

SHORT
COMMUNICATIONS

Reaction of Allyl Phenylcarbamate with 5-Methyl-4,5-dihydro-3*H*-2-benzazepine-3-spirocyclohexane *N*-Oxide

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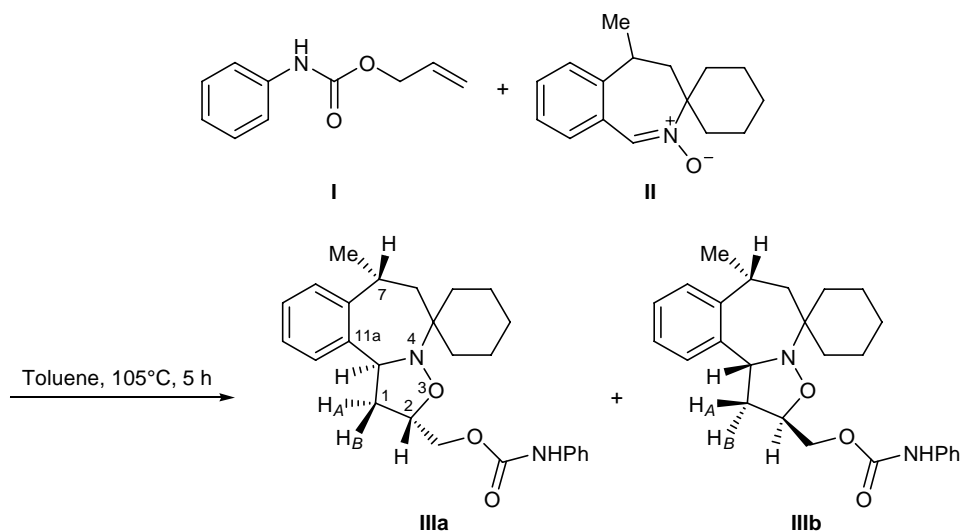
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Oxidation of secondary amines to the corresponding *N*-oxides with peroxy acids derived from Group VI transition metals (W, Mo) (which are prepared *in situ* from metal salts and hydrogen peroxide) is widely used in organic synthesis [1–6]. Accessibility of initial amines, simple experimental procedure, mild reaction conditions, high yields, and wide synthetic potential of the resulting nitrones ensured fast propagation of this method into the chemistry of heterocyclic compounds [7–12].

In the present communication we report the results of our study on the reaction of allyl phenylcarbamate (**I**) with 5-methyl-4,5-dihydro-3*H*-2-benzazepine-3-spirocyclohexane *N*-oxide (**II**). The latter was prepared in turn by intramolecular cyclization of 1-allyl-1-benzylaminocyclohexane in concentrated sulfuric acid at 70–80°C, followed by oxidation with hydrogen peroxide in aqueous acetone in the presence of 0.05 mol % of sodium tungstate at room temperature [13]. 1,3-Dipolar cycloaddition of compounds **I** and **II** was

effected by heating equimolar amounts of the reactants in boiling toluene for 5 h. Study of the product structure by IR and ¹H NMR spectroscopy showed that the reaction occurred in a regio- and stereoselective fashion with formation of 7-methyl-2-(phenylcarbamoyloxymethyl)-1,2,5,6,7,11b-hexahydrobenzo[*c*]-isoxazolo[2,3-*a*]azepine-5-spirocyclohexane as a mixture of two diastereoisomers **IIIa** and **IIIb**. The IR spectra of **IIIa** and **IIIb** lack absorption bands typical of the *N*-oxide moiety in initial compound **II** (1230, 928, 1647 cm⁻¹; stretching vibrations of the N→O and C=N bonds, respectively [13]), but bands belonging to stretching vibrations of the NH and carbamate carbonyl groups appeared at 3340 at 1720 cm⁻¹, respectively.

Compounds **IIIa** and **IIIb** are likely to be formed via *exo*-transition state as a result of approach of the carbamate **I** molecule to the *trans* or *cis* position with respect to the 5-methyl group in **II**. The regioselectivity is controlled by the lowest unoccupied molecular



orbital (LUMO) of nitron **II**, which is characterized by a larger contribution of the respective carbon atom [12]. Presumably, a considerable size of the phenylcarbamoyloxymethyl radical in allyl phenylcarbamate (**I**) is responsible for the observed stereoselectivity owing to destabilization of *endo*-transition state in the cycloaddition.

We succeeded in isolating by column chromatography only isomer **IIIa** as individual substance. Its steric structure was confirmed by two-dimensional NOESY technique: the NOESY spectrum contained no off-diagonal cross peaks due to interaction of the 7-H and 11a-H protons [11]. The high yield of compound **IIIa** indicates that it is formed as the major stereoisomer in the examined reaction.

7-Methyl-2-(phenylcarbamoyloxymethyl)-1,2,5,6,7,11b-hexahydrobenzo[*c*]isoxazolo[2,3-*a*]-azepine-5-spirocyclohexanes IIIa and IIIb. A mixture of 0.48 g (2.71 mmol) of allyl phenylcarbamate (**I**) and 0.66 g (2.71 mmol) of compound **II** in 30 ml of toluene was heated for 5 h at 105°C. The solvent was removed under reduced pressure, 15 ml of hexane was added to the residue, and the mixture was left to stand for 24 h for crystallization. Recrystallization of the product from carbon tetrachloride gave 0.98 g (89%) of a mixture of stereoisomers **IIIa** and **IIIb** as colorless crystals with mp 148–150°C.

Compound **IIIa**. Stereoisomer mixture **IIIa/IIIb** was subjected to chromatographic separation in a column (30×1 cm) charged with aluminum oxide (Brockmann activity grade 0) using hexane–ethyl acetate (3:1) as eluent. Yield 0.62 g (63%), mp 147–149°C, R_f 0.38 (hexane–ethyl acetate, 3:1). ^1H NMR spectrum, δ , ppm: 9.70 br.s (1H, NH), 7.48 d (2H, H_{arom} , $J = 8$ Hz), 7.27 t (2H, H_{arom} , $J = 8$ Hz), 7.21–7.12 m (4H, H_{arom}), 6.95 t (1H, H_{arom} , $J = 8$ Hz), 4.65 t (1H, 11a-H, $J = 8$ Hz), 4.27 d.d (1H, OCH₂, $J = 4$, 12 Hz), 4.15 m (1H, 2-H), 4.05 d.d (1H, OCH₂, $J = 4$, 12 Hz), 3.40 q (1H, 7-H, $J = 6$ Hz), 2.65 m and 2.23 m (1H each, 1-H_A, 1-H_B), 2.05 d (1H, 6-H_A, $J = 14.7$ Hz),

1.90 m (2H, 6-H_B, cyclohexane), 1.64 t (2H, cyclohexane, $J = 13.8$ Hz), 1.52–1.01 m (10H, 7-CH₃, cyclohexane). Found, %: C 74.02; H 7.27; N 7.01. C₂₆H₃₂N₂O₃. Calculated, %: C 74.29; H 7.62; N 6.67.

The IR spectra were recorded in the range from 4000 to 400 cm⁻¹ on an IKS-29 spectrophotometer from samples dispersed in mineral oil. The ^1H NMR spectra (including NOESY) were measured on a Bruker DRX-500 spectrometer (500 MHz) from solutions in DMSO-*d*₆.

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