Metal Oxide-Initiated Alkylation of Compounds Containing Activated Methene Groups with Terminal Alkenes[1]

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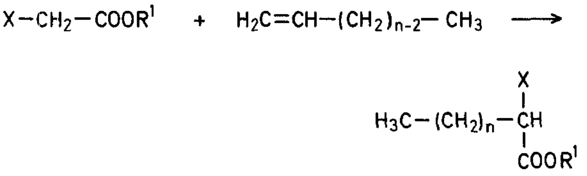
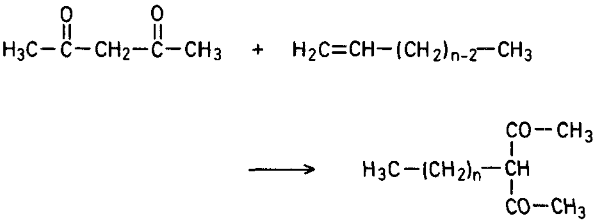
Malonic esters, acetoacetic esters, cyanoacetates, or acetylacetone, in which the displacement reaction on an α-hydrogen is enhanced by the two neighbouring activating groups, add in the presence of organic peroxides to 1-alkenes to give mono-*n*-alkyl esters **1** or mono-*n*-alkyl β-diketones **2** as main products[2-10].



$$X-CH_2-COOR^1 + H_2C=CH-(CH_2)_{n-2}-CH_3 \longrightarrow H_3C-(CH_2)_n-CH(X)-COOR^1$$

1

X = $COOR^2$, H_3C-CO-, $-CN$
R^1 = C_2H_5, C_3H_7, C_4H_9
n = 5, 7, 9

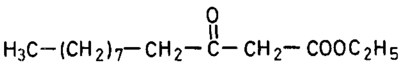


$$H_3C-\overset{O}{\overset{\|}{C}}-CH_2-\overset{O}{\overset{\|}{C}}-CH_3 + H_2C=CH-(CH_2)_{n-2}-CH_3 \longrightarrow H_3C-(CH_2)_n-CH(CO-CH_3)_2$$

2

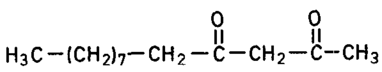
n = 5, 7, 9

The 1:1 adducts were obtained in yields varying between 54 and 79% in dependence on the mol ratio of ester or dione to 1-alkene and organic peroxide (10–30:1:0.1–0.3) at 105–160° (4 days/4 h); in the alkylation of ethyl acetoacetate and acetylacetone, the isomeric 1:1 adducts **3** and **4**, respectively, were simultaneously produced owing to formation of radicals arising by abstraction of hydrogen from the acetyl group and to interaction of these radicals with 1-octene[7].



$$H_3C-(CH_2)_7-CH_2-\overset{O}{\overset{\|}{C}}-CH_2-COOC_2H_5$$

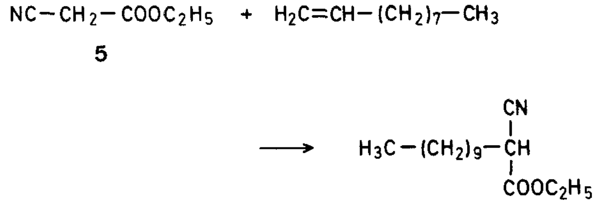
3



$$H_3C-(CH_2)_7-CH_2-\overset{O}{\overset{\|}{C}}-CH_2-\overset{O}{\overset{\|}{C}}-CH_3$$

4

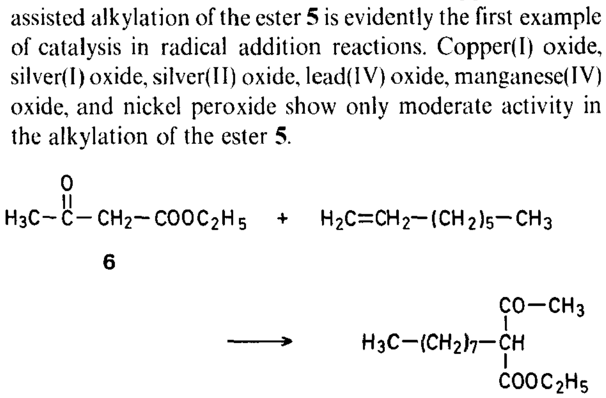
We now report that the alkylation of compounds containing activated methene groups, such as ethyl cyanoacetate (**5**), ethyl acetoacetate (**6**), diethyl malonate (**7**), or acetylacetone (**8**), with 1-alkenes can be effectively initiated by certain metal oxides. From the results summarized in the Table it follows that the 1:1 adducts **1** or **2** are formed with high selectivity under optimum and relatively mild reaction conditions in 49–87% yields.



$$NC-CH_2-COOC_2H_5 + H_2C=CH-(CH_2)_7-CH_3 \longrightarrow H_3C-(CH_2)_9-CH(CN)(COOC_2H_5)$$

5 **9**

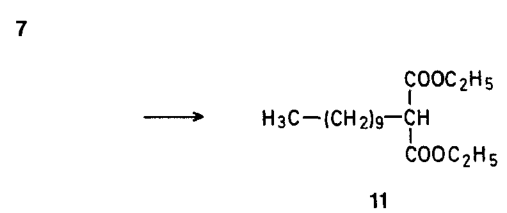
Copper(II) oxide was found to be most effective in the alkylation of the ester **5** with 1-alkenes; when, for example, **5** was allowed to react (80°, 2.5 h) with 1-decene in the presence of kieselguhr-supported copper(II) oxide at concentrations corresponding to a mol ratio of 50:1:0.05 (2.8% wt. of CuO on 1-decene), ethyl α-cyanododecanoate ($9 \equiv 1$; X = CN, $R^1 = C_2H_5$, n = 9) was formed in 84% yield. Recovered copper(II) oxide had unchanged activity after this and the next cycle and it behaved as a catalyst rather than as an initiating agent. When the reaction was repeated using the same concentrations of the reactants, but with di-*t*-butyl peroxide as initiator, only 33% of the adduct **9** was obtained at 95% conversion of 1-decene (140°, 2 h). This copper(II) oxide-assisted alkylation of the ester **5** is evidently the first example of catalysis in radical addition reactions. Copper(I) oxide, silver(I) oxide, silver(II) oxide, lead(IV) oxide, manganese(IV) oxide, and nickel peroxide show only moderate activity in the alkylation of the ester **5**.



$$H_3C-\overset{O}{\overset{\|}{C}}-CH_2-COOC_2H_5 + H_2C=CH_2-(CH_2)_5-CH_3 \longrightarrow H_3C-(CH_2)_7-CH(CO-CH_3)(COOC_2H_5)$$

6 **10**

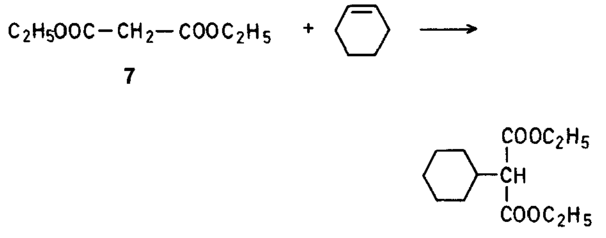
The silver(II) oxide- (or manganese(IV) oxide) initiated alkylation of the ester **6** with 1-octene gave the 1:1 adduct, ethyl α-acetyldecanoate ($10 \equiv 1$; X = CH_3CO, $R^1 = C_2H_5$, n = 7) in yields comparable with those obtained using di-*t*-butyl peroxide as initiator[6,7]; however, less than 1% of the isomeric ethyl 3-oxododecanoate (**3**) was formed in contrast to 6% of **3** in the di-*t*-butyl peroxide-initiated reaction[7]. Formation of the dimer, diethyl 2,3-diacetylsuccinate, was not observed. Silver(I) oxide and copper(II) oxide or lead(IV) oxide were less efficient in the alkylation of **6**.



$$C_2H_5OOC-CH_2-COOC_2H_5 + H_2C=CH-(CH_2)_7-CH_3 \longrightarrow H_3C-(CH_2)_9-CH(COOC_2H_5)_2$$

7 **11**

Manganese(IV) oxide, though less active than di-*t*-butyl peroxide, showed highest initiating efficiency in the alkylation of the diester **7** with 1-decene; the yields of diethyl *n*-decylmalonate ($11 \equiv 1$; X = $COOC_2H_5$, $R^1 = C_2H_5$, n = 9) were somewhat higher than those reported for the di-*t*-butyl peroxide induced alkylation reaction[5,6,8,9]



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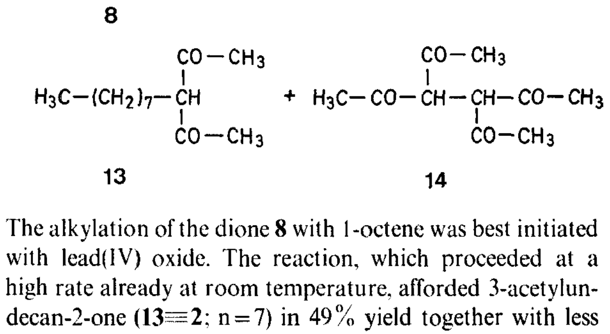
The known lower reactivity of cycloalkenes in radical addition reactions[11] led only to a moderate yield of diethyl cyclohexylmalonate (**12**) in the silver(II) oxide-initiated reaction of cyclohexene with the diester **7**.



$$H_3C-\overset{O}{\overset{\|}{C}}-CH_2-\overset{O}{\overset{\|}{C}}-CH_3 + H_2C=CH-(CH_2)_5-CH_3 \longrightarrow H_3C-(CH_2)_7-CH(CO-CH_3)_2 + H_3C-CO-CH(CO-CH_3)-CH(CO-CH_3)-CO-CH_3$$

8 **13** **14**

The alkylation of the dione **8** with 1-octene was best initiated with lead(IV) oxide. The reaction, which proceeded at a high rate already at room temperature, afforded 3-acetylundecan-2-one ($13 \equiv 2$; n = 7) in 49% yield together with less than 1% of the easily separable dimer, 3,4-diacetylhexane-2,5-dione (**14**); only traces of the isomeric 1:1 adduct, tridecane-2,4-dione (**4**) were detected in the product. Silver oxides and manganese(IV) oxide were less active; moreover, silver oxides yielded higher amounts of the dimer **14**. Significant amounts of lead(IV) oxide, manganese(IV) oxide, and silver oxides dissolved in the alkene-**8** mixture already at the very beginning of the reaction; under these circumstances, the acetylacetonates of the higher valent metals, which are only temporarily stable under the given reaction conditions, are presumably the actual initiating agents. Copper(II) oxide, which readily affords stable copper(II) acetylacetonate, showed no activity in this addition reaction. The high formation of the hardly separable isomer **4** (1 mol per 1.5–2.1 mol of **13**) in the di-*t*-butyl peroxide-initiated reactions was found to be in relation with the high degree of enolization of **8** in 1-octene-**8** mixtures[7]. The exclusive formation of the 1:1 adduct **13** in the metal oxide-initiated reaction indicates that this reaction proceeds in the presence of redox systems independently of the keto-enol equilibrium of the dione **8**. Results of investigations pursuing elucidation of this point will be reported in the near future.

Ethyl α-Cyanododecanoate (9):

The magnetically stirred suspension of copper(II) oxide (0.08 g; 0.001 mol) in the ester **5** (22.6 g; 0.2 mol) is heated under nitrogen at 85° and 1-decene (2.8 g; 0.02 mol) is added dropwise by means of a capillary tube during 3 h at such a rate as to maintain 50:1 mol ratio of **5** to 1-decene in the mixture. After further heating for 2 h, 98% of 1-decene is consumed and the yield of **9** reaches 83% (G.L.C.); the suspension is cooled to room tempera-

Table. Metal-Oxide Initiated Alkylation of Ethyl Cyanoacetate, Ethyl Acetoacetate, Diethyl Malonate, and Acetylacetone with 1-Alkenes and Cyclohexene (Reactions on 1–20 mmol Alkene Scale)

Ester or dione	Alkene	Metal oxide[a]	Molar ratio ester or dione:alkene :metal oxide	Reaction conditions (temp./time)	Overall alkene conversion [%]	Product and yield[b] [%]
5	1-decene	CuO[c]	50:1:0.05	80°/2.5 h	99	**9** 84
	1-decene[d]	CuO	10:1:0.05	85°/5 h	98	**9** 83 (75)
	1-decene	NiO_2	50:1:1	27–30°/4 h	90	**9** 62
	1-decene	PbO_2	50:1:1	150°/1 h	95	**9** 72[e]
	1-decene	MnO_2	50:1:1	100°/13 h	98	**9** 55
	1-decene	Cu_2O	50:1:0.1	80°/3 h	99	**9** 51
	1-decene	AgO	50:1:1	60°/1 h	>99	**9** 54
6	1-octene[f]	AgO	10:1:1	50°/1 h	99	**10** 57 (51)[g]
	1-octene	MnO_2	50:1:2	130°/4 h	91	**10** 54[g]
7	1-decene	MnO_2	50:1:2	170°/5 h	>99	**11** 71
	1-decene	MnO_2	200:1:2	170°/5.5 h	>99	**11** 87
	1-decene[h]	MnO_2	20:1:2	170°/16 h	99	**11** 84 (74)
	1-decene	AgO	50:1:2	80°/5.5 h	>99	**11** 65
	1-decene	Ag_2O	50:1:2	90°/4 h	>99	**11** 67
	cyclohexene	AgO	20:1:2	80°/6 h	81	**12** – (45)
8	1-octene	PbO_2	20:1:1	31°/5 h	99	**13** 49 (45)
	1-octene	AgO	20:1:2	60°/1.5 h	98	**13** 47[i]
	1-octene	Ag_2O	20:1:2	85°/0.5 h	99	**13** 49[i]

[a] Unless otherwise stated, metal oxides from the same sources were used as previously described[15,16]

[b] Yields based on the initial amount of alkenes and determined by G.L.C. utilizing authentic product samples as standards; figures in parentheses indicate isolated yields. Satisfactory microanalyses (C ±0.15%, H ±0.10%), and I.R. or N.M.R. spectra were obtained for all products.

[c] Kieselguhr-supported CuO (CuO, 50% by wt.); 1 wt. equivalent of CuO was used.

[d] 1-Decene was gradually added during 3 h at such a rate as to maintain a 50:1 mol ratio of **5** to 1-decene in the mixture which was then heated for further 2 h.

[e] Partial decomposition of **5** was observed.

[f] 1-Octene was gradually added during 45 min and the mixture was heated further for 15 min.

[g] Less than 1% of **3** was also formed.

[h] 1-Decene was gradually added during 12 h at such a rate as to maintain a 200:1 mol ratio of **7** to 1-decene in the mixture which was further heated for 4 h.

[i] The dimer **14** was also formed in 0.5–1% yield according to G.L.C.

ture, copper(II) oxide is filtered off and washed with acetone (3 × 5 ml). Combined filtrate and washings are freed of acetone by evaporation and the unreacted ester **5** is recovered by distillation in vacuo. Short-path distillation of the oily residue in vacuo gives the pure adduct **9** as a colorless liquid; yield 3.81 g (75%); b.p. 133–134°/1.5 torr (Ref.[12] b.p. 108–110°/0.05 torr).

$C_{15}H_{27}NO_2$	calc.	C 71.10	H 10.74
(253.4)	found	71.03	10.72

The I.R. spectrum was identical with that shown by an authentic sample[12]. Recovered copper(II) oxide was free of metallic copper and copper(I) oxide and exhibited unchanged activity.

3-Acetylundecan-2-one (13):

The suspension of lead(IV) oxide (4.8 g; 0.02 mol) in the dione **8** (40 g; 0.4 mol) and 1-octene (2.24 g; 0.02 mol) is magnetically stirred under nitrogen at 31° for 5 h. The conversion of 1-octene is 99% and the yield of **13** reaches 49% (G.L.C.). The mixture is cooled to 0° and the inorganic precipitate [mainly lead(II) acetonylacetonate] is filtered off and washed with diethyl ether (20 ml). Combined filtrate and washings are extracted with aqueous 4% nitric acid solution (4 × 10 ml), the aqueous layer is separated and washed with ether (2 × 15 ml). Combined organic layers and washings are treated with aqueous sodium hydrogen carbonate solution and dried ($MgSO_4$). The product is freed of diethyl ether and the unreacted dione **8** is recovered by distillation in vacuo. Short-path distillation of the oily residue in vacuo gives 2.05 g of the crude **13** and 2.25 g of undistillable telomers. The crude adduct **13** is cooled to 0°, the precipitated crude dimer **14** (0.05 g; yield 0.1%) is filtered off and recrystallized from ethanol; m.p. 188–189° (Ref.[13] m.p. 189–191°).

$C_{10}H_{14}O_4$	calc.	C 60.59	H 7.12
(198.2)	found	60.67	6.96

3,5,3′,5′-Tetramethyldipyrazol-4-yl prepared from the dimer **14** and hydrazine hydrate[14] had m.p. 298–300° (Ref.[14] m.p. 299–300°). Short-path distillation of the filtrate from the isolation of the crude **14** gave the pure adduct **13**; yield 1.90 g (45%); b.p. 130–132°/12 torr (Ref.[7] b.p. 64–65°/0.04 torr).

$C_{13}H_{24}O_2$	calc.	C 73.54	H 11.39
(212.3)	found	73.30	11.10

^{1}H-N.M.R. (in CCl_4 with respect to hexamethyldisilane): $\delta = 0.83$ (t, 3H, $C\underline{H}_3$); 1.25 (m, 14H, $C\underline{H}_2$); 2.03 (s, CH_3CO); 3.48 (t, $C\underline{H}$); 16.62 ppm (s, $C(OH){=}C$).

The retention time of **13** in G.L.C. (column 3 m × 3 mm, SE 302, 11.5% on Chromosorb W (30–60 mesh), 180°) was 17.7 min; the retention time of an authentic sample of **4**[7] was 20.8 min. Only traces of **4** were detected.

The copper(II) salt of the adduct **13** had m.p. 151° (Ref.[7] m.p. 152.5°).

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