A Free-Radical Acetonylation Method

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Among the derivatives of vinylic carbonochloridates[1], the *O-O-t*-butyl *O*-isopropenyl peroxycarbonate (**1**) can be used as a free-radical initiator. Studying its thermolysis in cyclohexane (**2a**), we have found that the reaction gives mainly cy-

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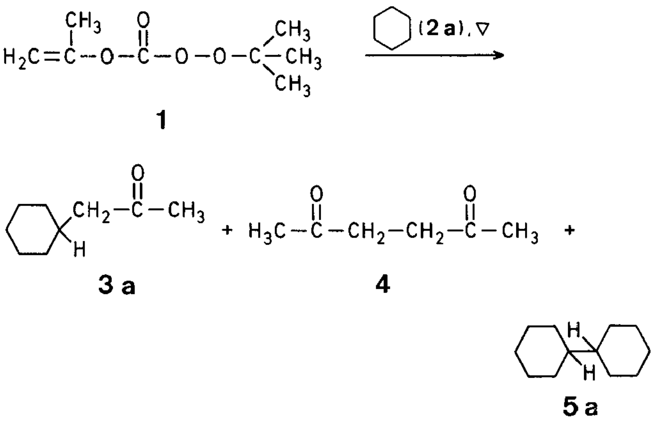
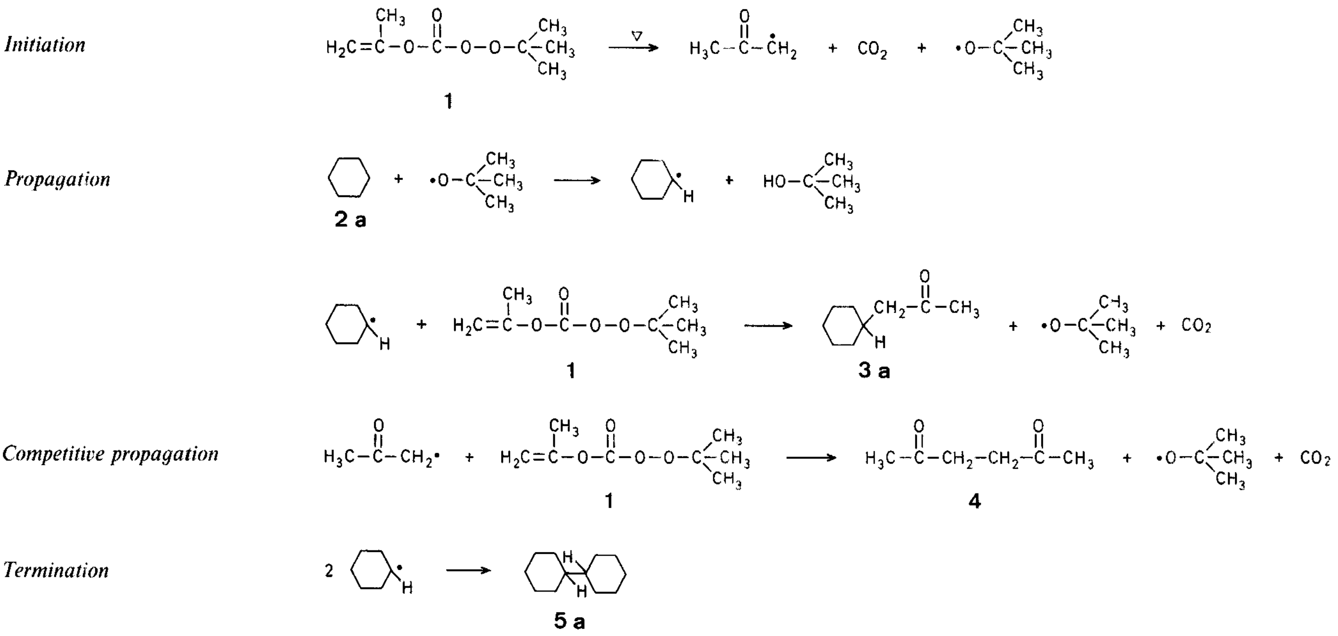
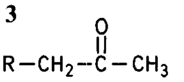
clohexylacetone **3a** with minor amounts of acetonylacetone (**4**) and bicyclohexyl (**5a**).



On the basis of chemical and kinetic data[2] it may be assumed that the reaction proceeds via a free-radical chain mechanism:



The high yields of cyclohexylacetone (**3a**) as well as the facile separation of the by-products (distillation) prompted us to attempt the preparation of compounds of the general formula 3


3

$R-CH_2-C(=O)-CH_3$

using various compounds R—H (**2**) as solvent instead of cyclohexane (**2a**). As expected, any compound capable of undergoing free-radical addition to alkenes[3] may thus be acetonylated. The reaction proceeds with cycloalkanes (**2a, b**), cyclic ethers (**2c, d**), saturated ketones (**2e, f**), alkanoic acids (**2g, h**) and esters (**2i**), alkanedioic esters such as succinic esters (**2j**) and malonic esters (**2k**), and alkanenitriles (**2l, m**); it cannot be successfully performed with solvents which give stabilized free radicals such as cumene [in this case, 2,5-hexanedione (**4**) is the main product].

The acetonylation is carried out at 130 °C using a 2.5 h reaction time. The ratios **1/2** given in the Table represent the optimum conditions. Whereas in the case of compounds **1a-f** the reaction is fairly independent from the concentration of the peroxycarbonate **1**, the yields of acetonylation products **3** obtained from compounds **1g-m** are somewhat lowered when a ratio **1/2** higher than 1/50 is used (with ratios 1/5 the yields are about half of the yields obtained using 1/50 ratios). In all cases, the isolation of products **3** is easy so that also higher peroxycarbonate concentrations may be used when only a small quantity of **2** is available.

As regards the preparative utility of our acetonylation method it compares favorably with the method of Ref.[4]. Although the yields of the acetonylation step are higher in the method of Ref.[4] our method may have the advantage of better overall yields since the preparation of peroxycarbonate **1** appears to be more efficient than the synthesis of 2-methoxyallyl bromide used as acetonylation reagent in the method of Ref.[4]; further, the method of Ref.[4] cannot be applied to the acetonylation of cycloalkanes and ethers whereas our method affords fairly good results in these cases.

O-O-t-Butyl *O*-Isopropenyl Peroxycarbonate (1):

Isopropenyl carbonochloridate (12.2 g, 0.1 mol) is added dropwise to a stirred, ice-cooled solution of *t*-butyl hydroperoxide (9.0 g, 0.1 mol) and pyridine (9.2 g, 0.11 mol) in pentane (100 ml). After the addition is complete stirring is continued at 0 °C for 1 h. Ice/water (40 ml) is added; the pentane solution is separated and washed with cold dilute hydrochloric acid (20 ml to eliminate excess pyridine). The organic layer is finally washed with saturated sodium chloride solution (40 ml) and dried with sodium sulfate. The pentane is removed at 25 °C under reduced pressure to give crude **1**; yield: 13 g (75%, based on isopropenyl carbonochloridate). In most cases, the crude compound **1** may be used in the acetonylation reaction. Purification may be achieved by column chromatography on Florisil® using pentane as eluent. [As with many peroxy compounds, a satisfactory microanalysis could not be obtained].

^{1}H-N.M.R. (CCl_4/TMS_{int}): $\delta = 4.5$-4.8 (m, 2H, $\underline{H}_2C{=}C$); 1.93 (s, 3H, $H_2C{=}C{-}C\underline{H}_3$); 1.28 ppm [s, 9H, $-C(C\underline{H}_3)_3$].

General C-Acetonylation Procedure (to give Compounds 3):

An autoclave containing the solution of *O-O-t*-butyl *O*-isopropenyl peroxycarbonate (**1**; 4.4 g, 0.025 mol) in the appropriate solvent (**2**; 0.125 mol for compounds **2a-f**; 1.25 mol for compounds **2g-m**) is heated at 130 °C in a thermostat oven for 2.5 h. Excess solvent is then distilled off and the residual product **3** distilled at reduced pressure (product **3h** is recrystallized from dichloromethane/hexane).

Acknowledgments are made to the Societé Nationale des Poudres et Explosifs (France) for a generous gift of isopropenyl carbonochloridate.

Table. *C*-Acetonylation of Substrates R—H (**2**) with *O*-*O*-*t*-Butyl *O*-Isopropenyl Peroxycarbonate (**1**)

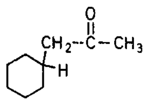
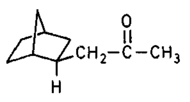
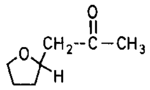
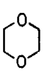
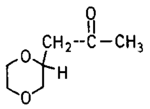
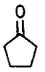
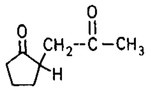
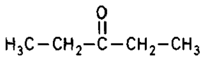
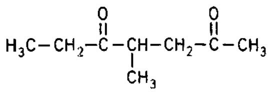
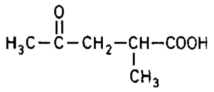
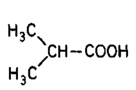
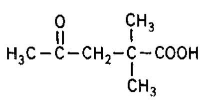
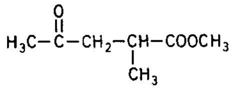
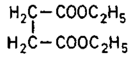
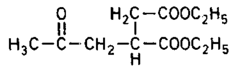
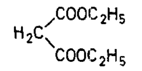
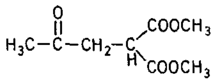
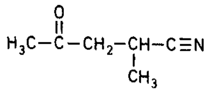
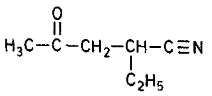
2, 3	Educt 2	Ratio **1/2**	Product 3	Yield[a] [%]	b.p./torr or m.p. [°C]	Lit. Data [°C] or Molecular formula	n_D^{20}	¹H-N.M.R. (CCl_4/TMS_{int}) δ [ppm]
a		1/5		55	b.p. 88-89°/20	b.p. 30°/0.1[5]	1.4274	0.8-2.0 (m, 11 H_{cycl}); 2.05 (s, 3 H, $CH_2{-}CO{-}C\underline{H}_3$); 2.1-2.4 (m, 2 H, $C\underline{H}_2{-}CO{-}CH_3$)
b		1/5	 (exo)	40	b.p. 99-101°/35	b.p. 90-93°/32[6]	1.4637	0.7-2.5 (m, 9 H_{cycl}); 2.04 (s, 3 H, $CH_2{-}CO{-}C\underline{H}_3$); 2.15-2.45 (m, 2 H, $C\underline{H}_2{-}CO{-}CH_3$)
c		1/5		25	b.p. 70-72°/20	[b]	1.4538	1.5-2.0 [m, 4 H, $C\underline{H}_2{-}C\underline{H}_2{-}CH$(acetonyl)—O]; 2.15 (s, 3 H, $CH_2{-}CO{-}C\underline{H}_3$); 2.2-2.8 (m, 2 H, $C\underline{H}_2{-}CO{-}CH_3$); 3.0-4.3 [m, 3 H, $C\underline{H}_2{-}O{-}C\underline{H}$(acetonyl)—]
d		1/5		41	b.p. 80-82°/20	$C_7H_{10}O_3$[c] (142.1)	1.4548	2.10 (s, 3 H, $CH_2{-}CO{-}C\underline{H}_3$); 2.2-2.7 (m, 2 H, $C\underline{H}_2{-}CO{-}CH_3$); 3.5-4.2 (m, 7 H_{cycl})
e		1/5		56	b.p. 120-121°/15	b.p. 112-113°/11[4]	1.4628	2.07 (s, 3 H, $CH_2{-}CO{-}C\underline{H}_3$); 0.8-3.1 (m, 9 H, 7 H_{cycl} + $C\underline{H}_2{-}CO{-}CH_3$)
f	 $H_3C{-}CH_2{-}\overset{O}{\overset{\|}{C}}{-}CH_2{-}CH_3$	1/5	 $H_3C{-}CH_2{-}\overset{O}{\overset{\|}{C}}{-}\underset{CH_3}{\underset{\vert}{C}H}{-}CH_2{-}\overset{O}{\overset{\|}{C}}{-}CH_3$	70	b.p. 90-92°/24	b.p. 62°/3[8]	1.4265	0.97 (t, 3 H, *J* = 7 Hz, $\underline{H}_3C{-}CH_2$); 1.02 (d, 3 H, *J* = 6.5 Hz, $CH{-}C\underline{H}_3$); 2.02 (s, 3 H, $CH_2{-}CO{-}C\underline{H}_3$); 2.1-3.0 (m, 5 H, $C\underline{H}_2{-}CO{-}\underset{\vert}{C\underline{H}}C\underline{H}_2{-}CO$)
g	$H_3C{-}CH_2{-}COOH$	1/50	 $H_3C{-}\overset{O}{\overset{\|}{C}}{-}CH_2{-}\underset{CH_3}{\underset{\vert}{C}H}{-}COOH$	52	b.p. 100-102°/0.5	b.p. 135-136°/8[9]	1.4438	1.15 (d, 3 H, *J* = 6.5 Hz, $CH{-}C\underline{H}_3$); 2.08 (s, 3 H, $\underline{H}_3C{-}CO{-}CH_2$); 2.2-3.3 (m, 3 H, $CO{-}C\underline{H}_2{-}C\underline{H}$); 11.8 (s, 1 H, OH)
h	 $(H_3C)_2CH{-}COOH$	1/50	 $H_3C{-}\overset{O}{\overset{\|}{C}}{-}CH_2{-}\underset{CH_3}{\overset{CH_3}{C}}{-}COOH$	41	m.p. 75-76°	m.p. 74.5-75°[c,10]	—	1.20 [s, 6 H, $C(C\underline{H}_3)_2$]; 2.05 (s, 3 H, $\underline{H}_3C{-}CO{-}CH_2$); 2.71 (s, 2 H, $H_3C{-}CO{-}C\underline{H}_2$); 12.0 (s, 1 H, OH)
i	$H_3C{-}CH_2{-}COOCH_3$	1/50	 $H_3C{-}\overset{O}{\overset{\|}{C}}{-}CH_2{-}\underset{CH_3}{\underset{\vert}{C}H}{-}COOCH_3$	57	b.p. 101-103°/25	b.p. 91-92°/20[11]	1.4240	1.11 (d, 3 H, *J* = 6.5 Hz, $CH{-}C\underline{H}_3$); 2.06 (s, 3 H, $\underline{H}_3C{-}CO{-}CH_2$); 2.1-3.2 (m, 3 H, $C\underline{H}_2{-}C\underline{H}$); 3.72 (s, 3 H, $COOC\underline{H}_3$)
j	 $H_2C{-}COOC_2H_5$ / $H_2C{-}COOC_2H_5$	1/50	 $H_3C{-}\overset{O}{\overset{\|}{C}}{-}CH_2{-}\underset{H}{\overset{H_2C-COOC_2H_5}{C}}{-}COOC_2H_5$	64	b.p. 80-82°/0.2	b.p. 135°/1.3[12]	1.4418	1.18 (t, 6 H, *J* = 7.3 Hz, $2\,COO{-}CH_2{-}C\underline{H}_3$); 2.10 (s, 3 H, $\underline{H}_3C{-}CO{-}CH_2$); 2.3-2.9 (m, 5 H, $C\underline{H}_2{-}C\underline{H}{-}C\underline{H}_2$); 4.02 (q, 4 H, *J* = 7.3 Hz, $2\,COO{-}C\underline{H}_2{-}CH_3$)

Table. (Continued)

2, 3	Educt 2	Ratio 1/2	Product 3	Yield[a] [%]	b.p./torr or m.p. [°C]	Lit. Data [°C] or Molecular formula	n_D^{20}	¹H-N.M.R. (CCl_4/TMS_{int}) δ [ppm]
k		1/50		52	b.p. 92-94°/0.5	b.p. 135-136°[13]	1.4357	2.11 (s, 3H, $\underline{H}_3C-CO-CH_2$); 3.0 (d, 2H, $J=6.0$ Hz; $H_3C-CO-C\underline{H}_2-CH$); 3.3 (t, 1H, $J=6.0$ Hz, $H_3C-CO-CH_2-C\underline{H}$); 3.6 (s, 6H, $2COOC\underline{H}_3$)
l	$H_3C-CH_2-C\equiv N$	1/50	 $H_3C-\overset{\overset{O}{\|}}{C}-CH_2-\underset{\underset{CH_3}{\mid}}{CH}-C\equiv N$	32	b.p. 105-107°/22	b.p. 68°/1[14]	1.4260	1.27 (d, 3H, $J=6.6$ Hz, $CH-C\underline{H}_3$); 2.10 (s, 3H, $\underline{H}_3C-CO-CH_2$); 2.4-3.3 (m, 3H, $C\underline{H}_2-C\underline{H}$)
m	$H_3C-CH_2-CH_2-C\equiv N$	1/50	 $H_3C-\overset{\overset{O}{\|}}{C}-CH_2-\underset{\underset{C_2H_5}{\mid}}{CH}-C\equiv N$	25	b.p. 83-85°/0.8	b.p. 85-87°/0.5[4]	1.4349	0.9-1.9 (m, 5H, $C\underline{H}_2-C\underline{H}_3$); 2.11 (s, 3H, $\underline{H}_3C-CO-CH_2$); 2.2-3.0 (m, 3H, $H_3C-CO-C\underline{H}_2-C\underline{H}$)

[a] Yield of isolated product (pure by G.L.C. analysis), based on **1**.

[b] The literature value[7], b.p. 96 °C/1 torr, seems to be incorrect.

[c] To our knowledge, product **3d** is a new compound.

calc.	C 59.11	H 7.11	O 33.78
found	59.16	7.15	33.7

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