Structural and reactivity studies of new organophosphorus amides

by

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ABSTRACT

The bicyclic substrates 1-oxo-2,8-diaryl-2,5,8-triaza-1λ^5-phosphabicyclo[3.3.0]-octane **3** were studied before. The molecular rearrangement of the alcoholysis product of **3** (the eight-membered ring compound 1-oxo-1-ethoxy-2,8-diaryl-2,5,8-triaza-1λ^5-phosphacyclooctane) to the five-membered ring isomer (the 1,3,2λ^5-diazaphospholidine system) is reasonably well understood for the *N,N*'-diaryl substituted substrates. It was decided to expand the studies of the bicyclic system **3** to other derivatives with aliphatic substituents on the nitrogen atoms (R=PhCH$_2$, Me, Et), as well as the thiophosphoryl and phosphine analogues of **3**.

Differences between the *N*-aryl and *N*-alkyl substrates were observed in the acid and base catalyzed solvolysis of the bicyclic substrate. The reactivity in the rearrangement of the solvolysis product, from an eight-membered ring to the five-membered ring isomer was also different. The *N,N'*-dialkyl substituted compounds rearranged much slower to the corresponding five-membered ring compounds than the *N,N'*-diaryl analogues.

The thiophosphoryl analoque of **3a** (R=Ph), 1-thio-2,8-diphenyl-2,5,8-triaza-1λ^5–phosphabicyclo[3.3.0]octane **11a** was prepared by reacting *bis*-(2-phenylamino-ethyl)amine with P(S)Cl$_3$ in the presence of a base. The alcoholysis product of **11a**, observed in ^{31}P NMR (δ_P 76), was the eight-membered ring compound **15**. This compound then rearranged to the five-membered ring isomer **16** during GC-MS analysis. This rearrangement is analogous to the rearrangement observed for the corresponding phosphoryl derivatives. Both the thiophosphoryl bicyclic **11a** and the phosphoryl bicyclic **3a** compounds were detected in the mass spectrum of compound **15**. This could be explained in terms of the thiono (P(S)OR) to thiolo (P(O)SR) rearrangement.

The NMR spectra of the phosphoryl and thiophosporyl bicyclic compounds **3a** and **11a** proved to have distinct differences in the aliphatic region as far as

coupling constants are concerned. From the crystal structures it was clear that the two halves (two five-membered rings) of **3a** and **11a** had remarkably different dihedral angles. The NMR data represented an average of the two rings, therefore they appear identical on the NMR-scale.

Comparing the dihedral angles as determined from NMR data, by utilization of the Karplus equation, with the dihedral angles obtained from X-ray diffraction data was only approximate. There was very little correlation between the experimental and the calculated dihedral angles for compounds **3a** and **11a**. An average value of the dihedral angles, resulting from NMR data, was not in agreement with the crystal structures.

The MM^+ force field of HyperChem® was adapted to perform molecular mechanical calculations in an effort to enhance the conceptualization of the properties and the behaviour of these new heterocyclic compounds. The calculated energies of the eight-membered ring and five-membered ring isomers, for all the different derivatives, confirmed that the rearrangement is thermodynamically controlled. The five-membered ring isomer in each case had lower total strain energy than the eight-membered ring isomer.

The thiono and thiolo isomers had comparable potential energies. The thiono isomer of the *N*-Benzyl derivative had a slightly lower potential energy than the thiolo isomer, for both the eight- and five-membered ring isomers. The calculated energies for both the thiono and the thiolo isomers suggested that the five-membered ring isomer was thermodynamically more stable than the eight-membered ring compound.

OPSOMMING

Die bisikliese verbinding 1-okso-2,8-diariel-2,5,8-triasa-1λ^5-fosfabisiklo[3.3.0]-oktaan **<u>3</u>**, is voorheen berei en bestudeer. Die molekulêre herrangskikking van die solvolise produk van **<u>3</u>**, die agtlidring 1-okso-1-alkoksie-2,8-diariel-2,5,8-triasa-1λ^5-fosfasiklooktaan na die vyflidring isomeer, die 1,3,2λ^5-diasa-fosfolidine sisteem, word redelik goed verstaan vir die verbindings met aromatiese substituente op stikstof. Die studie van die bisikliese sisteem **<u>3</u>** is uitgebrei na ander afgeleides met alifatiese substituente op stikstof sowel as die swawel analoë van **<u>3</u>**.

Die suur en basies gekataliseerde solvolise van **<u>3</u>** verloop verskillend vir die *N*-ariel en *N*-alkiel afgeleides. Verskille is ook waargeneem in die verloop van die agtlidring na vyflidring herrangskikking. Die *N,N*-dialkiel gesubstitueerde verbindings herrangskik na die ooreenstemmende vyflidring, maar veel stadiger as die *N,N*-diariel analoë.

Die swawel analoog van **<u>3a</u>**, 1-tio-2,8-difeniel-2,5,8-triasa-1λ^5-fosfabisiklo[3.3.0]-oktaan **<u>11a</u>** was berei deur *bis*-(2-fenielamino-etiel)amien met $P(S)Cl_3$ te laat reageer in die teenwoordigheid van ‘n basis. Die alkoholise produk van **<u>11a</u>** wat waargeneem is in ^{31}P NMR (δ_P 76) was die agtlidring isomer **<u>15</u>**. Hierdie produk herrangskik onder kondisies van GC-MS analise, na die vyflidring isomer **<u>16</u>**. Hierdie herrangskikking is in ooreenstemming met die herrangskikking in die ooreenkomstige fosforiel afgeleides. Beide die uitgangstof vir die alkoholise sowel as die suurstof analoog is waargeneem in die massaspektrum. Hierdie waarneming kan verklaar word aan die hand van die tiono (P(S)OR) na tiolo (P(O)SR) herrangskikking.

Die KMR spektra van die fosforiel en die tiofosforiel bisikliese verbindings **<u>3a</u>** en **<u>11a</u>** toon aansienlike verskille in die alifatiese gebied. Die kristalstruktuur data toon dat die twee helftes van die bisikliese verbindings **<u>3a</u>** en **<u>11a</u>** merkbaar

verskil in terme van die dihedrale hoeke. Die KMR data verteenwoordig ‘n gemiddelde van die twee ringe, dus vertoon die twee helftes identies op die KMR-skaal. Die vergelyking van die dihedrale hoeke, soos bepaal vanaf KMR data met behulp van die Karplus vergelyking, met die dihedrale hoeke wat verkry is uit X-straaldiffraksie data is in elke geval baie benaderd. Daar is min korrelasie tussen die eksperimentele en berekende dihedrale hoeke vir **3a** en **11a**. Die gemiddelde waarde soos verkry uit KMR data stem nie ooreen met die kristalstrukture nie.

Die MM^+ kragveld van HyperChem® is aangepas om die eienskappe en reaktiwiteit van die nuwe heterosikliese verbindings verder te bestudeer. Die berekende energieë van die aglidring en vyflidring isomere van al die verskillende afgeleides bevestig dat die herrangskikking termodinamies beheer word. In elke geval het die vyflidring isomeer ‘n laer energie as die agtlidring isomeer.

Die tiono en tiolo isomere het vergelykbare potensiële energieë. Die tiolo isomeer van die *N*-Bensiel afgeleide het ‘n effens laer energie as die tiono isomeer vir beide die aglidring as die vyflidring isomere. Vir beide die tiono en tiolo isomere, toon die berekende energieë dat die vyflidring isomeer termodinamies meer stabiel is as die aglidring isomeer.