(m, 2 H, Bam methylene), 7.10–8.30 (m, 9 H, aromatic plus exchangeable protons).

Anal.[9] Calcd for $C_{12}H_{16}N_2O_3S \cdot CF_3COOH$: C, 43.97; H, 4.45; N, 7.32. Found: C, 44.05; H, 4.61; N, 7.52.

***N*-*tert*-Butyloxycarbonyl-*S*-benzamidomethyl-L-cysteine (3).** A mixture of 1 (4.10 g, 11.1 mmol) and tetramethylguanidine (2.39 g, 22.3 mmol) in 30 mL of anhydrous dimethylformamide was stirred in an ice bath. To the cold reaction mixture was added dropwise and simultaneously *tert*-butyloxycarbonyl azide[6] (2.90 g, 22.3 mmol) and tetramethylguanidine (2.39 g, 22.3 mmol). The mixture was stirred at room temperature for 48 h, and the solvent was removed in vacuo. The residue was dissolved in water (60 mL) and extracted with ether (2 × 20 mL), and the aqueous phase was acidified, with cooling, by the addition of solid citric acid. The oil that separated was extracted with ethyl acetate (100 mL), and the organic phase was washed with water and dried over anhydrous $MgSO_4$. Upon removal of solvent, the product was obtained as a viscous oil that crystallized from ether: 3.75 g (95%); mp 141–142 °C; $[\alpha]^{25}_D$ −28.5° (*c* 1, methanol); R_f 0.8 (A); NMR ($CDCl_3$–Me_2SO-d_6, 5:1) δ 1.46 (s, 9 H, *t*-Bu), 3.16 (m, 2 H, Cys methylene), 4.30–4.80 (m, 3 H, Bam methylene and α-H), 6.40 (m, 1 H, NH), 7.35–8.32 (m, 6 H, aromatic and NH), 8.90 (m, 1 H, carboxyl hydrogen).

Anal. Calcd for $C_{16}H_{22}N_2O_5S$: C, 54.24; H, 6.22; N, 7.70. Found: C, 54.12; H, 6.34; N, 7.56.

***N*-*tert*-Butyloxycarbonyl-*N*-methyl-*S*-benzamidomethyl-L-cysteine Dicyclohexylammonium Salt (4).** Compound 4 was prepared by treatment of a mixture of **2** (12.3 g, 32.2 mmol) and tetramethylguanidine (6.88 g, 64.4 mmol) in 80 mL of dry dimethylformamide with *tert*-butyloxycarbonyl azide (8.36 g, 64.4 mmol) and tetramethylguanidine (6.88 g, 64.4 mmol) as described above for the preparation of **3**. The product **4** was isolated as an oil, which was taken up in cold ether and treated with dicyclohexylamine (5.98 g). The dicyclohexylammonium salt, which crystallized, was collected by filtration, washed with ether (15 mL), and dried to yield 17.2 g (97%) of **4**: mp 147–148 °C; $[\alpha]^{25}_D$ −95° (*c* 1, methanol); R_f 0.77 (A) 0.57 (B); NMR ($CDCl_3$) δ 0.9–2.1 (br m, 31 H, *t*-Bu and cyclohexyl), 2.9 (m, 5 H, *N*-methyl and Cys methylene), 4.3–4.9 (m, 3 H, Bam methylene and α-H), 7.4–8.2 (m, 6 H, aromatic and NH), 8.5–8.9 (br m, 2 H, ammonium NH).

Anal. Calcd for $C_{17}H_{24}N_2O_5S \cdot C_{12}H_{23}N$: C, 63.38; H, 8.56; N, 7.65. Found: C, 63.52; H, 8.66; N, 7.81.

***N*-*tert*-Butyloxycarbonyl-*S*-benzamidomethyl-L-cysteine *N*-Hydroxysuccinimide Ester (5).** A mixture of **3** (1.05 g, 3.0 mmol), *N*-hydroxysuccinimide (0.36 g, 3.0 mmol), and *N,N'*-dicyclohexylcarbodiimide (0.63 g, 3.0 mmol) in dry tetrahydrofuran (10 mL) was stirred at 0 °C for 2 h and then allowed to stand overnight in a refrigerator. The dicyclohexylurea was removed by filtration and the solvent removed in vacuo. The residue was taken up in ethyl acetate (30 mL), washed with 10% $NaHCO_3$ and water, and dried over $MgSO_4$. Removal of the solvent in vacuo gave an amorphous solid that was crystallized from 2-propanol to yield 0.97 g (72%) of ester **5**: mp 145–146 °C; $[\alpha]^{25}_D$ −117.5° (*c* 1, chloroform); R_f 0.86 (A); NMR ($CDCl_3$) δ 1.49 (s, 9 H, *t*-Bu), 2.90 (s, 4 H, succinimido protons), 3.30 (m, 2 H, Cys methylene), 4.83 (m, 3 H, Bam methylene and α-H), 5.78 (m, 1 H, NH), 7.33–8.28 (m, 6 H, aromatic and NH).

Anal. Calcd for $C_{20}H_{25}N_3O_7S$: C, 53.22; H, 5.54; N, 9.31. Found: C, 53.11; H, 5.64; N, 9.41.

Removal of the *S*-Benzamidomethyl Group. Compound 1 (37 mg, 0.1 mmol) was dissolved by warming in 5 mL of methanol–water (1:1). The clear solution was treated at room temperature with mercuric acetate (32 mg, 0.1 mmol) and the mixture was stirred for 1 h. Hydrogen sulfide was passed into the reaction mixture for 10 min and the precipitate was removed by filtration. TLC analysis (solvent A) showed that complete deblocking of 1 had occurred and that the product formed was cysteine as shown by comparison with an authentic sample.

Acknowledgment. Appreciation is expressed to the U.S. Public Health Service (National Cancer Institute, Grant CA 10653) for support of this work.

Registry No.—1, 64840-21-7; **2**, 64840-23-9; **3**, 33375-72-3; **4**, 64840-25-1; 4 free acid, 64840-24-0; **5**, 64852-94-4; L-cysteine hydrochloride, 52-89-1; *N*-hydroxymethylbenzamide, 6282-02-6; *N*-methyl-L-cysteine, 4026-48-6; *tert*-butyloxycarbonylazide, 1070-19-5; dicyclohexylamine, 101-83-7; *N*-hydroxysuccinimide, 6066-82-6.

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(8) The crude product was found to be reasonably pure and could be used to prepare the corresponding Boc derivatives without further purification.
(9) The analytical sample was prepared by recrystallization of 0.5 g of crystalline product from a minimum volume of water.

Reaction of Singlet Oxygen with Nitronate Salts, Conversion of Nitro Compounds into Carbonyls

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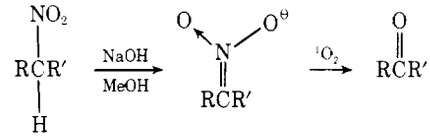
Methods for the conversion of nitro compounds to carbonyls have recently been summarized by McMurray and co-workers.[1] These workers reported that the ozonolysis of nitronate salts produces aldehydes and ketones in good yields. Unfortunately, this method uses ozone, which can react with other functional groups in a substrate, and also involves a relatively long workup procedure. Since singlet oxygen, like ozone, is an electrophilic species, it should also react very rapidly with nitronate results, but may react differently with the rest of the molecule. For example, ozone will react with a monosubstituted olefin,[2] whereas it is inert to singlet oxygen.[3]



Reaction of the nitronate salt with singlet oxygen, generated in situ using dye-sensitized photooxygenation, afforded the corresponding carbonyl compound rapidly and in good yield. Some of our results are given in Table I. When the nitronate salt of 5-nitro-1-hexene was treated with this procedure, 5-keto-1-hexene was obtained, whereas using ozone a ketoozonide would have been produced. To confirm that singlet oxygen was indeed the reactive species involved, 1,4-diazabicyclo[2.2.2]octane (Dabco), a known singlet oxygen quencher, was added.[4] In all cases there was no formation of ketone, indicating Dabco had quenched all the singlet oxygen produced.

In summary, singlet oxygen provides a more facile alternative procedure to the use of ozone for the preparation of carbonyl compounds from nitronate salts. Recently, a very convenient dry method was reported for the conversion of nitro groups into carbonyls.[5]

Experimental Section

General Reaction Procedure. A water-cooled immersion irradiation apparatus similar to the one described by Gollnick and Schenck was used.[6] O_2 was recirculated by a Cole–Parmer Masterflex Tubing Pump. The solutions were irradiated with a Sylvania Q/CL 500-W tungsten–halogen lamp operating at 110 V for 1 h. Oxygen uptake was measured by a gas burette.

The nitro compound (5.0 mM) in 10 mL of methanol with 1 mg of rose bengal added was treated with 1.1 equiv of NaOH (0.55 mL, 10 N) to form the nitronate salt. The solution was then cooled to 0 °C

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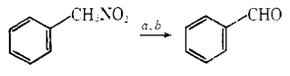
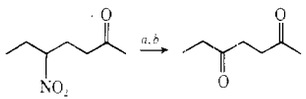
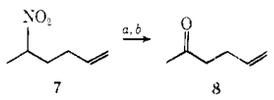
Table I. Oxidation of Nitronate Salts

Reaction	% yield with singlet oxygen	% yield with ozone[1]
 1 → 2	49	68
 3 → 4	60	83
$CH_3(CH_2)_5NO_2$ (5) → $CH_3(CH_2)_5CHO$ (6)	67	65
 7 → 8	66	

[a] OH^-. [b] Rose Bengal, $h\nu$, O_2.

and a stream of oxygen was bubbled through during the irradiation. After warming to room temperature, the solvent was removed in vacuo. The residue was dissolved in chloroform, washed with water, and dried over sodium sulfate. After removal of the solvent, the product was purified by distillation under reduced pressure in a Rinco Kugelrohr. Products were identified by spectral and gas chromatographic comparison with authentic samples. Quenching experiments were done as above adding 4.821 g (42.98 mM) of Dabco to the initial mixture. Gas chromatography of the worked up reaction indicated the absence of any carbonyl products.

Benzaldehyde (2) was prepared from α-nitrotoluene[7] 1 and identified by spectral comparison with an authentic sample: 49% yield.

Heptane-2,5-dione (4) was prepared from 5-nitroheptan-2-one[8] (3) and identified by spectral comparison with an authentic sample: 60% yield.

Octanal (6) was prepared from 1-nitrooctane[9] (5) and identified by spectral comparison with an authentic sample: 67% yield.

5-Nitro-1-hexene (7). Sodium borohydride reduction of 5-hexene-2-one afforded 5-hydroxy-1-hexene: bp 138 °C (lit.[10] bp 140 °C); NMR ($CDCl_3$) δ 3.78 (sextet, 1, J = 6.4 Hz, C-5) and 1.17 (d, 3, J = 6.4 Hz, C-6). Bromination of the alcohol with phosphorus tribromide gave 5-bromo-1-hexene: bp 100 °C (30 mm); NMR ($CDCl_3$) δ 4.14 (sextet, 1, J = 6.5 Hz, C-5), 1.68 (d, 3, C-6). Nitration of the bromohexene with sodium nitrite in dimethyl sulfoxide[9] afforded 5-nitro-1-hexene (7): bp 105 °C (30 mm); IR (film) 3020, 2925, 2850 (CH), 1630 (C=C), 1530, (NO_2), 1340, 990 (CH=CH_2), 915 (C=CH_2), 857 cm^{-1}; NMR ($CDCl_3$) δ 6.0–5.55 (m, 1, C-2), 5.2–4.9 (m, 2, C-1), 4.58 (br sextet, 1, J = 6.5 Hz, C-5), 2.3–1.6 (m, 4, C-3,4), 1.51 (d, 3, J = 6.5 Hz, C-6). Anal. Calcd for $C_6H_{11}NO_2$: C, 55.79; H, 8.58. Found: C, 55.72; H, 8.52.

5-Hexen-2-one (8) was prepared from 5-nitro-1-hexene (7) and identified by spectral comparison with an authentic sample: 66% yield.

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Registry No.—5-Hydroxy-1-hexene, 626-94-8; 5-bromo-1-hexene, 4558-27-4.

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Alkyl Inductive Effects: New-Model Systems for Defining Intrinsic Polar Substituent Effects by Fluorine-19 and Carbon-13 Nuclear Magnetic Resonance

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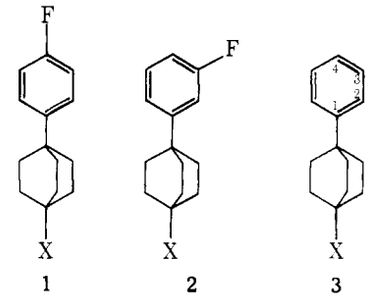
The inductive effects of alkyl substituents continue to attract interest. According to Taft and Levitt,[1] alkyl induction is significant and, together with polarizability effects, is quantitatively reflected by new σ_1 values (Me, −0.046; Et, −0.057; *i*-Pr, −0.065; *t*-Bu, −0.074) derived from a statistical analysis of gas-phase ionization potential data and polarizability "models".[2] The new scale parallels the inductive order of electron release (*t*-Bu > i-Pr > Et > Me) previously quantified (σ^*) from the rates of acid- and base-catalyzed hydrolyses of esters, such as RCO_2Et, by utilizing the Ingold–Taft relationship.[3] On the other hand, Charton[4] has recently concluded from a successful correlative analysis of rate data for base-catalyzed hydrolyses of such esters with steric parameters[5] that the σ^* scale is invalid and that it arises from an incomplete cancellation of steric effects in the Ingold–Taft relationship. The corollary of this conclusion is that the electrical effects of alkyl groups are unimportant in these reactions. A similar viewpoint has been expressed previously by Ritchie and Sager[6] on the basis that in many systems Taft correlations are as good when hydrogen and the aforementioned alkyl groups (and others) are all assigned $\sigma^* = 0$. However, this analysis has been, in the main, unaccepted by authors of modern physical organic texts[7] except for Hine[8] and Ritchie.[9]

Although Charton's analysis has been strongly criticized,[10,11] Bordwell and Fried[12] have presented equilibrium acidity data of carboxamides, $RCONH_2$, in dimethyl sulfoxide solution which offer strong experimental support for the beliefs expressed by Ritchie and Charton.

Recently, in connection with other studies,[13] we have had occasion to examine the effect of substituents on the ^{19}F chemical shifts of model systems 1 and 2, as well as the ^{13}C chemical shifts of C-4 in system 3, which indicate that these



1 2 3

phenylbicyclo[2.2.2]octyl skeletal frameworks are eminently suited for resolving whether or not alkyl inductive effects are significant, as well as testing the validity of the new σ_I values. In this regard, there are several beneficial aspects of these models. (i) They are stereochemically well-defined model systems in which the polar field effect emanating from substituent–substrate polarity can be assessed quantitatively in total isolation of other electronic mechanisms. Obviously, hyperconjugation involving the alkyl substituents is completely excluded by the rigid saturated framework intervening between the substituent and the phenyl ring, while polarizability effects should be negligible on the basis of distance dependency (r^{-6}).[14] These latter two phenomena are always

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