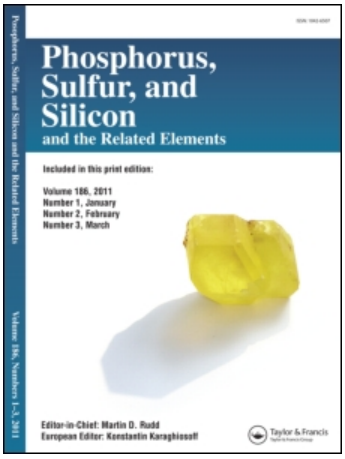


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Synthesis and Properties of 2-Amino-2-Arylethylphosphonic Acids and Derivatives

Ludwig Maier; Peter J. Diel

To cite this Article Maier, Ludwig and Diel, Peter J.(1996) 'Synthesis and Properties of 2-Amino-2-Arylethylphosphonic Acids and Derivatives', Phosphorus, Sulfur, and Silicon and the Related Elements, 109: 1, 341 — 344
To link to this Article: DOI: 10.1080/10426509608545160
URL: http://dx.doi.org/10.1080/10426509608545160

Phosphorus, Sulfur, and Silicon, 1996, Vols. 109-110, pp. 341-344
Reprints available directly from the publisher
Photocopying permitted by license only

SYNTHESIS AND PROPERTIES OF 2-AMINO-2-ARYLETHYLPHOSPHONIC ACIDS AND DERIVATIVES

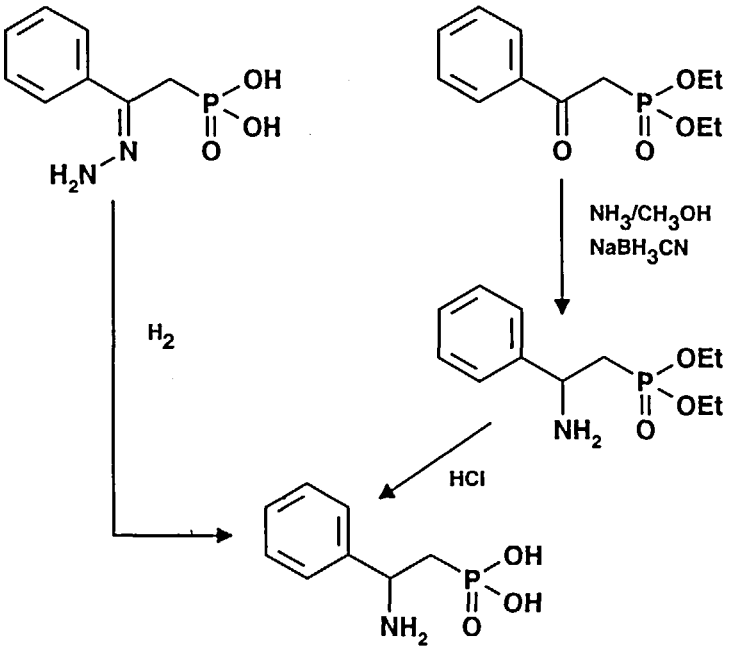
LUDWIG MAIER AND PETER J. DIEL
CIBA-GEIGY AG, Agricultural Division, CH-4002 Basel, Switzerland

ABSTRACT 2-Amino-2-arylethylphosphonic acids, **6a** to **6q** have been prepared from the corresponding 2-acetoxyimino- or 2-methoxy imino-2-arylethylphosphonates, **3** or **4**, by hydrogenation using Raney-Ni as a catalyst, followed by hydrolysis with HCl. **3** and **4** were obtained from the corresponding aryl-bromomethyl-ketoxime-O-acetates, **1**, or aryl-bromomethyl-O-methylketoximes, **2**, by an Arbuzov reaction with triethylphosphite.
Several of the 2-amino-2-arylethylphosphonic acids **6** show activity against Botrytis cinerea and Cercospora. Among the more active compounds were **6a**, **6b**, **6g** and **6k**, whereby **6b** and **6k** gave full protection against Botrytis cinerea (on apple) down to 60 ppm. The same compounds show also a weak inhibition of anthocyanin synthesis in vivo.[1]

Key words: 2-Amino-2-arylethylphosphonic acids; 2-amino-2-arylethylphosphonates; 2-acetoxyimino-2-arylethylphosphonates; 2-methoxyimino-2-arylethylphosphonates; Reduction of oximes; biological activity.

INTRODUCTION

A few years ago we reported on the synthesis and properties of 1-amino-2-arylethylphosphonic acids.[2] It was shown that several compounds of this type are strong inhibitors of PAL and anthocyanin synthesis and are also quite active botryticides. It seemed of interest to prepare the 2-amino-2-arylethylphosphonic acids and compare their biological activity with that of the 1-amino-2-arylethylphosphonic acids.
In the literature are already described some of these compounds. Thus Mastalerz et al.[3] obtained the unsubstituted 2-amino-2-phenylethylphosphonic acid, **6a**, by reduction of the hydrazon, and Varlet et al.[4] synthesized several compounds of this type by reductive amination of the corresponding keto-compounds (Scheme I)



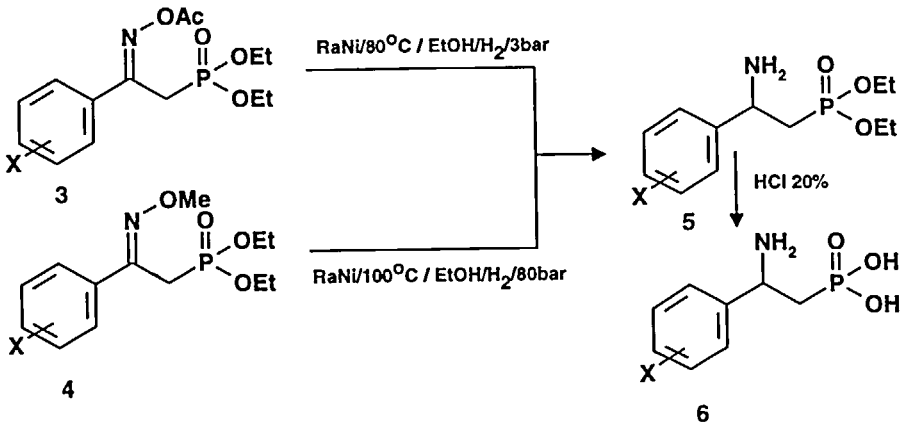
6a

Scheme I

Both methods need β-ketophosphonates as starting materials which are not so readily available. In the following we describe a new preparative procedure and also report on the biological activity of this type of compounds.

RESULTS AND DISCUSSION

To avoid the use of β-ketophosphonates we started with oxime acetates 1 or oxime ethers 2 of aryl-bromomethylketones which can be easily prepared. Treatment of these with triethylphosphite yields the 2-aryl-2-acetoxyiminoethylphosphonates 3[5] and 2-aryl-2-methoxyiminoethylphosphonates 4 in high yield (Scheme II).



Scheme II

Reduction of **3** with hydrogen in ethanol at 80°C and 3 bars and of **4** at 100°C and 80 bars in the presence of Raney-Ni as catalyst produced **5** in reasonable to good yields. It was observed that in general the reduction of **4** gave higher yields of **5** than that of **3**, e.g., reduction of **4k** ($X=CH_3$) yielded **5k** in 79.6% yield, whereas reduction of **3k** ($X=CH_3$) gave **5k** in only 51.5% yield. **4n** ($3,4\text{-}Cl_2$) and **4o** ($X=2,4\text{-}Cl_2$) were reduced to **5n** and **5o**, respectively, with zink in formic acid[6], in order to avoid dehalogenation.

Hydrolysis of 2-amino-2-arylethylphosphonates **5** with 20% HCl under reflux afforded 2-amino-2-arylethylphosphonic acids, **6**, (Scheme II) in good yields. Since the difluormethoxysubstituent in **5l** was cleaved with HCl, **5l** was converted to **6l** by dealkylation with trimethylbromosilane followed by hydrolysis with methanol.

BIOLOGICAL ACTIVITY

Like 1-amino-2-arylethylphosphonic acids[2] several of the 2-amino-2-arylethylphosphonic acids **6**, described in this paper, also show activity against Botrytis cinerea (on apple and cercospora (on peanuts). Among the more active compounds were **6a**, **6b**, **6g** and **6k**, whereby some of the compounds (**6b** and **6k**) gave full protection against Botrytis cinerea down to 60 ppm. In addition, the same compounds show a weak inhibition of anthocyanin synthesis in vivo (3.4% by 1 mM).

ACKNOWLEDGEMENT

We wish to thank Ciba-Geigy's Central Function Research for the hydrogenation experiments and the combustion analyses and Mr. H. Spörri and C. Devonas for experimental help. We particularly want to thank Professor N. Amrhein for providing the anthocyanin synthesis inhibition constants.

REFERENCES

1. Ciba Geigy AG, DOS 4 304 861 (1993); inv. P. J. Diel and L. Maier
2. L. Maier, Phosphorus, Sulfur, and Silicon, 53, 43 (1990); ibid., 62, 15 (1991).
3. G. Richtarski, M. Soroka, P. Mastalerz, and H. Starzemski, Rocz. Chem., 49, 2001 (1975); C.A., 85, 5776 (1976).
4. J. M. Varlet, N. Collignon, and P. Savignac, Tetrahedron, 37, 3713 (1981); Synthetic Commun., 8, 335 (1978).
5. Allied Corp., Jpn Kokai Tokkyo Koho, JP 58,128,394 (1983); C.A. 100, 6849p (1984).
6. J. Kowalik, L.Kupczyk-Subotkowska, and P. Mastalerz, Synthesis, 57 (1981).