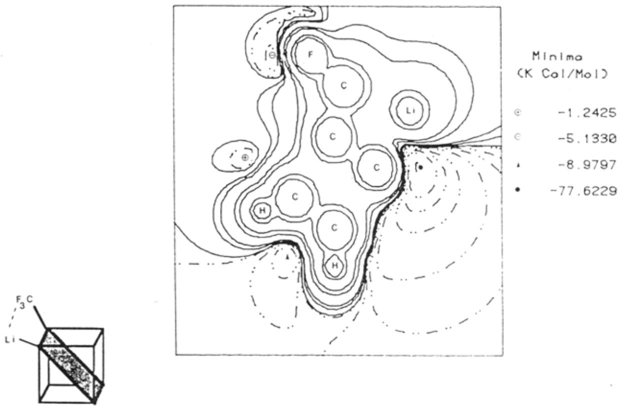

Figure 2. Calculated electrostatic potential of 2-lithio-1-(trifluoromethyl)cubane (**2b**) in a diagonal plane, as shown. Dashed contours correspond to negative potentials; the zero contour is shown. The magnitude of the other contours are in kcal/mol: −50.2, −37.6, −25.1, −12.5, −6.3, −3.1, −0.6, 3.1, 6.3, 31.4, 62.7, 314.0, 627.0. The locations and values of the minima are indicated.

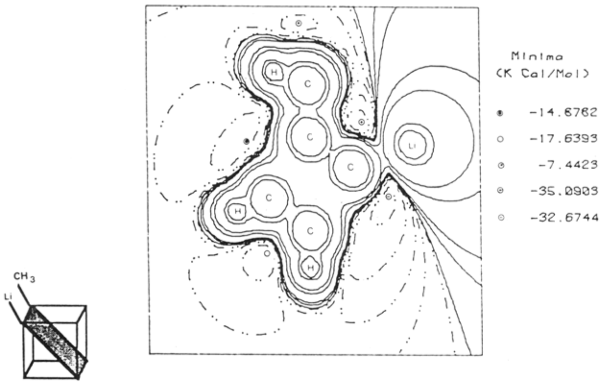

Figure 3. Calculated electrostatic potential of 2-lithio-1-methylcubane (**2c**) in a diagonal plane, as shown. Dashed contours correspond to negative potentials; the zero contour is shown. The magnitude of the other contours are in kcal/mol: −12.5, −6.3, −3.1, −0.6, 3.1, 6.3, 31.4, 62.7, 314.0, 627.0. The locations and values of the minima are indicated.

These are fully consistent with the observed reactive behavior of these molecules toward electrophiles.

In the present context, the key feature of Figure 1 is the negative channel to the lithiated carbon. This represents an important aspect of the activation of the ortho carbon by the 2-oxazoline directing group. When the latter is replaced by CF_3 as the directing agent (structure **2b**), this feature is modified to only a minor extent (Figure 2). The minimum near the ortho carbon is now −78 kcal/mol, which still corresponds to a very significant activation of this position toward electrophilic attack.

In marked constrast is the situation when CH_3 tries to take on the role of the directing group (**2c**). There is now no shifting of the lithium atom and no strongly negative channel to the ortho carbon (Figure 3); the minimum in that spatial region is now −33 kcal/mol. The picture is very much the same as that obtained earlier for lithiocubane.[7] There is clearly no activation of the ortho position.

Finally, Figure 4 shows the electrostatic potential for 2-lithio-1-nitrocubane (**2d**). There is again an interaction between the two substituents; the lithium is only 1.76 Å from the oxygen, while the sum of the van der Waals radii is 3.3 Å.[14] This produces a channel of negative potential to the lithiated (ortho) carbon, with a minimum of −68 kcal/mol (compared to −38 kcal/mol in that region for lithiocubane, without any second substituent). Thus NO_2 does definitely activate the ortho position toward electrophilic attack, although not as well as 2-oxazoline and CF_3.

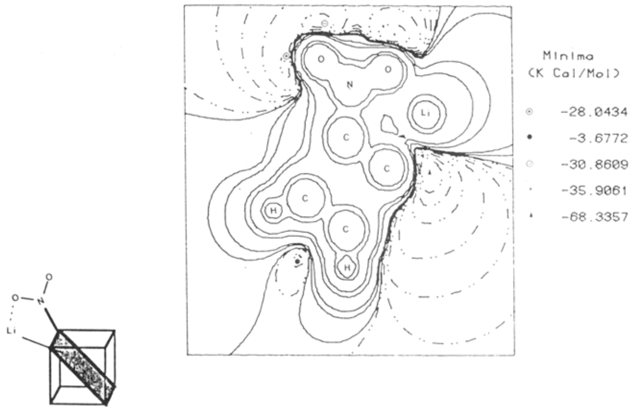

Figure 4. Calculated electrostatic potential of 2-lithio-1-nitrocubane (**2d**) in a diagonal plane, as shown. Dashed contours correspond to negative potentials; the zero contour is shown. The magnitude of the other contours are in kcal/mol: −37.6, −25.1, −12.5, −6.3, −3.1, −0.6, 3.1, 6.3, 31.4, 63.0, 314.0, 627.0. The locations and values of the minima are indicated.

Summary

We have carried out a computational assessment of the relative ortho directing powers of four different functional groups in terms of their tendencies to interact with an adjacent lithium substituent, thereby producing a channel of strongly negative electrostatic potential leading to the lithiated (ortho) carbon. In terms of the factors examined in this analysis, it appears that the nitro group should have at least a moderate ortho-directing capability.

Acknowledgment. We greatly appreciate very helpful discussions with Dr. Jane S. Murray. We also thank the U.S. Army Research Office for partial support of this work.

Registry No. **2a**, 111976-24-0; **2b**, 111976-25-1; **2c**, 111976-26-2; **2d**, 111976-27-3; CF_3, 2264-21-3; NO_2, 10102-44-0; CH_3, 2229-07-4; 2-oxazoline, 504-77-8.

Isolation of a Ketene Imine from the Decomposition of a Vinyl Azide

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Hassner and co-workers[1] have discussed recently the thermolysis of vinyl azides and suggested empirical rules for the formation of azirines and rearranged nitriles in this reaction. Whereas the thermal or photochemical loss of nitrogen is most likely a concerted process leading to an azirine,[2] formation of nitriles or of heterocyclic compounds

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(18) Politzer, P.; Jayasuriya, K. *J. Mol. Struct.* (*THEOCHEM*) **1986**, *135*, 245.

(19) Politzer, P.; Murray, J. S. In *Reactivity from Ground-State Structure*; Liebman, J., Greenberg, A., Eds.; VCH: Deerfield Beach, in press.

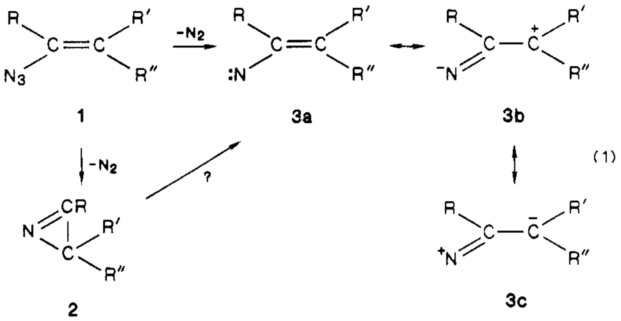
(1) Hassner, A.; Wiegand, N. M.; Gottlieb, H. *J. Org. Chem.* **1986**, *51*, 3176.

(2) For recent reviews, see: Hassner, A. In *Azides and Nitrenes, Reactivity and Utility*; Scriven, E. F. V., Ed.; Academic Press: Orlando, 1984; Chapter 2, p 35. Moore, H. W.; Goldish, D. M. In *The Chemistry of Functional Groups, Supp. D*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1983; Chapter 8, p 321.

0022-3263/88/1953-0679$01.50/0

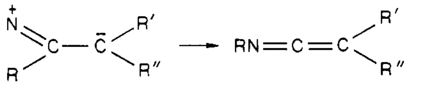
occurs frequently. It was noted, however, that only "in rare cases ketene imines are formed as major products".[1] There is apparently no case in which a ketene imine was isolated from such reactions, although it was sometimes trapped by added nucleophiles.

A key intermediate in these reactions is a vinylnitrene which is formed either directly from the vinyl azide 1 or by ring-opening of an intermediate azirine 2. The vinylnitrene is presented in eq 1 by three of its valence bond hybrids **3a–c**. Formation of nitriles was suggested to occur via migration of R to the cationic center of **3b**, whereas heterocyclic compounds could be formed by attack of the negative charge of **3b** on an electrophilic center present in R′ or R″.



(1)

We expect that the electronic distribution will be more closely represented by **3c** when R′ and R″ are electron-withdrawing groups. In that case, the migration of R to the positive nitrogen which will lead to ketene imine 4 (eq 2) will be more favored than migration of R to carbon in **3b**. Indeed, a few examples of products that can result from ketene imines trapped either by the solvent or by a nucleophile were previously reported by us[3] and by others[4] and relevant examples are shown in eq 3 and 4.


(2)

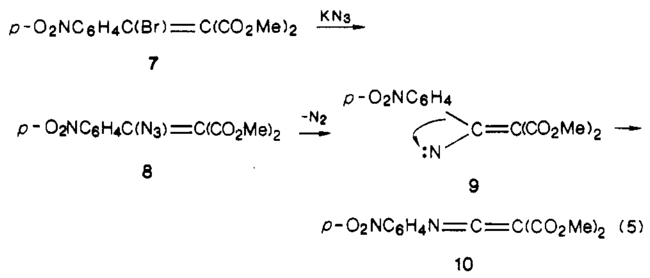
3 4

$$\underset{\mathbf{5}}{\mathrm{MeC(N_3){=}C(CN)_2}} \xrightarrow[\mathrm{ROH}]{-\mathrm{N_2}} \mathrm{MeNHC(OR){=}C(CN)_2} \qquad (3)^4$$

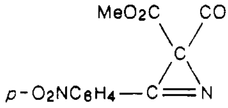
$$p\text{-}\mathrm{O_2NC_6H_4C(Cl){=}C(CN)CO_2Me} \xrightarrow{\mathrm{N_3^-/MeOH}} p\text{-}\mathrm{O_2NC_6H_4C(N_3){=}C(CN)CO_2Me} \xrightarrow{-\mathrm{N_2}} p\text{-}\mathrm{O_2NC_6H_4NHC(OMe){=}C(CN)CO_2Me} \qquad (4)^3$$

We report now the isolation of a ketene imine from a decomposition–rearrangement of a vinyl azide at room temperature.

Substitution of the bromine of dimethyl β-bromo-*p*-nitrobenzylidenemalonate (**7**)[5] with potassium or sodium azide in CH_3CN at room temperature gave initially vinyl azide **8**, which was observed by ^1H NMR.[6] **8** lost nitrogen under the reaction conditions and gave the ketene imine **10** presumably via rearrangement of the intermediate nitrene **9** (eq 5). The ketene imine was separated from **6** by crystallization.

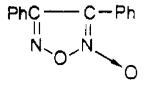


(5)



11

The assignment of **10** as a ketene imine rather than the isomeric azirine structure **11** is based on the appearance of an IR stretching band of medium intensity at 2100 cm^{-1}.[7] The C=N band in the azirine **11** should be <1800 cm^{-1}.[8] The appearance of only one signal in the ^1H NMR for the CO_2Me groups in both $CDCl_3$ and CD_3CN is consistent with this assignment. Hence, the combination of two electron-withdrawing CN and/or CO_2R groups gives the highly electrophilic vinyl azides **5**, **6**, and **8** which form the ketene imine in preference over other reaction routes. Electrophilic olefins activated by other electron-withdrawing groups can lead to other products via cyclization which involves the nitrogen and the R′ (or R″) group. The furoxan **12**[9] and the oxazole **13**[10] are formed by this route when **14** and **15** react with sodium azide.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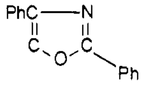
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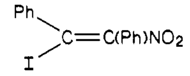
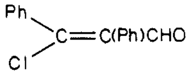


14



15

Experimental Section

To a solution of **7** (0.9 g, 2.7 mmol) in dry acetonitrile (100 mL) was added KN_3 (2.1 g, 26 mmol). The solution turned yellow and then orange. After stirring for 8 h at room temperature, pouring into water (300 mL), extraction with $CHCl_3$ (2 × 100 mL), drying, and evaporating, a viscous oily solid was obtained. ^1H NMR after 15 h showed the presence of a 15:85 mixture of **8** and the ketene imine **10**. Crystallization from benzene–hexane gave 1,1-bis(methoxycarbonyl)-*N*-*p*-nitrophenylketene imine (**10**) (95% pure, 0.9 g, 41%), mp 37 °C: IR ($CDCl_3$) ν_{max} 2100 (C=C=N, m), 1720 (CO_2Me, s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.81 (6 H, s, Me), 8.13, 8.44 (4 H, AA′BB′ q, J = 9 Hz); ^1H NMR (CD_3CN) δ 3.73 (6 H, s, Me), 8.20, 8.45 (4 H, AA′BB′ q, J = 9 Hz, Ar); ^{13}C NMR (CD_3CN) (proton decoupled) δ 53.4 (CH_3), 125.0, 131.2 (C_α,C_β,w), 125.5, 132.8 (Ar-C-2), Ar-C-3), 141.0, 146.0 (Ar-C-1, Ar-C-4, w), 167.6 (C=O);[11] mass spectra, m/z (rel abundance, assignment) 278 (2, M), 265 (3, M – CH), 234 (8, M – OMe – CH or M – CO_2), 220 (5, M – CO_2 –CH_2), 219 (4, M – COOMe), 205 (11, M – COOMe – CH_2 or M – COOMe – N), 203 (16, M – CH – 2 MeO), 178 (B, ?), 176 (19), 174 (30), 150 (83, B-CO), 148 (17, M – $C(CO_2Me)_2$), 135 (29, $O_2NC_6H_3N$), 122 (26, $C_6H_5NO_2$), 115 (53). Anal. Calcd for

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[3] Rappoport, Z.; Avramovitch, B. *J. Org. Chem.* **1982**, *47*, 1397.

[4] Friedrich, K. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 959.

[5] Rappoport, Z.; Gazit, A. *J. Org. Chem.* **1986**, *51*, 4107.

[6] The reaction of KN_3 with (E)-p-$O_2NC_6H_4C(Br){=}C(CO_2CH_3)$-$CO_2CD_3$ was recently described by Rappoport and Gazit Rappoport, Z.; Gazit, A. *J. Am. Chem. Soc.* **1987**, *109*, 6698–6710.

[7] The C=C=N stretching vibration is given at 2000 cm^{-1} in Nakanishi, K. *Infrared Absorption Spectroscopy*; Holden Day: San Francisco, 1962.

[8] Hassner, A.; Fowler, F. W. *J. Am. Chem. Soc.* **1968**, *90*, 2869.

[9] Rappoport, Z.; Topol, A. *J. Am. Chem. Soc.* **1980**, *102*, 406.

[10] Rappoport, Z.; Gazit, A. *J. Org. Chem.* **1985**, *50*, 3184.

[11] For comparison with the ^{13}C spectrum of p-$O_2NC_6H_4CH{=}C$-$(CO_2Et)_2$, see: Bottino, F. A.; Musumarra, G.; Rappoport, Z. *Magn. Reson. Chem.* **1986**, *24*, 31.

$C_{12}H_{10}N_2O_6$: C, 51.80; H, 3.60; N, 10.07. Found: C, 52.08; H, 3.86; N, 10.35.

A similar reaction mixture, worked up earlier and by NMR consisting of a 85:15 mixture of the azide **8** and the ketene imine **10** had the following spectral properties: IR ($CHCl_3$) ν_{max} 2150 cm^{-1} (N_3, s), 1730 (CO_2Me, s); ^1H NMR ($CDCl_3$) δ 3.59 (3 H, s, COOMe), 3.89 (3 H, s, COOMe), 7.61, 8.38 (4 H, AA′BB′ q, J = 8.8 Hz, Ar); ^1H NMR (CD_3CN) δ 3.50 (3 H, s, COOMe), 3.82 (3 H, s, COOMe), 7.66, 8.30 (4 H, AA′BB′ q, J = 8.8 Hz, Ar).

The ratio of **8** to **10** is likely to be dependent on the **7**/[N_3^-] ratio since **8** is formed in a bimolecular process and decomposes to **10** in a monomolecular one. Indeed, when 345 mM KN_3 and 26 mM of **7** in $CDCl_3$ were reacted, the two stages of reaction were clearly separated. Only **8** was observed up to 2.5 h (25% reaction) and ≥95% of **10** was formed after 168 h.

Acknowledgment. We are indebted to Professor A. Hassner for discussions and comments and to the Israel Commission for Basic Research, The Israel Academy for Sciences and Humanities, who supported the work.

Registry No. **7**, 103883-91-6; **8**, 110242-48-3; **10**, 110242-49-4.

Competitive RO-6 Neighboring Group Participation and Solvent-Assisted Displacement with 2-(2-Methoxyethoxy)ethyl Tosylate

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Pseudo-first-order rate constants for solvolysis of alkyl substrates have been assumed to be the sum of three contributing processes: solvent-assisted (k_s), neighboring group assisted (k_Δ), or nucleophilically unassisted (k_c), where the observed rate is defined by eq 1.[1] For almost

$$k_{obsd} = k_s + k_\Delta + k_c \qquad (1)$$

all substrates only one pathway is observed because it is energetically favorable over the others. There are, however, some borderline examples where two of these processes are simultaneously important. For example, linear free energy relationships were used to show that 3-aryl-2-propyl substrates undergo a change in mechanism as the aryl substituent is changed; for some aryl groups, the k_Δ pathway competes with the k_s pathway.[2]

We recently examined two structurally related substrates, **1** and **2**, which followed different pathways, **1** reacting by solvent assistance and **2** reacting by RO-3

$$\underset{\mathbf{1}}{MeOCH_2CH_2X} \qquad \underset{\mathbf{2}}{MeOCMe_2CH_2X}$$

$$\underset{\mathbf{3}}{MeOCH_2CH_2OCH_2CH_2X}$$

neighboring group participation.[3] The change in mechanism in going from structure **1** to **2** is obviously caused by the introduction of the *gem*-dimethyl groups. They serve two roles in **2**; first they serve to severely hinder direct displacement at C-1 and secondly they enhance neighboring oxygen participation. Geminal dimethyl substitution is said to favor neighboring group participation by operation of the Thorpe–Ingold effect.[4] Additionally with **2**-OBs, the *gem*-dimethyl groups stabilize the product of methoxy group migration, i.e., Me_2C^+–CH_2OMe.[3] The previous studies provide the basis for the present work which models the reactivity of simple polyethers like poly(ethylene glycol) (PEG) sulfonate esters.[5] In this report we have studied the polyether model substrate **3**-OTs, which has the opportunity for both RO-3 and RO-6 participation.

We used the trifluoroethanol (TFE)–ethanol (EtOH) probe[6] and the thiourea probe[7] to determine if **3**-OTs is

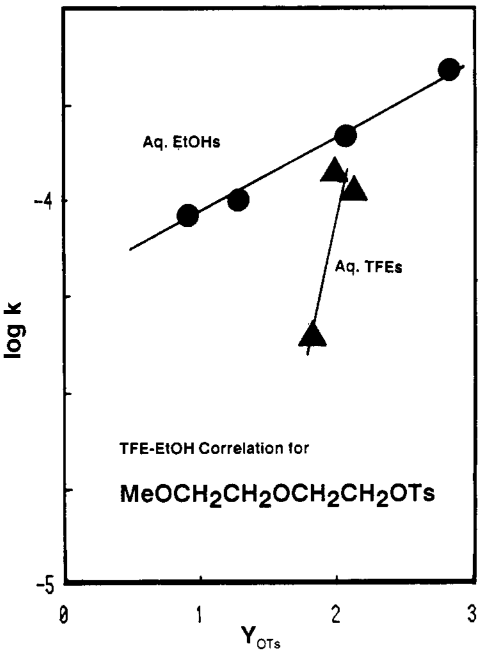

Figure 1. TFE–EtOH plot for **3**-OTs.

Table I. Solvolysis of 2-(2-Methoxyethoxy)ethyl Tosylate in 60% (v/v) Aqueous Ethanol at 85.0 °C with Added Thiourea

M, thiourea	10^4k (s^{-1})	k/k_0
0.0	0.90	1.00
0.1	2.30	2.55
0.2	3.39	3.76
0.5	5.07	5.64

Table II. Pseudo-First-Order Rates for the Solvolysis of 2-(2-Methoxyethoxy)ethyl Tosylate in Aqueous Ethanols (EtOH) and Trifluoroethanols (TFE) at 85 °C

solvent	10^4k (s^{-1})
60% (v/v) aqueous EtOH	0.90 + 0.01
50% (v/v) aqueous EtOH	0.99 + 0.03
40% (v/v) aqueous EtOH	1.45 + 0.03
30% (v/v) aqueous EtOH	2.19 + 0.11
97% (w/w) aqueous TFE	0.43 + 0.02
70% (w/w) aqueous TFE	1.17 + 0.22
50% (w/w) aqueous TFE	1.03 + 0.083

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(1) Winstein, S.; Allred, E.; Heck, R.; Glick, R. *Tetrahedron* **1958**, *3*, 1.

(2) (a) Harris, J. M. *Prog. Phys. Org. Chem.* **1974**, *11*, 89. (b) Lancelot, C. J.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1969**, *91*, 4291, 4296, 4297. (c) Lancelot, C. J.; Harper, J. J.; Schleyer, P. v. R. *Ibid.* **1969**, *91*, 4294. Harris, J. M.; Schadt, F. L. (d) Schleyer, P. v. R.; Lancelot, C. J. *Ibid.* **1969**, *91*, 7508.

(3) McManus, S. P.; Karaman, R. M.; Sedaghat-Herati, R.; Neamati-Mazraeh, N.; Hovanes, B. A.; Paley, M. S.; Harris, J. M. *J. Org. Chem.* **1987**, *52*, 2518.

(4) Review: Eliel, E. L. *Stereochemistry of Carbon Compounds*; McGraw-Hill: New York, 1962; p 197. See also: Eliel, E. L.; Knox, D. E. *J. Am. Chem. Soc.* **1985**, *107*, 2946. Eliel, E. L.; Clawson, L.; Knox, D. E. *J. Org. Chem.* **1986**, *50*, 2707.

(5) McManus, S. P.; Karaman, R. M., Shannon, T. G.; Hovatter, T. W.; Hovanes, B. A.; Paley, M. S.; Harris, J. M. *Polym. Preprints* (*Am. Chem. Soc., Polym. Chem. Div.*) **1987**, *28*(2), 276.

(6) Raber, D. J.; Neal, W. C., Jr.; Dukes, M. D.; Harris, J. M.; Mount, D. L. *J. Am. Chem. Soc.* **1978**, *100*, 8137. Harris, J. M.; Mount, D. L.; Smith, M. R.; Neal, W. C., Jr.; Dukes, M. C.; Raber, D. J. *Ibid.* **1978**, *100*, 8147.

(7) McManus, S. P.; Neamati-Mazraeh, N.; Karaman, R. M.; Harris, J. M. *J. Org. Chem.* **1986**, *51*, 4876.