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## Synthesis, Bleaching Activity, and Germination Promoting Activity of 3,4-Disubstituted-4H-1,2,4-triazoles

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A series of 3,4-disubstituted-4H-1,2,4-triazoles was prepared and evaluated for their activity to cause bleaching injury in lettuce seedlings and to promote germination of lettuce seeds at a high temperature of 30 °C. In the 3-propargylthio-4-substituted-4H-1,2,4-triazole series, the 3,4-dichlorophenyl analog **8** with the highest bleaching activity promoted the seed germination at 30 °C, however, its activity was much less than that of fluridone, an inhibitor of abscisic acid biosynthesis. 4-Phenyl-3-(4-trifluoromethylphenyl)-4H-1,2,4-triazole (**30**) showed germination promoting activity comparable to that of compound **8**. There was no apparent correlation between the ability of 4-phenyl-3-substituted-4H-1,2,4-triazoles to cause bleaching injury and the germination promoting activity on lettuce seeds at 30 °C.

### INTRODUCTION

It is evident that abscisic acid (ABA) and gibberellins play essential roles for seed dormancy and germination (Hilhorst and Karssen, 1992). ABA biosynthesis via carotenoids has been shown to be involved in the onset of dormancy during seed maturation (Le Page-Degivy *et al.*, 1990). Grappin *et al.*, (2000) have found that fluridone, an inhibitor of carotenoid biosynthesis, is efficient in breaking dormancy by preventing the accumulation of ABA in imbibed dormant seeds of *Nicotiana plumbaginifolia*.

It is well known that the germination of lettuce seed is inhibited by high temperature, but at lower temperatures germination occur or recommence after a period of time (Gray, 1975). Yoshioka *et al.* (1998) have found that fluridone causes a decrease in ABA content of lettuce seeds at a high temperature of 33 °C and promotes germination, indicating that ABA plays a decisive role in the regulation of seed germination at supraoptimal temperatures as well.

Since ABA is involved in not only seed dormancy and germination but also induction of physiological responses to the environmental stresses such as drought (Stewart and Voetberg, 1985) and freezing (Chen and Gusta, 1983), inhibitors of ABA biosynthesis would be a useful plant growth regulator as well as an effective tool in studies of plant physiology. We have previously reported that a new series of 3-propargylthio-4-(substituted phenyl)-4H-1,2,4-triazoles caused bleaching symptoms by the inhibition of  $\beta$

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-carotene formation (Takehara *et al.*, 1995), probably by inhibiting phytoene desaturase as fluridone does. To discover ABA biosynthesis inhibitors of novel structure we synthesized additional 3,4-disubstituted 4*H*-1,2,4-triazoles and evaluated their bleaching activity and germination promoting activity on lettuce seeds.

## MATERIALS AND METHODS

### Synthesis

All melting points (mp) are uncorrected. <sup>1</sup>H-NMR spectra were recorded on JNM-EX400 spectrometer with tetramethylsilane as an internal standard and all samples were prepared in deuteriochloroform.

3-Mercapto-4-phenyl-4*H*-1,2,4-triazole (**III**), 4-phenyl-3-propargylthio-4*H*-1,2,4-triazole (**IV**) and 4-(3,4-dichlorophenyl)-3-propargylthio-4*H*-1,2,4-triazole (**8**) were prepared according to the procedure reported previously (Takehara *et al.*, 1995). 1-Formyl-4-substituted-3-thiosemicarbazide (**I**) and 3-mercapto-4-substituted-4*H*-1,2,4-triazoles (**II**) were similarly prepared starting from the corresponding isothiocyanate. 3-Cyclohexylmethylthio-4-phenyl-4*H*-1,2,4-triazole (**23**)

To a solution of 0.8 g of (**III**) in 25 ml of acetone was added 0.94 g of K<sub>2</sub>CO<sub>3</sub>. After stirring for 1 hr at room temperature, to the mixture was added 0.96 g of cyclohexylmethyl bromide and then heated to reflux for 3 hr. After filtration, the filtrate was concentrated and the product was extracted with ethyl acetate. The ethyl acetate solution was washed with water, 5% NaOH solution and brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the residue was chromatographed on silica gel by eluting with hexane and ethyl acetate (2:1) to afford **23** (1.2 g, 97%) as an oil. <sup>1</sup>H-NMR δ: 0.9–1.9 (11H, m), 3.20 (2H, d, *J*=6.8 Hz), 7.3–7.7 (3H, m), 8.27 (1H, s).

Compounds **1–7** and **9–11** were similarly prepared from the corresponding (**II**) and propargyl bromide.

3-Propargylthio-4-propyl-4*H*-1,2,4-triazole (**1**). Yield 65%. <sup>1</sup>H-NMR δ: 0.97 (3H, t, *J*=7.6 Hz), 1.82 (2H, m), 2.27 (1H, s), 3.96 (4H, m), 8.20 (1H, s).

4-Butyl-3-propargylthio-4*H*-1,2,4-triazole (**2**). Yield 77%. <sup>1</sup>H-NMR δ: 0.96 (3H, t, *J*=7.3 Hz), 1.35 (2H, q, *J*=7.5 Hz), 1.76 (2H, m), 2.29 (1H, s), 3.96 (4H, m), 8.21 (1H, s).

4-*tert*-Butyl-3-propargylthio-4*H*-1,2,4-triazole (**3**). Yield 65%. mp 85–86°C. <sup>1</sup>H-NMR δ: 1.57 (9H, s), 2.26 (1H, s), 4.13 (2H, s), 8.21 (1H, s).

4-Cyclohexyl-3-propargylthio-4*H*-1,2,4-triazole (**4**). Yield 92%. mp 48–49°C. <sup>1</sup>H-NMR δ: 1.2–2.1 (10H, m), 2.28 (1H, s), 3.9–4.1 (3H, m), 8.25 (1H, s).

4-(3-Nitrophenyl)-3-propargylthio-4*H*-1,2,4-triazole (**5**). Yield 80%. mp 148–149°C. <sup>1</sup>H-NMR δ: 2.28 (1H, s), 4.06 (2H, s), 7.7–7.8 (2H, m), 8.32 (1H, s), 8.4 (2H, m).

4-(3-Acetylphenyl)-3-propargylthio-4*H*-1,2,4-triazole (**6**). Yield 73%. mp 138–139°C. <sup>1</sup>H-NMR δ: 2.26 (1H, t, *J*=2.7 Hz), 2.67 (3H, s), 4.06 (2H, d, *J*=2.9 Hz), 7.58–7.60 (1H, m), 7.68 (1H, t, *J*=8.1 Hz), 7.97 (1H, s), 8.09 (1H, d, *J*=7.8 Hz), 8.36 (1H, s).

4-(4-Acetylphenyl)-3-propargylthio-4*H*-1,2,4-triazole (**7**). Yield 72%. mp 124–125°C. <sup>1</sup>H-NMR δ: 2.26 (1H, s), 2.67 (3H, s), 4.06 (2H, s), 7.50 (2H, d, *J*=8.3 Hz), 8.14 (1H, d, *J*=8.3 Hz), 8.37 (1H, s).

4-Naphthyl-3-propargylthio-4*H*-1,2,4-triazole (**9**). Yield 91%. <sup>1</sup>H-NMR δ: 2.03 (1H, s), 3.98 (2H, s), 7.3–7.7 (5H, m), 8.0–8.1 (2H, m), 8.37 (1H, s).

4-Benzyl-3-propargylthio-4H-1,2,4-triazole (**10**). Yield 55%. <sup>1</sup>H-NMR  $\delta$ : 2.28 (1H, s), 3.88 (2H, s), 5.16 (2H, s), 7.2–7.4 (5H, m), 8.21 (1H, s).

4-(2-Phenylethyl)-3-propargylthio-4H-1,2,4-triazole (**11**). Yield 83%. <sup>1</sup>H-NMR  $\delta$ : 2.27 (1H, s), 3.04 (2H, t,  $J=7.1$  Hz), 3.91 (2H, s), 4.23 (2H, t,  $J=7.1$  Hz), 7.0–7.1 (2H, m), 7.2–7.3 (3H, m), 7.89 (1H, s).

Analogously compounds **12–21** were prepared from the corresponding (**II**) and benzyl bromide.

3-Benzylthio-4-propyl-4H-1,2,4-triazole (**12**). Yield 61%. <sup>1</sup>H-NMR  $\delta$ : 0.84 (3H, t,  $J=7.3$  Hz), 1.62 (2H, q,  $J=7.3$  Hz), 3.65 (2H, t,  $J=7.1$  Hz), 4.41 (2H, s), 7.2–7.3 (5H, m), 8.11 (1H, s).

4-Allyl-3-benzylthio-4H-1,2,4-triazole (**13**). Yield 58%. <sup>1</sup>H-NMR  $\delta$ : 4.2–4.3 (2H, m), 4.38 (2H, s), 5.07 (1H, d,  $J=17$  Hz), 5.21 (1H, d,  $J=9.3$  Hz), 5.6–5.7 (1H, m), 7.2–7.3 (5H, m), 8.10 (1H, s).

3-Benzylthio-4-butyl-4H-1,2,4-triazole (**14**). Yield 76%. <sup>1</sup>H-NMR  $\delta$ : 0.88 (3H, t,  $J=7.3$  Hz), 1.22 (2H, q,  $J=7.5$  Hz), 1.56 (2H, m), 3.68 (2H, t,  $J=7.3$  Hz), 4.41 (2H, s), 7.2–7.3 (5H, m), 8.10 (1H, s).

3-Benzylthio-4-tert-butyl-4H-1,2,4-triazole (**15**). Yield 65%. mp 101–102 °C. <sup>1</sup>H-NMR  $\delta$ : 1.59 (9H, s), 4.58 (2H, s), 7.3–7.4 (5H, m), 8.19 (1H, s).

3-Benzylthio-4-cyclohexyl-4H-1,2,4-triazole (**16**). Yield 68%. <sup>1</sup>H-NMR  $\delta$ : 1.1–1.4 (5H, m), 1.7–1.9 (5H, m), 3.71 (1H, s), 4.39 (2H, s), 7.2–7.3 (5H, m), 8.15 (1H, s).

4-(3-Acetylphenyl)-3-benzylthio-4H-1,2,4-triazole (**17**). Yield 75%. mp 101–102 °C. <sup>1</sup>H-NMR  $\delta$ : 2.62 (3H, s), 4.48 (2H, s), 7.3–7.4 (1H, m), 7.59 (1H, t,  $J=7.8$  Hz), 7.79 (1H, t,  $J=2.0$  Hz), 8.31 (1H, s).

4-(4-Acetylphenyl)-3-benzylthio-4H-1,2,4-triazole (**18**). Yield 83%. mp 112–113 °C. <sup>1</sup>H-NMR  $\delta$ : 2.64 (3H, s), 4.50 (2H, s), 7.2–7.4 (7H, m), 8.05 (2H, d,  $J=8.8$  Hz), 8.31 (1H, s).

3-Benzylthio-4-naphthyl-4H-1,2,4-triazole (**19**). Yield 33%. mp 148–149 °C. <sup>1</sup>H-NMR  $\delta$ : 4.46 (2H, s), 7.2–7.3 (6H, m), 7.9–8.0 (2H, m), 8.32 (1H, s).

4-Benzyl-3-benzylthio-4H-1,2,4-triazole (**20**). Yield 63%. mp 98–99 °C. <sup>1</sup>H-NMR  $\delta$ : 4.39 (2H, s), 4.83 (2H, s), 7.0–7.3 (10H, m), 8.04 (1H, s).

3-Benzylthio-4-(2-phenylethyl)-4H-1,2,4-triazole (**21**). Yield 75%. <sup>1</sup>H-NMR  $\delta$ : 2.82 (2H, t,  $J=7.1$  Hz), 3.92 (2H, t,  $J=7.1$  Hz), 4.39 (2H, s), 6.95 (2H, s), 7.2–7.3 (8H, m), 7.79 (1H, s).

Compounds **31** and **32** were prepared by reacting (**III**) with phenethyl bromide and 1-bromo-2-butyne, respectively.

4-Phenyl-3-(2-phenylethylthio)-4H-1,2,4-triazole (**31**). Yield 83%. <sup>1</sup>H-NMR  $\delta$ : 3.09 (2H, t,  $J=8.0$  Hz), 3.52 (2H, t,  $J=8.0$  Hz), 7.1–7.5 (10H, m), 8.29 (1H, s).

3-(2-Butynylthio)-4-phenyl-4H-1,2,4-triazole (**32**). Yield 36%. mp 122 °C. <sup>1</sup>H-NMR  $\delta$ : 1.78 (3H, t,  $J=2.7$  Hz), 4.00 (2H, q,  $J=2.6$  Hz), 7.3–7.4 (2H, m), 7.5–7.6 (3H, m), 8.31 (1H, s).

3-tert-Butylthio-4-phenyl-4H-1,2,4-triazole (**22**).

A mixture of 0.65 g (3.7 mmole) of (**III**), 1.0 g (4.6 mmole) of *tert*-butyl trichloroacetimidate and boron trifluoride etherate (0.4 ml) in 25 ml of dichloromethane was stirred at room temperature for 16 hr. After adding solid NaHCO<sub>3</sub> (0.3 g), the precipitate was filtered off and the filtrate was concentrated in vacuo. The product was extracted with

ethyl acetate and the ethyl acetate solution was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the residue was chromatographed on silica gel by eluting with hexane–ethyl acetate (1:2) to give 0.58 g (68%) of **22**, mp 98 °C. <sup>1</sup>H-NMR δ: 1.41 (9H, s), 7.31–7.33 (2H, m), 7.51 (3H, m), 8.36 (1H, s).

*4-Phenyl-3-phenylthio-4H-1,2,4-triazole (24).*

A mixture of 3.0 g (16.9 mmole) of (**III**), 0.86 g (4.2 mmole) of iodobenzene, 0.54 g (8.5 mmole) of copper powder and 2.34 g (16.9 mmole) of K<sub>2</sub>CO<sub>3</sub> in 10 ml of DMF was stirred at 90–100 °C for 5.5 hr. The reaction mixture was allowed to cool to room temperature and then to the mixture was added ethyl acetate. After filtration, the product was extracted with ethyl acetate. The ethyl acetate solution was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated in vacuo. The residue was chromatographed on silica gel by eluting with hexane–ethyl acetate (1:2) to afford 0.64 g (59%) of **24**, mp 92 °C. <sup>1</sup>H-NMR δ: 7.2–7.3 (7H, m), 7.4–7.6 (3H, m), 8.36 (1H, s).

Compounds **25–30** were prepared in the same manner as compound **24** with use of the corresponding substituted iodobenzene instead of iodobenzene.

*3-(3-Chlorophenylthio)-4-phenyl-4H-1,2,4-triazole (25).* Yield 53%. <sup>1</sup>H-NMR δ: 7.2–7.3 (6H, m), 7.4–7.5 (3H, m), 8.39 (1H, s).

*3-(4-Chlorophenylthio)-4-phenyl-4H-1,2,4-triazole (26).* Yield 42%. mp 119–120 °C. <sup>1</sup>H-NMR δ: 7.2–7.3 (6H, m), 7.4–7.5 (3H, m), 8.36 (1H, s).

*3-(3-Methoxyphenylthio)-4-phenyl-4H-1,2,4-triazole (27).* Yield 16%. <sup>1</sup>H-NMR δ: 3.71 (3H, s), 6.7–6.8 (3H, m), 7.13 (1H, t, *J*=7.8 Hz), 7.2–7.4 (5H, m), 8.36 (1H, s).

*3-(4-Methoxyphenylthio)-4-phenyl-4H-1,2,4-triazole (28).* Yield 41%. mp 92–93 °C. <sup>1</sup>H-NMR δ: 3.77 (3H, s), 6.77 (2H, d, *J*=8.8 Hz), 7.15–7.25 (4H, m), 7.4–7.5 (3H, m), 8.30 (1H, s).

*4-Phenyl-3-(3-trifluoromethylphenylthio)-4H-1,2,4-triazole (29).* Yield 19%. mp 120–121 °C. <sup>1</sup>H-NMR δ: 7.2–7.5 (9H, m), 8.39 (1H, s).

*4-Phenyl-3-(4-trifluoromethylphenylthio)-4H-1,2,4-triazole (30).* Yield 46%. mp 115–116 °C. <sup>1</sup>H-NMR δ: 7.2–7.3 (3H, m), 7.37 (2H, d, *J*=8.3 Hz), 7.4–7.5 (4H, m), 8.42 (1H, s).

*4-Phenyl-3-(2-heptynylthio)-4H-1,2,4-triazole (33).*

To a solution of 0.8 g of 4-phenyl-3-propargylthio-4H-1,2,4-triazole (**IV**) and 0.8 g of *n*-butyl iodide in 30 ml of DMF was added 0.3 g of sodium hydride at room temperature. After stirring for 1 day at room temperature, saturated NH<sub>4</sub>Cl solution was added to the mixture, and the product was extracted with ethyl acetate. The ethyl acetate solution was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated. The residue was chromatographed on silica gel by eluting with hexane–ethyl acetate (1:1) to give 0.33 g (33%) of **33**, mp 46–47 °C. <sup>1</sup>H-NMR δ: 0.84 (3H, t, *J*=7.3 Hz), 1.24 (2H, m), 1.40 (2H, m), 2.18 (2H, m), 4.73 (2H, t, *J*=3.2 Hz), 7.35–7.39 (2H, m), 7.50–7.57 (3H, m), 8.36 (1H, s).

*4-Phenyl-3-(4-phenylbut-2-ynylthio)-4H-1,2,4-triazole (34)* was similarly prepared from (**IV**) and benzyl bromide. <sup>1</sup>H-NMR δ: 3.57 (2H, t, *J*=2.7 Hz), 4.75 (2H, t, *J*=2.7 Hz), 7.09 (2H, m), 7.22 (5H, m), 7.48 (3H, m), 8.33 (1H, s).

## Bioassay

Seven varieties of lettuce (*Lactuca sativa* L.) used for this study were purchased from Takii Company Ltd. (Kyoto, Japan).

#### Germination test.

A filter paper in a Petri dish (9 cm in diameter) was soaked with 1 ml of acetone solution containing fluridone or a test compound. After evaporation of the solvent, 20 seeds were placed on the filter paper and 5 ml of deionized water was added. The Petri dishes were incubated in darkness at temperature of 20 or 30 °C. At the designated time after sowing, germinated seeds were scored. The germination promoting activity of the compounds synthesized was evaluated by the counts of germinated seeds eight days after sowing.

#### Bleaching activity.

Lettuce (*Lactuca sativa* L. cv Sacramento) seedling tests were performed by the same method as described previously (Yamada *et al.*, 1992). Seeds were incubated for 4 days at 25 °C under 12 hr photoperiod. The bleaching activity was evaluated on a scale of 0–4 according to the following categories: 0, no visual change compared with the control; 1, faintly bleaching of the cotyledon; 2, intermediate between 1 and 3; 3, slightly remaining green color; 4, complete bleaching (no green color). Two replicates were used for each concentration.

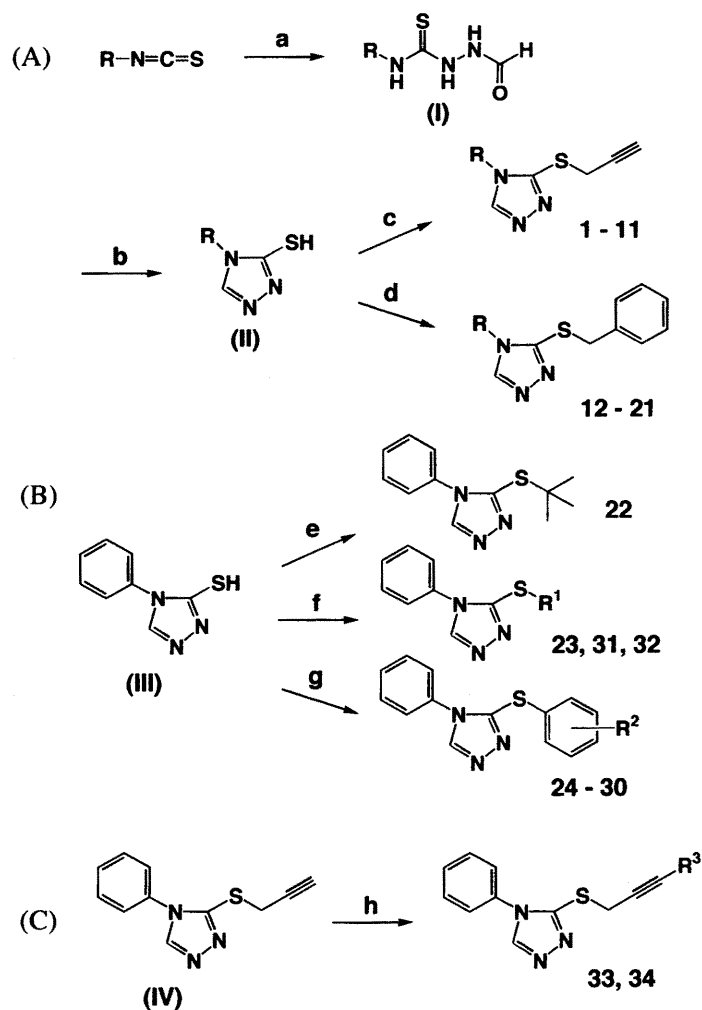
## RESULTS AND DISCUSSION

### Synthesis

A variety of 4-substituted-3-substituted thio-4*H*-1,2,4-triazoles were prepared according to the route depicted in Fig. 1. 1-Formyl-4-substituted-3-thiosemicarbazides (**I**) were prepared by reaction of the corresponding alkyl or aryl isothiocyanide with formylhydrazine as shown in Fig. 1 (A). Cyclization of the thiosemicarbazide **I** by heating with potassium hydroxide aqueous solution afforded 3-mercapto-4-substituted 4*H*-1,2,4-triazoles (**II**), which were treated with propargyl bromide and benzyl bromide to give 3-propargylthio-4-substituted-4*H*-1,2,4-triazoles (**1–11**) and 3-benzylthio-4-substituted-4*H*-1,2,4-triazoles (**12–21**), respectively. Treatment of 3-mercapto-4-phenyl-4*H*-1,2,4-triazole (**III**) with *tert*-butyltrichloroacetimidate and boron trifluoride etherate afforded 3-*tert*-butylmercapto-4-phenyl-4*H*-1,2,4-triazole (**22**) [Fig. 1 (B)]. Alkylation of **III** with alkyl bromide or aralkyl bromide gave the corresponding 4-phenyl-3-substituted thio-4*H*-1,2,4-triazoles (**23**, **31** and **32**). 3-Arylthio-4-phenyl-4*H*-1,2,4-triazoles (**24–30**) were prepared by treatment of **III** with aryl iodide in the presence of copper powder in DMF. 4-Phenyl-4*H*-1,2,4-triazoles having a 2-alkynylthio group at the 3-position (**33** and **34**) were prepared by alkylation of **IV** with alkyl halide as illustrated in Fig. 1 (C).

### Biological activity

We first examined the response of seed germination at 20 and 30 °C for seven varieties of lettuce (Table 1). At 20 °C all of the varieties showed more than 95% germination two days after sowing. At 30 °C Sacramento, Cisco and Berkeley varieties gave percentage germination figures between 65% and 85%, while Winter Cisco, Legacy and Green Wave varieties showed less than 15% germination. No seeds of Ballade variety germinated at 30 °C two days after sowing. Since significant difference in response to temperature was found in Ballade variety, this variety was used to examine the



**Fig. 1.** Synthesis of 3-substituted thio-4-substituted-4*H*-1,2,4-triazoles  
 Reagents and conditions: (a) formylhydrazine, THF, reflux; (b) 1) aq. KOH, 60–70 °C, 2) aq. HCl; (c) propargyl bromide, K<sub>2</sub>CO<sub>3</sub>, acetone, room temperature; (d) benzyl bromide, K<sub>2</sub>CO<sub>3</sub>, acetone, room temperature; (e) *tert*-butyltrichloroacetimidate, boron trifluoride etherate, CH<sub>2</sub>Cl<sub>2</sub>, room temperature; (f) R<sup>1</sup>-Br, K<sub>2</sub>CO<sub>3</sub>, acetone, room temperature; (g) substituted iodobenzene, copper powder, K<sub>2</sub>CO<sub>3</sub>, DMF, 90–100 °C; (h) R<sup>3</sup>-Br or R<sup>3</sup>-I, NaH, DMF, room temperature.

**Table 1.** Percentage germination of seeds of lettuce varieties at 20 and 30 °C

Variety	(% Seed germination <sup>a</sup> )	
	Temperature (°C)	
Sacramento	30	100
Cisco	30	95
Winter Cisco	20	100
Berkeley	30	100
Legacy	20	100
Ballade	30	95
Green Wave	20	95

<sup>a</sup> 48 hr after sowing**Table 2.** Effect of fluridone on the germination of lettuce (cv. Ballade) seeds

Treatment	Treatment period (day)	(% Seed germination <sup>a</sup> )		
		2	5	8
Fluridone (30 μM)		10	50	85
Control		0	0	5

<sup>a</sup> Condition: 30 °C in darkness





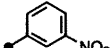
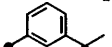

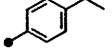


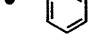
germination promoting activity of compounds at 30 °C.

The effect of fluridone on germination of Ballade variety at 30 °C was examined (Table 2). In the presence of 30 μM fluridone, 85% of the seeds germinated, whereas in the control the germination rate was only 5% eight days after sowing. Although fluridone stimulated germination at 30 °C, the timing of germination was markedly delayed as compared with that at 20 °C. These results suggest that the maintenance of high ABA content might be responsible for high-temperature inhibition of germination in Ballade variety, based on the results of Yoshioka *et al.* (1998) for another lettuce variety (Grand Rapids), in which fluridone caused a decrease in ABA content at high temperatures and restored the seed germination.

Table 3 shows the germination promoting activity and bleaching activity of 3-propargylthio-4-substituted-4H-1,2,4-triazoles. As previously reported (Takehara *et al.*, 1995), the 3,4-dichlorophenyl analog **8** caused strong bleaching injury against lettuce seedlings. The introduction of an electron-withdrawing group such as a nitro or acetyl substituent on the benzene ring (**5-7**) led to a drastic decrease in bleaching activity. Replacement of the 3,4-dichlorophenyl group with an alkyl group in compound **8** gave much lower activity (**1-4**). The naphthyl analog **9** had no visible bleaching injury at 250 μM, while the



**Table 3.** Germination promoting activity and bleaching activity of 3-propargylthio-4-substituted-4*H*-1,2,4-triazoles

No.	R	(% ) Seed germination at 200 $\mu$ M	Bleaching activity	
			50	250
1		7	0	1
2		10	1	2
3		0	0	0
4		10	0	1
5		10	0	0
6		8	0	1
7		9	0	1
8		28	4	4
9		2	0	0
10		2	1	3
11		11	2	3






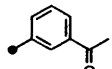
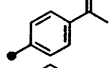


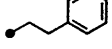
benzyl (**10**) and the phenethyl (**11**) analogs showed moderate activity.

Compound **8** with strong bleaching activity promoted the seed germination at 30 °C, however, its activity was much less than that of fluridone. Other compounds in Table 3 had much lower activity than compound **8**. There seems to be some correlation between the ability of these 3-propargylthio-4-substituted-4*H*-1,2,4-triazoles to cause bleaching injury and to promote the seed germination in lettuce.

Further, a new series of 3-benzylthio-4-substituted-4*H*-1,2,4-triazoles (Table 4) and 4-phenyl-3-substituted-4*H*-1,2,4-triazoles (Table 5) were synthesized and evaluated for their activity. None of the 3-benzylthio analogs in Table 4 caused complete bleaching injury at 250  $\mu$ M. Among these compounds, only the 3-acetylphenyl analog **17** was slightly effective in promoting seed germination, although its bleaching activity was not observed even at a high concentration of 250  $\mu$ M.

In the 4-phenyl-1,2,4-triazole series (Table 5), the 4-trifluoromethylphenyl analog

**Table 4.** Germination promoting activity and bleaching activity of 3-benzylthio-4-substituted-4H-1,2,4-triazoles

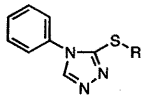





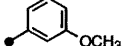
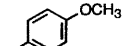
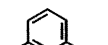
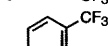
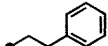

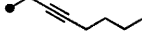
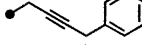
No.	R	(% ) Seed germination at 200 $\mu$ M	Bleaching activity	
			50	250
12		6	0	0
13		1	0	0
14		0	0	1
15		0	0	1
16		10	1	2
17		17	0	0
18		8	0	0
19		8	0	0
20		0	1	2
21		2	0	2

**30**, which had comparatively weak bleaching activity, showed germination promoting activity comparable to that of compound **8**. The *tert*-butyl (**22**), 3-chlorophenyl (**25**) and 4-chlorophenyl (**26**) analogs slightly promoted seed germination. It is noteworthy that the germination promoting activity of these 4-phenyl-3-substituted-4H-1,2,4-triazoles was not correlated with their bleaching activity. Although it remains to be seen whether or not compound **30** inhibits ABA synthesis to promote germination at high temperature, compound **30** might be a structurally novel class of leads for the development of new plant growth regulators.

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**Table 5.** Germination promoting activity and bleaching activity of 4-phenyl-3-substituted-4*H*-1,2,4-triazoles

No.	 R	(%) Seed germination at 200 $\mu$ M	Bleaching activity	
			50	250
22		19	0	0
23		3	0	2
24		2	1	2
25		19	2	3
26		18	1	3
27		13	0	0
28		11	1	2
29		6	1	2
30		31	1	3
31		2	0	2
32		9	3	4
33		0	0	1
34		4	0	1

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