Synthesis and Bleaching Activity of 1-Ethyl- and 1-Propyl-5-Substituted Imidazoles

Naotaka Yamada, Eiichi Kuwano, and Morifusa Eto
Department of Agricultural Chemistry, Kyushu University, Fukuoka 812, Japan

Z. Naturforsch. **48c**, 301–306 (1993); received November 5, 1992

1,5-Disubstituted Imidazoles, Bleaching Activity

Twenty-eight 1-ethyl- and 1-propyl-5-substituted imidazoles were synthesized and their bleaching activity was evaluated by using the lettuce seedling test. 5-Phenyl-1-propylimidazole (**1**) caused distinct chlorosis, while none of the compounds with various alkenyl groups at the 5-position of the imidazole ring showed this bleaching activity. Introduction of a bromo, chloro, fluoro, methyl or trifluoromethyl group at the 4-position on the benzene ring of compound **1** increased the activity in comparison with that of compound **1.** 5-[4-(3-Chlorobenzyloxy)phenyl]-1-ethylimidazole (**15**) and 1-ethyl-5-[4-(3-methylbenzyloxy)phenyl]imidazole (**21**), analogs with a large substituent at the 4-position on the benzene ring, also caused pronounced chlorosis in the lettuce seedlings. Both compounds **1** and **15** at 30 ppm decreased total carotenoid content in the lettuce seedlings to less than 40% of that in the control, and the reduction of total carotenoid content correlated well with treatment dose.

Introduction

We have previously reported that 1-ethyl- and 1-propyl-5-phenylimidazoles caused chlorosis of lettuce seedlings, and that the presence of both substituents at the 1- and 5-position of the imidazole ring was essential for the bleaching activity [1]. In the 1-ethyl-5-phenylimidazole series, the introduction of a benzyloxy group at the 4-position on the benzene ring increased the activity compared with that of non-substituted phenyl analog, while the 2- and 3-benzyloxyphenyl analogs had no activity. The size of the substituent at the 1-position of the imidazole ring strongly influenced the activity. Only the 1-ethyl and the 1-propyl analogs caused distinct chlorosis, otherwise the activity fell off sharply with increasing or decreasing size of the alkyl group at the 1-position. Representative compounds showing marked activity, 5-phenyl-1-propylimidazole (**1**), 5-(4-benzyloxyphenyl)-1-ethylimidazole and 1-ethyl-5-stilbenylimidazole have been described [2]. However, the mode of action of these imidazole compounds is uncertain. Several bleaching herbicides such as norflurazon, fluridone and difunon are well-known to interfere with carotenoid biosynthesis by inhibiting maily the desaturation reactions of phytoene [3]. We therefore examined whether or not 1,5-disubstituted imidazoles affect the carotenoid content in the plant. We report structure-activity relationships of new 1-ethyl- and 1-propyl-5-substituted imidazoles, and the effect of representative compounds on the total carotenoid content in lettuce seedlings.

Reprint requests to Dr. E. Kuwano.

Verlag der Zeitschrift für Naturforschung,
D-W-7400 Tübingen
0939–5075/93/0300–0301 $ 01.30/0

Materials and Methods

Chemicals

All melting points (m.p.) are uncorrected. ^{1}H NMR spectra were determined with a JEOL FX-100 spectrometer, using tetramethylsilane as an internal standard, and samples were prepared in deutero-chloroform.

5-Phenyl-1-propylimidazole (**1**), 5-[(*E*)-2,6-dimethyl-1,5-heptadienyl]-1-propylimidazole (**12**), 5-(4-benzyloxy)-1-ethylimidazole (**13**), 5-[4-(2-chlorobenzyloxy)phenyl]-1-ethylimidazole (**14**), 5-[4-(3-chlorobenzyloxy)phenyl]-1-ethylimidazole (**15**), 5-[4-(4-chlorobenzyloxy)phenyl]-1-ethylimidazole (**16**), 1-ethyl-5-[4-(3-methoxybenzyloxy)-phenyl]imidazole (**23**) and 1-ethyl-5-[4-(4-methoxybenzyloxy)phenyl]imidazole (**24**) were prepared according to the procedure previously [1, 2].

5-(2-Chlorophenyl)-1-propylimidazole (**2**). A mixture of chlorobenzaldehyde (2.8 g, 20 mmol), *n*-propylamine (1.77 g, 30 mmol) and anhydrous magnesium sulfate (7.22 g, 60 mmol) in 50 ml of dichloromethane was stirred for 3 h at room temperature and then refluxed for 1 h. Magnesium

Dieses Werk wurde im Jahr 2013 vom Verlag Zeitschrift für Naturforschung in Zusammenarbeit mit der Max-Planck-Gesellschaft zur Förderung der Wissenschaften e.V. digitalisiert und unter folgender Lizenz veröffentlicht: Creative Commons Namensnennung-Keine Bearbeitung 3.0 Deutschland Lizenz.

This work has been digitalized and published in 2013 by Verlag Zeitschrift für Naturforschung in cooperation with the Max Planck Society for the Advancement of Science under a Creative Commons Attribution-NoDerivs 3.0 Germany License.

Zum 01.01.2015 ist eine Anpassung der Lizenzbedingungen (Entfall der Creative Commons Lizenzbedingung „Keine Bearbeitung") beabsichtigt, um eine Nachnutzung auch im Rahmen zukünftiger wissenschaftlicher Nutzungsformen zu ermöglichen.

On 01.01.2015 it is planned to change the License Conditions (the removal of the Creative Commons License condition "no derivative works"). This is to allow reuse in the area of future scientific usage.

sulfate was filtered off and the filtrate was concentrated. The residue was dissolved in 50 ml of methanol, and to the mixture was added tosylmethylisocyanide (TosMIC; 4.69 g, 24 mmol) and anhydrous potassium carbonate (7.33 g, 40 mmol). After refluxing for 3 h, the solvent was evaporated and 50 ml of water was added to the residue. The product was extracted with ethyl acetate twice, and the combined ethyl acetate solution was washed with brine and dried over anhydrous sodium sulfate. After removal of the solvent, the residue was chromatographed on silica gel by elution with hexane–ethyl acetate (1 : 1) and ethyl acetate. Concentration of the ethyl acetate eluate afforded 3.5 mg (0.8%) of **2.** NMR δ: 0.79 (3H, t, J = 7 Hz), 1.33–1.79 (2H, m), 3.76 (2H, t, J = 7 Hz), 7.01 (1H, s), 7.11–7.66 (5H, m).

Compounds **3, 5,** and **7–12** were prepared in the same manner as **2** with use of a corresponding aldehyde, instead of 2-chlorobenzaldehyde.

5-(3-Chlorophenyl)-1-propylimidazole (**3**). Yield 2.5%. NMR δ: 0.83 (3H, t, J = 7 Hz), 1.38–1.86 (2H, m), 3.91 (2H, t, J = 7 Hz), 7.02 (1H, s), 7.04–7.39 (4H, m), 7.52 (1H, s).

5-(4-Fluorophenyl)-1-propylimidazole (**5**). Yield 0.96%. NMR δ: 0.82 (3H, t, J = 7 Hz). 1.38–1.83 (2H, m), 3.88 (2H, t, J = 7 Hz), 6.86–7.19 (5H, m), 7.50 (1H, s).

$C_{14}H_{15}N_2O_4F$ (oxalate salt)
Calcd C 57.14 H 5.14 N 9.52%,
Found C 57.18 H 5.25 N 9.26%.

5-(4-Methylphenyl)-1-propylimidazole (**7**). Yield 6.6%. NMR δ: 0.81 (3H, t, J = 7 Hz), 1.40–1.84 (2H, m), 2.38 (3H, s), 3.88 (2H, t, J = 7 Hz), 6.98 (1H, s), 7.05–7.34 (4H, m), 7.49 (1H, s).

$C_{15}H_{18}N_2O_4$ (oxalate salt)
Calcd C 62.06 H 6.25 N 9.65%,
Found C 61.96 H 6.30 N 9.44%.

5-(4-Trifluoromethylphenyl)-1-propylimidazole (**8**). Yield 0.29%. NMR δ: 0.84 (3H, t, J = 7 Hz), 1.38–1.87 (2H, m), 3.94 (2H, t, J = 7 Hz), 6.95–7.78 (6H, m).

$C_{15}H_{15}N_2O_4F_3$ (oxalate salt)
Calcd C 52.33 H 4.39 N 8.14%,
Found C 52.08 H 4.52 N 8.21%.

5-(2-Methyl-1-propenyl)-1-propylimidazole (**9**). Yield 40%. NMR δ: 0.91 (3H, t, J = 7 Hz), 2.47–2.91 (8H, m), 3.79 (2H, t, J = 7 Hz), 5.84 (1H, s), 6.91 (1H, s), 7.35 (1H, s).

$C_{12}H_{18}N_2O_4$ (oxalate salt)
Calcd C 56.68 H 7.13 N 11.02%,
Found C 56.62 H 7.17 N 10.39%.

5-(1,3-Pentadienyl)-1-propylimidazole (**10**). Yield 14%. NMR δ: 0.92 (3H, t, J = 7 Hz), 1.50–1.94 (5H, m), 3.84 (2H, t, J = 7 Hz), 5.60–6.80 (4H, m), 7.10 (1H, s), 7.34 (1H, s).

5-(1-Octenyl)-1-propylimidazole (**11**). Yield 33%. NMR δ: 0.92 (6H, t, J = 7 Hz), 1.10–1.96 (10H, m), 2.04–2.32 (2H, m), 3.82 (2H, t, J = 7 Hz), 5.84–6.26 (2H, m), 7.02 (1H, s), 7.32 (1H, s).

$C_{16}H_{26}N_2O_4$ (oxalate salt)
Calcd C 61.94 H 8.39 N 9.03%,
Found C 61.85 H 8.44 N 8.94%.

5-[(E)-2,6-dimethyl-1,5-heptadienyl]-1-propylimidazole (**12**). Yield 25%. NMR δ: 0.92 (3H, t, J = 7 Hz), 1.62 (3H, s), 1.70 (3H, s), 1.86 (3H, d, J = 2 Hz), 2.00–2.50 (4H, m), 3.80 (2H, t, J = 7 Hz), 4.90–5.28 (1H, m), 5.88 (1H, s), 6.94 (1H, s), 7.38 (1H, s).

$C_{17}H_{26}N_2O_4$ (oxalate salt)
Calcd C 63.35 H 8.07 N 8.70%,
Found C 63.25 H 7.93 N 8.54%.

Compounds **4** and **6** were prepared in the same manner as that used for compound **1** from the corresponding formamide and propylamine [1].

5-(4-Chlorophenyl)-1-propylimidazole (**4**). Yield 52%. NMR δ: 0.82 (3H, t, J = 7 Hz), 1.40–1.84 (2H, m), 3.89 (2H, t, J = 7 Hz), 6.84–7.60 (6H, m).

$C_{14}H_{15}N_2O_4Cl$ (oxalate salt)
Calcd C 54.11 H 4.87 N 9.02%,
Found C 54.12 H 4.83 N 8.75%.

5-(4-Bromophenyl)-1-propylimidazole (**6**). Yield 18%. NMR δ: 0.83 (3H, t, J = 7 Hz), 1.40–1.84 (2H, m), 3.90 (2H, t, J = 7 Hz), 6.84–7.61 (6H, m).

$C_{14}H_{15}N_2O_4Br$ (oxalate salt)
Calcd C 47.34 H 4.26 N 7.89%,
Found C 47.32 H 4.31 N 7.88%.

1-Ethyl-5-[4-(2-fluorobenzyloxy)phenyl]imidazole (**17**). To a suspension of sodium hydride (60% in oil; 0.2 g, 5 mmol) in dimethylformamide

(10 ml) was added dropwise 1-ethyl-5-(4-hydroxyphenyl)imidazole [4] (0.8 g, 4.25 mmol) in 5 ml of dimethylformamide at 0–5 °C, and the mixture was stirred for 1 h at room temperature. To the ice-cooled mixture was added 2-fluorobenzyl chloride (0.93 g, 6.4 mmol). After stirring for 24 h at room temperature, 50 ml of water was added to the mixture and the product was extracted with diethyl ether twice. The combined ether solution was washed with 5% sodium hydroxide solution and brine, and dried over anhydrous sodium sulfate. After removal of the solvent, the residue was chromatographed on silica gel by elution with hexane–ethyl acetate (1 : 1) and ethyl acetate. Concentration of the ethyl acetate eluate afforded 0.45 g (39%) of **17.** NMR δ: 1.31 (3H, t, J = 7 Hz), 3.95 (2H, q, J = 7 Hz), 5.13 (2H, s), 6.78–7.58 (10H, m).

$C_{20}H_{19}N_5O_2F$ (oxalate salt)
Calcd C 69.17 H 4.96 N 7.25%,
Found C 69.09 H 5.01 N 7.03%.

Compounds **18–22** and **25–28** were prepared in the same manner as compound **17** with use of a corresponding benzyl halide, instead of 2-fluorobenzyl chloride.

1-Ethyl-5-[4-(3-fluorobenzyloxy)phenyl]imidazole (**18**). Yield 57%. NMR δ: 1.31 (3H, t, J = 7 Hz), 3.95 (2H, q, J = 7 Hz), 5.07 (2H, s), 6.70–7.56 (10H, m).

$C_{20}H_{19}N_5O_2F$ (oxalate salt)
Calcd C 62.17 H 4.96 N 7.25%,
Found C 61.95 H 5.03 N 7.14%.

1-Ethyl-5-[4-(4-fluorobenzyloxy)phenyl]imidazole (**19**). Yield 75%. NMR δ: 1.31 (3H, t, J = 7 Hz), 3.95 (2H, q, J = 7 Hz), 5.03 (2H, s), 6.82–7.59 (10H, m).

$C_{20}H_{19}N_5O_2F$ (oxalate salt)
Calcd C 62.17 H 4.96 N 7.25%,
Found C 62.12 H 5.05 N 7.13%.

1-Ethyl-5-[4-(2-methylbenzyloxy)phenyl]imidazole (**20**). Yield 27%. NMR δ: 1.33 (3H, t, J = 7 Hz), 2.43 (3H, s), 3.99 (2H, q, J = 7 Hz), 5.06 (2H, s), 6.87–7.60 (10H, m).

$C_{21}H_{22}N_2O_5$ (oxalate salt)
Calcd C 65.96 H 5.80 N 7.33%,
Found C 65.75 H 5.85 N 7.20%.

1-Ethyl-5-[4-(3-methylbenzyloxy)phenyl]imidazole (**21**). Yield 35%. NMR δ: 1.29 (3H, t, J = 7 Hz), 2.35 (3H, s), 3.93 (2H, q, J = 7 Hz), 5.01 (2H, s), 6.82–7.57 (10H, m).

$C_{21}H_{22}N_2O_5$ (oxalate salt)
Calcd C 78.05 H 6.89 N 9.58%,
Found C 77.97 H 6.87 N 9.35%.

1-Ethyl-5-[4-(4-methylbenzyloxy)phenyl]imidazole (**22**). Yield 43%. NMR δ: 1.30 (3H, t, J = 7 Hz), 2.35 (3H, s), 3.95 (2H, q, J = 7 Hz), 5.02 (2H, s), 6.87–7.60 (10H, m).

$C_{21}H_{22}N_2O_5$ (oxalate salt)
Calcd C 78.05 H 6.89 N 9.58%,
Found C 78.28 H 6.92 N 9.21%.

1-Ethyl-5-[4-(3-trifluoromethylbenzyloxy)-phenyl]imidazole (**25**). Yield 28%. NMR δ: 1.30 (3H, t, J = 7 Hz), 3.94 (2H, q, J = 7 Hz), 5.10 (2H, s), 6.77–7.76 (10H, m).

$C_{21}H_{19}N_2O_5F_3$ (oxalate salt)
Calcd C 59.63 H 4.75 N 6.95%,
Found C 58.90 H 4.83 N 6.86%.

1-Ethyl-5-[4-(3,4-dichlorobenzyloxy)phenyl]-imidazole (**26**). Yield 32%. NMR δ: 1.30 (3H, t, J = 7 Hz), 3.92 (2H, q, J = 7 Hz), 5.00 (2H, s), 6.71–7.56 (9H, m).

1-Ethyl-5-[4-(2,4-dichlorobenzyloxy)phenyl]-imidazole (**27**). Yield 25%. NMR δ: 1.31 (3H, t, J = 7 Hz), 3.95 (2H, q, J = 7 Hz), 5.12 (2H, s), 6.77–7.67 (9H, m).

$C_{20}H_{18}N_2O_5Cl_2$ (oxalate salt)
Calcd C 55.89 H 4.47 N 6.21%,
Found C 54.70 H 4.31 N 6.25%.

1-Ethyl-5-[4-(3,5-dichlorobenzyloxy)phenyl]-imidazole (**28**). Yield 52%. NMR δ: 1.31 (3H, t, J = 7 Hz), 3.95 (2H, q, J = 7 Hz), 5.02 (2H, s), 6.81–7.05 (3H, m), 7.13–7.37 (5H, m), 7.52 (1H, s).

$C_{20}H_{18}N_2O_5Cl_2$ (oxalate salt)
Calcd C 55.89 H 4.47 N 6.21%,
Found C 55.09 H 4.30 N 6.30%.

Bioassay

Lettuce (*Lactuca sativa* L. *cv.* sacramento) seedling tests were performed by the same method as that described previously [2]. Four days after treatment, the degree of chlorosis was assessed on a scale of 0–4 according to the following categories:

0, no visual change compared with the control; 1, faintly bleaching at the edges of the leaves; 2, intermediate between 1 and 3; 3, a small green area remaining on the leaves; 4, complete bleaching. The bleaching activity from each treatment is indicated by the average results from 60 seedlings.

Determination of the carotenoid content

Carotenoid extraction was done according to the methods of Allen *et al.* [5]. Fresh lettuce leaves were cut 4 days after treatment and stored at 0 °C in the dark for 1 h. Then 0.5 g of leaves were immersed in an aqueous 80% acetone solution (10 ml) at 0 °C for 30 min and homogenated in an ice-cooled water-bath. The homogenate was filtered through a glass filter by suction, and the residue was washed with an iced aqueous 80% (v/v) acetone solution until all visible pigments had been removed (20–25 ml). The volume of combined solution was made up to 50 ml, and the absorbance values at 480, 645 and 663 nm were measured with a Shimadzu spectrophotometer (UV-2100). The total carotenoid content was determined by using Allen's equation [5]. The total carotenoid content in the treated plants was calculated as percentage of that in the control. Each experiment was repeated four times.

Results and Discussion

Synthesis

The 1,5-disubstituted imidazoles were prepared by using tosylmethylisocyanide (TosMIC) according to a method described by van Leusen *et al.* [6]. 1-Propyl-5-substituted imidazoles were synthesized by reaction of the aldimines derived from propylamine and aldehydes with TosMIC in the presence of potassium carbonate as a base in methanol (Fig. 1 A). Similar cyclization reaction of N-(4-hydroxybenzylidene)ethylamine derived from 4-hydroxybenzaldehyde and ethylamine with TosMIC afforded 1-ethyl-5-(4-hydroxyphenyl)-imidazole, which was alkylated by an appropriate alkyl halide to give 1-ethyl-5-(4-alkyloxyphenyl)-imidazoles in a fairly good yield (Fig. 1 B).

Biological activities

Table I shows the bleaching activity of 1-propyl-5-substituted imidazoles on lettuce seedlings. 1-Propyl-5-phenylimidazole (**1**) caused complete chlorosis at a concentration more than 50 ppm as described previously [1]. The introduction of a 4-chloro substituent on the benzene ring (**4**) extremely increased the activity in comparison with that observed for compound **1,** while the 2-chlorophenyl analog **2** gave much lower activity. The 3-chlorophenyl analog **3** showed much higher activity than compound **1** at a lower concentration, however, in contrast to compound **1,** it did not cause complete chlorosis even at a high concentration of 100 ppm. The data indicates that the *para* substituent on the benzene ring is necessary for high activity. The introduction of a fluoro (**5**), bromo (**6**), methyl (**7**) or trifluoromethyl (**8**) substituent at the 4-position on the benzene ring also in-

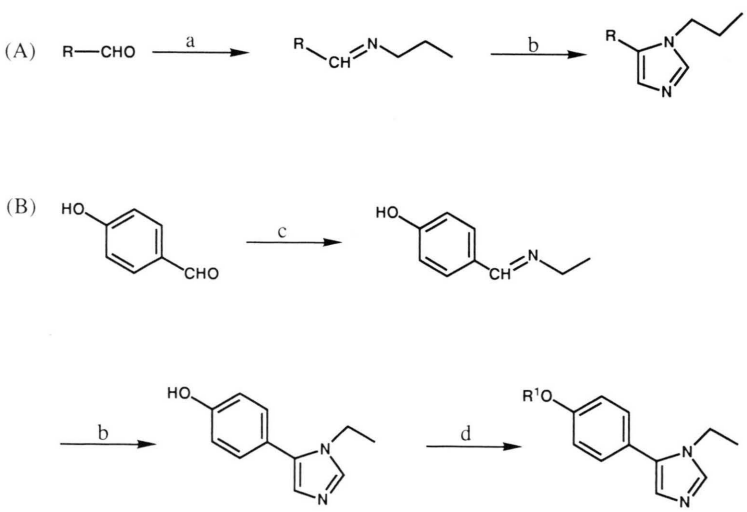
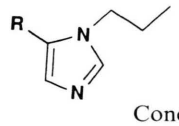
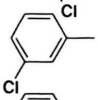
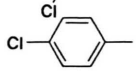
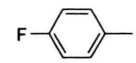
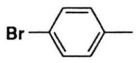
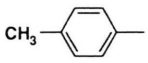
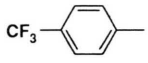
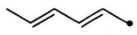
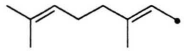


Fig. 1. Synthesis of 1,5-disubstituted imidazoles. Reagents: (a) $C_3H_7NH_2$, $MgSO_4$, CH_2Cl_2; (b) TosMIC, K_2CO_3, CH_3OH; (c) $C_2H_5NH_2 \cdot HCl$, NEt_3, $MgSO_4$ CH_2Cl_2; (d) R^1X, NaH, DMF.

Table I. Bleaching activity of 5-substituted 1-propylimidazoles.



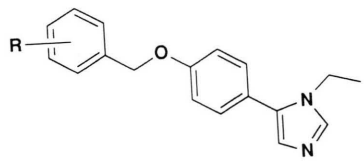
No.	R	Concentration [ppm] 3	5	10	30	50	100
1			0	1	2	4	4
2					0	1	3
3		1	2	2	2	3	3
4		2	3	4	4	4	4
5		0	1	3	4	4	4
6		1	3	4	4	4	4
7		0	2	3	4	4	4
8		0	1	3	4	4	4
9							0
10							0
11							0
12							0

For rating: see Materials and Methods.

creased the activity in comparison with that of compound **1.** All of these compounds induced complete chlorosis at 30 ppm. On the other hand, none of the compounds with alkenyl groups at the 5-position of the imidazole ring (compounds **9–12**) showed the bleaching activity even at 100 ppm, indicating that the presence of a benzene ring is essential for the activity. Thus, among the 1-propyl-5-(4-substituted phenyl)imidazole series, the 4-chlorophenyl analog **4** was the most active and caused distinct chlorosis at 3 ppm.

In our previous study, 1-ethyl-5-(4-benzyloxyphenyl)imidazole (**13**) was found to show high bleaching activity as well as compound **1.** However, introduction of other alkyloxy substituents such as a methoxy, butyloxy or hexyloxy group at the 4-position on the benzene ring greatly diminished the activity. There was little difference in activity between 1-propyl-5-(4-benzyloxyphenyl)-imidazole and the 1-ethyl analog **13** [2]. We synthesized additional 1-ethyl-5-(4-benzyloxyphenyl)-imidazole analogs and evaluated their bleaching activity (Table II). In the 5-(4-benzyloxyphenyl)-imidazole series, the introduction of a 3-chloro substituent (**15**) into the benzyl group of compound **13** increased the activity in comparison with that of compound **13,** while 2-chloro (**14**) and 4-chlorobenzyloxyphenyl (**16**) analogs showed much lower activity than that of compound **13.** The bleaching activity of these 5-(4-benzyloxyphenyl)imidazole analogs is very dependent on the position of the substituent at the benzyl group. The analogs having various substituents such as a

Table II. Bleaching activity of 5-substituted 1-ethylimidazoles.



No.	R	Concentration [ppm] 10	30	50	100
13	H	1	3	4	4
14	2-Cl		0	1	1
15	3-Cl	1	4	4	4
16	4-Cl		0	1	2
17	2-F	0	3	4	4
18	3-F	1	4	4	4
19	4-F	0	1	2	4
20	2-CH_3			0	1
21	3-CH_3	2	4	4	4
22	4-CH_3	0	1	2	3
23	3-CH_3O	0	2	4	4
24	4-CH_3O				0
25	3-CF_3	0	1	2	4
26	3,4-Cl				0
27	2,4-Cl		0	1	2
28	3,5-Cl			0	1

For rating: see Materials and Methods.

fluoro (**18**), methyl (**21**) or methoxy (**23**) group at the 3-position of the benzyl group possessed much higher bleaching activity than the corresponding 2- or 4-substituted benzyloxyphenyl analogs. Among them, 3-chlorobenzyloxyphenyl (**15**) and 3-methylbenzyloxyphenyl (**21**) analogs showed the highest activity. However, the additional introduction of a chloro substituent at the 4- (**26**) or 5-position (**28**) in compound **15** gave analogs with negligible bleaching activity. It is noteworthy that there is little difference in activity between compounds **1** and **15** on lettuce seedlings, although their steric structures are quite different.

Both compounds **1** and **15** markedly reduced the total carotenoid content in the lettuce seedlings four days after treatment (Fig. 2). Lettuce seedlings treated with 30 ppm of these compounds showed more than a 60% decrease in total carotenoid content compared with that of control, and the reduction of total carotenoid content correlated well with the treated dosage. This result suggests that compounds **1** and **15** may cause chlorosis by inhibiting carotenoid biosynthesis.

A number of substituted imidazoles, as well as substituted triazoles, pyridines and pyrimidines, are well known to inhibit cytochrome P-450 [7]. Rogerson *et al.* have reported that 1,5-disubstituted imidazoles were the most effective inhibitors of microsomal cytochrome P-450 among the substituted imidazoles tested [8]. Recently, a novel 1,5-disubstituted imidazole herbicide, CGA 201029/

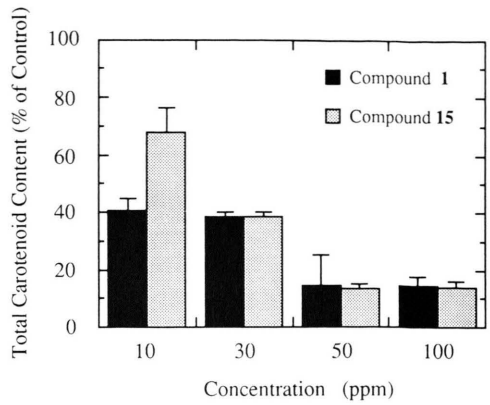


Fig. 2. Effect of 1,5-disubstituted imidazoles on total carotenoid content in 4-day-old lettuce leaves. Vertical bars represent standard deviation.

R 69020 [methyl 1-(2,2-dimethylindan-1-yl)imidazole-5-carboxylate], has been shown to block sterol biosynthesis in plants by inhibiting obtusifoliol 14-methyl demethylase, which is a microsomal cytochrome P-450 [9]. It remains to be seen whether or not the mode of action of the 1,5-disubstituted imidazoles described in this article involves cytochrome P-450 inhibition.

Acknowledgement

The authors thank Dr. Lawrence G. Harshman of University of California, Davis, for his critical reading and improvement of this manuscript.

[1] M. Kikuchi, E. Kuwano, Y. Nakashima, and M. Eto, Biosci. Biotech. Biochem. **56,** 161–162 (1992).
[2] N. Yamada, E. Kuwano, M. Kikuchi, and M. Eto, Biosci. Biotech. Biochem. **56,** 1943–1948 (1992).
[3] G. Sandmann and P. Böger, in: Target Sites of Herbicide Action (P. Böger and G. Sandmann, eds.), pp. 25–44, CRC Press, Boca Raton, FL 1989.
[4] M. Kikuchi, E. Kuwano, Y. Nakashima, and M. Eto, J. Fac. Agr., Kyushu Univ. **36,** 83–92 (1991).
[5] J. T. O. Kirk and R. L. Allen, Biochem. Biophys. Res. Commun. **21,** 523–530 (1965).
[6] A. M. van Leusen, J. Wildeman, and O. H. Oldenziel, J. Org. Chem. **42,** 1153–1159 (1977).
[7] P. R. Ortiz de Montellano and N. O. Reich, in: Cytochrome P-450 (P. R. Ortiz de Montellano, ed.), pp. 273–314, Plenum Press, New York 1986.
[8] T. D. Rogerson, C. F. Wilkinson, and K. Hetnarski, Biochem. Pharmac. **26,** 1039–1042 (1977).
[9] L. Streit, M. Moreau, J. Gaudin, E. Ebert, and H. V. Bossche, Pestic. Biochem. Physiol. **40,** 162–168 (1991).