

Synthesis, herbicidal and insecticidal efficacy of *N*-hydroxy-1,4-epoxycyclohex-5-en-2,3-dicarboximide and its *O*-substituted derivatives

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N-Hydroxy-1,4-epoxycyclohex-5-en-2,3-dicarboximide and its *O*-alkyl, *O*-alkenyl, *O*-aralkyl, and *O*-acyl derivatives were synthesized. Some of the prepared compounds were found to have a relatively low herbicidal and insecticidal efficiency.

Starting from our experience with *N*-hydroxy-bicyclo[2.2.1]hept-5-en-2,3-dicarboximide and its derivatives as possible pesticides [1], in the present work we focused our attention on the synthesis of epoxy analogs of the mentioned compounds as well as on the investigation of their herbicidal and insecticidal efficacy.

Experimental

The synthesized compounds, their physical constants, analytical data, and yields are given in Table 1. Melting points were determined on a Kofler block.

N-Hydroxy-1,4-epoxycyclohex-5-en-2,3-dicarboximide (I)

Hydroxylammonium chloride (4.17 g, 0.06 mole) and sodium hydroxide (2.40 g, 0.06 mole) were simultaneously dissolved in water (50 ml). On dissolution, 1,4-epoxycyclohex-5-en-2,3-dicarboxylic anhydride (8.3 g, 0.05 mole) was added. The reaction mixture was refluxed for 10 minutes and then allowed to react for 1 hour at room temperature. After cooling the reaction mixture to 12–15°C a white crystalline compound was obtained. Its melting point after twofold crystallization from ethanol using charcoal was 215–217°C.

N-Alkoxy-1,4-epoxycyclohex-5-en-2,3-dicarboximides (II–XV)

N-Hydroxy-1,4-epoxycyclohex-5-en-2,3-dicarboximide *I* (9.06 g, 0.05 mole) was dissolved in the solution of sodium hydroxide (2.00 g, 0.05 mole) in the mixture of water (40 ml) and ethanol (100–250 ml). After dissolution, alkyl halogenide (0.055–0.07 mole; when preparing compounds *II–IV*, *VII*, *VIII*, *X–XIV* it was alkyl iodide, *V* and *VI* alkyl bromide, *IX* and *XV* alkyl chloride) was added and the reaction mixture was

Table 1

Characteristic of the synthesized compounds

| Compound | Formula | <i>M</i> | Calculated/found | | | Yield [%] | M.p. [°C] |
|-------------|----------------------|----------|------------------|------|------|--------------|--------------|
| | | | % C | % H | % N | | |
| <i>I</i> | $C_8H_7NO_4$ | 181.14 | 53.04 | 3.89 | 7.73 | 82.8 | 215—217 |
| | | | 53.20 | 4.06 | 7.87 | | |
| <i>II</i> | $C_9H_9NO_4$ | 195.17 | 55.38 | 4.65 | 7.18 | 69.4 | 156.5—157.5 |
| | | | 55.45 | 4.78 | 7.00 | | |
| <i>III</i> | $C_{10}H_{11}NO_4$ | 209.20 | 57.41 | 5.30 | 6.70 | 53.5 | 77—79 |
| | | | 57.33 | 5.11 | 6.70 | | |
| <i>IV</i> | $C_{11}H_{13}NO_4$ | 223.22 | 59.18 | 5.87 | 6.28 | 60.9 | 100—101.5 |
| | | | 59.37 | 5.75 | 6.42 | | |
| <i>V</i> | $C_{11}H_{13}NO_4$ | 223.22 | 59.18 | 5.87 | 6.28 | 63.6 | 111—112.5 |
| | | | 59.23 | 5.70 | 6.18 | | |
| <i>VI</i> | $C_{11}H_{11}NO_4$ | 221.21 | 59.72 | 5.01 | 6.33 | 63.3 | 71—73 |
| | | | 59.77 | 4.90 | 6.11 | | |
| <i>VII</i> | $C_{12}H_{15}NO_4$ | 237.25 | 60.75 | 6.37 | 5.90 | 60.5 | 63—65 |
| | | | 60.78 | 6.49 | 5.88 | | |
| <i>VIII</i> | $C_{12}H_{15}NO_4$ | 237.25 | 60.75 | 6.37 | 5.90 | 64.0 | 64—66 |
| | | | 60.49 | 6.28 | 5.70 | | |
| <i>IX</i> | $C_{12}H_{12}ClNO_4$ | 269.68 | 53.44 | 4.49 | 5.19 | 51.9 | 98—99.5 |
| | | | 53.70 | 4.61 | 5.14 | | |
| <i>X</i> | $C_{13}H_{17}NO_4$ | 251.27 | 62.14 | 6.82 | 5.57 | 40.6 | 60—62 |
| | | | 61.97 | 6.60 | 5.40 | | |
| <i>XI</i> | $C_{15}H_{21}NO_4$ | 279.33 | 64.49 | 7.58 | 5.01 | 39.3 | 37—38 |
| | | | 64.56 | 7.71 | 4.93 | | |
| <i>XII</i> | $C_{16}H_{23}NO_4$ | 293.35 | 65.51 | 7.90 | 4.77 | 83.9 | 56—57 |
| | | | 65.59 | 7.80 | 4.53 | | |
| <i>XIII</i> | $C_{24}H_{39}NO_4$ | 405.56 | 71.07 | 9.70 | 3.45 | 49.2 | 78.5—79.5 |
| | | | 71.40 | 9.78 | 3.22 | | |
| <i>XIV</i> | $C_{13}H_{15}NO_4$ | 249.26 | 62.64 | 6.07 | 5.62 | 48.9 | 144.5—146 |
| | | | 62.80 | 5.98 | 5.77 | | |
| <i>XV</i> | $C_{15}H_{13}NO_4$ | 271.26 | 66.41 | 4.83 | 5.16 | 98.1 | 108.5—110.5 |
| | | | 66.37 | 5.02 | 4.88 | | |
| <i>XVI</i> | $C_{10}H_9NO_5$ | 223.18 | 53.81 | 4.06 | 6.27 | 68.1 | 141—142.5 |
| | | | 53.95 | 4.20 | 6.21 | | |
| <i>XVII</i> | $C_{15}H_{11}NO_5$ | 285.25 | 63.15 | 3.89 | 4.91 | 74.0 | 145—147 |
| | | | 63.28 | 4.03 | 4.66 | | |

heated under reflux for 1—6 hours. Decolourizing with charcoal and evaporation of the solution gave a white crystalline compound recrystallized from the mixture of benzene—cyclohexane (1 : 1).

N-Acetoxy-1,4-epoxycyclohex-5-en-2,3-dicarboximide (*XVI*)

To the solution of *N*-hydroxy-1,4-epoxycyclohex-5-en-2,3-dicarboximide *I* (18.1 g, 0.10 mole) in glacial acetic acid (30 ml), acetyl chloride (15.7 g, 0.20 mole) was added. The reaction mixture was heated under reflux for 30 minutes. Then the solvent as well as the remaining acetyl chloride was distilled off under reduced pressure and twofold amount of water was added to the oily residue. The crude compound was crystallized from the mixture of acetone—ethanol (1 : 1).

N-Benzoyloxy-1,4-epoxycyclohex-5-en-2,3-dicarboximide (XVII)

N-Hydroxy-1,4-epoxycyclohex-5-en-2,3-dicarboximide *I* (18.1 g, 0.10 mole), benzoyl chloride (14.1 g, 0.10 mole), and *N,N*-diethylaniline (15.0 g, 0.10 mole) were heated under reflux for 1 hour in benzene (50 ml). After decolourizing with charcoal, the solvent was distilled off under reduced pressure, water (150 ml) was added to the residue and boiled for 5 minutes. The crude product was crystallized from the mixture of tetrahydrofuran—ethanol—water (2 : 2 : 1) using charcoal.

Results and discussion

The compounds of the mentioned types were prepared to compare their pesticidal efficacy with that of the earlier synthesized methane analogs [1] and their 1,4,5,6,7,7-hexachloro derivatives [2] (Chart 1).

The yields of the *O*-alkyl derivatives depended on the reactivity of the starting alkyl halogenides as well as on the consistence and solubility of the formed products. We have not prepared a great number of *O*-acyl derivatives because our previous works [1, 2] showed that the pesticidal efficacy of *O*-acyl derivatives was much lower than that of the *O*-alkyl ones.

We investigated the herbicidal effect of the synthesized compounds *I*—*XVII* in standard screening tests applied preemergence and postemergence in oats (*Avena sativa*), proso (*Panicum miliaceum*), white mustard (*Sinapis alba*), and buckwheat (*Polygonum vulgare*).

Though among other synthesized compounds the endomethylene [1] and the saturated [3] analogs proved to be herbicidally effective, the tests showed that the majority of the synthesized compounds was not efficient. Some of these compounds, however, had a specific effect on buckwheat but did not attack oats, proso, and white mustard at all. They were effective only at higher concentrations. Some of these compounds applied at 15 kg/ha preemergence and at 5 kg/ha postemergence were more effective than the standard (2,4-D). However, with decreasing concentration the efficacy decreased rapidly to zero in most cases (Table 2).

Only *O*-methyl (*II*) and *O*-ethyl (*III*) derivatives were effective when applied pre-emergence. The first one strongly hindered the growing of buckwheat while the second one caused plant dying to 80—100%. The effect of *O*-*sec*-butyl derivative (*VIII*) was qualitatively different; at 15 kg/ha hindered the sprouting of plants.

Table 2

Herbicidal efficacy of the synthesized compounds and standards applied preemergence and postemergence in buckwheat

| Application | kg/ha | Synthesized compounds | | | | | | Standards | | | |
|---------------|-------|-----------------------|-----------|------------|-----------|----------|-------------|-----------|-------|-----|------|
| | | <i>I</i> | <i>II</i> | <i>III</i> | <i>IV</i> | <i>V</i> | <i>VIII</i> | Atrazine | 2,4-D | PCA | DNOC |
| Preemergence | 15 | 0 | 3.5 | 5 | 0 | 0 | 5 | 5 | 2.5 | 5 | |
| | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 2.5 | 3.5 | |
| Postemergence | 5 | 2 | 5 | 5 | 5 | 5 | 0 | | 4.5 | | 5 |
| | 1 | 1 | 0 | 2 | 0 | 0 | 0 | | 3.5 | | 5 |

Classification scale: 0—5; 0 = intact, 5 = totally destroyed.

Table 3

Insecticidal efficacy of the synthesized compounds and standards

| | Synthesized compounds | | | | | | | | | | | | | | | Standard |
|---------------------------------------|-----------------------|-----------|------------|-----------|----------|-----------|------------|-------------|-----------|----------|------------|-----------|------------|-------------|--------------------|----------|
| | <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>XIV</i> | <i>XV</i> | <i>XVI</i> | <i>XVII</i> | | |
| <i>Musca domestica</i> — contact | 0 | 0.5 | 0.5 | 1.5 | 2 | 1 | 3 | 4.5 | 0.5 | 4.5 | 1 | 0.5 | 0.5 | 0.5 | 6.5 (Malathione) | |
| <i>Calandra granaria</i> | 0.5 | 0.5 | 0 | 0.5 | 0 | 0 | 0 | 1.5 | 0.5 | 0 | 0 | 0 | 1.5 | 0 | 10 (Malathione) | |
| <i>Tetranychus urticae</i> — contact | 1.5 | 1.5 | 1.5 | 0.5 | 2 | | 1 | 1.5 | 1 | 2.5 | 1 | 2 | 2 | 2 | 10 (Acarithione) | |
| <i>Tetranychus urticae</i> — ovicidal | 0 | 1.5 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0.5 | 0 | 0 | 0 | 0 | 10 (Acarithione) | |
| <i>Aphis fabae</i> — contact | 0 | 0 | 4 | 5 | 1.5 | 0 | 3 | 0 | 0.5 | 3.5 | 1.5 | 0.5 | 0 | 0 | 10 (Phosphothione) | |

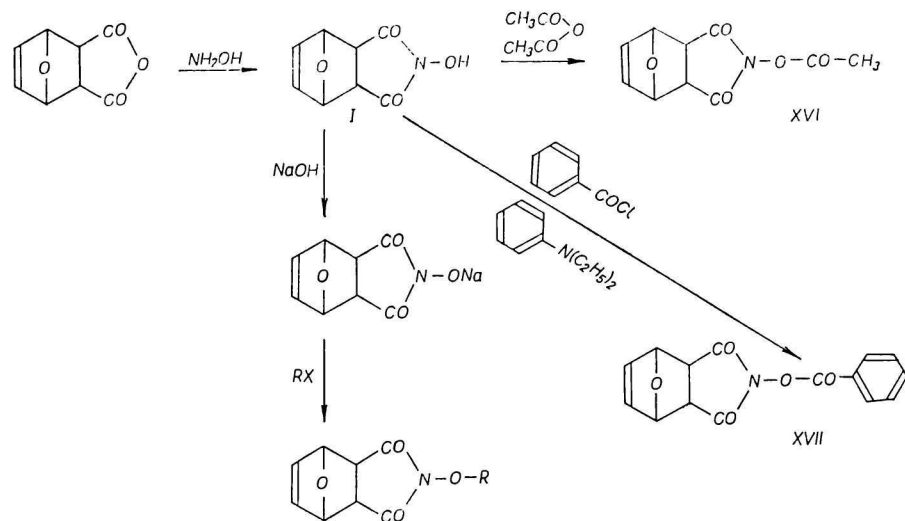



Chart 1

II–IV, VII, VIII, X–XIV: X = I; VI, VII: X = Br; IX, XV: X = Cl.

II: R = $-\text{CH}_3$; III: R = $-\text{CH}_2-\text{CH}_3$; IV: R = $-\text{CH}_2-\text{CH}_2-\text{CH}_3$; V: R = $-\text{CH}(\text{CH}_3)_2$; VI: R = $-\text{CH}_2-\text{CH}=\text{CH}_2$;
 VII: R = $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_3$; VIII: R = $-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$; IX: R = $-\text{CH}_2-\text{CH}=\text{C}(\text{Cl})\text{CH}_3$;
 X: R = $-\text{CH}_2-\text{CH}_2-\text{CH}(\text{CH}_3)_2$; XI: R = $-\text{CH}_2-(\text{CH}_2)_5-\text{CH}_3$; XII: R = $-\text{CH}_2-(\text{CH}_2)_6-\text{CH}_3$;

XIII: R = $-\text{CH}_2-(\text{CH}_2)_{14}-\text{CH}_3$; XIV: R = $-\text{CH}$ $\begin{array}{c} \text{CH}_2-\text{CH}_2 \\ | \\ \text{CH}_2-\text{CH}_2 \end{array}$

XV: R = $-\text{CH}_2-$ 

The basic hydroxy derivative (I) caused the necrosis of leaves only when applied postemergence. *O*-Methyl (II), *O*-ethyl (III), *O*-*n*-propyl (IV), and *O*-isopropyl (V) derivatives at 5 kg/ha caused plant dying to 80–100%. The *O*-ethyl derivative at 1 kg/ha still caused the necrosis of leaves. Consequently, it was the most effective compound among the synthesized ones. *O*-Alkyl (with the alkyl > C₄), *O*-alkenyl, and *O*-acyl derivatives were not effective at all.

The insecticidal efficacy of the synthesized compounds was investigated on *Musca domestica* (contact) against Malathione as standard, on *Calandra granaria* against Malathione, on *Tetranychus urticae* (acaricido-contact and acaricido-ovicidal) against Acarithione, on *Aphis fabae* (contact) against Phosphothione, and on *Macrosiphoniella sanborni* (systemic) against Intrathione.

O-Alkyl (with alkyl up to C₅), *O*-alkenyl, *O*-benzyl, and *O*-acyl derivatives were tested as insecticides. The results are in Table 3. The efficacy of the synthesized compounds did not reach that of the standards.

The tested compounds were not or only slightly efficient on *Macrosiphoniella sanborni*, *Calandra granaria*, and *Tetranychus urticae*. On *Tetranychus urticae* the *O*-isoamyl derivative was the most effective (contact).

On *Aphis fabae* the *O*-alkyl derivatives with primary alkyl were most effective (contact); the optimal effect was reached at C₃. Compounds with the secondary alkyl and *O*-alkenyl derivatives as well as the basic hydroxy derivative (I) and the *O*-acyl derivatives were only slightly or not at all effective.

The contact efficacy of *O*-alkyl derivatives on *Musca domestica* increased with the increasing alkyl and was optimal at C₄–C₅. The secondary branched alkyls were more effective than the unbranched primary ones contrary to the tests on *Aphis fabae*.

The values in Table 3 are the mean efficacies of the tested compounds and standards at two different concentrations. The main deficiency of the synthesized compounds is the rapid decrease of their efficacies with decreasing concentration. For instance, the efficacy of compound X at 5000 p.p.m. was equal to 80% efficacy of the standard at the same concentration but at 500 p.p.m. only to 26%.

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