Cycloaddition of Vinyl Isocyanate to 1,3-Dipoles

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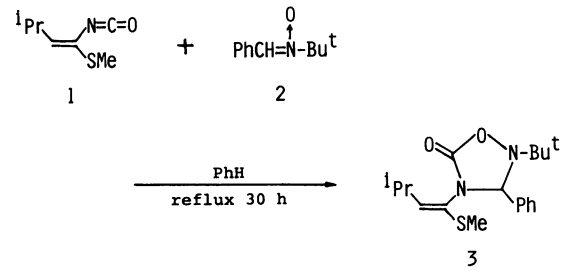
Synopsis. 1,2-Cycloadditions of 3-methyl-1-(methylthio)-1-butenyl isocyanate with *N*-*t*-butyl-α-toluenimine *N*-oxide and with *in situ*-generated *N*-*t*-butyl-α-methyl-α-lactam afforded an oxadiazolidinone derivative and a hydantoin derivative in 100 and 46% yields, respectively.

Vinyl isocyanates are known to undergo 1,2- and/or 1,4-cycloaddition reactions with several unsaturated compounds and have been often utilized in heterocyclic synthesis.[1,2] Previously we reported synthesis and 1,4-cycloaddition reactions of α-alkylthio(or arylthio)vinyl isocyanates,[3] which are expected to be reagents equivalent to acyl isocyanates[4] because the (alkylthio)vinyl group is easily converted to a carbonyl group.[5] Here we wish to report 1,2-cycloaddition reactions of 1,3-dipoles to the (alkylthio)vinyl isocyanate leading to heterocycles having the (alkylthio)vinyl substituent.

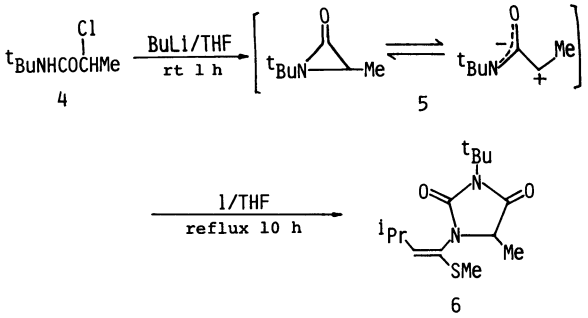
Reaction of (*E*)-3-methyl-1-(methylthio)-1-butenyl isocyanate (**1**) and *N*-*t*-butyl-α-toluenimine *N*-oxide (**2**) in refluxing benzene for 30 h under a nitrogen atmosphere to give 2-*t*-butyl-4-[3-methyl-1-(methylthio)-1-butenyl]-3-phenyl-1,2,4-oxadiazolidin-5-one (**3**) quantitatively.



1 2 3

The structure of the oxadiazolidone **3** was determined by spectral data and elemental analysis. The IR spectrum of **3** shows a strong carbonyl absorption at 1740 cm^{-1} as well as a weak one at 1625 cm^{-1} due to the olefinic bond. In the NMR spectrum, two methyl doublets were observed at δ 0.17 and 0.93 (relative area 3H, respectively). These are assignable to the isopropyl group whose methyl groups became nonequivalent by the presence of the asymmetric carbon in the oxadiazolidine ring. The unusual higher shift of one of the methyl signals is due to the deshielding effect by the phenyl ring.

As another candidate for a 1,3-dipole, it is known that an α-halo amide generates an α-lactam and/or a 1,3-dipole such as **5** upon treatment with a strong base.[6] Thus the α-chloropropanamide **4** was reacted with the isocyanate **1** after treatment with butyllithium. 1,2-Cycloadditon again occurred to give the hydantoin derivative **6**. The IR spectrum of **6** showed two carbonyl absorptions at 1770 and 1715 cm^{-1} and a weak one at 1630 cm^{-1} due to the C=C bond. In the NMR spectrum, two doublets of the nonequivalent methyl group of the isopropyl function was observed at δ 0.95 and 1.13. The



mass spectrum as well as elemental analysis showed good agreement with the structure of the hydantoin **6**.

Thus the two heterocyclic compounds having a thiovinyl substituent were prepared by 1,2-cycloaddition of the (alkylthio)vinyl isocyanate with the 1,3-dipoles. Higher convertibility of the thiovinyl group, as is already mentioned, will enable further conversion of the compounds into various heterocycles and it will increase utility of the (alkylthio)vinyl isocyanates.

Experimental

A melting point was determined on a Yanagimoto micro melting point apparatus and melting and boiling points were uncorrected. ^{1}H-NMR spectra were obtained with a JOEL JNM PMX-60 spectrometer in $CDCl_3$ using TMS as an internal standard. IR spectra were taken on a JASCO IRA-1 spectrophotometer. Mass spectrometry was performed on a Hitachi RMU-6E spectrometer at an ionizing voltage of 70 eV.

Materials. (*E*)-3-Methyl-1-(methylthio)-1-butenyl isocyanate (**1**: bp 31—34 °C/267 Pa) and *N*-*t*-butyl-α-toluenimine *N*-oxide (**2**) were prepared according to the literatures.[3,7] *N*-*t*-Butyl-2-chloropropanamide (**4**) was prepared from *N*-*t*-butylamine and 2-chloropropionyl chloride by the usual manner. Commercially available butyllithium (15% in hexane) was used.

The Reaction of the Isocyanate 1 with the N*-Oxide 2.* A solution of **1** (1.7 g, 10 mmol) and **2** (1.9 g, 10 mmol) in dry benzene (20 ml) was stirred at reflux for 30 h. The reaction mixture was concentrated and chromatographed on a SiO_2 column to give 3.6 g (100%) of 2-*t*-butyl-4-[3-methyl-1-(methylthio)-1-butenyl]-3-phenyl-1,2,4-oxadiazolidin-5-one (**3**): mp 147—148 °C (colorless needles from benzene–hexane); IR (Nujol) 1740 (C=O) and 1625 cm^{-1} (C=C); ^{1}H-NMR δ=0.17 (3H, d, *J*=6.8 Hz, Me), 0.93 (3H, d, *J*=6.4 Hz, Me), 1.18 (9H, s, *t*Bu), 1.8—2.3 (1H, m, CH), 2.30 (3H, s, SMe), 5.57 (1H, d, *J*=10.2 Hz, =CH), 5.83 (1H, s, CH), 7.2—7.7 (5H, m, Ph); MS *m*/*z* 247 (M^+—BuNO). Found: C, 64.71; H, 7.99; N, 8.29%. Calcd for $C_{18}H_{26}N_2O_2S$: C, 64.85; H, 7.84; N, 8.38%.

The Reaction of the Isocyanate 1 with the 1,3-Dipole 5. To a solution of the amide **4** (1.56 g, 9.6 mmol) in THF (20 ml) was added dropwise a solution of butyllithium in hexane (6.4 ml, 9.6 mmol) and the mixture was stirred for 1 h at room temperature. To this mixture was added a solution of the isocyanate **1** (1.5 g, 9.6 mmol) in THF (10 ml) at 0 °C and was stirred for 10 h at reflux. After removal of THF

and addition of cold water, the reaction mixture was extracted (ether), dried (Na_2SO_4), and chromatographed on a SiO_2 column to give 1.3 g (46%) of 1-*t*-butyl-4-methyl-3-[3-methyl-1-(methylthio)-1-butenyl]-2,5-imidazolidinedione (**6**): bp 60 °C (bath temp)/66 Pa by pot distillation; IR (neat) 1770 (C=O), 1715 (C=O), and 1630 cm^{-1} (C=C); ^{1}H-NMR δ=0.95 (3H, d, J=6.2 Hz, Me), 1.13 (3H, d, J=6.2 Hz, Me), 1.37 (3H, d, J=7.0 Hz, Me), 1.62 (9H, s, *t*Bu), 2.12 (3H, s, SMe), 2.2—2.6 (1H, m, CH), 4.17 (1H, q, J=7.0 Hz, CH), 5.72 (1H, d, J=10.0 Hz, =CH); MS *m/z* 284 (M^+). Found: C, 58.83; H, 8.60; N, 9.57; S, 11.22%. Calcd for $C_{14}H_{24}N_2O_2S$: C, 59.13; H, 8.51; N, 9.85; S, 11.26%.

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