

단 신

2,4,5-Imidazolidinetrione기를 포함한 새로운 Saccharin 유도체의 합성

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Synthesis of the New Saccharin Derivatives Containing 2,4,5-Imidazolidinetrione Group

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Saccharin derivatives have been widely studied for the use of phytocides, herbicides and insecticides.^{1,3} 2,4,5-Imidazolidinetriones are known for their herbicide, plantgrowth regulator, and fungicide properties.^{4,7}

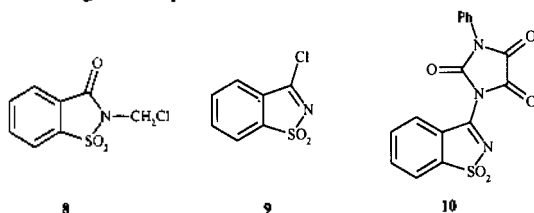
In the development of new agrochemicals, we chose to associate benzisothiazole and 2,4,5-imidazolidinetrione groups as a new structure in which each part could serve as an active component for the desired property. In order to obtain a new agrochemical, we planned first to synthesize a chlorinated precursor **4** to introduce 1,2-benzisothiazole-3-one-1,1-dioxide (Saccharin).

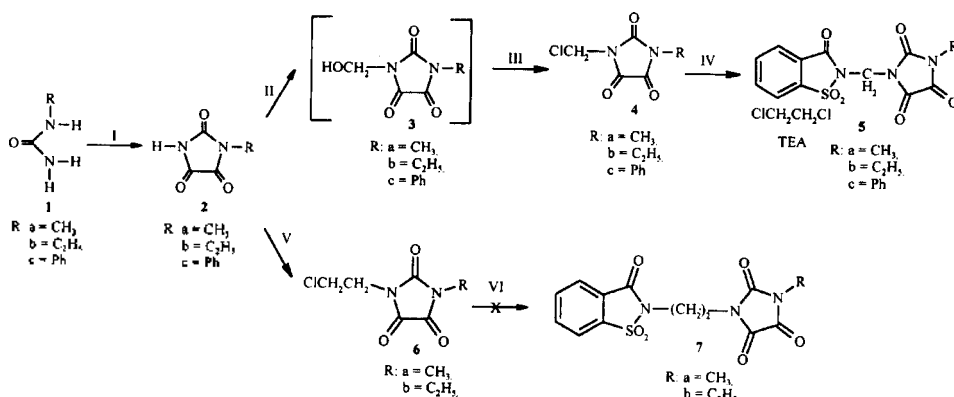
The base-catalyzed condensation between *N*-alkyl(or phenyl)imidazolidinetrione **2**^{8,9} and paraformaldehyde (Scheme 1) in aqueous solution allowed us a mixture of the expected *N*-hydroxymethyl derivative **3** and **2**. However, the instability of **3** made its isolation very difficult. The use of column chromatography as a method of purification failed, whatever the eluent or support (silica gel, alumina) used, because the *R_f* value is the same for the two compounds. For this reason, the next chlorination step, using a large excess of thionyl chloride, was realized starting directly from a mixture of **3** and **2**. The chlorinated precursor **4** was easily isolated by column chromatography (silica gel, CH₂Cl₂) and the

product has a much higher *R_f* value than the starting material.

When chlorinated products **4** were allowed to react with 1,2-benzisothiazole-3-one-1,1-dioxide, saccharin derivatives **5** containing 2,4,5-imidazolidinetrione group were obtained in good yields as shown in the Table 1.

We also tried to obtain various saccharin derivatives, but the reaction of saccharin and *N*-chloroethyl-*N*-methylimidazolidinetrione **6** synthesized by using dichloroethane with triethylamine did not occur. It was found that compound **4** is more reactive than compound **6**. We attempted the reaction of *N*-alkyl(or phenyl)imidazolidinetrione **2** and *N*-(chloromethyl)saccharin **8** formed by *N*-(hydroxymethyl)saccharin with thionyl chloride, but we did not obtain compound **5**. We also attempted to synthesize compound **10** from 3-chloro-1,2-benzisothiazole-1,1-dioxide (BID-Cl) **9** and compound **2**, but we did not gain compound **10**.





Reagents and reaction conditions: (I) Benzene, r.t., COCICICO (II) $(\text{CH}_2\text{O})_6$, K_2CO_3 (III) SOCl_2 (IV) saccharin, THF, TEA (V) $\text{ClCH}_2\text{CH}_2\text{Cl}$, TEA (VI) saccharin, THF, TEA

Scheme 1. Synthesis of saccharin derivatives 5 using N-chloromethyl precursor 4.

Table 1. Physical data from 2,4,5-imidazolidinetriones 2 to saccharin derivatives 5

Entry	Reactant	Product	Yield ^a (%)	mp (°C)
1	1a	2a	92	146-147
2	1b	2b	85	121-123
3	1c	2c	90	203-204
4	2a	4a	62	149-150
5	2b	4b	81	83-84
6	2c	4c	70	130-131
7	4a	5a	52	192-193
8	4b	5b	54	182-183
9	4c	5c	50	191-192

^a Yields are isolated yields

The typical experimental procedure for *N*-(*N*'-phenyl-*N*'-methylimidazolidinetrionyl)saccharin is as follows: To a solution of *N*-phenyl-*N*'-chloromethylimidazolidinetrione (2.38 g, 10 mmol) in dry THF (15 ml) under nitrogen at room temperature was added solution of saccharin (2.01 g, 11 mmol) and triethylamine (1.2 ml) in dry THF (15 ml). The reaction mixture was stirred at room temperature for 30 minutes. After 30 minutes, the reaction mixture was refluxed at 55~60 °C for 5hr. The reaction mixture was cooled again to room temperature and THF (50 ml) was added. The combined organic layers were dried over anhydrous Na_2SO_4 , filtered and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel eluted with only CH_2Cl_2 , to provide the *N*-(*N*'-phenyl-*N*'-methylimidazolidinetrionyl)saccharin 5c as a white crystalline solid (1.93 g, 50%). mp 191~192 °C; $^1\text{H NMR}$ (200 MHz, CDCl_3) δ 5.84 (s, 2H, CH_2), 7.4~8.1 (m, 9H, phenyl);

Mass m/z (rel. intensity, %) 385 ($[\text{M}]^+$, 40), 196 (100), 91, 77. Biological tests for the phytocides, herbicides, and insecticides of the new saccharin derivatives 5 containing 2,4,5-imidazolidinetrione group are in progress.

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- Methylimidazolidinetrione 2a**, yield 92%; mp 146-147°C; IR (ν , KBr, cm^{-1}) 3230, 2732, 1748, 1620, 1460, 1320, 1120; Mass, m/z (rel. intensity, %) 128 ($[\text{M}]^+$, 100), 100 (55), 70 (35), 56 (60). **Ethylimid-**

azolidinetrione 2b. yield 85%; mp 121-123 °C; IR (ν , KBr, cm^{-1}) 3160, 2990, 2850, 1782, 1422, 1351, 1064; Mass m/z (rel. intensity, %) 142 ($[\text{M}]^+$, 100), 114 (30), 86 (5), 70 (30), 56 (50). **Phenylimidazolidinetrione 2c.** yield 90%; mp 203-204 °C; IR (ν , KBr, cm^{-1}) 3245, 3066, 1793, 1736; $^1\text{H NMR}$ (200 MHz, DMSO-d_6) δ 7.3-7.56 (m, 5H, phenyl), 12.27 (s, 1H, NH). ***N*-Chloromethyl-*N'*-methylimidazolidinetrione 4a.** yield 50%; mp 149-150 °C; IR (ν , KBr, cm^{-1}) 1731.7, 1459, 1407, 1306, 1129; Mass m/z (rel. intensity, %) 179 ($[\text{M}+2]^+$, 5), 176 ($[\text{M}]^+$, 20), 141 (100) 113 (30), 94 (5), 70 (35), 56 (85); $^1\text{H NMR}$ (200 MHz, CDCl_3) δ 3.23 (s, 3H, CH_3), 5.40 (s, 2H, CH_2Cl). ***N*-Chloromethyl-*N'*-Ethylimidazolidinetrione 4b.** yield 64%; mp 83-84 °C; IR (ν , KBr, cm^{-1}) 2982, 2865, 1735, 1409, 1298, 1208, 1128; Mass m/z (rel. intensity, %) 192 ($[\text{M}+1]^+$, 5), 190 ($[\text{M}-1]^+$, 10), 175 (2), 162 (1), 154 (30), 127 (15), 99 (10), 70 (45), 56 (100). $^1\text{H NMR}$ (200 MHz, CDCl_3) δ 1.27-1.34 (t, 3H, CH_3), 3.70-3.81 (q, 2H, CH_2Cl), 5.39 (s, 2H, CH_2Cl). ***N*-Chloromethyl-*N'*-phenylimidazolidinetrione 4c.** yield 70%; mp 130-131 °C; IR (ν , KBr, cm^{-1}) 1780, 1730, 1500, 1440, 1295, 1190; Mass m/z (rel. intensity, %) 238 ($[\text{M}]^+$, 27),

119 (100), 91 (23); $^1\text{H NMR}$ (200 MHz, CDCl_3) δ 5.6 (s, 2H, CH_2Cl), 7.4-7.5 (m, 5H, phenyl). ***N*-(*N'*-Methyl-*N''*-methylimidazolidimetryl)saccharin 5a.** yield 40%; mp 192-193 °C; IR (ν , KBr, cm^{-1}) 1749, 1453, 1340, 1291, 1245, 1179; Mass m/z (rel. intensity, %) 323 ($[\text{M}]^+$, 1), 259 (15), 223 (4), 196 (100), 174 (20), 169 (17), 132 (20), 121 (5), 104 (22), 76 (15), 70 (9); $^1\text{H NMR}$ (200 MHz, Acetone-d_6) δ 3.14 (s, 3H, CH_3), 5.70 (s, 2H, CH_2), 8.05-8.21 (m, 4H, phenyl). ***N*-(*N'*-Ethyl-*N''*-methylimidazolidinetrionyl)saccharin 5b.** yield 54%; mp 182-183 °C; IR (ν , KBr, cm^{-1}) 2981, 2885, 1746, 1425, 1340, 1293, 1251, 1180, 1115; ; Mass m/z (rel. intensity, %) 337 ($[\text{M}]^+$, 2), 273 (8), 223 (4), 196 (100), 174 (15), 169 (14), 132 (20); $^1\text{H NMR}$ (200 MHz, Acetone-d_6) δ 1.18-1.28 (t, 3H, CH_3), 3.64-3.75 (q, 2H, CH_2), 5.70 (s, 2H, $\text{N-CH}_2\text{-N}$), 8.02-8.22 (m, 4H, phenyl). ***N*-(*N'*-Phenyl-*N''*-methylimidazolidinetrionyl)saccharin 5c.** yield 50%; mp 191- 192 °C; IR (ν , KBr, cm^{-1}) 1785, 1750, 1410, 1330, 1290, 1250; Mass m/z (rel. intensity, %) 385 ($[\text{M}]^+$, 40), 196 (100), 169 (20), 119 (80), 91 (45), 77 (33); $^1\text{H NMR}$ (200 MHz, CDCl_3) δ 5.84 (s, 2H, CH_2), 7.4-8.1 (m, 9H, phenyl).