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N,N-DIETHYLBENZENESELENAMIDE: A USEFUL REAGENT FOR THE DIRECT SELENENYLATION OF ALDEHYDES

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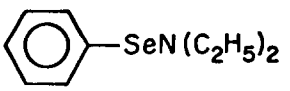
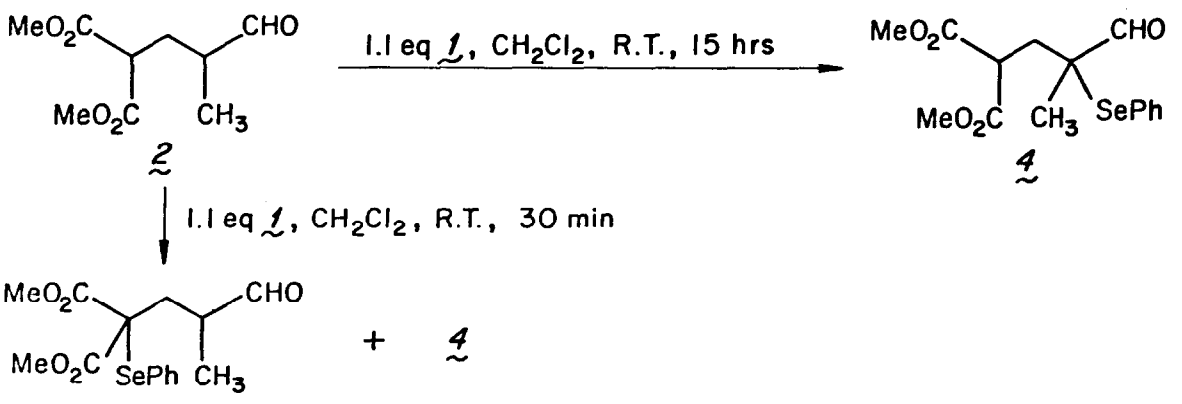
Abstract: N,N-Diethylbenzeneselenamide reacts selectively with aldehydes, under mild conditions, to give α-phenylselenoaldehydes.

N,N-Diethylbenzeneselenamide 1 reacts smoothly with β-dicarbonyl compounds to give α-phenylseleno derivatives.[1] While attempting to use this reaction to convert the malonic



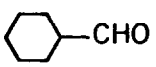
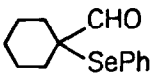
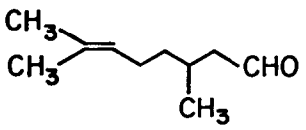
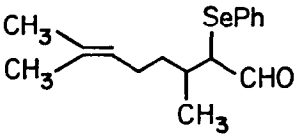
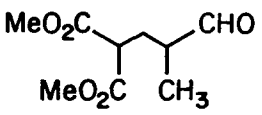
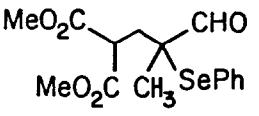
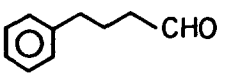
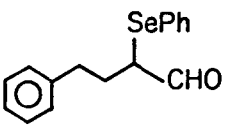
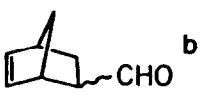
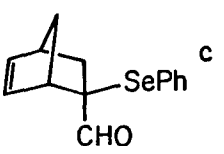
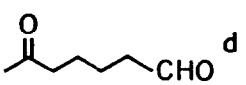
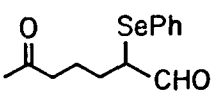
1

ester 2 into its α-phenylseleno derivative, 3, we were surprized to find that after 15 hours at room temperature in CH_2Cl_2, the major reaction product was the α-phenylselenoaldehyde 4 (Scheme 1). At short reaction times (<30 min), we isolated a mixture of 3 and 4. Since dimethyl malonate itself could be selenenylated (60% yield) under similar condition, we suspected that the initial reaction product was in fact 3, and that this product rearranged to 4 under the reaction conditions. In support of this hypothesis, a mixture of 3 and 4 was transformed predominantly into 4 upon treatment with diethylamine in CH_2Cl_2 at R.T.



Scheme 1

Table 1

Aldehyde	Reaction Conditions	α-Phenylseleno Aldehyde (Yield)[a]
	1.25 eq *1*, CH_2Cl_2, 6 hrs, R.T.	 (87%)
	1.0 eq *1*, CH_2Cl_2, 45 min, R.T.	 (78%)
	1.1 eq *1*, CH_2Cl_2, 15 hrs, R.T.	 (60%)
	1.0 eq *1*, CH_2Cl_2, 5 min, −78°C	 (78%)
 [b]	1.25 eq *1*, CH_2Cl_2, 24 hrs, R.T.	 [c] (84%)
 [d]	1.0 eq *1*, CH_2Cl_2, 5 min, R.T.	 (72%)

a) All yields refer to compounds isolated by column chromatography as yellow oils and characterized by ^1H NMR, IR, and MS.[7]

b) The individual epimers gave the same exo/endo product ratio (3:1, with the presumed major epimer drawn), as would be expected on the basis of the proposed mechanism.

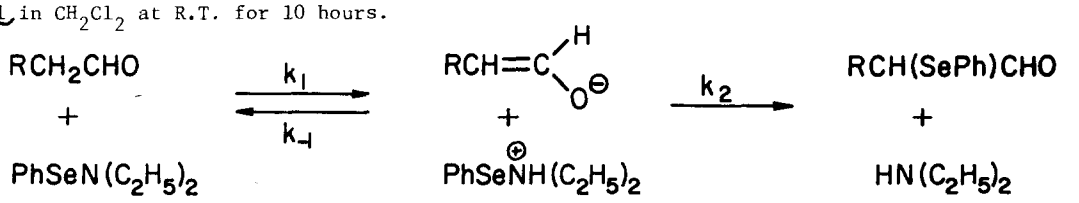
c) Bicyclo[2.2.1]hepta-2,5-diene-2-carboxaldehyde was produced from the epimeric phenylselenides by oxidation to the selenoxides at −78°C with 1.0 eq m-CPBA, followed by elimination at room temperature.

d) 2-Oxo-heptanal was produced via the ozonolysis of 1-methylcyclohexene.

Since compounds of the type $R_2CHCR(SePh)CHO$ can be converted easily into α,β-unsaturated aldehydes via oxidation and elimination,[2] we thought it would be useful to see whether the reaction of 1 with a variety of aldehydes would result in direct selenenylation. To our delight, we observed the selective formation of the desired α-phenylselenoaldehydes in good to excellent yields. The results of these experiments are summarized in Table I.

Several aspects of these results deserve attention. One is the experimental simplicity of the transformation. Although two methods for the preparation of α-phenylselenoaldehydes have been reported recently,[3,4] these require the prior preparation of either enol ethers or of enamines. The present procedure, which requires neither strong acid nor base, represents the first high-yield method for the direct formation of α-phenylselenoaldehydes from unactivated aldehydes.

A notable feature of this reaction is its specificity for attack adjacent to an aldehyde function. If enolate anion formation is the rate determining step in this process (see Scheme 2), then the observed selectivity can be explained on the basis of the greater kinetic acidity of aldehydes compared to ketones. (It has been reported that the rate of α-hydrogen exchange of isobutyraldehyde is 10-100 times greater than that of diisopropyl ketone, using hydroxide ion in H_2O at 25-35°C.[5,6]) Additionally, we observed that 4-phenylbutan-2-one, 4-phenylbutyl acetate, and methyl 4-phenylbutyrate gave no observable selenenylated products when treated with 1.1 eq of 1 in CH_2Cl_2 at R.T. for 10 hours.



Scheme 2

N,N-Diethylbenzeneselenamide can be prepared easily from PhSeCl and 2 eq of $HNEt_2$ as described by Reich.[1] Although 1 is difficult to purify, it is quite stable when stored in a freezer under anhydrous conditions. Selenenylations were carried out by adding 1 via syringe to ~0.3 M solutions of aldehyde in dry CH_2Cl_2 at the appropriate temperature. The reaction mixture was stirred until the starting material was consumed. Solvent was then removed, and the products isolated by column chromatography.

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7. 1-Phenylselenocyclohexanecarboxaldehyde: ^{1}H NMR (90 MHz, $CDCl_3$): δ=9.21, 1H, s; 7.2-7.6, 5H, m; 1.1-2.1, 10H, m. IR(CCl_4): 1714, 2710, 1585 cm^{-1}. MS m/e(rel. int.): 268(68), 266(37), 239(42), 237(21), 158(59), 156(30), 111(58), 93(47), 81(100).
2-Phenylseleno-3,7-dimethyloct-6-enal: ^{1}H NMR (90 MHz, $CDCl_3$): δ=9.42, 1H, overlapping d, J=5Hz; 7.2-7.6, 5H, m; 5.20-5.25, 1H, m; 3.49, 1H, overlapping dd, J=5,7Hz; 1.4-2.2, 11H, m; 1.08, 1.14, 3H, d, J=7Hz. IR (CCl_4): 1716, 2720, 1582 cm^{-1}. MS m/e(rel. int.): 310(5), 308(3), 135(60), 83(92), 71(100), 41(82).
2-Carbomethoxy-4-formyl-4-phenylselenomethylpentanoate: ^{1}H NMR (90 MHz, $CDCl_3$): δ=9.22, 1H, s; 7.2-7.6, 5H, m; 3.73, 3H, s; 3.70, 3H, s; 3.7, 1H, m; 2.25-2.6, 2H, m; 1.32, 3H, s. IR (CCl_4): 1762, 1743, 1712, 2720, 1580 cm^{-1}. MS m/e(rel. int.): 358(6), 356(3), 201(92), 169(34), 157(30), 137(100).
2-Phenylseleno-4-phenylbutanal: ^{1}H NMR (90 MHz, $CDCl_3$): δ=9.44, 1H, d, J=3Hz; 7.1-7.6, 5H, m; 3.57, 1H, dt, J=3,8Hz; 2.80, 2H, t, J=8Hz; 1.7-2.3, 2H, m. IR(CCl_4): 1718, 2720, 1580 cm^{-1}. MS m/e(rel. int.): 304(11), 302(6), 157(13), 147(24), 129(38), 117(37), 91(100).
Bicyclo[2.2.1]hept-5-ene-2-phenylseleno-2-carboxaldehyde: ^{1}H NMR (90 MHz, $CDCl_3$): δ=9.48, 0.22H, s; 9.27, 0.78H, s; 7.2-7.6, 5H, m; 6.43, 0.22H, dd, J=3,6Hz; 6.20, 1H, m; 5.98, 0.78H, dd, J=3,6Hz; 3.16, 0.22H, m; 3.00, 1.78H, m; 2.2-2.4, 1H, m; 1.87, 1H, m; 1.55-1.75, 1H, m; 1.15-1.4, 1H, m. IR (CCl_4): 1710, 2710, 1580 cm^{-1}. MS m/e(rel. int.): 278(40), 276(21), 212(99), 210(50), 183(73), 157(23), 155(12), 121(29). 103(30), 91(89), 86(24), 84(37), 77(100)
2-Phenylseleno-6-oxo-heptanal: ^{1}H NMR (90 MHz, $CDCl_3$): δ=9.46, 1H, d, J=3Hz; 7.2-7.6, 5H, m; 3.61, 1H, m; 2.50, 2H, m; 2.15, 3H, m; 1.80, 4H, m. IR(CCl_4): 1718, 1580, 2720 cm^{-1}. MS m/e(rel. int.): 284(8), 282(4), 157(11), 127(16), 97(11), 81(12), 78(10), 77(10), 43(100).

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