Original Article

Synthesis and Herbicidal Activity of New 2-(1-Carbamoyl-1,2,4-triazol-3-ylsulfonyl)alkanoates

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A series of new 2-(1-*N,N*-dialkylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)alkanoates were synthesized and examined for herbicidal activity against weeds. The herbicidal efficacy varied with the substituents at the α -position of the alkoxycarbonyl group and on the nitrogen atom of the carbamoyl moiety. Among the compounds synthesized, 1-*N,N*-dialkylcarbamoyl-1,2,4-triazole derivatives having a branched alkyl group at the α -position of the alkoxycarbonyl group exhibited the most potent herbicidal activity. The chirality of the α -position had no effect on the activity. On the basis of biological evaluations, isopropyl 2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)-4-methylpentanoate was selected as a promising herbicidal candidate for transplanted rice. Studies on structure-activity relationships using the hydrophobicity parameter $\log k'$ revealed that hydrophobicity markedly influenced the herbicidal activity.

Key words: 2-(1-*N,N*-dialkylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)alkanoates, herbicidal activity, chirality, hydrophobicity.

INTRODUCTION

Herbicidally active 3-(substituted sulfonyl)-1,2,4-triazole-1-carboxamide derivatives were first reported in 1974,¹⁾ and since then structural modifications in the sulfonyl group have yielded numerous 3-arylsulfonyl- and 3-alkylsulfonyl-1,2,4-triazole-1-carboxamides.^{2–5)} A successful modification of the 3-arylsulfonyl derivatives led to the discovery of a novel rice herbicide, cafenstole,³⁾ having a mesitylsulfonyl group at the 3-position of the triazole ring. Although 3-alkylsulfonyl-1,2,4-triazole derivatives having a carbamoyl⁴⁾ or acyl⁵⁾ group on the neighboring carbon atom of the sulfonyl moiety have already been produced, a 1,2,4-triazole derivative with an alkoxycarbonyl group at the same position has not. In this paper, we describe the synthesis and herbicidal activities of 2-(1-*N,N*-dialkylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)alkanoates (Fig. 1).⁶⁾ Furthermore, an optically active 2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)-4-methylpentanoate was prepared and its herbicidal activity was compared with that of the racemic mixture. In addition, we discuss briefly the relationship between herbicidal activity and hydrophobicity.

MATERIALS AND METHODS

1. Instrumental Analysis

Chemical structures were confirmed by ¹H NMR. ¹H NMR spectra were recorded on a JEOL JNM-A500 NMR spectrometer with tetramethylsilane (TMS) as an internal standard. HRMS spectra were recorded on a JMS-SX 102A. FAB spectra were obtained using glycerol as a matrix. Melting points were determined on a Yanagimoto or Büchi micromelting point apparatus and are uncorrected. Optical rotations were measured using a JASCO P-1020 polarimeter.

2. Synthesis of Compounds

The procedure used for synthesizing 2-(1-*N,N*-dialkylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)alkanoates (**v**) is shown in Fig. 2. The reaction of 3-mercapto-1,2,4-triazole (**i**) with various α -haloalkanoates (**ii**) afforded the corresponding sulfides (**iii**), which, when treated with dialkylcarbamoyl chloride, gave 2-(1-*N,N*-dialkylcarbamoyl-1,2,4-triazol-3-ylthio)alkanoates (**iv**). Oxidation of the triazoles (**iv**) with *m*-chloroperbenzoic acid (*m*CPBA) produced the sulfonyl derivatives (**v**). Alternatively, (1-*N,N*-dialkylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)acetate derivatives (**v-a**) could be converted to the desired compounds (**v**) by a reaction with various

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Fig. 1 General structure of 2-(1-*N,N*-dialkylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)alkanoates.

alkylation reagents in the presence of a base. Typical procedures are described as follows.

2.1 Isopropyl 2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylthio)-4-methylpentanoate

An acetonitrile solution (80 ml) of 3-mercapto-1,2,4-triazole (5.06 g, 50.0 mmol), isopropyl 2-chloro-4-methylpentanoate (9.64 g, 50.0 mmol) and potassium carbonate (5.18 g, 37.4 mmol) was refluxed for 3.5 hr and cooled to room temperature. After the addition of potassium carbonate (5.18 g, 37.4 mmol) and diethylcarbamoyl chloride (6.5 ml, 51.4 mmol), the solution was stirred at room temperature for 18 hr. The mixture was then added to a 1N hydrochloric acid solution (100 ml) and extracted with ethyl acetate (50 ml $\times$ 3). The combined organic layers were washed with brine (50 ml), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (ethyl acetate/hexane = 1/3) to give isopropyl 2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylthio)-4-methylpentanoate as a colorless oil (7.34 g, 41.2%). ^1H NMR (CDCl_3 , TMS) δ ppm: 0.95 (3H, d, $J = 6.4$ Hz, $\text{CH}_2\text{-CH-CH}_3$), 0.98 (3H, d, $J = 6.1$ Hz, $\text{CH}_2\text{-CH-CH}_3$), 1.20 (3H, d, $J = 6.1$ Hz, O-CH- CH_3), 1.21 (3H, d, $J = 6.4$ Hz, O-CH- CH_3), 1.29 (6H, t, $J = 7.0$ Hz, $(\text{CH}_3\text{-CH}_2)_2\text{-N}$), 1.71–1.84 (2H, m, $\text{CH}_2\text{-CH-CH}_3$), 1.86–1.92 (1H, m, $\text{CH}_2\text{-CH-CH}_3$), 3.40–3.80 (4H, m, $(\text{CH}_3\text{-CH}_2)_2\text{-N}$), 4.26–4.30 (1H, m, $\text{SO}_2\text{-CH}$), 5.02 (1H, qq, $J = 6.1$ and 6.4 Hz, O-CH), 8.75 (1H, s, triazole).

2.2 Isopropyl 2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)-4-methylpentanoate

To a chloroform solution (10 ml) of isopropyl 2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylthio)-4-methylpentanoate (0.903 g, 2.59 mmol), was added *m*CPBA (70%, 1.50 g, 6.08 mmol) at 0°C. The mixture was warmed to room temperature and stirred for 6 hr. A saturated sodium hydrogen carbonate solution (20 ml) was added, the organic layer was separated, and then the aqueous layer was extracted with chloroform (10 ml $\times$ 2). The combined organic layers were washed with brine (10 ml), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (ethyl acetate/hexane = 1/2) to give isopropyl 2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)-4-methylpentanoate as a white solid (0.985 g, 97.9%). mp: 52.3–52.8°C; ^1H NMR (CDCl_3 , TMS) δ ppm: 0.94 (3H, d, $J = 6.7$ Hz, $\text{CH}_2\text{-CH-CH}_3$), 0.96 (3H, d, $J = 6.7$ Hz, $\text{CH}_2\text{-CH-CH}_3$), 1.22 (3H, d, $J = 6.4$ Hz, O-CH- CH_3), 1.23 (3H, d, $J = 6.4$ Hz, O-CH- CH_3), 1.32 (6H, t, $J = 7.0$ Hz, $(\text{CH}_3\text{-CH}_2)_2\text{-N}$), 1.60–1.70 (1H, m, $\text{CH}_2\text{-CH-CH}_3$), 1.98 (1H, ddd, $J = 3.4$, 9.2 and 13.4 Hz, $\text{CH}_2\text{-CH-CH}_3$), 2.13 (1H, ddd, $J = 5.2$, 11.3 and 13.4 Hz, $\text{CH}_2\text{-CH-CH}_3$), 3.50–3.70 (4H, m, $(\text{CH}_3\text{-CH}_2)_2\text{-N}$), 4.24 (1H, dd, $J = 3.4$ and 11.3 Hz, $\text{SO}_2\text{-CH}$), 5.03 (1H, sep, $J = 6.4$ Hz, O-CH), 8.91 (1H, s, triazole); HR-FABMAS: Found ($\text{M} + \text{H}^+$): 389.1859, Calcd. for $\text{C}_{16}\text{H}_{29}\text{N}_4\text{O}_5\text{S}$ ($\text{M} + \text{H}$): 389.1837.

2.3 Isopropyl 2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)-4-methylpentanoate

To an *N,N*-dimethylformamide (DMF) suspension (2 ml) of sodium hydride (60%, 155 mg, 3.88 mmol) was added a DMF solution (8 ml) of isopropyl (1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)acetate (1.16 g, 3.49 mmol) at 0°C under an argon atmosphere and the resulting mixture was stirred for 30 min. After an addition of isobutyl iodide (0.42 ml, 3.56 mmol), the mixture was stirred for 3 hr while gradually being warmed to

Fig. 2 Routes for the synthesis of 2-(1-*N,N*-dialkylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)alkanoates.

Table 1 Physicochemical data of compounds 1–16.

No	mp (°C)	High-resolution MS ^{a)} (<i>M</i> + <i>H</i>)	¹ H NMR (CDCl ₃) ^δ (ppm)
1	58.5–59.0	305.0918 (C ₁₀ H ₁₇ N ₄ O ₅ S=305.0920)	1.25 (6H, t), 3.61 (4H, q), 3.75 (3H, s), 4.44 (2H, s), 9.01 (1H, s)
2	oil	319.1070 (C ₁₁ H ₁₉ N ₄ O ₅ S=319.1076)	1.31 (6H, t), 1.73 (3H, d), 3.63 (4H, q), 3.75 (3H, s), 4.19 (1H, q), 8.92 (1H, s)
3	oil	333.1237 (C ₁₂ H ₂₁ N ₄ O ₅ S=333.1233)	1.05 (3H, t), 1.32 (6H, t), 2.26 (2H, m), 3.60 (4H, q), 3.76 (3H, s), 4.16 (1H, t), 8.90 (1H, s)
4	77.0–77.5	347.1370 (C ₁₃ H ₂₃ N ₄ O ₅ S=347.1389)	0.96 (3H, t), 1.29 (2H, m), 1.31 (6H, t), 2.07 (2H, m), 3.60 (4H, q), 3.75 (3H, s), 4.24 (1H, t), 8.90 (1H, s)
5	79.0–80.0	347.1388 (C ₁₃ H ₂₃ N ₄ O ₅ S=347.1389)	1.11 (3H, d), 1.23 (3H, d), 1.31 (6H, t), 2.69 (1H, m), 3.60 (4H, q), 3.74 (3H, s), 4.17 (1H, d), 8.89 (1H, s)
6	oil	361.1550 (C ₁₄ H ₂₅ N ₄ O ₅ S=361.1546)	0.90 (3H, t), 1.20–1.40 (10H, m), 2.10–2.20 (2H, m), 3.45–3.60 (4H, m), 3.76 (3H, s), 4.20–4.30 (1H, m), 8.93 (1H, s)
7	65.0–66.0	361.1529 (C ₁₄ H ₂₅ N ₄ O ₅ S=361.1546)	0.92 (3H, d), 0.95 (3H, d), 1.20–1.30 (1H, m), 1.31 (6H, t), 1.96–2.12 (2H, m), 3.60 (4H, q), 3.75 (3H, s), 4.30 (1H, dd), 8.90 (1H, s)
8	oil	361.1545 (C ₁₄ H ₂₅ N ₄ O ₅ S=361.1546)	0.92 and 0.93 (total 3H, each t), 1.23 and 1.32 (total 3H, each d), 1.32 (6H, t), 1.45–1.73 (2H, m), 2.47 (1H, m), 3.60 (4H, q), 3.73 and 3.74 (total 3H, each s), 4.25 and 4.36 (total 1H, each d), 8.90 and 8.90 (total 1H, each s)
9	oil	375.1700 (C ₁₅ H ₂₇ N ₄ O ₅ S=375.1702)	0.90 (3H, t), 0.92 (3H, t), 1.32 (6H, t), 1.59–1.68 (1H, m), 1.71–1.84 (3H, m), 2.20–2.30 (1H, m), 3.50–3.70 (4H, m), 3.73 (3H, s), 4.44 (1H, d), 8.90 (1H, s)
10	oil	345.1242 (C ₁₃ H ₂₁ N ₄ O ₅ S=345.1233)	0.37–0.43 (1H, m), 0.52–0.58 (1H, m), 0.72–0.85 (2H, m), 1.32 (6H, t), 1.47–1.55 (1H, m), 3.50–3.70 (5H, m), 3.79 (3H, s), 8.92 (1H, s)
11	oil	373.1542 (C ₁₅ H ₂₅ N ₄ O ₅ S=373.1546)	1.30–1.35 (7H, m), 1.37–1.46 (1H, m), 1.52–1.85 (5H, m), 2.13–2.21 (1H, m), 2.52–2.65 (1H, m), 3.50–3.70 (4H, m), 3.74 (3H, s), 4.19 (1H, d), 8.92 (1H, s)
12	oil	375.1702 (C ₁₅ H ₂₇ N ₄ O ₅ S=375.1702)	0.87 and 0.88 (total 3H, each t), 0.90 and 0.91 (total 3H, each d), 1.10–1.20 (1H, m), 1.32 (6H, t), 1.35–1.50 (1H, m), 1.90 and 2.25 (total 1H, each ddd), 2.00–2.10 (1H, m), 2.13 and 2.16 (total 1H, each ddd), 3.50–3.70 (4H, m), 3.76 (3H, s), 4.29 and 4.33 (total 1H, dd), 8.91 (1H, s)
13	oil	359.1387 (C ₁₄ H ₂₃ N ₄ O ₅ S=359.1389)	0.10–0.20 (2H, m), 0.50–0.60 (2H, m), 0.70–0.90 (1H, m), 1.32 (6H, t), 2.05 (1H, ddd), 2.14 (1H, ddd), 3.50–3.70 (4H, m), 3.78 (3H, s), 4.35 (1H, dd), 8.91 (1H, s)
14	79.2–80.3	401.1851 (C ₁₇ H ₂₉ N ₄ O ₅ S=401.1859)	0.84–1.02 (2H, m), 1.10–1.30 (3H, m), 1.32 (6H, t), 1.60–1.77 (6H, m), 1.96–2.14 (2H, m), 3.50–3.70 (4H, m), 3.76 (3H, s), 4.33 (1H, dd), 8.91 (1H, s)
15	96.0–97.5	377.1136 (C ₁₃ H ₂₁ N ₄ O ₇ S=377.1131)	1.32 (6H, t), 3.27 (2H, d), 3.60 (4H, q), 3.72 (3H, s), 3.75 (3H, s), 4.78 (1H, t), 8.91 (1H, s)
16	oil	372.1335 (C ₁₄ H ₂₂ N ₅ O ₅ S=372.1342)	1.26 (6H, t), 1.80 (2H, m), 2.14–2.47 (4H, m), 3.53 (4H, q), 3.70 (3H, s), 4.26 (1H, t), 8.88 (1H, s)

^{a)} Values in parentheses are theoretical values for the given formula of the compounds.

room temperature and then for a further 3.5 hr at 60°C. It was then added to a 1N hydrochloric acid solution (20 ml) and extracted with ethyl acetate (10 ml × 3). The combined organic layers were washed with brine (15 ml), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (ethyl acetate/hexane = 1/3) to give isopropyl 2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)-4-methylpentanoate as a white solid (0.72 g, 53.0%).

Various 2-(1-*N,N*-dialkylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)alkanoates were synthesized in a similar manner. The physical and spectral data of representative compounds are summarized in Table 1.

3. Evaluation of Herbicidal Activity

3.1 Pre-emergence application under flooded conditions

A plastic pot (30 cm²) was filled with clay loam soil (clay: 24.9%, total carbon: 1.8%, pH: 5.3) and the soil was flooded after addition of fertilizer. Soil containing seeds of *Monochoria vaginalis* (Mv) was spread in the pot and then seeds of *Echinochloa oryzicola* (Eo, barnyardgrass), broadleaf weeds (Bw) and *Scirpus juncooides* (Sj,

Japanese bulrush) were sown. After the transplanting of rice seedlings at the 2-leaf stage (*Oryza sativa* (Os), cv. Koshihikari), the pot was maintained flooded to a depth of 2 cm.

Each test compound was dissolved in a mixture of dimethyl sulfoxide (1.0 ml) and 1,3-dimethyl-2-imidazolidinone (0.1 ml), and the solution was diluted with water containing an emulsifier (Sorpul 2564) to give an aqueous emulsion. The final concentration of Sorpul was 0.02%. This emulsion was slowly added to the water surface at five rates ranging from 10 to 500 g a.i./ha just after the transplanting of the rice seedlings (pre-emergence application; +0). Fourteen days after the treatment, weed control and rice injury were evaluated using a visual rating scale of 0 (no weed or crop injury) to 10 (complete kill of weed or crop), and the results obtained in two replications are shown in Tables 2 to 6. Based on the data, the dose giving a score of 8 against *Echinochloa oryzicola* was determined as the ED₈₀ (mol/ha).

3.2 Pre-emergence application under upland soil conditions

A rectangle plastic pot (60 cm²) was filled with gardening soil (Kureha Chemical Co.). Seeds of *Echinochloa*

Table 1 Physicochemical data of compounds 17–32. (continued)

No	mp (°C)	High-resolution MS ^{a)} (<i>M</i> + <i>H</i>)	¹ H NMR (CDCl ₃) δ (ppm)
17	oil	395.1389 (C ₁₇ H ₂₃ N ₄ O ₅ S=395.1389)	1.32 (6H, t), 3.42 (1H, dd), 3.55 (1H, dd), 3.50-3.70 (4H, m), 3.65 (3H, s), 4.52 (1H, dd), 7.15-7.30 (5H, m), 8.92 (1H, s)
18	oil	359.1394 (C ₁₄ H ₂₃ N ₄ O ₅ S=359.1389)	1.32 (6H, t), 1.62-1.67 (3H, m), 2.78-3.00 (2H, m), 3.50-3.70 (4H, m), 3.74 (3H, s), 4.24 and 4.26 (total 1H, each d), 5.25-5.45 (1H, m), 5.55-5.65 (1H, m), 8.92 (1H, s)
19	oil	359.1388 (C ₁₄ H ₂₃ N ₄ O ₅ S=359.1389)	1.32 (6H, t), 1.75 (3H, s), 2.85-2.90 (2H, m), 3.50-3.70 (4H, m), 3.74 (3H, s), 4.44 (1H, dd), 4.74 (1H, s), 4.84 (1H, s), 8.92 (1H, s)
20	oil	375.1716 (C ₁₅ H ₂₇ N ₄ O ₅ S=375.1702)	0.93 (3H, d), 0.96 (3H, d), 1.24 (3H, t), 1.32 (6H, t), 1.60-1.70 (1H, m), 1.98 (1H, ddd), 2.14 (1H, ddd), 3.50-3.70 (4H, m), 4.20 and 4.21 (total 2H, each q), 4.28 (1H, dd), 8.91 (1H, s)
21	oil	389.1861 (C ₁₆ H ₂₉ N ₄ O ₅ S=389.1859)	0.92 (3H, t), 0.94 (3H, d), 0.96 (3H, d), 1.32 (6H, t), 1.60-1.69 (3H, m), 1.97 (1H, ddd), 2.15 (1H, ddd), 3.50-3.70 (4H, m), 4.11 (2H, t), 4.29 (1H, dd), 8.91 (1H, s)
22	52.3-52.8	389.1837 (C ₁₆ H ₂₉ N ₄ O ₅ S=389.1859)	0.94 (3H, d), 0.96 (3H, d), 1.22 (3H, d), 1.23 (3H, d), 1.32 (6H, t), 1.60-1.70 (1H, m), 1.98 (1H, ddd), 2.13 (1H, ddd), 3.50-3.70 (4H, m), 4.24 (1H, dd), 5.03 (1H, sep), 8.91 (1H, s)
23	oil	403.2016 (C ₁₇ H ₃₁ N ₄ O ₅ S=403.2015)	0.92 (3H, t), 0.93 (3H, d), 0.96 (3H, d), 1.32 (6H, t), 1.30-1.38 (2H, m), 1.60 (2H, t), 1.60-1.70 (1H, m), 1.97 (1H, ddd), 2.15 (1H, ddd), 3.50-3.70 (4H, m), 4.14 (2H, t), 4.29 (1H, dd), 8.91 (1H, s)
24	oil	403.2019 (C ₁₇ H ₃₁ N ₄ O ₅ S=403.2015)	0.92 (3H, d), 0.94 (3H, d), 1.22 (3H, d), 1.23 (3H, d), 1.32 (6H, t), 1.60-1.70 (1H, m), 1.90-1.94 (1H, m), 1.97 (1H, ddd), 2.16 (1H, ddd), 3.50-3.70 (4H, m), 3.93 (2H, d), 4.31 (1H, dd), 8.91 (1H, s)
25	oil	403.2016 (C ₁₇ H ₃₁ N ₄ O ₅ S=403.2015)	0.94 (3H, d), 0.96 (3H, d), 1.32 (6H, t), 1.42 (9H, s), 1.64-1.73 (1H, m), 1.96 (1H, ddd), 2.12 (1H, ddd), 3.50-3.70 (4H, m), 4.19 (1H, dd), 8.92 (1H, s)
26	oil	417.2170 (C ₁₈ H ₃₃ N ₄ O ₅ S=417.2172)	0.90 (3H, t), 0.94 (3H, d), 0.96 (3H, d), 1.32 (6H, t), 1.24-1.34 (4H, m), 1.61 (2H, t), 1.60-1.70 (1H, m), 1.97 (1H, ddd), 2.15 (1H, ddd), 3.50-3.70 (4H, m), 4.13 (2H, t), 4.29 (1H, dd), 8.91 (1H, s)
27	oil	361.1548 (C ₁₄ H ₂₅ N ₄ O ₅ S=361.1546)	0.94 (3H, d), 0.96 (3H, d), 1.22 (3H, d), 1.23 (3H, d), 1.62-1.71 (1H, m), 1.97 (1H, ddd), 2.15 (1H, ddd), 3.20 (3H, brs), 3.33 (3H, brs), 4.26 (1H, dd), 5.04 (1H, sep), 8.90 (1H, s)
28	oil	417.2171 (C ₁₈ H ₃₃ N ₄ O ₅ S=417.2172)	0.94 (3H, d), 0.96 (3H, d), 1.20 (3H, d), 1.21 (3H, d), 1.30-1.58 (12H, brs), 1.63-1.71 (1H, m), 1.99 (1H, ddd), 2.15 (1H, ddd), 3.80-4.20 (2H, m), 4.25 (1H, dd), 5.03 (1H, sep), 8.80 (1H, s)
29	oil	429.2174 (C ₁₉ H ₃₅ N ₄ O ₅ S=429.2172)	0.93 (3H, d), 0.96 (3H, d), 1.08-2.02 (18H, m), 2.16 (1H, ddd), 3.09 (3H, s), 4.06-4.28 (2H, m), 5.03 (1H, sep), 8.86 (1H, s)
30	oil	423.1704 (C ₁₉ H ₂₇ N ₄ O ₅ S=423.1702)	0.88 (3H, d), 0.92 (3H, d), 1.20 (3H, d), 1.21 (3H, d), 1.50-1.64 (1H, m), 1.67-1.80 (1H, m), 1.88-2.06 (1H, m), 3.57 (3H, s), 3.93-4.06 (1H, m), 5.01 (1H, sep), 7.11-7.22 (2H, m), 7.31-7.43 (3H, m), 8.75 (1H, s)
31	oil	403.1653 (C ₁₆ H ₂₇ N ₄ O ₅ S=403.1651)	0.94 (3H, d), 0.96 (3H, d), 1.22 (3H, d), 1.23 (3H, d), 1.62-1.72 (1H, m), 1.97 (1H, ddd), 2.13 (1H, ddd), 3.68-4.05 (8H, m), 4.25 (1H, dd), 5.03 (1H, sep), 8.91 (1H, s)
32	oil	387.1703 (C ₁₆ H ₂₇ N ₄ O ₅ S=387.1702)	0.93 (3H, d), 0.96 (3H, d), 1.21 (3H, d), 1.23 (3H, d), 1.60-1.74 (1H, m), 1.93-2.06 (5H, m), 2.16 (1H, ddd), 3.69-3.73 (2H, m), 3.94-3.99 (2H, m), 4.26 (1H, dd), 5.04 (1H, sep), 8.99 (1H, s)

^{a)} Values in parentheses are theoretical values for the given formula of the compounds.

crus-galli (Ec, barnyardgrass), *Digitaria ciliaris* (Dc, southern crabgrass), *Chenopodium album* (Ca, common lambsquarters), and *Zea mays* (Zm, corn) were sown on the surface and covered with a small amount of the same soil. An emulsion of each test compound prepared as described above was diluted and uniformly sprayed over the soil surface at three rates ranging from 100 to 1000 g a.i./ha. Fourteen days after the treatment, weed control and corn injury were visually evaluated using the rating scale described above. The results obtained in two replications are shown in Table 2.

4. Determination of hydrophobic properties (log *k'*) by HPLC

HPLC measurements were performed using a Shimadzu Model LC-6A liquid chromatography system equipped with a C-R5A recorder and a SOD-10AV UV detector. The column was an ODS reversed-phase column (150 mm × 4.6 mm ϕ , Tosoh ODS 120T). The mobile phase (1.0 ml/min) consisted of acetonitrile-water (60:40). The capacity factor *k'* as a hydrophobicity index was calculated as follows: $k' = (t_r - t_0)/t_0$ where t_r is the retention time of the test compound and t_0 is the solvent front. The logarithm of *k'* is given in Table 7.

RESULTS AND DISCUSSION

1. Synthesis

2-(1-*N,N*-dialkylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)-alkanoates (**v**) having various substituents at the α -position of the alkoxycarbonyl group were synthesized by reacting 3-mercapto-1,2,4-triazole (**i**) with a variety of α -haloalkanoates (**ii**), followed by treatment with dialkylcarbamoyl chloride and oxidation of the sulfur atom. This method was not always successful, however, because of the limited availability of α -haloalkanoates (**ii**). In the course of studying more effective methods, we found that various substituents could be introduced into the methylene group of (1-*N,N*-alkylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)acetates (**v-a**) by reacting them with alkyl halides in the presence of a base. This method made it possible to synthesize target products with various substituents at the desired α -position.

Although the carbamoylation of **iii** could give rise to three regioisomers, the 1-, 2-, and 4-carbamoyl forms, the 1-carbamoyl form was the major product. This high regioselectivity is considered to be caused by steric hindrance at the 2*N*- and 4*N*-positions by the substituted alkylthio group situated at the 3-position. Structural

Table 2 Herbicidal activity of methyl 2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylsulfonfyl) alkanooates on pre-emergence application under paddy and upland conditions.

No	R ¹	Herbicidal activity ^{a)}								
		Paddy (50 g a.i./ha)					Upland (500 g a.i./ha)			
		EO ^{b)}	BW ^{c)}	MV ^{d)}	SJ ^{e)}	OS ^{f)}	EC ^{g)}	DC ^{h)}	CA ⁱ⁾	ZM ^{j)}
1	H	1	1	1	1	1	4	5	3	1
2	CH ₃	1	1	1	1	1	6	8	6	2
3	C ₂ H ₅	6	1	1	1	1	6	5	4	3
4	C ₃ H ₇	10	6	6	6	1	10	10	10	5
5	(CH ₃) ₂ CH	10	9	10	10	4	8	9	9	3
6	C ₄ H ₉	9	3	4	1	1	9	9	10	5
7	(CH ₃) ₂ CHCH ₂	10	10	10	10	1	10	10	10	4
8	C ₂ H ₅ C(CH ₃)H	10	8	6	9	1	9	10	10	4
9	(C ₂ H ₅) ₂ CH	10	9	10	8	1	10	9	9	3
10	cyclo-C ₃ H ₅	1	1	1	1	1	9	10	8	2
11	cyclo-C ₅ H ₉	10	9	10	10	1	9	9	9	8
12	C ₂ H ₅ C(CH ₃)HCH ₂	9	8	4	8	1	9	9	10	2
13	cyclo-C ₃ H ₅ CH ₂	10	9	10	6	1	9	9	10	6
14	cyclo-C ₆ H ₁₁ CH ₂	10	5	1	1	1	4	1	4	2
15	CH ₃ OCOCH ₂	1	1	1	1	1	5	6	3	1
16	NCCH ₂ CH ₂ CH ₂	1	1	1	1	1	9	9	9	7
17	C ₆ H ₅ CH ₂	5	1	1	1	1	1	1	3	1
18	CH ₂ =CHC(CH ₃)H	6	1	1	1	1	9	9	9	7
19	CH ₂ =C(CH ₃)CH ₂	9	9	10	6	1	10	10	10	4
cafenstrole ^{k)}	-	10	10	10	10	1	9	9	10	6

^{a)} DAT: 14 days; Rating scale: 0 (no weed or crop injury) - 10 (complete kill of weed or crop). ^{b)} Eo: *Echinochloa oryzicola*. ^{c)} Bw: broadleaf weed. ^{d)} Mv: *Monochoria vaginalis*. ^{e)} Sj: *Scirpus juncoides*. ^{f)} Os: *Oryza sativa*. ^{g)} Ec: *Echinochloa crus-galli*. ^{h)} Dc: *Digitaria ciliaris*. ⁱ⁾ Ca: *Chenopodium album*. ^{j)} Zm: *Zea mays*. ^{k)} *N,N*-Diethylcarbamoyl-3-mesitylsulfonyl-1,2,4-triazole-1-carboxamide.

Fig. 3 Routes for the synthesis of isopropyl (*R*)-2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylsulfonfyl)-4-methylpentanoate.

assignment of **v** was accomplished by ¹H NMR analysis. A chemical shift in the ring proton at the 5-position was expected to be observed at a lower field because of the magnetic deshielding anisotropy caused by the carbonyl

group of the carbamoyl moiety, and actually these protons in **v** were observed at δ 8.8–9.0 ppm as shown in Table 1. On the other hand, it was reported that the ring protons at the 5-position of the 2- and 4-carbamoyl

forms were observed at δ 8.0 and 8.5 ppm, respectively.¹⁾ Based on these findings, the regiochemistry of **v** was determined as the structure shown in Fig. 2.

Optically active isopropyl 2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)-4-methylpentanoate was prepared by the procedure outlined in Fig. 3. The reaction of 3-mercapto-1,2,4-triazole with isopropyl (*S*)-4-methyl-2-tosyloxypentanoate (**S-35**) yielded the sulfide (**R-36**), which, when treated with diethylcarbamoyl chloride, gave isopropyl (*R*)-2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylthio)-4-methylpentanoate (**R-37**). Isopropyl (*S*)-4-methyl-2-tosyloxypentanoate (**S-35**) was easily obtained by esterification of a commercially available L-leucic acid followed by tosylation in the presence of pyridine. Oxidation of the triazole (**R-37**) with *m*CPBA gave the isopropyl (*R*)-2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)-4-methylpentanoate (**R-22**) in a 57.5% enantiomer excess (*ee*).

The corresponding *S*-enantiomer was obtained in a similar manner using isopropyl (*R*)-2-chloro-4-methylpentanoate (**R-35**), however, the optical purity (10.8% *ee*) was too low for herbicidal evaluation.

2. Herbicidal Activity and Crop Safety

2.1 Effect of the substituent R^1

Table 2 summarizes pre-emergence herbicidal activities of and crop injuries caused by methyl 2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)alkanoates having various substituents (R^1) at the α -position of the methoxycarbonyl group. Under paddy conditions, compounds **1** (R^1 =H), **2** (R^1 =CH₃) and **3** (R^1 =C₂H₅) showed poor herbicidal activity. However, compounds bearing alkyl groups with more than 3 carbon chains exhibited higher levels of activity against all weeds tested than compounds **1**, **2** and **3**. Notably, the introduction of branched alkyl groups such as isopropyl (**5**), isobutyl

Table 3 Herbicidal activity of 2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)-4-methylpentanoates on pre-emergence application under paddy conditions.

No	R^2	Dose (g a.i./ha)	Herbicidal activity ^{a)}				Injury ^{a)} Os ^{f)}
			Eo ^{b)}	Bw ^{c)}	Mv ^{d)}	Sj ^{e)}	
7	CH ₃	50	10	10	10	10	1
		25	10	7	5	8	1
20	C ₂ H ₅	50	10	6	9	9	1
		25	9	5	4	3	1
21	C ₃ H ₇	50	10	10	10	10	1
		25	9	6	6	7	1
22	(CH ₃) ₂ CH	50	10	10	10	10	1
		25	10	9	10	9	1
23	C ₄ H ₉	50	10	8	10	10	1
		25	10	6	9	10	1
24	(CH ₃) ₂ CHCH ₂	50	8	6	10	10	1
		25	4	3	4	3	1
25	(CH ₃) ₃ C	50	9	1	1	1	1
		25	3	1	1	1	1
26	C ₅ H ₁₁	50	4	6	1	4	1
		25	4	3	1	1	1
cafenstrole ^{g)}	-	50	10	10	10	10	1
		25	10	9	10	9	1

^{a)} DAT: 14 days; Rating scale: 0 (no weed or crop injury) - 10 (complete kill of weed or crop). ^{b)} Eo: *Echinochloa oryzicola*. ^{c)} Bw: broadleaf weed.

^{d)} Mv: *Monochoria vaginalis*. ^{e)} Sj: *Scirpus juncoides*. ^{f)} Os: *Oryza sativa*.

^{g)} *N,N*-Diethylcarbamoyl-3-mesitylsulfonyl-1,2,4-triazole-1-carboxamide.

(7) and cyclopentyl (11) groups remarkably enhanced the herbicidal efficacy. Herbicidal activities of alkenyl derivatives (18, 19) were lower than those of the corresponding alkyl derivatives (7, 8). The introduction of a functional group such as methoxycarbonyl (15), cyano (16) or phenyl (17) group into the alkyl group of R¹ reduced the herbicidal activity. Among the compounds tested, isobutyl derivative (7) exhibited the strongest herbicidal activity and excellent selectivity for rice. These compounds inhibited the germination of annual weeds and their herbicidal effect was similar to that of other 3-(substituted sulfonyl)-1,2,4-triazole-1-carboxamide derivatives such as cafenstrole. Under upland conditions, almost all compounds tested exhibited strong herbicidal activities at the cost of severe corn injury.

2.2 Effect of the substituent R²

Herbicidal activities and crop injuries for 2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)-4-methylpentanoates (7, 20–26) are shown in Table 3. These results suggest that the carbon chain length and bulkiness of the alkyl group R² influenced the herbicidal activity. That is, compounds 21, 22 and 23 having alkyl groups with 3 to 4 carbon chains were most active against all the weeds tested and further elongation of the carbon chain (26) or introduction of a bulky group (25) reduced the activity. Among these compounds, the isopropyl derivative (22) exhibited excellent herbicidal activity and crop safety, its activity being nearly equal to that of cafenstrole.

2.3 Effect of substituents R³ and R⁴ of the carbamoyl moiety

In the aforementioned triazole derivatives, the substituent at the 1-position of the triazole ring is fixed with the *N,N*-diethylcarbamoyl group like in cafenstrole. Recently, a new tetrazolinone derivative, fentrazamide,⁷⁾ which has an *N*-cyclohexyl-*N*-ethylcarbamoyl group on the tetrazolinone ring, has been developed as a rice herbicide. To examine the effect of the substituent of the carbamoyl moiety, the herbicidal activities of compounds 22 and 27 to 32 having substituents representative of R³ and R⁴ were evaluated (Table 4). In these compounds, R¹ and R² were fixed as isobutyl and isopropyl groups, respectively, because this combination was most effective for herbicidal efficacy as described above. Table 4 clearly shows that the diethylcarbamoyl derivative (22) was much more active than the other compounds, meaning that diethyl groups as R³ and R⁴ were most suitable for the triazole derivatives.

2.4 Effect of the alkoxycarbonyl group

To elucidate the importance of the alkoxycarbonyl group to the herbicidal activity, an alkyl derivative (33)¹⁾ without an ester moiety and an amide derivative (34)⁴⁾ were synthesized and their herbicidal activities compared with those of a sufficiently active compound (7). As shown in Table 5, though the alkyl derivative (33) com-

Table 4 Herbicidal activity of isopropyl 2-(1-*N,N*-dialkylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)-4-methylpentanoates on pre-emergence application under paddy conditions.

No	R ³	R ⁴	Herbicidal activity ^{a)} (50 g a.i./ha)			
			Eo ^{b)}	Bw ^{c)}	Mv ^{d)}	Sj ^{e)}
27	CH ₃	CH ₃	6	4	1	1
22	C ₂ H ₅	C ₂ H ₅	10	10	10	10
28	(CH ₃) ₂ CH	(CH ₃) ₂ CH	6	6	1	3
29	cyclo-C ₆ H ₁₁	CH ₃	3	5	1	1
30	C ₆ H ₅	CH ₃	2	4	1	1
31	-CH ₂ CH ₂ OCH ₂ CH ₂ -		1	1	1	1
32	-CH ₂ CH ₂ CH ₂ CH ₂ -		4	3	1	1

^{a)} DAT: 14 days; Rating scale: 0 (no weed or crop injury) - 10 (complete kill of weed or crop). ^{b)} Eo: *Echinochloa oryzicola*. ^{c)} Bw: broadleaf weed. ^{d)} Mv: *Monochoria vaginalis*. ^{e)} Sj: *Scirpus juncoides*.

Table 5 Herbicidal activity of compounds 7, 33 and 34.

No	R ⁵	Herbicidal Activity ^{a)}				
		Paddy (50 g a.i./ha.)				
		Eo ^{b)}	Bw ^{c)}	Mv ^{d)}	Sj ^{e)}	Os ^{f)}
7	COOMe	10	10	10	10	1
33	H	10	5	1	1	1
34	CON(C ₂ H ₅) ₂	1	1	1	1	2

^{a)} DAT: 14 days; Rating scale: 0 (no weed or crop injury) - 10 (complete kill of weed or crop). ^{b)} Eo: *Echinochloa oryzicola*. ^{c)} Bw: broadleaf weed. ^{d)} Mv: *Monochoria vaginalis*. ^{e)} Sj: *Scirpus juncoides*. ^{f)} Os: *Oryza sativa*.

pletely controlled Eo, it showed poor activity against other weeds at a rate of 50 g a.i./ha. Furthermore, the amide derivative (34) did not exhibit herbicidal activity against all weeds tested at the same dosage. Consequently, the alkoxycarbonyl group is considered to play an important role in enhancing herbicidal efficacy in the present triazole heterocycles.

2.5 Effect of chirality

It is reported that the primary mode of action of cafenstrole is the inhibition of the biosynthesis of very long chain fatty acids (VLCFAs) like chloroacetamide-class herbicides including butachlor, dimethenamid and metolachlor.^{8,9)} The sensitivity of fatty acid elongation depends on chemical structure and stereochemistry. For example, the *S*-enantiomers of dimethenamid and metolachlor are active, whereas the *R*-enantiomers are

Table 6 Herbicidal activity of **R-22** and **RS-22** on pre-emergence application under paddy conditions.

R-22	RS-22						
No	ee ^{a)} (%)	Dose (g a.i./ha)	Herbicidal activity ^{b)}				Injury ^{b)}
			Eo ^{c)}	Bw ^{d)}	Mv ^{e)}	Sj ^{f)}	Os ^{g)}
R-22	57.5	50	10	9	10	9	1
		25	9	6	4	4	1
		10	5	4	1	1	1
RS-22	0	50	10	9	10	10	1
		25	9	9	4	6	1
		10	4	4	1	3	1

^{a)} Determined by HPLC analysis on a CHIRALCEL OF (Hexane/2-Propanol = 60/40, UV 220 nm). ^{b)} DAT: 14 days; Rating scale: 0 (no weed or crop injury) - 10 (complete kill of weed or crop). ^{c)} Eo: *Echinochloa oryzicola*. ^{d)} Bw: broadleaf weed. ^{e)} Mv: *Monochoria vaginalis*. ^{f)} Sj: *Scirpus juncoides*. ^{g)} Os: *Oryza sativa*.

inactive. Our 2-(1-*N,N*-dialkylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)alkanoates have one chiral carbon center. Therefore, isopropyl (*R*)-2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)-4-methylpentanoate (**R-22**) was synthesized in order to compare it with its racemate (**22**). As shown in Table 6, no apparent difference in activity could be detected in this experiment, indicating that the chirality does not contribute to a specific phytotoxic or regulating activity. Couderchet *et al.*¹⁰⁾ proposed that the appropriate chirality would be maintained in the *N*-substituent of the amide moiety in chloroacetamide-class herbicides and such an amide is essential structurally for potent activity. Therefore, it is presumed that the sulfonyl moiety of the present triazole derivatives may not be an effective component for the active site of the target enzyme.

3. Relationship between Herbicidal Activity and Hydrophobicity

As the biological activity of agrochemicals, in general, depends on physico-chemical characteristics such as hydrophobicity, and steric as well as electronic properties, we examined the relationship between the herbicidal potency and hydrophobicity of 2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)alkanoates. The hydrophobicity parameter is usually expressed as a logarithm of the partition coefficient ($\log P$) in *n*-octanol/water.¹¹⁾ However, since the amounts of compounds synthesized were not enough for the measurement of their partition coefficient, the logarithm of the capacity factor (k') determined from the retention time for reversed-phase HPLC was used as the hydrophobicity parameter.¹²⁻¹⁴⁾ It is known that $\log k'$ values are

Table 7 Herbicidal activity and hydrophobicity parameter.

No	$\log k'$	$\log 1/ED_{80}$ ^{a)}		
		Obsd	Calcd ^{b)}	Δ ^{c)}
1	0.36	0.18	-0.13	0.31
2	0.41	-0.10	0.13	-0.23
3	0.49	0.74	0.50	0.24
4	0.58	1.14	0.82	0.32
5	0.56	1.24	0.76	0.48
6	0.69	0.90	1.10	-0.20
7	0.68	1.26	1.08	0.18
8	0.66	0.95	1.04	-0.09
9	0.76	1.40	1.20	0.20
10	0.47	0.24	0.41	-0.17
11	0.69	1.27	1.10	0.17
12	0.79	0.99	1.23	-0.24
13	0.60	0.95	0.88	0.07
14	0.94	1.20	1.21	-0.01
15	0.45	-0.04	0.32	-0.36
16	0.41	0.05	0.13	-0.08
17	0.69	0.60	1.10	-0.50
18	0.63	0.65	0.97	-0.32
19	0.63	0.95	0.97	-0.02
20	0.78	1.27	1.22	0.05
21	0.90	1.41	1.24	0.17
22	0.89	1.41	1.25	0.16
23	1.04	1.30	1.06	0.24
24	1.03	0.91	1.08	-0.17
25	0.99	1.00	1.15	-0.15
26	1.18	0.62	0.66	-0.04

^{a)} ED_{80} : Rate (mol/ha) to provide 80% control of *Echinochloa oryzicola*.

^{b)} Using Eq. 1.

^{c)} Δ : Obsd - Calcd.

significantly correlated with the *n*-octanol/water partition coefficient.¹⁵⁻¹⁷⁾ Table 7 shows the $\log k'$ values and herbicidal activities ($\log 1/ED_{80}$) against *Echinochloa oryzicola* (Eo) of 2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)alkanoates (**1-26**). A regression analysis was performed on the activities ($\log 1/ED_{80}$), using $\log k'$ values, and Eq. 1 was obtained at the 95% confidence level.

$$\begin{aligned} \log 1/ED_{80} &= -5.66(\pm 0.98)(\log k')^2 + 9.68 \\ &\quad (\pm 1.48)(\log k') - 2.88(\pm 0.52) \quad (1) \\ n &= 26, r^2 = 0.73, s = 0.47, F_{2,23} = 31.77 \end{aligned}$$

In Eq. 1, n is the number of compounds used, r^2 is the correlation coefficient, s is the standard deviation and $F_{m,n-m-1}$ is the *F* ratio where m is the number of independent variables. The values in parentheses are 95% confidence intervals. Equation 1 indicates the parabolic relationship between $\log 1/ED_{80}$ values and $\log k'$ values, and predicts an optimum $\log k'$ value of ca. 0.86 (Fig. 4). The $\log 1/ED_{80}$ values calculated with Eq. 1 are shown in Table 7. The $\log k'$ value (0.89) of iso-

Fig. 4 Plot of $\log k'$ versus $\log 1/ED_{80}$ of 2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)alkanoates, **1** to **26**.

propyl 2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)-4-methylpentanoate (**22**) exhibiting the strongest herbicidal activity approximates the optimum, 0.86. This result reveals that herbicidal activity against Eo is markedly affected by molecular hydrophobicity. However, some compounds deviated from the regression curve shown in Fig. 4, indicating that hydrophobicity is not the only factor governing the activity. In particular, the benzyl derivative (**17**) deviated markedly from the curve. Steric and electronic properties are likely to influence the activity, too.

In conclusion, the present study demonstrated that isopropyl 2-(1-*N,N*-diethylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)-4-methylpentanoate (**22**) showed the most potent herbicidal activity against all the weeds tested with a wide safety margin between rice and Eo, and this compound is a promising candidate for further development. No difference in the herbicidal activities of the enantiomers could be detected in this experiment. Furthermore, the SAR study indicated that there is a good correlation between the hydrophobicity parameter $\log k'$ and the herbicidal activities against *Echinochloa oryzicola* (Eo) of the 2-(1-*N,N*-dialkylcarbamoyl-1,2,4-triazol-3-ylsulfonyl)alkanoates examined, and that the $\log k'$ value is useful for the evaluation of herbicidal activity.

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要 約

新規な 2-(1-carbamoyl-1,2,4-triazol-3-ylsulfonyl)alkanoate 誘導体の合成と除草活性

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一連の新規な 2-(1-*N,N*-ジアルキルカルバモイル-1,2,4-トリアゾール-3-イルスルホニル) アルカン酸エステル誘導体を合成し, 種々の雑草に対する除草活性を調べた。除草活性はアルコキシカルボニル基の α 位の置換基とカルバモイル部の窒素原子上の置換基により変化した。合成した全ての化合物の中で, アルコキシカルボニル基の α 位に分岐状のアルキル基を有する 1-*N,N*-ジアルキルカルバモイル-1,2,4-トリアゾール誘導体が高い除草活性を示した。 α 位のキラリティーは除草活性に効果を及ぼさなかった。生物評価に基づいて, 2-(1-*N,N*-ジエチルカルバモイル-1,2,4-トリアゾール-3-イルスルホニル)-4-メチルペンタン酸イソプロピルが, 移植水稻用除草剤としての候補化合物として選ばれた。疎水性パラメータ $\log k'$ を用いた構造活性相関 (SAR) の研究より, 疎水性が除草活性に顕著な影響を及ぼしていることが明らかとなった。