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New Methods and Reagents in Organic Synthesis. 43.¹⁾ A New Synthesis of *tert*-Butyl Peroxycarboxylates Using Diethyl Phosphorocyanidate (DEPC)

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Condensation of carboxylic acids with *tert*-butyl hydroperoxide has been smoothly achieved by the use of diethyl phosphorocyanidate and triethylamine under mild reaction conditions, giving *tert*-butyl peroxycarboxylates in good yields.

Keywords—*tert*-butyl peroxycarboxylate; diethyl phosphorocyanidate; *tert*-butyl hydroperoxide; carboxylic acid; triethylamine; α -effect

Peroxycarboxylic acid esters are utilized as initiators for radical polymerization and are interesting as intermediates for the decarboxylation of carboxylic acids.³⁾ They are generally prepared by the acylation of hydroperoxides with acid chlorides, acid anhydrides, or imidazolides in the presence of a base. To our knowledge, no report has described the direct condensation of carboxylic acids with hydroperoxides.

We have already shown that diethyl phosphorocyanidate (DEPC, $(C_2H_5O)_2P(O)CN$), in combination with carboxylic acids and bases, can be efficiently used for N-acylation, S-acylation, and C-acylation, giving carboxylic acid amides,⁴⁾ peptides,⁵⁾ thiol esters,⁶⁾ acylmalonate derivatives,⁷⁾ α -nitroketones,⁸⁾ and oxazoles.⁹⁾ However, O-acylation of alcohols with carboxylic acids using DEPC under similar reaction conditions does not proceed efficiently,⁴⁾ possibly because of the weaker nucleophilicity of alcohols. Since hydroperoxides in the presence of a base seemed to be more reactive toward carbon electrophiles because of the α -effect,¹⁰⁾ we thought the O-acylation of hydroperoxides with carboxylic acids using DEPC in the presence of a base might proceed much more smoothly, giving synthetically useful

TABLE I. Condensation of *m*-Chlorobenzoic Acid
with *tert*-Butyl Hydroperoxide

Run	Reaction solvent	Method ^{a)}	Yield (%)
1	C ₆ H ₅ CH ₃	A	62
2	C ₆ H ₅ CH ₃	B	55
3	CH ₂ Cl ₂	A	56
4	CH ₃ CN	A	61
5	CH ₃ CN	B	75
6	HCON(CH ₃) ₂	A	61
7	HCON(CH ₃) ₂	B	92

a) Order of addition of reagents: Method A, (1) *m*-chlorobenzoic acid, (2) DEPC, (3) triethylamine, (4) *tert*-butyl hydroperoxide; Method B, (1) *m*-chlorobenzoic acid, (2) *tert*-butyl hydroperoxide, (3) triethylamine, (4) DEPC.

TABLE II. Preparation of *tert*-Butyl Peroxycarboxylates ($\text{RCO}_2\text{O}-\text{C}(\text{CH}_3)_3$) by the Direct Condensation of Carboxylic Acids with *tert*-Butyl Hydroperoxide

Compd. No.	R-	Yield (%)	Appearance (mp, °C)	IR ^{a)} $\nu_{\text{C=O}}$	NMR ^{b)} δ ppm (9H, s, $(\text{CH}_3)_3\text{C}$)	Molecular formula	Analysis (%)		MS M^+ (m/e) Calcd (Found)
							Calcd	Found	
							C	H	
I		95	Colorless oil	1750	1.38	$\text{C}_{12}\text{H}_{16}\text{O}_4$	—	—	224.10486 (224.10467)
II		88	Colorless cryst. ^{c)} (126–127)	1740	1.39	$\text{C}_{13}\text{H}_{17}\text{NO}_4$ ^{d)}	62.14 (62.30)	6.82 7.02)	—
III		83	Colorless oil	1750	1.39	$\text{C}_{12}\text{H}_{14}\text{O}_5$	—	—	238.08412 (238.08333)
IV		92	Colorless oil	1760	1.41	$\text{C}_{11}\text{H}_{13}\text{ClO}_3$	—	—	228.05532 (228.05529)
V		70	Yellow cryst. ^{e)} (77.5–78) ^{f)}	1755	1.45	$\text{C}_{11}\text{H}_{13}\text{NO}_5$	—	—	—
VI		60	Colorless oil	1772	1.38	$\text{C}_{11}\text{H}_{13}\text{NO}_5$ ^{g)}	55.23 (54.96)	5.48 5.44)	—
VII		98	Colorless oil	1755	1.46	$\text{C}_{15}\text{H}_{16}\text{O}_3$	—	—	244.10994 (244.11017)
VIII	$\text{CH}_3(\text{CH}_2)_{16}-$	64	Colorless cryst. (38.5–40)	1780	1.31	$\text{C}_{22}\text{H}_{44}\text{O}_3$	74.10 (73.70)	12.44 12.20)	—
IX		46	Colorless oil	1765	1.31	$\text{C}_{15}\text{H}_{24}\text{O}_3$	71.39 (71.89)	9.59 10.05)	—

a) Determined in Nujol or as a film.

b) Determined in deuteriochloroform using tetramethylsilane as an internal standard.

c) Recrystallized from diethyl ether–hexane. d) Analysis of N, 5.57 (5.46).

e) Recrystallized from hexane. f) Lit. mp 79 °C (ref. 12). g) Analysis of N, 5.85 (5.77).

peroxycarboxylic acid esters in higher yields.

In fact, carboxylic acids have been smoothly condensed with *tert*-butyl hydroperoxide by the use of DEPC and triethylamine under mild reaction conditions to give *tert*-butyl peroxycarboxylates in good yields:

Suitable reaction conditions have been explored for the condensation of *m*-chlorobenzoic acid with *tert*-butyl hydroperoxide as a model reaction. As summarized in Table I, *N,N*-dimethylformamide is the solvent of choice. A slight excess (1.5 eq) of DEPC and triethylamine is necessary to conduct the reaction smoothly. The order of addition of reagents significantly affects the yield, and method B (Table I), in which DEPC is finally added to a mixture of the carboxylic acid, *tert*-butyl hydroperoxide, and triethylamine, gives the best result. The use of diphenyl phosphorazidate (DPPA, $(\text{C}_6\text{H}_5\text{O})_2\text{P}(\text{O})\text{N}_3$)^{5,6,11} in place of DEPC under similar reaction conditions was disappointing, and only the formation of the carboxylic acid azide was observed.

Method B is a general one for the preparation of *tert*-butyl peroxycarboxylates, as summarized in Table II. Various aromatic acids are efficiently used for O-acylation of *tert*-butyl hydroperoxide. Condensation of aliphatic or alicyclic acids with *tert*-butyl hydroperoxide seems to proceed less efficiently than that of aromatic acids.

Experimental

Commercial *tert*-butyl hydroperoxide (80%) was used without purification. Silica gel (70–230 mesh ASTM, Merck Art. 7734) was used for column chromatography.

General Procedure for Preparation of *tert*-Butyl Peroxycarboxylates (Table II)—*tert*-Butyl hydroperoxide (180 mg, 2 mmol) in *N,N*-dimethylformamide (5 ml) was added to a carboxylic acid (2 mmol) cooled in an ice-methanol bath, followed by the addition of triethylamine (304 mg, 3 mmol) in *N,N*-dimethylformamide (5 ml). DEPC (489 mg, 3 mmol) in *N,N*-dimethylformamide (5 ml) was slowly added, and the mixture was stirred in the ice-methanol bath for 1.5 h, then at room temperature for 2 h (in the preparations of VI and VIII, the mixture was stirred overnight). Ethyl acetate–benzene (2:1, 120 ml) was added to the reaction mixture, and the organic layer was successively washed with 40 ml each of water, saturated aqueous sodium bicarbonate, water, 10% aqueous citric acid, water, and saturated aqueous sodium chloride, then dried over sodium sulfate. The mixture was concentrated *in vacuo* below 30 °C, and the residue was purified by column chromatography with diethyl ether–hexane (for I, II, IV, and VII), benzene–hexane (for III, VI, and VIII), or benzene (for V and IX), giving the peroxycarboxylate.

References and Notes

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