chiral center influences the stereoselectivity of the Grignard addition.) Adduct **13** and its stereoisomers were cleaved[14] and reduced to **14** and its stereoisomers as previously described.[8,9]

Ozonization of the phenyl group (Scheme V) required prior protection of the hydroxyl functions in **14** by trifluoroacetylation to **15**. No epimerization at the tertiary carbinol center occurred in this process, in as much as **15** could be hydrolyzed back to **14** without overall change. Ozonization of **15** adsorbed on silica gel[16] to acid **16** followed by hydrolysis to **17** and lactonization to (−)-malyngolide proceeded in moderate (36–43%) yield in the various series (cf. Table I).

Malyngolide can be readily distinguished from epimalyngolide by the proton NMR pattern of the CH$_2$OH group. Malyngolide displays a characteristic AB pattern centered at 3.57 ppm, $J = 12$ Hz (3.47, 3.67 ppm) whereas epimalyngolide shows a highly degenerate AB pattern with unresolved inner peaks at 3.60 ppm and very small outer peaks, $J = 12$ Hz. Since the enantiomeric purity of (*R*)-**7** was 96.8% and the reaction **7** + **10** (Scheme IV) was 98% diastereoselective, it may be calculated that the (−)-malyngolide synthesized should be 97.4% diastereomerically pure[17] and 100% enantiomerically pure *provided* no epimerization occurs in the course of the reactions shown in Scheme V. The proton NMR spectrum of (−)-malyngolide indicated about 4% epimalyngolide, which was removed chromatographically. The final product had $[\alpha]^{20}_{D}$ −13.4° (CHCl$_3$, *c* 2.01) [lit.[1] [α] −13.0°, lit.[5a] [α] −12.3°, lit.[5b] [α] −12.7°], proton NMR spectrum[18] identical with that of the natural product, ^{13}C NMR, mass, and IR spectra as reported.[1]

The combination of (*S*)-**7** and **12** in analogous manner produced (+)-malyngolide, calculated diastereomeric purity 95.5%, enantiomeric purity 99.9%; the proton NMR spectrum indicated 4% epimalyngolide. After purification the malyngolide had $[\alpha]^{20}_{D}$ +12.4° (CHCl$_3$, *c* 2.02). We believe the slightly low rotation to be due to a nonstereoisomeric impurity.[19] Combination of (*R*)-**7** and **12** was the worst of the four studied, giving (−)-epimalyngolide (5-epimalyngolide) in a calculated diastereomeric purity of only 87.6% (but still 99.8% enantiomerically pure). Proton NMR confirmed the presence of 13% malyngolide, which was, however, readily removed by column chromatography to give pure epimalyngolide, $[\alpha]^{20}_{D}$ −20.8° (CHCl$_3$, *c* 2.04). In contrast, the combination of (*S*)-**7** and **10** gave very pure (+)-epimalyngolide (2-epimalyngolide), calculated diastereomeric purity 95.4%, enantiomeric purity 100%, found malyngolide content 2%, $[\alpha]^{20}_{D}$ +21.2° (CHCl$_3$, *c* 2.005) after purification [lit.[5a] [α] +19.1°; lit.[5b] [α] 17°].

Rotations of the unseparated (and therefore diastereomerically impure) intermediates **14** are included in Table I. The high rotation of (2*R*,5*R*)-**14** is evidently not due to high purity but rather to contamination with the higher rotating (2*R*,5*S*) epimer.

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[16] Klein, H.; Steinmetz, A. *Tetrahedron Lett.* **1975**, 4249.

[17] This is the expected percentage of malyngolide in the malyngolide–epimalyngolide mixture, *not* the diastereomeric excess.

[18] We thank Professor T. Mukaiyama for supplying us with proton NMR spectra of (−)-malyngolide and (+)-epimalyngolide.

[19] The fact that the calculated and found percentages of epimeric impurities agreed within experimental error in all four cases is an indication that no epimerization and hence no racemization occurred in the course of the synthesis.

Synthesis of 2-(4-Nitroaryl)propionate Esters

Summary: Alkyl 2-chloropropionates react with nitroaromatic compounds on treatment with base to give alkyl 2-(4-nitroaryl)propionates in good yield.

Sir: Only a few methods of effecting nucleophilic aromatic substitution for hydrogen are synthetically useful.[1] Makosza and coworkers reported that nitroarenes are alkylated by certain carbanions bearing leaving groups at the anionic carbon atoms (Scheme I).[2] Although the success of this process is quite dependent on the substrates and reaction conditions, some leaving group-substituted sulfones[2a], nitriles[2b], sulfoxides[2e] phosphine oxides[2c], and phosphonates[2c] were effectively employed as nucleophiles.

We report the alkylation of nitroaromatic compounds by a new class of nucleophiles, α-halocarboxylic esters. Specifically, use of the readily available and relatively inexpensive 2-chloropropionate esters provides access to 2-(4-nitrophenyl)propionates in good yield with high regioselectivity (Scheme II). These reactions do not work well in the NaOH–Me$_2$SO system frequently used by Makosza[2] but proceed readily in DMF or *N*,*N*-dimethylacetamide (DMAc) using NaH, potassium *tert*-butoxide (PTB), or sodium *tert*-butoxide as base. Substrates, reaction conditions, products, and yields are shown in Table I. In each case only a single isomer was observed and products always resulted from reaction at the unsubstituted 4-position.

A typical procedure consists of dropwise addition of 1 equiv each of ester and arene onto an ice-cold mixture of 2 equiv of base in solvent. The reactions are quite exothermic[3] and occur immediately on mixing the reactants. The rate of reactant addition is adjusted to maintain the desired temperature. After reaction is complete the crude mixture is partitioned between 1 N HCl and diethyl ether. The products are isolated from the ether phase by distillation or chromatography.

Examination of Table I shows that variation of the nitroaromatic ring substituents and variation of the alcohol portion of the esters had little effect on the yields of products. However, the reaction of phenyl 2-chloropropionate with nitrobenzene under the conditions most suitable for the alkyl ester reactions does not give the anticipated arylpropionate product. In a NaH–DMF system this reaction affords only phenyl 2-phenoxy-

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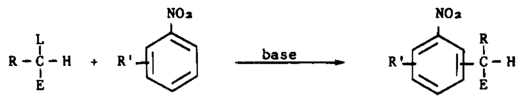
[1] For reviews, see: Chupakhin, O. N.; Postouskii, I. Ya. *Uspekhi Khimii* **1976**, *45*, 908. de Boer, Th. J.; Dirkx, I. P. In "The Chemistry of the Nitro and Nitroso Groups"; Fever, H., Ed.; Interscience: New York, 1969; Vol. 1, p 554. Also see: Armillotta, N.; Bartoli, G.; Bosco, M.; Dalpozzo, R. *Synthesis* **1982**, 836 and references cited therein.

[2] (a) Golinski, J.; Makosza, M. *Tetrahedron Lett.* **1978**, *3495*. (b) Makosza, M.; Winiarski, J. *J. Org. Chem.* **1980**, *45*, 1534. (c) Makosza, M.; Golinski, J. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 451. (d) Makosza, M. *Int. Conf. Chem. Biotechnol. Biol. Act. Nat. Prod.* (*Proc.*), 1st, **1982**, *Issue* 2, 480–490. (e) Makosza, M.; Golinski, J.; Pankowski, J. *Synthesis* **1983**, 40.

[3] The reaction temperature must be kept below about 50 °C so that the thermal runaway reaction between NaH and DMF is avoided. See: Buckley, J.; Webb, R. L.; Laird, T.; Ward, R. J. *Chem. Eng. News* **1982**, *60*, 5.

Scheme I



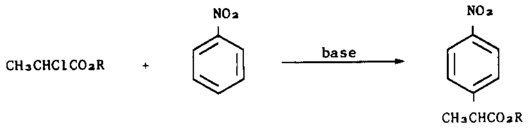
L = leaving group

E = stabilizing group

R = H, alkyl

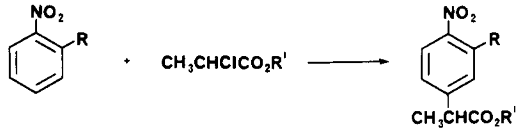
R' = H, halogen, alkoxy, thioalkoxy, aryl

Scheme II



R = alkyl group

Table I. Reactions of Nitroarenes with 2-Chloropropionate Esters[a]



R	R′	base	solvent	temp, °C	yield, %
H	Me	NaH	DMF	20–30	66
H	Et	Me_3COK	DMF	−5–0	80
Cl	Me	NaH	DMF	25–30	68
Cl	Et	Me_3CONa	DMAc	−5–0	83
F	Me	NaH	DMF	0–10	58
F	Me	Me_3COK	DMF	−5–0	55
F	Et	Me_3COK	DMF	−5–0	75
F	*t*-Bu	Me_3COK	DMF	−5–0	65
OPh	Me	Me_3COK	DMF	0–5	56

[a] All new compounds gave satisfactory proton magnetic resonance, infrared and mass spectral data and combustion analyses.

propionate and unreacted nitrobenzene. When PTB is used as base only a trace of phenyl 2-(4-nitrophenyl)propionate is observed; the major components of the product mixture are phenol and nitrobenzene. Apparently phenyl 2-chloropropionate is too susceptible to ester cleavage to be used under these conditions.

Although the mechanism of nitroarylpropionate formation is not yet understood, it is reasonable to envision a Meisenheimer salt intermediate of the type suggested by Makosza. We have observed that bases able to remove the acidic proton from alkyl 2-chloropropionates do not necessarily effect alkylation. For example, methyl 2-chloropropionate and nitrobenzene do not react when treated with a mixture of potassium carbonate and a phase-transfer catalyst in DMF, conditions under which the Darzens reaction between this ester and various aldehydes occurs.[4] This suggests that the pathway may be more complex than rate-determining nucleophilic attack followed by fast elimination of HCl or hydride transfer. Results of further investigations of the mechanism and scope of this useful alkylation reaction are forthcoming.

Registry No. Nitrobenzene, 98-95-3; 2-chloronitrobenzene, 88-73-3; 2-fluoronitrobenzene, 1493-27-2; 2-phenoxynitrobenzene, 2216-12-8; methyl 2-chloropropionate, 17639-93-9; ethyl 2-chloropropionate, 535-13-7; *tert*-butyl 2-chloropropionate, 40058-88-6; methyl 2-(4-nitrophenyl)propionate, 50415-69-5; ethyl 2-(4-nitrophenyl)propionate, 50712-64-6; methyl 2-(3-chloro-4-nitrophenyl)propionate, 24646-28-4; ethyl 2-(3-chloro-4-nitrophenyl)propionate, 50537-08-1; methyl 2-(3-fluoro-4-nitrophenyl)propionate, 86790-39-8; ethyl 2-(3-fluoro-4-nitrophenyl)propionate, 78543-07-4; *tert*-butyl 2-(3-fluoro-4-nitrophenyl)propionate, 88430-80-2; methyl 2-(4-nitro-3-phenoxyphenyl)propionate, 88430-81-3.

Supplementary Material Available: Experimental procedure and spectral and analytical data for methyl 2-(3-fluoro-4-nitrophenyl)propionate and spectral and analytical data for *tert*-butyl 2-(3-fluoro-4-nitrophenyl)propionate and methyl 2-(4-nitro-3-phenoxyphenyl)propionate (2 pages). Ordering information is given on any current masthead page.

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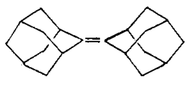
(4) Gladiali, S.; Soccolini, F. *Synth. Commun.* **1982**, *12*, 355.

Electron-Transfer Conversion of Isopropylideneadamantane to its Dioxetane

Summary: Adamantylideneadamantane (1) yields its dioxetane 2 by reaction with $^3O_2$ and catalytic tris(*o,p*-dibromophenyl)aminium hexachloroantiminate (4) at −78 °C in CH_2Cl_2 with a chain length of over 800. Isopropylideneadamantane (5) produces its dioxetane 6 under the same conditions with a chain length of greater than 60.

Sir: Adamantylideneadamantane (1) gives a long-lived radical cation[1] that reacts with oxygen to give a species of greater oxidizing power, causing the characteristic $\overline{\text{E}}\text{C}\overline{\text{E}}$ wave form to be observed in its cyclic voltammogram.[2,3] The dioxetane 2 is produced in a catalytic reaction for which average chain lengths of 8–24[3] and 78[4] have been reported from coulometry studies of the electrochemically catalyzed reaction. Ando and co-workers[4] employed other olefins with "protected" alkyl groups (ones that hold the α-hydrogens in the nodal plane of the π system). They showed that the olefin radical cation–$^3O_2$ reaction produces dioxetane nonstereospecifically, in contrast to the dicyanoanthracene-sensitized photochemical reaction, which proceeds by reaction of olefin radical cation with oxygen radical anion. Chemical oxidants also produce 2 from 1 and $^3O_2$. Use of tris(*p*-bromophenyl)aminium hexachloroantiminate (3) only consumes olefin very slowly, and although $NOPF_6$ and NO_2PF_6 cause rapid reaction, other products than 2 predominate if enough oxidant is employed to consume 1.[2] We report here reaction conditions that make the olefin radical cation–$^3O_2$ dioxetane formation synthetically useful, and its extension to an olefin having methyl substitution, showing that "protection" of all alkyl groups is not necessary for efficient dioxetane formation.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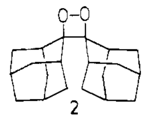

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(2) Nelsen, S. F.; Akaba, R. *J. Am. Chem. Soc.* **1981**, *103*, 2096.
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