Pyridazines, LVIII[1]:
1-Phenyl-1-pyridazinyl-2-substituted Ethenes,
Synthesis and Configuration**

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Summary. Starting from phenyl pyridazinyl ketones 1 and 3 various 1-phenyl-1-pyridazinyl-2-substituted ethenes (2a-c, 4, 5a, b, 6a, b, 7–9) were prepared by Wittig-Horner- oder Wittig-type reactions. Configurational assignments of these novel compounds were achieved by NOE difference spectroscopy.

Keywords. Phenyl-4-pyridazinylmethanone; Phenyl-3-pyridazinylmethanone; Phenyl-pyridazinyl-ethenes, configuration of; NOE-difference spectroscopy.

Introduction

The 1,1-diarylethene system represents an essential subunit of a wide variety of bio-active compounds. In particular, mono-aza congeners (i.e. 1-phenyl-1-pyridyl-2-substituted ethenes) have been investigated in detail and several interesting drugs (antidepressants [3, 5], nonsedating antihistaminics [5], antithrombotics [6–8]) emerged from these studies. Diaza-analogous systems in which one of the aryl moieties is a pyridazine nucleus, however, so far remained totally unexplored.

On the other hand, it has been shown recently that replacement of the azine system in certain pyridine-derived drug molecules [9–11] by the pyridazine system may afford compounds with improved biological activity or reduced cytotoxicity.

These findings now prompted us to investigate Wittig-Horner-type carbonylolefination reactions of phenyl pyridazinyl ketones in order to gain access to novel synthetic intermediates potentially useful for bio-isosterism studies. This approach

** Dedicated with best wishes to Prof. Dr. M. Pailer on the occasion of his 80th anniversary
to the title compounds was chosen in view of the convenient availability of phenyl 4-pyridazinyl ketone (I) [13, 14] and the isomeric 3-pyridazinyl derivative (3) [15, 16]. An economical large scale preparation for the latter ketone has been elaborated quite recently [2].

**Results and Discussion**

**Syntheses**

Phenyl 4-pyridazinyl ketone (1) was found to react smoothly with diethyl benzylphosphonate/sodium hydride (15 h, 25°) to afford a 70% yield of 2a. Under these mild conditions we also succeeded in the preparation of the olefins 2b and 2c in satisfactory yields. Whereas these reactions of 1 afforded Z-isomers almost exclusively (only traces of the E-isomers could be detected by glc/ms), treatment of phenyl 3-pyridazinyl ketone (3) with diethyl cyanomethylphosphonate or diethyl ethoxycarbonylmethylphosphonate under analogous conditions gave mixtures of Z and E olefins (Scheme 1). Separation of compounds 5a, 6a and 5b, 6b simply could be achieved by means of medium pressure liquid chromatography (yields of pure products: 5a 59%, 6a 19%; 5b 30%, 6b 48%). When diethyl benzylphosphonate was employed as the Wittig-Horner reagent, also the ketone 3 was transformed into a single isomer 4. In this case however, the new phenyl substituent and the heteroaromatic ring are in trans position as shown by NOE experiments (see below).

\[ \text{Scheme 1} \]

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