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ALLERGENIC α-METHYLENE-γ-BUTYROLACTONES. A CONVENIENT SHORT ONE-CARBON DEGRADATION OF ISOALANTOLACTONE FROM VINYLSULFOXIDES.

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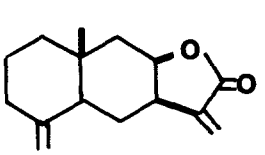
Summary : 13-Norisoalantolactone 9 was prepared in seven steps from isoalantolactone.

The mechanism of allergic contact dermatitis to α-methylene-γ-butyrolactones can be studied in guinea pigs, using ^{14}C-labelled lactones[1]. We have recently described a one-carbon degradation of isoalantolactone 1 based on the Pummerer rearrangement of phenylsulfoxide 2[2]. Migration of the exocyclic C_4 double bond could not be avoided and nor-lactone 3 was obtained. We described here a new degradation where the nonrearranged norisoalantolactone could be obtained in good yield.



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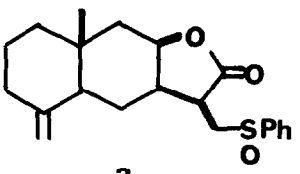

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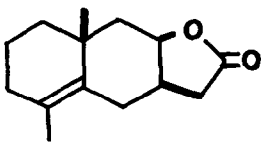

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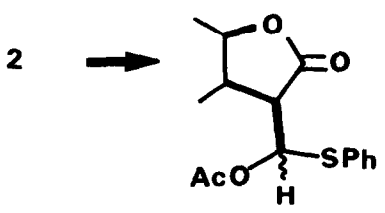
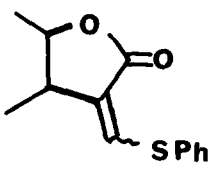
Pummerer rearrangement of sulfoxide 2 leads to diasteromeric acetates 4, 5, along with vinylsulfides 6 which could not be hydrolyzed[2].



4, 5



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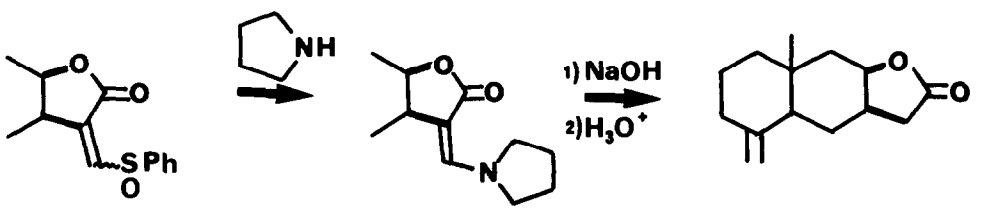
We have found that the vinylsulfoxides 7 (derived from 6) were extremely sensitive to nucleophiles such as amines, leading, with good yields, to enamines. For instance, when compound 7 was treated with 4 equivalents of pyrrolidine in CH_2Cl_2 at room temperature for

ten minutes, a crystalline compound 8 (Z isomer, mp 215-218 dec, ir 1 705 1 620, nmr : 0.86 (s, 3H, $C_{10}\underline{CH}_3$), 1.93 (m, 4H, $\underline{CH}_2$-$\underline{CH}_2$), 2.6-3.3 (m, 1H, H_7), 3.46 (m,4H, $N(\underline{CH}_2)_2$), 4.1-4.5 (m, 1H, H_8), 4.48 and 4.78 (2 broad s, 2H, C_4=CH_2), 7.36 (broad s, 1H, H_a, C=$\underline{CH}$N) was obtained, along with the E-isomer (oil). The mixture of enamines 8 (obtained without purification from sulfoxide 7) was treated with a base (6N NaOH in EtOH) for 8 h under reflux, pH was adjusted to 4 and extraction gave a hydroxyacid which lactonized slowly.



7 8 9

13-Norisoalantolactone 9 was isolated by column chromatography as a crystalline compound (mp 130-132°, 60% yield). IR and NMR spectra were identical with those reported in the literature[3].

Since the α-acetoxysulfide 5 can easily be transformed into vinylsulfide 6 through NaOMe treatment, the sequence described above provides an efficient facile route to one-carbon degraded α-methylene-γ-lactones. ^{14}C-labelled isoalantolactone can be prepared from 9 using a known sequence of transformations[4].

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