 mmHg), $[\alpha]^{23}_D$ +51.0° (neat), 98.9% ee.

Registry No. KAPA, 56038-00-7; BH_3·SMe_2, 13292-87-0; Ipc_2BH, 21947-87-5; (+)-α-pinene, 7785-70-8; (−)-β-pinene, 18172-67-3; (−)-α-pinene, 7785-26-4; benzaldehyde, 100-52-7.

Diphthalimido Carbonate: A New Reagent for Active Ester Synthesis

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Active amino acid esters from *N*-hydroxyphthalimide/dicyclohexylcarbodiimide have found wide use in peptide chemistry.[1] During the study on the reactions of

Table I. Reaction of DPC with Carboxylic Acids

acid	solvent	catalyst	rctn time, h	yield of ester, %	DPC recovd, %
benzoic	THF	none	120	23	73
benzoic	THF	pyridine	72	37	48
benzoic	THF	triethylamine	6	92	
benzoic	acetonitrile	pyridine	72	90	
acetic	THF	pyridine	72	10	76
acetic	THF	triethylamine	6	100	

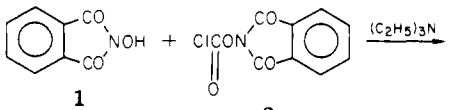
Table II. Reaction of DPC with *N*-Carbobenzoxy Amino Acids

amino acid	rctn time, h	yield, %	mp, °C	$[\alpha]^{22}_D$ (concn)[a]
L-Pro	20	89 (98)[b]	104-106 (109)[c]	−82.1 (−81.9)[c] (*c* 1.0)
L-Phe	20	89 (96)[b]	108-109 (109)[c]	−44.2 (−44.6)[c] (*c* 2.0)
L-Leu	20	85 (93)[b]	110-111 (112)[c]	−33.3 (−34.0)[c] (*c* 1.0)

[a] In acetic acid. [b] Yield before recrystallization. [c] Literature[7] values.

the hydroxy group in *N*-hydroxy imides,[2-5] diphthalimido carbonate (DPC) was considered of interest as a simple carboxyl-activating reagent similar to carbonyldiimidazole. DPC would exhibit appreciable reactivity toward carboxyl groups owing to the acidity of the leaving group, *N*-hydroxyphthalimide.[2,6] We now report the new reagent, DPC, which should make the active esters more conveniently accessible.

DPC was prepared from *N*-hydroxyphthalimide (1) and *N*-[(chlorocarbonyl)oxy]phthalimide (2) in dry tetrahydrofuran (THF). It was obtained in a high yield and



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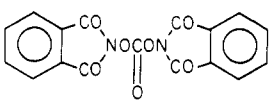
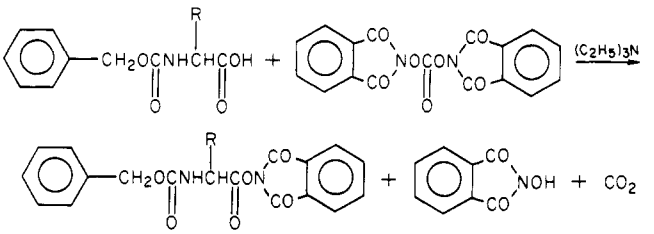


DPC

easily purified by recrystallization from ethyl acetate to give colorless granular crystals. DPC is a stable compound and can be kept at room temperature over a long period. It begins to decompose at 153 °C in thermogravimetry in air (5 °C/min) without showing a clear melting point.

Before the reaction with amino acids, DPC was subjected to the reaction with benzoic and acetic acids in order to establish the general reactivity of the carbonate. The reaction proceeded only reluctantly in THF at room temperature but quite smoothly in the presence of a basic catalyst. Triethylamine was far more effective than pyridine, giving quantitative yields of the esters as shown in Table I. Acetonitrile seemed to be another suitable solvent as it resulted in a high yield even with pyridine. The reaction mixture was, however, heterogeneous all the way, which made it difficult to determine the end point.

As suggested from the above results, the reactions of DPC with *N*-carbobenzoxy amino acids were carried out in THF, triethylamine being used as a catalyst. Although



the reactions progressed heterogeneously in the initial stage, all the mixtures became clear solutions within 20 h, indicating the completion of the esterification. The products were isolated by a simple procedure, including concentration of the solutions followed by removal of *N*-hydroxyphthalimide by washing with an aqueous alkaline solution. As shown in Table II, yields were almost quantitative as expected and much higher than those (65–73%) obtained by the conventional *N*-hydroxyphthalimide/dicyclohexylcarbodiimide method.[7] These results implied that DPC exhibited similar reactivity to disuccinimido carbonate, which was recently reported to give high yields of the corresponding esters.[8] An advantage of DPC seems to be that *N*-hydroxyphthalimide can be recovered quantitatively with ease after the reaction as is distinct from *N*-hydroxysuccinimide.[2]

All the active esters prepared here showed good crystallizability and were readily purified by recrystallization. Furthermore, they were optically pure judging from the specific rotation data, and no appreciable extent of racemization was detected. Consequently, in addition to being easy to prepare and handle, DPC was confirmed to be a convenient reagent for synthesis of active amino acid esters.

Experimental Section

N-[(Chlorocarbonyl)oxy]phthalimide was synthesized by chlorocarbonylation of *N*-hydroxyphthalimide with trichloromethyl chloroformate.[5,9] *N*-Carbobenzoxy amino acids were obtained commercially. All the solvents used were purified by the usual manner.

Diphthalimido Carbonate (DPC). A solution of 0.979 g (6 mmol) of *N*-hydroxyphthalimide and 0.84 mL (0.61 g, 6 mmol)

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of triethylamine in 100 mL of dry THF was cooled with an ice-water bath, whereupon 1.354 g (6 mmol) of *N*-[(chlorocarbonyl)oxy]phthalimide was added. Stirring was continued at 5 °C for 15 min and further at room temperature for 3 h. Triethylamine hydrochloride precipitated and was removed by filtration and washed thoroughly with THF. The combined filtrates were evaporated under reduced pressure to give 2.01 g (95%) of DPC as a slightly yellow solid. On recrystallization from dry ethyl acetate, it gave 1.78 g (84%) of colorless granular crystals, which showed no clear melting point. It began to lose weight at 153 °C in thermogravimetry in air (5 °C/min): ^{1}H NMR ($CDCl_3$) δ 7.70–8.00 (m, Ar H); IR (KBr) 1740, 1790, 1850 (C=O) cm^{-1}.

Anal. Calcd for $C_{17}H_8N_2O_7$: C, 57.96; H, 2.30; N, 7.95. Found: C, 57.41; H, 2.20; N, 7.93.

Reaction of DPC with *N*-Carbobenzoxy Amino Acids. A typical example is as follows. *N*-(Carbobenzoxy)-L-proline (1.247 g, 5 mmol) was dissolved in 20 mL of dry THF, and 1.762 g (5 mmol) of DPC and a drop of triethylamine were added to the solution. The reaction mixture became a clear solution after about 4 h of stirring. The reaction was discontinued after 20 h. The solvent was evaporated under reduced pressure to give a pale-yellow oil. It was dissolved in chloroform, washed consecutively with an aqueous sodium bicarbonate solution and water, and then dried over sodium sulfate. After removal of chloroform, 1.94 g (98%) of the product was obtained as a colorless oil, which, on standing at room temperature, crystallized. It was recrystallized from ethyl acetate/petroleum ether to give 1.75 g (89%) of white granular crystals: mp 104–106 °C (lit.[7] mp 109 °C); $[\alpha]^{22}_D$ −82.1° (*c* 1.0, acetic acid) (lit.[7] $[\alpha]^{22}_D$ −81.9°); IR (KBr) 1690, 1740, 1790, 1810 (C=O) cm^{-1}.

Registry No. 1, 524-38-9; 2, 15263-19-1; DPC, 78816-91-8; *N*-hydroxyphthalimide benzoate, 58585-84-5; *N*-hydroxyphthalimide acetate, 17720-64-8; *N*-(carbobenzyloxy)-L-proline, 1148-11-4; *N*-(carbobenzoyloxy)-L-phenylalanine, 1161-13-3; *N*-(carbobenzoyloxy)-L-leucine, 2018-66-8; hydroxyphthalimide *N*-(carbobenzyloxy)-prolinate, 83025-91-6; hydroxyphthalimide *N*-(carbobenzyloxy)-phenylalanate, 83025-92-7; hydroxyphthalimide *N*-(carbobenzyloxy)leucinate, 83025-93-8.

Addition of Electrogenerated Cyanomethyl Anions to Fluorenone and Its Schiff Bases. Indirect Evidence of the Formation of an Unstable Cyclopropyl Cyanide Derivative as a Key Intermediate

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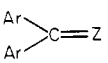
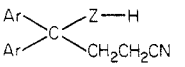
In a previous publication on the electroreductive cyclopropylcarbonylation in acetonitrile (MeCN) of fluorenone and of the Schiff bases 1 and 2, we have reported the



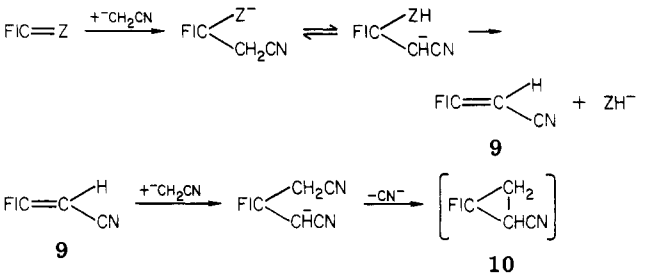
1, Ar = Ph; Z = NPh
2, Ar_2 = Fl; Z = NPh
3, Ar_2 = Fl; Z = NPh-*p*-Cl



4, Ar_2 = Fl; Z = O
5, Ar = Ph; Z = NPh
6, Ar_2 = Fl; Z = NPh

Fl

Scheme I[a]

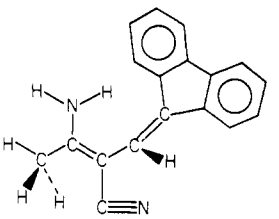


[a] Z = O, NPh, NPh-*p*-Cl; for Fl, see structure 1-6.

unexpected formation of the nitrile derivatives 4–6 as minor compounds.[1]

To explain these results, we have suggested a mechanism in which a reductive cleavage of an intermediate acrylonitrile occurs (Scheme VI of ref 1).

We now report new results that have been obtained by adding electrogenerated $^-CH_2CN$ anions to fluorenone and its Schiff bases 2 and 3. The conjugated 3-aminoacrylonitrile (*E*)-7 is the major compound isolated from all experiments.



(*E*)-7

It is suggested that nucleophilic additions of CH_2CN to fluorenone and its Schiff bases 2 and 3 lead to an unstable key intermediate, 10, which is further transformed to (*E*)-7. Taking into account the results and their interpretation, we reconsider the origin of the nitrile derivatives 4–6 isolated by the experimental conditions of ref 1.

Results and Discussion

Cyanomethyl anions have been electrogenerated by two ways:[2-7] (1) A strong base, such as an aromatic ketone radical anion or the azobenzene dianion, is electrogenerated in MeCN, from which it abstracts a proton;[2-6] (2) a reductive cleavage of cyanomethyl derivatives is performed in DMF.[4-7] Prior to this work, the addition of electrogenerated CH_2CN^- to aromatic carbonyl groups has been reported for a series of aromatic aldehydes and ketones, including benzophenone,[2-5] the formation of 3-substituted glutaronitriles has been observed in several cases.

Under our experimental conditions, azobenzene (2×10^{-3} M) is reduced to its dianion in MeCN. After consumption of 2 F, one of the substrates (10^{-3} M) is added to the catholyte. The mixture is allowed to stand for 3 h. The compounds contained in the catholyte are then isolated.

Besides traces of unidentified nitrile derivatives and a mixture of azo- and hydrazobenzene, a major cyano com-

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