

## SUBSTITUENT EFFECTS ON HYDROLYTIC STABILITY AND HERBICIDAL ACTIVITY OF 3-ARYLMIDAZOLIDINE-2,4-DIONES

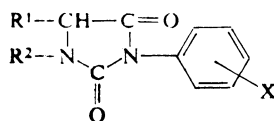
Alexandr ČEGAN and Miroslav VEČEŘA

*Department of Organic Chemistry,  
Institute of Chemical Technology, 532 10 Pardubice*

Received November 7th, 1983

Twenty-one derivatives of imidazolidine-2,4-dione have been prepared by reactions of substituted amino acids with aryl isocyanates in aqueous medium. Pre- and post-emergent herbicidal activities of all the compounds have been tested, and stability of five derivatives has been followed in aqueous medium within the pH range from 7.6 to 13.0. The highest pre-emergent herbicidal activity has been found with the derivatives *XI*–*XVI* which inhibit the growth of most indicator plants at the doses of 1.6 kg/ha. The derivatives studied are relatively stable in aqueous medium, the hydrolysis half-life of the compound *XI* being 9 days at pH 8.

Imidazolidine-2,4-diones (hydantoins) show both fungicidal<sup>1–3</sup> and herbicidal effects<sup>4,5</sup>. Other papers<sup>6,7</sup> deal with herbicidal and fungicidal tests of the substituted imidazolidine-2,4-diones proposed for use in agriculture. Although the imidazolidine-2,4-dione derivatives are used in agriculture to a limited extent only, they are interesting due to their relatively good pesticidal activity and, especially, low toxicity for fish and warm-blooded animals<sup>1</sup>.



|             | R <sup>1</sup> | R <sup>2</sup>  | X                   |              | R <sup>1</sup>  | R <sup>2</sup>  | X                   |
|-------------|----------------|-----------------|---------------------|--------------|-----------------|-----------------|---------------------|
| <i>I</i>    | H              | H               | 3-CH <sub>3</sub>   | <i>XII</i>   | H               | CH <sub>3</sub> | 4-Cl                |
| <i>II</i>   | H              | H               | H                   | <i>XIII</i>  | H               | CH <sub>3</sub> | 4-F                 |
| <i>III</i>  | H              | H               | 4-Cl                | <i>XIV</i>   | H               | CH <sub>3</sub> | 3-Cl                |
| <i>IV</i>   | H              | H               | 3-Cl                | <i>XV</i>    | H               | CH <sub>3</sub> | 3-CF <sub>3</sub>   |
| <i>V</i>    | H              | H               | 3,4-Cl <sub>2</sub> | <i>XVI</i>   | H               | CH <sub>3</sub> | 3,4-Cl <sub>2</sub> |
| <i>VI</i>   | H              | H               | 2,5-Cl <sub>2</sub> | <i>XVII</i>  | H               | CH <sub>3</sub> | 3-NO <sub>2</sub>   |
| <i>VII</i>  | H              | H               | 4-NO <sub>2</sub>   | <i>XVIII</i> | H               | CH <sub>3</sub> | 4-NO <sub>2</sub>   |
| <i>VIII</i> | H              | CH <sub>3</sub> | 4-OCH <sub>3</sub>  | <i>XIX</i>   | CH <sub>3</sub> | H               | H                   |
| <i>IX</i>   | H              | CH <sub>3</sub> | 4-CH <sub>3</sub>   | <i>XXI</i>   | CH <sub>3</sub> | H               | 4-Cl                |
| <i>X</i>    | H              | CH <sub>3</sub> | 3-CH <sub>3</sub>   | <i>XXI</i>   | CH <sub>3</sub> | H               | 3-Cl                |
| <i>XI</i>   | H              | CH <sub>3</sub> | H                   |              |                 |                 |                     |

To find the basic relations between substitution and herbicidal activity and hydrolytic stability, we synthesized the derivatives *I–XXI* of imidazolidine-2,4-dione. Pre- and postmergent herbicidal activity of all the derivatives was determined as well as the hydrolysis rate constants of selected compounds in the pH range 7.6–1.0.

## EXPERIMENTAL

### Reagents

The 3-arylimidazolidine-2,4-diones *I–VII*, 3-aryl-1-methylimidazolidine-2,4-diones *VIII* to *XVIII*, and 3-aryl-5-methylimidazolidine-2,4-diones *XIX–XXI* were prepared by reactions of 2-aminoethanoic, N-methyl-2-aminoethanoic, and 2-aminopropanoic acids, respectively, with the corresponding aryl isocyanates. The aryl isocyanate (0.11 mol) was added to solution of 0.1 mol acid and 6.8 g potassium hydroxide in 40 ml water with stirring during 4 h. The mixture was left to stand at room temperature 24 h. The precipitated diarylurea was then filtered off, and the filtrate was acidified with 20 ml 15% hydrochloric acid. The crystalline hydantoic acid was then filtered off and cyclized by boiling with 30 ml 15% hydrochloric acid for 1 h. The products were recrystallized from a 2 : 1 ethanol–water mixture. Physical constants of the compounds are given in Tables I and II.

### Kinetic Measurements

All the kinetic measurements of the selected derivatives of imidazolidine-2,4-dione were carried out spectrophotometrically. The concentration decrease of the starting compound was followed at 240 nm either continuously or discontinuously. In the former case 2.5 ml buffer solution

TABLE I  
Physical constants of the studied 3-arylimidazolidine-2,4-diones

| Compound   | Yield, % | M.p., °C  | M.p., °C (ref.) |
|------------|----------|-----------|-----------------|
| <i>I</i>   | 93       | 119–121   | 123(8)          |
| <i>II</i>  | 95       | 152–155   | 154–155(9)      |
| <i>III</i> | 92       | 173–175   | 174(8)          |
| <i>IV</i>  | 94       | 145–147.5 | 157–147.5(9)    |
| <i>V</i>   | 94       | 217–118   | 216–217(8)      |
| <i>VII</i> | 92       | 217–220   | 220(8)          |
| <i>IX</i>  | 85       | 116–117.5 | 114–117(5)      |
| <i>X</i>   | 87       | 52–53     | 49–52(5)        |
| <i>XI</i>  | 92       | 107.5–109 | 108–109(5)      |
| <i>XII</i> | 90       | 119–120   | 117.5–118.5(5)  |
| <i>XIV</i> | 83       | 81.5–83   | 84–86(5)        |
| <i>XVI</i> | 92       | 147–148   | 148–149(10)     |
| <i>XIX</i> | 79       | 167–169   | 171–172(11)     |

of the chosen pH was placed in a 1 cm quartz cell and tempered at 25°C, whereupon 0.1 ml solution of the derivative in dioxane was added with a doser (the concentrations were  $3 \cdot 10^{-3} \text{ mol l}^{-1}$  for the derivatives *II*, *IV*, and *XI*, and  $5 \cdot 10^{-3} \text{ mol l}^{-1}$  for *XIX* and *XXI*). The extinction was recorded with a Unicam SP 800 or a Specord UV-VIS apparatus. Within the pH region from 7.6 to 8.8 the discontinuous method was adopted to follow the concentration decrease of the starting compound: 96 ml buffer was placed in 150 ml flask located in a thermostat and, after 15 min, 4 ml dioxane solution of the investigated substance (of the above-given concentrations) was quickly added. At definite time intervals samples were withdrawn from the flask, and — after cooling in ice — their extinctions were measured at 25°C with the Unicam SP 800 spectrophotometer.

The rate constants were calculated from the equation  $kt = 2.303 \log ((E_0 - E)/(E_t - E))$ , where  $k$  is the rate constant in  $\text{s}^{-1}$ ,  $E_0$ ,  $E_t$ , and  $E$  mean the extinctions at  $t = 0$ , at a time  $t$ , and after 9 reaction half-lives, respectively. The hydrolysis rate constants measured at 40–60°C were recalculated to 25°C by means of the equation  $\log k = \log A - E/19.147T$ . The obtained values of logarithms of the hydrolysis rate constants of compounds *II*, *IV*, *XI*, *XIX*, and *XXI* are given in Table III.

TABLE II  
Physical constants of the studied 3-arylimidazolidine-2,4-diones

| Compound     | M.p., °C<br>(yield, %) | Formula<br>(mol.mass)                                              | Calculated/Found |      |       |
|--------------|------------------------|--------------------------------------------------------------------|------------------|------|-------|
|              |                        |                                                                    | % C              | % H  | % N   |
| <i>VI</i>    | 184–187<br>(86)        | $\text{C}_9\text{H}_6\text{Cl}_2\text{N}_2\text{O}_2$<br>(245.1)   | 44.11            | 2.47 | 11.43 |
|              |                        |                                                                    | 44.32            | 2.98 | 11.10 |
| <i>VIII</i>  | 117–120<br>(88)        | $\text{C}_{11}\text{H}_{12}\text{N}_2\text{O}_3$<br>(220.2)        | 60.05            | 5.49 | 12.72 |
|              |                        |                                                                    | 60.31            | 5.30 | 12.89 |
| <i>XIII</i>  | 119–120<br>(70)        | $\text{C}_{10}\text{H}_9\text{FN}_2\text{O}_2$<br>(208.2)          | 57.68            | 4.36 | 13.46 |
|              |                        |                                                                    | 57.38            | 4.42 | 13.05 |
| <i>XV</i>    | 75–77<br>(81)          | $\text{C}_{11}\text{H}_9\text{F}_3\text{N}_2\text{O}_2$<br>(258.2) | 51.17            | 3.51 | 10.85 |
|              |                        |                                                                    | 50.85            | 3.65 | 11.07 |
| <i>XVII</i>  | 144–145<br>(85)        | $\text{C}_{10}\text{H}_9\text{N}_3\text{O}_4$<br>(245.3)           | 51.04            | 3.86 | 17.86 |
|              |                        |                                                                    | 51.35            | 3.62 | 17.92 |
| <i>XVIII</i> | 163–165<br>(68)        | $\text{C}_{10}\text{H}_9\text{N}_3\text{O}_4$<br>(235.3)           | 51.04            | 3.86 | 17.86 |
|              |                        |                                                                    | 50.85            | 3.77 | 17.62 |
| <i>XX</i>    | 167–168.5<br>(75)      | $\text{C}_{10}\text{H}_9\text{ClN}_2\text{O}_2$<br>(224.6)         | 53.47            | 4.04 | 12.47 |
|              |                        |                                                                    | 53.27            | 4.09 | 12.55 |
| <i>XXI</i>   | 131–134<br>(72)        | $\text{C}_{10}\text{H}_9\text{ClN}_2\text{O}_2$<br>(224.6)         | 53.47            | 4.04 | 12.37 |
|              |                        |                                                                    | 53.16            | 4.08 | 12.45 |

## Biochemical Measurements

The herbicidal tests were carried out with the concentrations of 5 or 1.5 kg active substance per 1 ha in pre- and post-emergent application using the following procedure: The substrate (clayey-sandy soil) was placed in vessels having 0.04 m<sup>2</sup> surface and 5.5 cm height, the indicator plants were sown therein and watered. The tested substances were applied in aqueous emulsion of the above-given concentrations. The vessels were regularly watered and the plants were twice evaluated: (1) after three days and (2) after three weeks, the second evaluation being conclusive. The degrees 0–5 characterizing the effects of the tested substances were chosen according to the following scale: 0 healthy plants, 1 little attacked plants, 2 distinctly attacked plants, 3 strongly attacked plants, 4 plants heavily damaged, 5 dead or non-germinated plants. The post-emergent application was carried out with grown up plants which were sprayed with 0.5% and 0.1% emulsion of the tested substance in water. The plants were watered in such way that the substances applied were not washed down from the leaves. The evaluation was carried out in the above-mentioned intervals using the same scale. The results are presented in Tables IV–VI.

## RESULTS AND DISCUSSION

The dependence of  $\log k$  vs pH given in Fig. 1 shows that substituents at various positions of the imidazolidine-2,4-dione molecule affect the hydrolysis rate but slightly. Course of the dependences confirms the previously published<sup>13</sup> general hydrolysis mechanism of imidazolidine-2,4-diones which is characterized by slow, rate-limiting addition of hydroxyl ion to carbonyl carbon at 4 position. The dif-

TABLE III

Values of  $\log k$  of hydrolysis of the compound *II*, *IV*, *XI*, *XIX*, and *XXI* at 25°C

| pH    | <i>II</i>           | <i>IV</i>           | <i>XI</i>           | <i>XIX</i>          | <i>XXI</i>          |
|-------|---------------------|---------------------|---------------------|---------------------|---------------------|
| 7.60  | —                   | —                   | —                   | –4.932 <sup>a</sup> | —                   |
| 7.93  | –5.952 <sup>a</sup> | —                   | –5.682 <sup>a</sup> | –4.802 <sup>a</sup> | –4.432 <sup>a</sup> |
| 8.89  | –5.055 <sup>a</sup> | –5.100 <sup>a</sup> | –4.580 <sup>a</sup> | –4.585 <sup>a</sup> | –4.205 <sup>a</sup> |
| 9.80  | –4.110 <sup>a</sup> | –3.980 <sup>a</sup> | –3.967 <sup>a</sup> | –3.472              | –3.457              |
| 10.46 | –3.493              | –3.328              | –3.258              | –2.910              | –3.282              |
| 11.15 | –2.525              | –2.575              | –2.610              | –2.608              | –2.427              |
| 11.50 | –2.350              | –2.290              | –2.295              | —                   | –2.156              |
| 12.10 | –1.847              | –1.642              | –1.692              | –1.852              | –1.782              |
| 12.50 | –1.650              | –1.517              | –1.353              | –1.713              | –1.629              |
| 12.90 | –1.563              | –1.442              | –1.005              | –1.604              | –1.583              |
| 13.05 | —                   | —                   | —                   | –1.552              | –1.500              |

<sup>a</sup> The extrapolated  $\log k$  value.

ferences between the pH profiles of the individual derivatives are ascribed to changed acidity or basicity of these derivatives due to different substitution of hydrogen atoms in the imidazolidine-2,4-dione molecule. In the case of the derivative *II* it is

TABLE IV

Pre-emergent herbicidal activity of the compounds *I*–*XXI* at the concentration of 5 kg/ha

| Plant                    | <i>I</i> | <i>II</i> | <i>III</i> | <i>IV</i> | <i>V</i> | <i>VI</i> | <i>VII</i> | <i>VIII</i> | <i>IX</i> | <i>X</i> | <i>XI</i> | <i>XII</i> |
|--------------------------|----------|-----------|------------|-----------|----------|-----------|------------|-------------|-----------|----------|-----------|------------|
| <i>Avena sativa</i>      | 0        | 0         | 0          | 0         | 0        | 0         | 0          | 1           | 3         | 3        | 2         | 4          |
| <i>Fagopyrum vulgare</i> | 0        | 0         | 0          | 0         | 0        | 0         | 0          | 4           | 4         | 3        | 5         | 5          |
| <i>Sinapis alba</i>      | 0        | 0         | 0          | 0         | 0        | 0         | 0          | 3           | 5         | 5        | 5         | 5          |
| <i>Panicum miliaceum</i> | 0        | 0         | 0          | 0         | 0        | 0         | 0          | 2           | 1         | 0        | 3         | 5          |
| <i>Lepidium sativum</i>  | 0        | 0         | 0          | 0         | 0        | 0         | 0          | 2           | 3         | 2        | 4         | 5          |

| Plant               | <i>XIII</i> | <i>XIV</i> | <i>XV</i> | <i>XVI</i> | <i>XVII</i> | <i>XVIII</i> | <i>XIX</i> | <i>XX</i> | <i>XXI</i> | S <sup>a</sup> |
|---------------------|-------------|------------|-----------|------------|-------------|--------------|------------|-----------|------------|----------------|
| <i>A. sativa</i>    | 3           | 3          | 2         | 4          | 2           | 0            | 0          | 1         | 1          | 5              |
| <i>F. vulgare</i>   | 5           | 5          | 3         | 5          | 2           | 2            | 1          | 2         | 2          | 5              |
| <i>S. alba</i>      | 5           | 5          | 5         | 5          | 3           | 3            | 2          | 3         | 2          | 5              |
| <i>P. miliaceum</i> | 1           | 1          | 1         | 5          | 0           | 0            | 0          | 1         | 1          | 5              |
| <i>L. sativum</i>   | 3           | 5          | 4         | 5          | 1           | 0            | 0          | 1         | 1          | 5              |

<sup>a</sup> Standard.

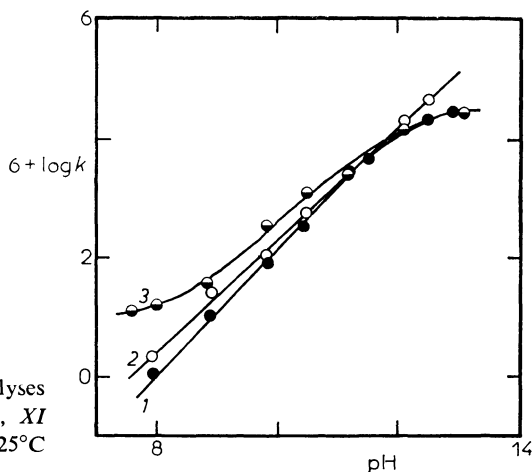


FIG. 1

The pH dependence of  $\log k$  of hydrolyses of imidazolidine-2,4-dione *II* (curve 1), *XI* (straight line 2), and *XIX* (curve 3) at 25°C

possible that a non-reactive anion is formed by deprotonation in strongly basic medium (see Eq. (A)). This anion is stabilized by resonance, and thereby the con-

TABLE V  
Pre-emergent herbicidal activity of the compounds VIII–XVII at the concentration of 1.6 kg/ha

| Plant                          | VIII | IX | X | XI | XII | XIII | XIV | XV | XVI | XVII | S <sup>a</sup> |
|--------------------------------|------|----|---|----|-----|------|-----|----|-----|------|----------------|
| <i>Avena sativa</i>            | 0    | 0  | 2 | 1  | 1   | 2    | 2   | 2  | 0   | 0    | 5              |
| <i>Beta vulgaris</i>           | 0    | 0  | 0 | 4  | 5   | 4    | 0   | 3  | 0   | 0    | 5              |
| <i>Brassica napus</i>          | 0    | 0  | 0 | 2  | 4   | 0    | 3   | 3  | 2   | 0    | 5              |
| <i>Avena fatua</i>             | 0    | 0  | 2 | 2  | 2   | 2    | 2   | 3  | 0   | 0    | 5              |
| <i>Vicia sativa</i>            | 1    | 0  | 0 | 1  | 0   | 1    | 0   | 0  | 0   | 0    | 5              |
| <i>Sinapis alba</i>            | 2    | 2  | 3 | 3  | 3   | 3    | 3   | 4  | 5   | 2    | 5              |
| <i>Amaranthus</i> <sup>b</sup> | 0    | 0  | 0 | 3  | 2   | 2    | 3   | 2  | 5   | 0    | 5              |
| <i>Linum</i> <sup>c</sup>      | 0    | 0  | 0 | 2  | 1   | 2    | 1   | 2  | 0   | 0    | 5              |
| <i>Fagopyrum vulgare</i>       | 3    | 1  | 1 | 5  | 4   | 4    | 5   | 4  | 4   | 0    | 5              |

<sup>a</sup> Standard, <sup>b</sup> *Amaranthus retroflexus*, <sup>c</sup> *Linum usitatissimum*.

TABLE VI  
Post-emergent herbicidal activity of the compounds I–XXI at the concentration of 5 kg/ha

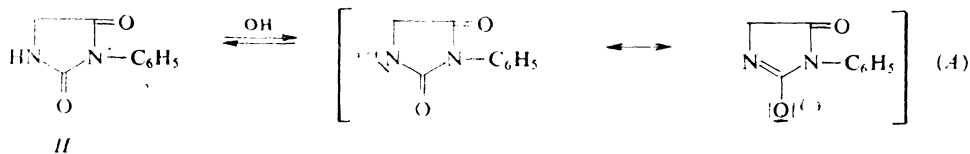
| Plant               | I | II | III | IV | V | VI | VII | VIII | IX | X | XI | XII |
|---------------------|---|----|-----|----|---|----|-----|------|----|---|----|-----|
| <i>A. sativa</i>    | 0 | 0  | 0   | 0  | 0 | 0  | 0   | 0    | 1  | 1 | 2  | 3   |
| <i>F. vulgare</i>   | 0 | 0  | 2   | 2  | 0 | 0  | 0   | 2    | 2  | 3 | 3  | 4   |
| <i>S. alba</i>      | 2 | 1  | 2   | 2  | 0 | 0  | 0   | 3    | 3  | 4 | 3  | 4   |
| <i>P. miliaceum</i> | 0 | 0  | 0   | 0  | 0 | 0  | 0   | 1    | 1  | 1 | 1  | 4   |
| <i>L. sativum</i>   | 0 | 0  | 0   | 0  | 0 | 0  | 0   | 2    | 3  | 3 | 3  | 5   |

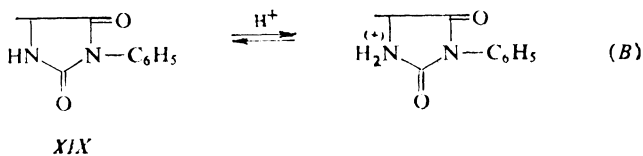
| Plant               | XIII | XIV | XV | XVI | XVII | XVIII | XIX | XX | XXI | S <sup>a</sup> |
|---------------------|------|-----|----|-----|------|-------|-----|----|-----|----------------|
| <i>A. sativa</i>    | 2    | 2   | 3  | 4   | 0    | 0     | 0   | 0  | 1   | 5              |
| <i>F. vulgare</i>   | 3    | 3   | 4  | 4   | 1    | 1     | 0   | 1  | 1   | 5              |
| <i>S. alba</i>      | 3    | 4   | 4  | 5   | 2    | 2     | 1   | 2  | 2   | 5              |
| <i>P. miliaceum</i> | 1    | 2   | 1  | 4   | 0    | 0     | 1   | 2  | 2   | 5              |
| <i>L. sativum</i>   | 4    | 5   | 4  | 5   | 0    | 0     | 0   | 1  | 1   | 5              |

<sup>a</sup> Standard.

centration of the reactive base of 3-phenylimidazolidine-1,4-dione in the reaction mixture is lowered, and the hydrolysis rate decreases with increasing pH. This fact is also confirmed by the published<sup>12</sup> value of the dissociation constant of the compound *II* ( $pK_A = 12.5$ ). Compound *XI* cannot form such anion, because the 1-nitro-



gen atom carries methyl group instead of hydrogen. This fact makes itself felt in the pH profile by the linear course of the dependence of  $\log k$  vs pH in the whole pH range. Substitution of hydrogen at 5-carbon atom by methyl group introduces another possibility of acid-base equilibrium, *viz.* in neutral medium. In contrast to compound *XI* (with two hydrogen atoms at 5 position), compound *XIX* carries one methyl group at the 5-carbon atom, and hyperconjugation effect of this methyl group enables the protonation of 1-nitrogen atom at a higher pH than in the case of compounds *II* and *XI* (Eq. (B)). Thus the more reactive protonated 3-phenyl-



-5-methylimidazolidine-2,4-dione is formed which reacts with the present nucleophiles ( $\text{OH}^-$  and  $\text{H}_2\text{O}$ ) much faster than the non-protonated substrate does. With respect to decreasing  $\text{OH}^-$  ion concentration in the region below pH 8, solvolysis with water molecules becomes increasingly significant, and the dependence of  $\log k$  vs pH becomes non-linear.

From the results of herbicidal tests given in Tables IV – VI it is obvious that some derivatives of imidazolidine-2,4-dione show relatively good herbicidal activity. Moreover, the results confirm strong dependence of herbicidal activity on the overall structure of the molecule. So, *e.g.* 3-(3-chlorophenyl)imidazolidine-2,4-dione (*IV*), which is quite inefficient at the concentration of 5 kg/ha, acquires – by substitution of hydrogen atom at 1 position by methyl group – a large herbicidal activity which makes itself felt as low as at the concentration of 1.6 kg/ha. On the contrary, introduction of methyl group into 5 positions brings generally an only small increase in herbicidal activity at the concentration of 5 kg/ha. Similar relations were also found with further derivatives of 3-arylimidazolidine-2,4-diones. Substitution in the 3-phenyl ring affects

the herbicidal activity fundamentally, too, though the effect is not so large as in the previous case. The most efficient derivatives were *XI*–*XV* with methyl group at 1 position and non-substituted phenyl group at 3 position (or with 3- or 4-Cl, F, or CF<sub>3</sub> groups in the 3-phenyl ring).

*The authors are indebted to Mr F. Benda, Research Institute of Agrochemical Technology, Bratislava, for carrying out the herbicidal tests.*

#### REFERENCES

1. Fujinami A., Ozaki T., Yamamoto S.: Ger. Offen. 1 958 183 (4. 6. 1970); Chem. Abstr. 73, 35 376 (1970).
2. Singhal C. H.: Ger. Offen. 2 123 860 (2. 12. 1971); Chem. Abstr. 76, 85 825 (1972).
3. Hubele A.: Ger. Offen. 2 441 601 (13. 3. 1975); Chem. Abstr. 82, 170 955 (1975).
4. Takeo S.: Japan Kokai 74 66 829 (28. 6. 1974); Chem. Abstr. 82, 81 697 (1975).
5. Kroll H.: US 3 134 663 (26. 5. 1964); Chem. Abstr. 61, 3117 (1964).
6. Wegler R.: *Chemie der Pflanzenschutz und Schädlingsbekämpfungsmittel*, Band 5. *Herbizide*, p. 292, 615. Springer, Berlin 1977.
7. Fujinami A., Nobumasa T., Toschiro K., Nobuyuki K.: Agr. Biol. Chem. 36, 1623 (1972).
8. Hill J. A., Kelsey E. B.: J. Amer. Chem. Soc. 44, 2362 (1922).
9. Johnson T. B., Pfau G. H., Hodge W. W.: J. Amer. Chem. Soc. 34, 1048 (1912).
10. Friedman E.: Beitr. Chem. Physiol. Path. 11, 160 (1908).
11. Bailey J. R., Randolph C. P.: Chem. Ber. 41, 2500 (1908).
12. Bergon M., Valmon J. P.: J. Chem. Soc., Perkin Trans. 2, 1978. 493.

Translated by J. Panchartek.