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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	$C_6H_5CH_3$	A	62
2	$C_6H_5CH_3$	B	55
3	CH_2Cl_2	A	56
4	CH_3CN	A	61
5	CH_3CN	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 (RCO_2O–$C(CH_3)_3$) by the Direct Condensation of Carboxylic Acids with *tert*-Butyl Hydroperoxide

Compd. No.	R–	Yield (%)	Appearance (mp, °C)	IR[a] $\nu_{C=O}$	NMR[b] δ ppm (9H, s, $(CH_3)_3C$)	Molecular formula	Analysis (%) Calcd (Found) C	Analysis (%) Calcd (Found) H	MS M^+ (*m/e*) Calcd (Found)
I	CH_3O-C$_6$H$_4$-	95	Colorless oil	1750	1.38	$C_{12}H_{16}O_4$	—		224.10486 (224.10467)
II	CH_3CONH-C$_6$H$_4$-	88	Colorless cryst.[c] (126—127)	1740	1.39	$C_{13}H_{17}NO_4$[d]	62.14 (62.30	6.82 7.02)	—
III	H_2C(O)$_2$C$_6$H$_3$-	83	Colorless oil	1750	1.39	$C_{12}H_{14}O_5$	—		238.08412 (238.08333)
IV	Cl-C$_6$H$_4$-	92	Colorless oil	1760	1.41	$C_{11}H_{13}ClO_3$	—		228.05532 (228.05529)
V	O_2N-C$_6$H$_4$-	70	Yellow cryst.[e] (77.5—78)[f]	1755	1.45	$C_{11}H_{13}NO_5$	—		—
VI	NO_2-C$_{10}$H$_7$	60	Colorless oil	1772	1.38	$C_{11}H_{13}NO_5$[g]	55.23 (54.96	5.48 5.44)	—
VII	C$_{10}$H$_7$-	98	Colorless oil	1755	1.46	$C_{15}H_{16}O_3$	—		244.10994 (244.11017)
VIII	$CH_3(CH_2)_{16}$–	64	Colorless cryst. (38.5—40)	1780	1.31	$C_{22}H_{44}O_3$	74.10 (73.70	12.44 12.20)	—
IX	C$_{10}$H$_{15}$-	46	Colorless oil	1765	1.31	$C_{15}H_{24}O_3$	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:

$$RCO_2H + (CH_3)_3COOH \xrightarrow[(C_2H_5)_3N]{(C_2H_5O)_2P(O)CN} RCO_2OC(CH_3)_3$$

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, $(C_6H_5O)_2P(O)N_3$)[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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