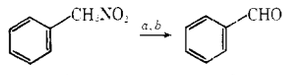
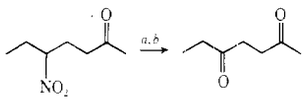
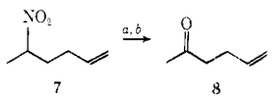
Table I. Oxidation of Nitronate Salts

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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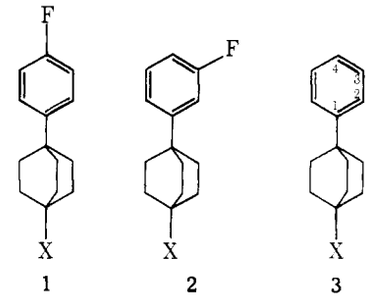
The inductive effects of alkyl substituents continue to attract interest. According to Taft and Levitt,[1] alkyl induction is significant and, together with polarizability effects, is quantitatively reflected by new σ_1 values (Me, −0.046; Et, −0.057; *i*-Pr, −0.065; *t*-Bu, −0.074) derived from a statistical 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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Table I. Substituent Chemical Shifts (SCS) [a] for Systems 1, 2, and 3

Substituent (X)	^{19}F SCS, Cyclohexane 1	Cyclohexane 2	DMF 1	DMF 2	^{13}C SCS,[b] Cyclohexane 3
Me	0.09	0.00	0.07	0.00	0.00
Et	0.07	0.00	0.07	0.00	0.00
i-Pr	0.05		0.05		0.03
t-Bu	0.03		0.02		0.03

[a] Chemical shifts (ppm) referenced to parent compound (X = H); a positive sign denotes deshielding. [b] X = H (c-C_6D_{12}, relative to Me_4Si): 125.73 (C-4).[28]

concomitant effects to be dubiously disentangled from inductive perturbations when assessing alkyl substituent effects in other model systems. (ii) Steric and solvation effects, problems associated with chemical reactivity studies, are completely excluded. (iii) ^{19}F and ^{13}C chemical shifts can be readily measured in a nonpolar solvent such as cyclohexane; hence, the substituent chemical shifts (SCS) can be considered *intrinsic* measures of substituent induction applicable to the gas phase. (iv) DSP correlations[15] of good precision are obtained between the SCS of **1** (eq 1a and 1b), **2** (eq 2a and 2b), and **3** (eq 3) and available substituent parameters[15,16] for a basis set of substituents, which indicate that the sensitivity of these systems to polar effects (ρ_I values) is more than adequate to assess the question of alkyl induction.

$$SCS = 2.49\sigma_I + 0.18\sigma_R^0 \text{ (cyclohexane; } f = 0.13\text{; SD} = 0.13, n = 14) \quad (1a)$$

$$SCS = 1.50\sigma_I + 0.02\sigma_R^0 \text{ (DMF; } f = 0.09\text{; SD} = 0.05\text{; } n = 13) \quad (1b)$$

$$SCS = 1.49\sigma_I + 0.14\sigma_R^0 \text{ (cyclohexane; } f = 0.07\text{; SD} = 0.05\text{; } n = 8) \quad (2a)$$

$$SCS = 0.63\sigma_I + 0.11\sigma_R^0 \text{ (DMF; } f = 0.11\text{; SD} = 0.03\text{; } n = 7) \quad (2b)$$

$$SCS = 1.34\sigma_I + 0.23\sigma_R^0 \text{ (cyclohexane; } f = 0.07\text{; SD} = 0.04\text{; } n = 8) \quad (3)$$

Accordingly, we have synthesized a number of appropriate alkyl derivatives of **1**, **2**, and **3**[17] and measured their NMR spectra (^{19}F and ^{13}C). A scrutiny of the data listed in Table I leads to two important conclusions. First, it can be seen that the expected SCS,[18] based on the polar sensitivity parameters (ρ_I) for **1**, **2**, and **3** and the new σ_I scale, are not realized in these model systems. Surprisingly, for **1**, the most sensitive system to polar effects, all the alkyl ^{19}F SCS are *positive*, implying, if taken at face value, *electron withdrawal* in the order Me > Et > *i*-Pr > *t*-Bu! This result is dramatically exemplified by the spectrum (Figure 1) of a mixture in cyclohexane of all the alkyl derivatives of **1** as well as the parent compound (X = H). The compounds were present in the ratio 1:1:1.5:2:1 (total concentration did not exceed 10%, w/w). However, since polar effects in system **1** are greatly attenuated by changing the solvent from cyclohexane to DMF (see eq 1a and 1b), the observed constancy of the shifts in **1** (cyclohexane and DMF) indicates unambiguously that their origin is definitely *not* polar in nature and, moreover, that polar effects for all the alkyl groups attached to an sp^3-hybridized carbon must be *zero*.[19] This conclusion is strongly reinforced by the observed SCS for systems **2** and **3** (Table I). Note that, within experimental error, they are all *zero*. The inescapable conclusion, therefore, is that the new σ_I scale (and the old σ^* scale) is invalid as a measure of intrinsic inductive effects of alkyl groups, as suggested by Ritchie,[9] Charton,[4] and Bordwell.[12] Undoubtedly, the new σ_I scale for alkyl groups embodies predominantly the effects of hyperconjugation and polarizability, both having fairly similar structural dependencies with regards to branching.[20] It is important to note that Houk and co-workers[20] have recently presented correlations of data from various model systems which reveal the importance of alkyl hyperconjugation on the ionization potentials of species employed for deriving the new σ_I scale.[2] There may also be a small polar contribution to the σ_I values when the alkyl groups are attached to an sp^2-hybridized carbon center.[1,19]

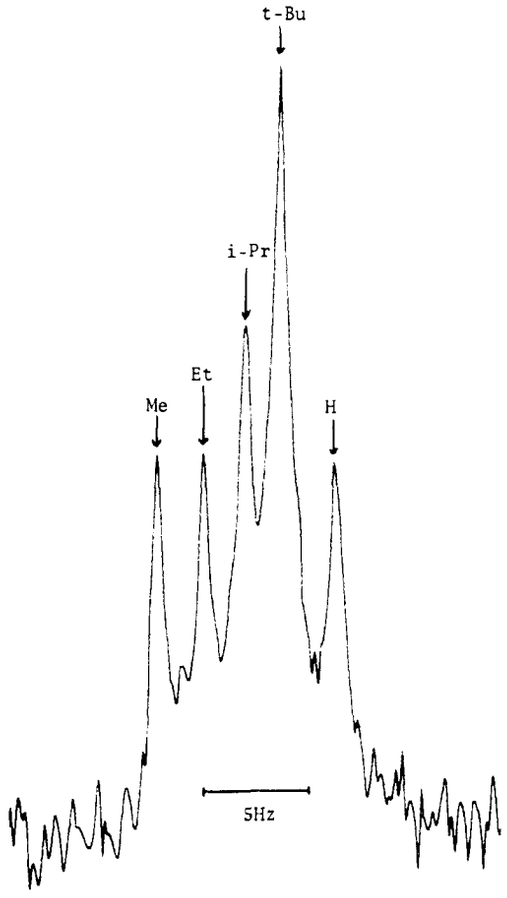

Figure 1. The 84.66-MHz ^{19}F NMR proton-decoupled spectrum of a mixture of **1** (X = H, Me, Et, *i*-Pr, and *t*-Bu) in cyclohexane.

Secondly, we believe that the "anomalous" downfield shifts induced by alkyl substitution in system **1**, but not observed in **2** and **3**, reflect small but significant changes in the hyperconjugative interaction between the phenyl and bicyclo[2.2.2]octyl moieties due to substitution at the bridgehead. Several considerations lead to this conclusion. (i) In **1**, the para orientation of the fluorophenyl tag is extremely sensitive to mesomeric effects which are relatively *constant* with respect to solvent changes (ρ_R = 31.0 and 31.85 for cyclohexane and DMF, respectively).[21] Hence, even a change of 0.005 in the σ_R^0 value[22] of the bicyclo[2.2.2]octyl group on bridgehead substitution would produce a chemical-shift perturbation of ~0.15 ppm in **1**. (ii) In **2**, the meta orientation of the fluorophenyl tag ($\rho_R \approx 0$) is virtually insensitive to mesomeric effects.[23] (iii) In **3**, although the carbon monitor (^{13}C SCS of C-4) is para orientated and, therefore, quite sensitive to resonance effects (ρ_R = 20.7 for cyclohexane),[21] sensitivity considerations (^{13}C SCS are ca. one-half the magnitude of ^{19}F SCS for a given electronic perturbation)[24] suggest that any mesomeric perturbation here should be approximately one-third of that observed in **1**. Hence, "anomalous" shifts similar to those observed in **1** are not detected in **3**, since their magnitude are

within the limits of experimental error for measuring the ^{13}C chemical shifts (see Experimental Section).

The only possible corollary which follows from this conclusion is that the angular relationship of the C–C bonds with respect to the π electron system at the point of attachment of the bicyclo[2.2.2]octyl moiety, an important factor determining the magnitude of σ–π interactions,[25] can be perturbed by substituent-induced structural changes of the saturated skeletal framework. The fact that this phenomenon is observed in a bicyclo[2.2.2]octyl framework made considerably rigid by phenyl group "anchoring", together with other noted apparent manifestations of substituent-induced structural distortions of caged systems,[26] suggests that strong reservations must be held concerning the use of fairly flexible model systems for precisely defining *weak* intrinsic polar effects. In particular, this applies to the quinuclidine system which has been heralded as a source of such information.[27] Here the probe is an integral part of the skeletal framework and, thus, is probably responsive to structural changes. Interestingly, although the ionization of 4-substituted quinuclidinium perchlorates indicates that the effects of alkyl substituents adhere to the σ^* scale,[10,27a] it should be noted that, according to this model system, Me and Et are electron withdrawing while *i*-Pr and *t*-Bu are electron donating! The disclosures in this paper suggest that these results are anomalous and, moreover, are probably a consequence of changes in the ionization potential of the nitrogen lone pair electrons due to hybridization adjustments effected by substituent-induced structural changes. Solvation factors may also be an important contributing factor.

Experimental Section

Compounds. 1-Methyl-4-*p*-fluorophenylbicyclo[2.2.2]octane (1, X = CH_3). A solution of 1 (X = Cl; 1.0g; 0.0042 mol)[28] and trimethylaluminum[29] (0.60 g; 0.0084 mol) in 1,2-dichloroethane[30] (5 mL) was stirred under a nitrogen atmosphere for 24 h at 50 °C. The reaction mixture was then cooled to −70 °C before methanol (10 mL) was added carefully to destroy excess trimethylaluminum. The mixture was then allowed to come to room temperature and quenched with dilute sulfuric acid before workup in the usual manner. Sublimation afforded 1 (X = CH_3; 0.8 g; 87%): mp 43.5–47 °C; ^1H NMR ($CDCl_3$) δ 0.84 (3 H, s, aliphatic), 1.18–2.00 (12 H, m, aliphatic), 6.78–7.43 (4 H, m, aromatic).

Anal. Calcd for $C_{15}H_{19}F$: C, 82.5; H, 8.8. Found: C, 82.8; H, 8.9.

1-Ethyl-4-*p*-fluorophenylbicyclo[2.2.2]octane (1, X = C_2H_5). 1 (X = Cl; 1.0 g; 0.0042 mol)[28] was treated with excess triethylaluminum under the same conditions described above for alkylation with trimethylaluminum. Similar workup procedures afforded a white solid (90%) after sublimation. A quantitative analysis by a combination of GLC and mass spectral determinations indicated that the product was a mixture of 1 (X = C_2H_5; *m/e* 232) and 1 (X = H; *m/e* 204) in the ratio of 7:3, respectively. Since the latter compound is the appropriate parent compound employed as an internal reference in the measurement of ^{19}F SCS, no attempt was made to purify the compound.

1-Isopropyl-4-*p*-fluorophenylbicyclo[2.2.2]octane [1, X = $CH(CH_3)_2$]. A solution of 1 (X = $COCH_3$; 3 g; 0.012 mol)[28] in ether (25 mL) was added dropwise to an ether solution of methyllithium (2 M; 0.013 mol) at −70 °C. The reaction mixture was allowed to come to room temperature and stirred for 1 h before workup in the usual manner. The crude alcohol [1, X = $C(CH_3)_2OH$; 3.0 g; 94%] was treated with hydrogen chloride in the manner described by Brown and Rei[31] to afford 1 [X = $C(CH_3)_2Cl$; 3.2 g; 81%]. A mixture of the crude chloride [1, X = $C(CH_3)_2Cl$; 0.8 g; 0.0029 mol] and tri-*n*-butyltin hydride[32] (1.2 g; 0.0041 mol) was irradiated with a Hanovia 500-W UV lamp. After 1 h, the suspension changed into a clear homogeneous liquid. The reaction mixture was dissolved in hexane (5 mL) and then treated with bromine until the solution was reddish-brown in color. The mixture was then passed through a column of alumina to remove organotin salts. The hexane was removed under reduced pressure to yield a residue which was recrystallized from aqueous ethanol to afford fine white needles of 1 [X = $CH(CH_3)_2$; 0.53 g; 75%]: mp 53.5–55 °C; ^1H NMR ($CDCl_3$) δ 0.82 (6 H, d, aliphatic, J_{HH} = 6 Hz), 1.04–1.99 (13 H, m, aliphatic), 6.77–7.41 (4 H, m, aromatic).

Anal. Calcd for $C_{17}H_{23}F$: C, 82.9; H, 9.4. Found: C, 82.9; 9.5.

1-*tert*-Butyl-4-*p*-fluorophenylbicyclo[2.2.2]octane [1, X = $C(CH_3)_3$]. A solution of crude 1 [X = $C(CH_3)_2Cl$; 1.0 g; 0.0036 mol] in methylene chloride (10 mL) at −70 °C was treated with an excess of trimethylaluminum according to the procedure described by Kennedy and co-workers.[29] After standard workup, sublimation of the residue and then recrystallization from methanol afforded white needles of 1 [X = $C(CH_3)_3$; 0.7 g; 76%]: mp 103.5–106.5 °C; ^1H NMR ($CDCl_3$) δ 0.83 (9 H, s, aliphatic), 1.34–1.99 (12 H, m, aliphatic), 6.78–7.47 (4 H, m, aromatic).

Anal. Calcd for $C_{18}H_{25}F$: C, 83.0; H, 9.7. Found: C, 82.7; H, 9.7.

1-Methyl-4-*m*-fluorophenylbicyclo[2.2.2]octane (2, X = CH_3). Prepared from 2 (X = Cl)[28] by the same procedure described above for 1 (X = CH_3). Distillation afforded a colorless oil: bp 120 °C (1 mm); $n^{22}D$ 1.5185; ^1H NMR ($CDCl_3$) δ 0.85 (3 H, s, aliphatic), 1.20–2.05 (12 H, m, aliphatic), 6.65–7.35 (4 H, m, aromatic).

Anal. Calcd for $C_{15}H_{19}F$: C, 82.5; H, 8.8. Found: C, 82.7; H, 8.8.

1-Ethyl-4-*m*-fluorophenylbicyclo[2.2.2]octane (2, X = C_2H_5). Prepared from 2 (X = Cl)[28] by the same procedure described above for 1 (X = C_2H_5). The mixture of 2 (X = C_2H_5 and H), shown to be in the ratio of 7:3, respectively, by a combination of GLC and mass spectrometry, was not separated for the reasons cited above for 1 (X = C_2H_5).

1-Methyl-4-phenylbicyclo[2.2.2]octane (3, X = CH_3). Prepared from 3 (X = Cl)[28] as described above for 1 (X = CH_3). The compound was sublimed and recrystallized from methanol to afford white needles: mp 47.5–49.5 °C (lit.[33] 50–52 °C); ^1H NMR ($CDCl_3$) δ 0.83 (3 H, s, aliphatic), 1.29–2.02 (12 H, m, aliphatic), 7.07–7.42 (5 H, m, aromatic).

Anal. Calcd for $C_{15}H_{20}$: C, 89.9; H, 10.1. Found: C, 90.0; H, 10.2.

1-Ethyl-4-phenylbicyclo[2.2.2]octane (3, X = C_2H_5). Prepared from 3 (X = $COCH_3$)[28] by the Wolf–Kishner[34] reduction procedure in 88% yield. The compound was recrystallized from aqueous methanol to afford white needles: mp 33.5–34 °C (lit.[33] 36–38 °C); ^1H NMR ($CDCl_3$) δ 0.59–2.06 (17 H, m, aliphatic), 7.06–7.43 (5 H, m, aromatic).

1-Isopropyl-4-phenylbicyclo[2.2.2]octane [3, X = $CH(CH_3)_2$]. 3 (X = $COCH_3$; 4.5 g; 0.02 mol)[28] was converted to the tertiary alcohol 3 [X = $C(CH_3)_2OH$; 3.9 g; 81%] and then the chloride 3 [X = $C(CH_3)_2Cl$; 86%] by the same procedures described above for the corresponding derivatives of 1. The crude chloride was treated with lithium/*tert*-butyl alcohol[34] in tetrahydrofuran and then workedup in the usual manner. Sublimation of the product afforded 3 (X = $CH(CH_3)_2$; 78%): mp 63–65 °C (lit.[33] mp 60–62 °C); ^1H NMR ($CDCl_3$) δ 0.82 (6 H, d, aliphatic; J_{HH} = 6 Hz) 1.04–2.02 (13 H, m, aliphatic), 7.02–7.42 (5 H, m, aromatic).

1-*tert*-Butyl-4-phenylbicyclo[2.2.2]octane [3, X = $C(CH_3)_3$]. Prepared from crude 3 [X = $C(CH_3)_2Cl$] in the same manner outlined above for 1 [X = $C(CH_3)_3$]. The product was sublimed and recrystallized from methanol to afford white needles of 3 [X = $C(CH_3)_3$; 88%]: mp 108–111.5 °C; ^1H NMR ($CDCl_3$) δ 0.82 (9 H, s, aliphatic), 1.34–1.99 (12 H, m, aliphatic), 7.06–7.42 (5 H, m, aromatic).

Anal. Calcd for $C_{18}H_{26}$: C, 89.2; H, 10.8. Found: C, 89.2; H, 10.6.

Spectra. The ^{19}F and ^{13}C NMR spectra were obtained at 84.66 and 67.89 MHz, respectively, on Bruker spectrometers. The proton broad-band decoupled ^{19}F NMR spectra (spectral width of 2.5 Hz/cm) were obtained for cyclohexane and DMF solutions containing 5% (w/w) of 1 or 2 and 2% (w/w) of the appropriate parent compound (X = H).[28] The ^{19}F SCS can be considered accurate to better than 0.01 ppm. The samples for proton-decoupled ^{13}C NMR spectra were prepared in deuteriocyclohexane (5 mol %) with $(CH_3)_4Si$ as an internal standard. A sweep of 15 000 Hz was used, and 16K data points were collected and transformed to 8K real data points. The ^{13}C chemical shifts are considered to be accurate to ±0.03 ppm.

^1H NMR spectra were measured with a Varian A-60 spectrometer. Gas chromatographic analysis was performed on a Varian 1740 gas chromatograph using a 10-ft column of 5% SE-30 on 100/120 Chromosorb W. Mass spectra were recorded on an AEI MS30 spectrometer.

Acknowledgments. We thank Monash University (Dr. J. Weigold) for the use of their NMR facilities as well as the Australian Research Grants Committee for providing access to the National NMR Center.

Registry No.—1 (X = CH_3), 64872-36-2; 1 (X = C_2H_5), 64872-37-3; 1 [X = $CH(CH_3)_2$], 64872-38-4; 1 [X = $C(CH_3)_3$], 64872-39-5; 1 (X = Cl), 61541-33-1; 1 (X = $COCH_3$), 64872-40-8; 1 [X = $C(CH_3)_2OH$],

64872-41-9; **1** [X = $C(CH_3)_2Cl$], 64872-42-0; **2** (X = CH_3), 64872-43-1; **2** (X = C_2H_5), 64872-44-2; **2** (X = Cl), 64872-45-3; **3** (X = CH_3), 23062-66-0; **3** (X = C_2H_5), 23062-67-1; **3** [X = $CH(CH_3)_2$], 23102-73-0; **3** [X = $C(CH_3)_3$], 64872-46-4; **3** (X = Cl), 33732-68-2; **3** (X = $COCH_3$), 64872-47-5; **3** [X = $C(CH_3)_2OH$], 64872-48-6; **3** [X = $C(CH_3)_2Cl$], 64872-49-7; trimethylaluminum, 75-24-1; triethylaluminum, 97-93-8; tributyltin hydride, 688-73-3.

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Regiospecificity and Conformational Specificity in Oxime Alkylation of a Geometrical Enantiomeric Isomer[1a]

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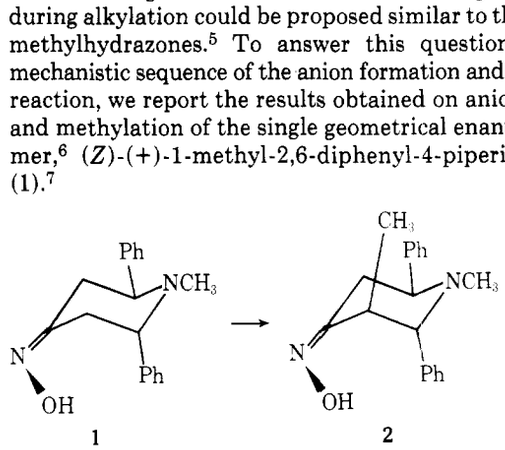
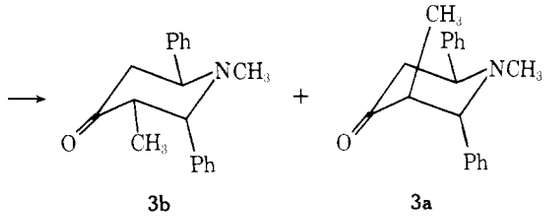
The reactions of electrophiles with the anions of oximes,[1] oxime ethers,[2] dialkylhydrazones,[3] and nitrosamines[1a,4] have been shown to occur with bond formation on the cisoid carbon and perpendicular to the plane of the functional group. This suggests that a cisoid arrangement of four overlapping p orbitals having six electrons produces more stable molecular orbitals than the transoid arrangement. These conclusions are based on structural assignments of the product of electrophilic reactions with the anion, and, although undoubtedly correct, do not provide absolute evidence for the stereochemistry of the reaction pathway. Recently, the dimethylhydrazone anion was shown to be formed by initial removal of the transoid proton with subsequent rearrangement of the stereochemistry to the cisoid anion before alkylation. This observation requires some reevaluation of the stereochemical specificity of the reactions of oximes. A process involving rotation about the carbon–nitrogen bond or inversion at nitrogen prior to or during alkylation could be proposed similar to that of the dimethylhydrazones.[5] To answer this question about the mechanistic sequence of the anion formation and electrophilic reaction, we report the results obtained on anion formation and methylation of the single geometrical enantiomeric isomer,[6] (*Z*)-(+)-1-methyl-2,6-diphenyl-4-piperidone oxime (**1**).[7]



1 **2**



3b **3a**

A sample of **1** ($[\alpha]^{25}_D$ +26.34° (*c* 0.331 g/100 mL); EtOH 95%) was shown to be 87% optically pure by ^1H NMR analysis of the NCH_3 in the presence of the chiral shift reagent Eu(tfc)$_3$.[10] The dianion of **1** was prepared with *n*-butyllithium and alkylated with methyl iodide to give 88% of (*Z*)-(2*R*,3*R*,6*S*)-1,3-dimethyl-2,6-diphenyl-4-piperidone oxime (**2**) ($[\alpha]^{25}_D$ −30.76° (*c* 0.331 g/100 mL); EtOH 95%). The optical purity of **2** was shown to be 86% based on the integration of the NMe signals or 80% based on the CMe signals. Since the singlet of the NCH_3 probably gave a more accurate analysis,

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