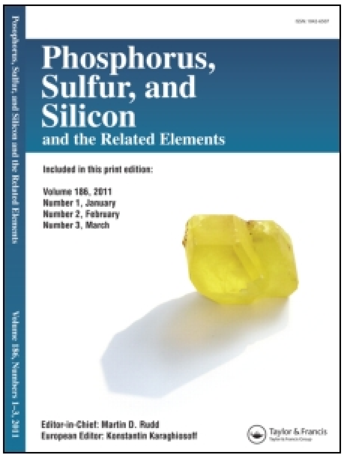

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

What are the Requirements in the Glyphosate Molecule in Order to be Herbicidally Active?

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To cite this Article Maier, Ludwig(1999) 'What are the Requirements in the Glyphosate Molecule in Order to be Herbicidally Active?', Phosphorus, Sulfur, and Silicon and the Related Elements, 144: 1, 429 — 432
To link to this Article: DOI: 10.1080/10426509908546273
URL: http://dx.doi.org/10.1080/10426509908546273

Phosphorus, Sulfur and Silicon, 1999, Vol. 144-146, pp. 429-432
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What are the Requirements in the Glyphosate Molecule in Order to be Herbicidally Active?

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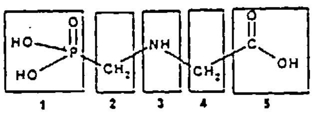
The synthesis of Glyphosate derivatives and the requirements for herbicidal activity shall be discussed.

Keywords: Glyphosate derivatives; herbicidal activity

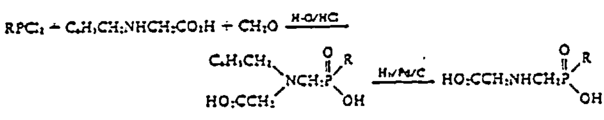
N-Dihydroxyphosphonylmethylglycine is the most active phosphorus containing herbicide[1]. What are the requirements for herbicidal activity? To answer this question, we have segmented the molecule into five sections as shown below:



We have undertaken synthetic efforts to vary each of the five molecule segments widely. At the same time the biological activity of the compounds prepared were determined. The following variations were synthesized:

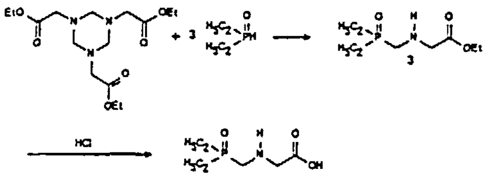
Segment 1: HO-groups on phosphorus replaced by $HOCH_2$, R, $HOOCCH_2NHCH_2$
Segment 2: CH_2 replaced by cyclopropyl
Segment 3: H on nitrogen replaced by CH_3, NH_2, $HOOCCH_2NHCH_2$
Segment 4: CH_2 replaced by cyclopropyl; furthermore compounds prepared where a cycloaliphatic ring is substituted between segments 2 and 3, 2 and 4, or 3 and 4
Segment 5: COOH replaced by CHO, tetrazole, and SO_3H

Let us start with segment 1. We have tried to substitute one or both HO-groups by other groups. Thus the interaction of hypophosphorous acid with formaldehyde gives hydroxymethylphosphonous acid. This acid when treated with formaldehyde and benzylglycine yields hydroxymethyl-N-benzyl-N-glycinomethylphosphinic acid in 88% yield[2]. Instead of phosphonous acids, alkylphosphonous dihalides my be used in this Mannich type reaction[2]. As is well known, these compounds react with water with the formation of phosphonous acids. Also a phosphinic acid is formed, when hypophosphorous acid is treated with two equivalents of formaldehyde and N-benzylglycine[3].

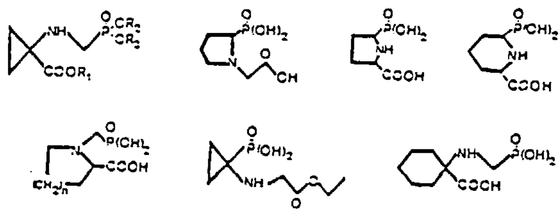


The benzyl derivatives can easily be debenzylated with H_2 in the presence of 5% Pd/C as a catalyst in acetic acid or alcohol-water as solvent. All phosphinic acids are obtained as crystalline solids with high decomposition points.

To replace both HO-groups on phosphorus by alkyl groups secondary phosphine oxides were heated with tris(N-ethoxycarbonylmethyl)-hexahydrotriazine. This afforded a high yield of the corresponding phosphine oxides which on hydrolysis gave a quantitative yield of N-glycinomethyl-dialkylphosphine oxides as crystalline solids[4,5].

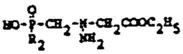


The same compounds were obtained by the interaction of aminomethyl-dialkylphosphine oxides and bromoacetic acid followed by hydrolysis with HCl.
All compounds described so far showed a much weaker herbicidal activity than Glyphosate, e.g. methyl-N-glycinomethylphosphinic acid controls only some weeds at 4 kg/ha but not all weeds as Glyphosate does[1].
To get a better insight into the structure-activity relationship of this class of compounds it seemed of interest to synthesize cyclic compounds which still contain the structural element of Glyphosate. The following compounds were synthesized[6]:



All cyclic Glyphosate derivatives were tested for herbicidal activity against seven weeds pre- and postemergent. At 4 kg/ha no activity could be detected.
What are the requirements on nitrogen? It is known that the N-benzyl-, N-phosphonylmethyl-, N-hydroxycarbonylmethyl- and N-methyl-Glyphosate showed only week herbicidal activity. On the other hand N-hydroxy-Glyphospate is an active herbicide but less active than Glyphosate[1].

For this reason we synthesized N-amino-Glyphosate:



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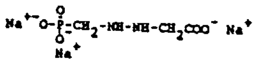
	a	b
R_2	OH	CH_3

and aza-Glyphosate:



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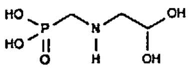
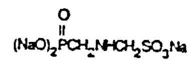
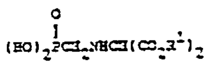
These two compounds exhibit plant growth regulating properties at 4 kg/ha[7].
Replacement in segment 5 of the COOH-group by CHO[8], tetrazole and SO_3H[9] produced herbicidally inactive compounds:

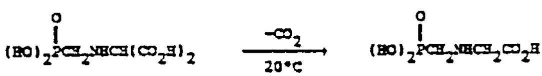




Of all the compounds synthesized only the formulated N-di(methoxycarbonyl)methyl-aminomethylphosphonic acid has about the same herbicidal activity than Glyphosate[10].



It is found that the activity is due to a decomposition product i.e. Glyphosate methyl ester.



Thus any change of the structure of the Glyphosate molecule results in a decrease of the herbicidal activity.

References

[1] J. F. Franz, in "Advances in Pesticide Science", eds. H. Geissbühler, G. T. Brooks and P. C. Kearney, Pergamon Press, Vol. 2, p. 139 (1979).
[2] L. Maier, Phosphorus and Sulfur, **11**,139 (1981).
[3] L. Maier and M. J. Smith, Phosphorus and Sulfur, **8**, 67 (1980).
[4] L. Maier, Phosphorus, Sulfur and Silicon, **63**, 237 (1991).
[5] L. Maier and H. Spörri, Phosphorus, Sulfur and Silicon, **70**, 59 (1992).
[6] P. J. Diel and L. Maier, Phosphorus and Sulfur, **20**, 313 (1984).
[7] P. J. Diel and L. Maier, Phosphorus and Sulfur, **39**, 159 (1988).
[8] L. Maier and T. Winkler, Phosphorus, Sulfur and Silicon, **63**, 65 (1991).

[9] L. Maier, Phosphorus, Sulfur and Silicon, **47,** 43 (1990).
[10] L. Maier, Phosphorus and Sulfur, **36,**1 (1988).