In conclusion, we report the first NOESY spectrum of a paramagnetic metalloprotein which exhibits line widths at half-height greater than 1000 Hz at 360 MHz. Moreover, these studies have facilitated the assignment of several of the observed isotropically shifted signals. These data also establish for the first time that a carboxylate moiety resides at the active site of Uf. Our studies suggest that NOESY spectra can be obtained for isotropically shifted proton signals which are comparatively broad, provided that the T_1 values are sufficiently long to allow NOE buildup to occur. We estimate T_1 values greater than 10 ms to provide ample time to observe NOE buildup for systems of this type.

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Additions of Malononitrile Radicals to Alkenes: New Examples of 1,2-Asymmetric Induction in Iodine and Phenylselenium Transfer Reactions

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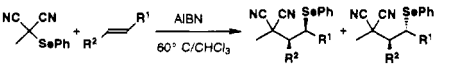
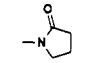
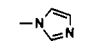
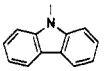
One of the current frontiers in radical chemistry is the control of acyclic stereochemistry,[1] and recent work has focused on 1,2-asymmetric induction.[2-4] We have introduced iodomalononitriles as useful reagents for radical addition and annulation reactions (eq 1, X = I),[5] and we felt that these or related reagents would be especially useful for study of 1,2-asymmetric induction in radical reactions.[4b] In attempting to study asymmetric reactions of heteroatom-substituted radicals, we learned that iodomalononitriles do not add cleanly to oxygen-, sulfur-, or nitrogen-substituted alkenes (R^1 = OR, SR, NR_2).[6] To solve this problem, we introduce a new class of reagents, (phenylseleno)malononitriles (X = SePh),[7,8] and describe the first examples of asymmetric selenium transfer reactions of benzylic (R^1 = Ph), oxygen-substituted (R^1 = OR), sulfur-substituted (R^1 = SPh), and nitrogen-substituted (R^1 = NR_2) radicals. Perhaps most importantly, additions of iodomalononitriles to disubstituted alkenes provide the first examples of high 1,2-asymmetric induction in reactions of alkyl radicals bearing no conjugating substituents (X = I, R^1 = alkyl).

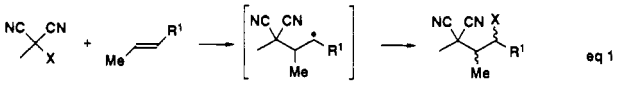
Table I. Additions of **1** to Alkenes



1 2 3-syn (if $R^2 \neq H$) 3-anti

Alkene 2	R^1	R^2	Time	Yield[a]	syn/anti (or cis/trans)
a	C_4H_9	H	40 h	97%	-
b	C_6H_5	H	120 h	84%	-
c	OC_2H_5	H	2 h	96%	-
d	$OCOCH_3$	H	24 h	97%	-
e	SC_6H_5	H	2 h	97%	-
f		H	5 h	91%	-
g		H	120 h[b]	84%	-
h		H	16 h	97%	-
i	$-CH_2CH_2CH_2-$		120 h	55%	(0/100)
j	$-OCH_2CH_2CH_2-$		120 h	78%	(30/70)
k	C_6H_5	CH_3	240 h	80%	80/20
l	OC_2H_5	CH_3[c]	70 h	92%	25/75
m	SC_6H_5	CH_3[c]	40 h	73%	10/90
n	See entry h	CH_3	120 h	70%	90/10

[a] Procedure: A $CHCl_3$ solution of **1** (0.1 M), the alkene (2-3 equiv), and AIBN (5%) was heated at 60 °C. For slow reactions, additional AIBN (5%) was added once per day. After **1** was consumed, the solvent was evaporated and the product was purified by chromatography on silica gel (ether/hexanes, 1/10). [b] Ten equivalents of alkene used. [c] *E*/*Z* mixture.



eq 1

X = I, succeeds for R^1 = alkyl, phenyl; fails for R^1 = OR, SR, NR_2
X = SePh, suceeds for R^1 = phenyl, OR, SR, NR_2; fails for R^1 = alkyl

syn or anti

Methyl(phenylseleno)malononitrile (**1**) is readily available by the reaction of the anion of methylmalononitrile with benzeneselenenyl bromide. In a typical addition reaction (Table I, entry a), selenomalononitrile **1**, 1-hexene, and AIBN were heated in $CHCl_3$ at 60 °C. After 40 h, the reaction was complete, and we isolated adduct **3a** in 97% yield. Reactions of **1** with other monosubstituted alkenes are summarized in Table I, entries a-h. Additions occur not only with alkyl- and phenyl-substituted alkenes (which form adducts with iodomalononitriles[4]) but also with *O*-alkyl-, *O*-acyl-, *S*-phenyl, *N*-heterocycle-, and *N*-acyl-substituted alkenes (which do not form adducts with iodomalononitriles). These reactions do not occur in the absence of AIBN, and we believe that a standard radical chain mechanism is involved. The malononitrile radical adds to the alkene, and the adduct radical abstracts a phenylselenium group[7,8] from the (phenylseleno)-malononitrile to give the product **3a** and the starting radical.

Entries i-n in Table I summarize the additions of **1** to representative 1,2-disubstituted alkenes. Although reaction times can be very long (3-10 days), yields are consistently high. Product ratios do not change over time, so we believe that the observed ratios are kinetically controlled. Regioselectivities are very high

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(2) Recent leading references to carbonyl-substituted radicals: (a) Hart, D. J.; Huang, H. C.; Krishnamurthy, R.; Schwartz, T. *J. Am. Chem. Soc.* **1989**, *111*, 7507. (b) Guindon, Y.; Lavallee, J. F.; Llinas-Brunet, M.; Horner, G.; Rancourt, J. *J. Am. Chem. Soc.* **1991**, *113*, 9701. (c) Bulliard, M.; Zehnder, M.; Giese, B. *Helv. Chim. Acta* **1991**, *74*, 1600. (d) Hart, D. J.; Krishnamurthy, R. *Synlett* **1991**, 412. (e) Curran, D. P.; Abraham, A. C.; Liu, H. *J. Org. Chem.* **1991**, *56*, 4335. (f) Beckwith, A. L. J.; Hersperger, R.; White, J. M. *J. Chem. Soc., Chem. Commun.* **1991**, 1151. (g) Snider, B. B.; Wan, B. Y.-F.; Buckmann, B. O.; Foxmann, B. M. *J. Org. Chem.* **1991**, *56*, 328. (h) Phosphine oxide-substituted radicals: Brandi, A.; Cicchi, S.; Goti, A.; Pietrusiewicz, K. M. *Tetrahedron Lett.* **1991**, *32*, 3265.

(3) Oxygen-substituted radicals: Giese, B.; Damm, W.; Dickhaut, J.; Wetterich, F.; Sun, S.; Curran, D. P. *Tetrahedron Lett.* **1991**, *32*, 6097.

(4) Benzylic radicals: (a) Giese, B.; Bulliard, M.; Zeitz, H.-G. *Synlett* **1991**, 425. (b) Curran, D. P.; Thoma, G. *Tetrahedron Lett.* **1991**, *32*, 6307.

(5) (a) Curran, D. P.; Seong, C.-M. *J. Am. Chem. Soc.* **1990**, *112*, 9401. (b) Curran, D. P.; Seong, C. M. *Tetrahedron* **1992**, *48*, 2157, 2175.

(6) Iodomalonic esters did not add to such alkenes either. Curran, D. P.; Chen, M.-H.; Spletzer, E.; Seong, C. M.; Chang, C.-T. *J. Am. Chem. Soc.* **1989**, *111*, 8872.

(7) Selenium-transfer additions of Se-heteroatom bonds are well known. Examples and leading references: (a) Back, T. G.; Krishna, M. J. *J. Org. Chem.* **1988**, *53*, 2533. (b) Back, T. G.; Krishna, M. V.; Muralidharan, K. R. *Tetrahedron Lett.* **1987**, *28*, 1737. (c) Toru, T.; Seko, T.; Maekawa, E.; Ueno, Y. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1927. (d) Ogawa, A.; Yokayama, H.; Yokayama, K.; Masawaki, T.; Kambe, N.; Sonoda, N. *J. Org. Chem.* **1991**, *56*, 5721.

(8) Byers and co-workers recently reported examples of phenylselenium-transfer addition and cyclizations of selenomalonic esters. (a) Byers, J. H.; Gleason, T. G.; Knight, K. S. *J. Chem. Soc., Chem. Commun.* **1991**, 354. (b) Byers, J. H.; Lane, C. G. *Tetrahedron Lett.* **1990**, *31*, 5697. (c) See also: Kropp, P. J.; Fryxell, G. E.; Tubergen, M. W.; Hager, M. W.; Harris, G. D., Jr.; McDermott, T. P., Jr.; Tornero-Velez, R. *J. Am. Chem. Soc.* **1991**, *113*, 7300.

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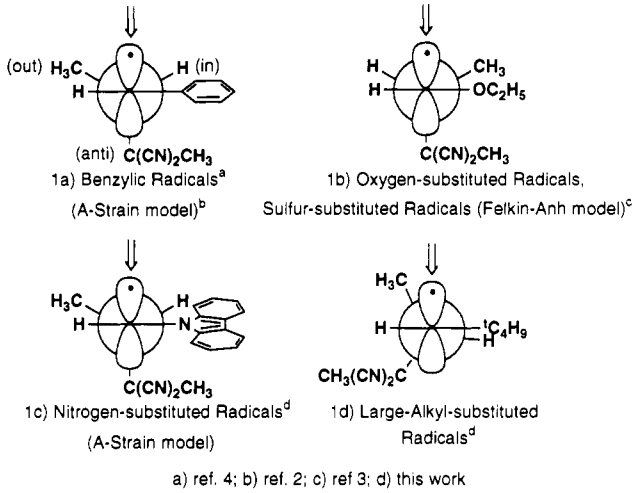
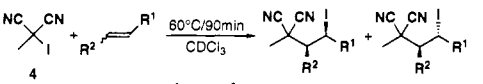


a) ref. 4; b) ref. 2; c) ref 3; d) this work

Figure 1. Transition state models for 1,2-induction.

(no regioisomers were detected in any reactions) and follow expected trends for additions of electrophilic radicals.[9] Stereoselectivities in additions to cyclic alkenes also follow established trends: five-membered rings give high trans selectivity (single isomer, entry i), and six-membered rings give modest trans selectivity (70/30, entry j).[10] For acyclic alkenes, addition to styrene **2k** gives modest syn selectivity (80/20, entry k) while addition to *N*-aryl enamine **2n** gives good syn selectivity (90/10, entry n).[11] In contrast, addition to enol ether **2l** gives modest anti selectivity (25/75, entry l), and addition to phenylthio enol ether **2m** gives good anti selectivity (10/90, entry m).[11]

All documented examples of 1,2-induction in radical reactions (including those above) involve conjugated radicals. To probe the reactions of alkyl radicals, we conducted iodine transfer reactions of **4** with a short series of disubstituted alkenes (**2o–q**), and the results are summarized in eq 2. There was no selectivity in the addition of **4** to **2o**, modest syn selectivity in the addition to **2p** (75/25), and very high syn selectivity in the addition to **2q** (98/2).[11] This level of selectivity is impressive, especially considering that iodine transfer from an iodomalononitrile to an alkyl radical is an extremely rapid reaction.[12]



2	R^1	R^2	equiv 2	5-syn /5-anti	Yield
o	C_2H_5	C_2H_5	3	~ 50/50	50%
p	i-C_3H_7	CH_3	3 (15)	75/25	40% (90%)
q	t-C_4H_9	CH_3	6 (20)	98/2	40% (80%)

eq 2

Figure 1 shows models for each of the 1,2-induction reactions. At this early stage, we consider only the size effects of the malononitrile group; further experiments will be needed to identify any electronic or stereoelectronic contributions. The large majority of existing examples of 1,2-induction follow an A-strain model (Figure 1a);[2,4] a conjugating substituent on the radical-bearing carbon dictates that the smallest substituent on the adjacent stereocenter (hydrogen) occupies the "inside" position. The medium group is "outside", and the large group is "anti". Selenium-, iodine-,[4b] and deuterium-transfer[4b] reactions of the benzylic radical derived from β-methylstyrene all follow this model (Figure 1a) and give similar syn selectivities (80/20 to 85/15). We and Giese have recently shown that oxygen-substituted radicals do not follow the A-strain model and, instead, follow a "Felkin–Anh" model;[3] the medium-sized group is inside, and the hydrogen is outside (Figure 1b). Addition of **1** of **2l** is indeed in line with this radical version of the Felkin–Anh model. The sulfur-substituted radical derived from addition of **1** to **2m** gives even higher "Felkin–Anh" selectivity than its oxygen couterpart. Geometric parallels[1] between enamines,[13a] iminium ions, and nitrogen-substituted radicals suggest that the nitrogen-substituted radicals should follow the A-strain model rather than the Felkin–Anh model (Figure 1c); again the results agree (entry m). Finally, the series of additions in eq 2 shows for the first time that conjugation is not indispensable. If the substituent on the radical center becomes large enough, then excellent syn selectivity can be expected (see **5q**). For this reaction, we tentatively suggest the model in Figure 1d. We suspect that conformations of these types of radicals (and ultimately of the transition states) are restricted by the need for the large group on the radical to be distant from both the medium and large groups on the adjacent stereocenter.

Even though selenium transfer[7] must be slower than iodine transfer, the replacement of iodine by phenylselenium significantly extends the scope of malononitrile radical chemistry by permitting additions to classes of alkenes that are not well-behaved in additions of iodomalononitriles. The additions of selenomalononitrile **1** have already opened new directions in 1,2-asymmetric induction, and further new preparative directions should be revealed by the union of these radical reactions with organoselenium-based methods in organic synthesis.

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Supplementary Material Available: Procedures for the synthesis of **1** and **4**, characterization and structure assignments for all products of 1,2-induction reactions, and complete details of the X-ray crystal structure of **5q**-syn (11 pages). Ordering information is given on any current masthead page.

(9) (a) Giese, B. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 753. (b) Giese, B.; Horler, H.; Leising, M. *Chem. Ber.* **1986**, *119*, 444. (c) Renaud, P.; Schubert, S. *Synlett* **1991**, 624. (d) Renaud, P.; Vionnet, J. P.; Vogel, P. *Tetrahedron Lett.* **1991**, *32*, 3491.

(10) Giese, B. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 969.

(11) Full details of configurational assignments are provided in the supplementary material.

(12) See ref 5b and the following: Curran, D. P.; Bosch, E.; Kaplan, J.; Newcomb, M. *J. Org. Chem.* **1989**, *54*, 1826.

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Mechanism of Rhodium(III)-Catalyzed Methyl Acrylate Dimerization

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Recently we reported a highly efficient Rh-based catalytic system[1] for the selective tail-to-tail dimerization of methyl acrylate (MA) to dimethyl hexenedioates, precursors to adipic acid, which is an intermediate in nylon-66 production.[1-3] The catalytic cycle is entered by protonation of $Cp^*Rh(C_2H_4)_2$, **1**, in the presence of MA.[4] The catalyst is deactivated by loss of H_2 to give the

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(3) For references to Pd-, Ni-, and Ru-based acrylate dimerization catalysts, see footnotes 4 and 5 of ref 1.

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