Synthesis and Herbicidal Properties of 3-(2-Oxo-1-Imidazolidinyliminomethyl)Indoles

Aldo Andreani*, Alessandra Locatelli and Mirella Rambaldi

Università di Bologna, Dipartimento di Scienze Farmaceutiche, Via Belmeloro 6, 40126 Bologna, Italy

Received June 13, 1994

The reaction of 1-substituted 2-chloroindole-3-carboxaldehydes with 1-amino-2-imidazolidinone gave a series of 1-substituted 2-chloro-3-(2-oxo-1-imidazolidinyliminomethyl)indoles which were evaluated as potential herbicides. The level of biological activity was not sufficient to warrant further investigation.

J. Heterocyclic Chem., **32**, 49 (1995).

The imidazolinone herbicides are a new class of compounds discovered [1] and developed [2-6] by American Cyanamid. Commercial formulations such as Arsenal®, Assert®, Pursuit® and Scepter® contain, as active ingredients, imidazolinones belonging to the general formula **1** (Scheme 1). According to a recent paper [7] they act as uncompetitive inhibitors of acetohydroxyacid synthase.

A Shell team [8] took into consideration a great number of related compounds **2**, acting as photosynthesis inhibitors, in order to evaluate the effect of the following features on the biological activity: substituents on the phenyl ring (R); nature of the linkage; nature of the bridge (ring size); presence of carbon or eteroatoms in the point indicated by **a**.

Scheme I

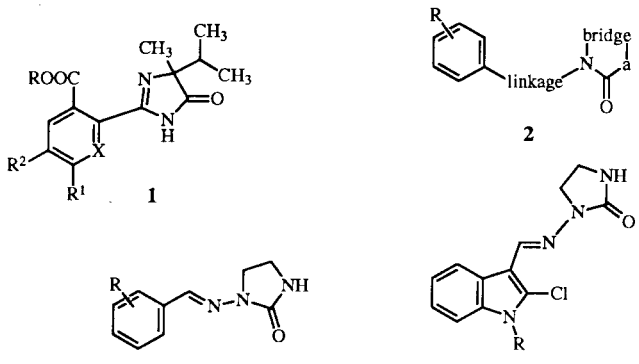

Table I
Compounds **4a-e**

Compound	R	Formula (mw)	Mp, °C	Calculated/Found %C	%H	%N	ν_{max} cm^{-1}	δ [a] ppm in $(CD_3)_2SO$	m/z (%)
4a	H	$C_{12}H_{11}ClN_4O$ (262.7)	274-275 dec	54.87 55.15	4.22 3.98	21.33 21.46	3170, 1725, 1710, 1265, 1230, 745	3.45 m, 2H (im), 3.77 m, 2H (im), 7.07 s, 1H (NH), 7.20 m, 2H (ind), 7.34 m, 1H (ind), 7.68 s, 1H (CH), 8.28 m, 1H (ind), 12.20 broad s, 1H (ind NH)	264 (M+2, 25), 262 (M+, 55), 176 (M-im, 72), 150 (100), 87 (47)
4b	CH_3	$C_{13}H_{13}ClN_4O$ (276.7)	225-227 dec	56.42 56.70	4.73 4.77	20.25 20.12	3420, 3230, 1700, 1275, 1230, 735	3.43 m, 2H (im), 3.75 m, 2H (im), 3.79 s, 3H (CH_3), 7.08 s, 1H (NH), 7.30 m, 2H (ind), 7.57 m, 1H (ind), 7.76 s, 1H (CH), 8.42 m, 1H (ind)	278 (M+2, 13), 276 (M+, 42), 190 (M-im, 100), 150 (24), 85 (13)
4c	CH_2CH_3	$C_{14}H_{15}ClN_4O$ (290.7)	210-212 dec	57.83 58.02	5.20 5.31	19.27 19.59	3280, 1720, 1675, 1265, 1220, 730	1.30 t, 3H (CH_3, J = 7.5), 3.49 m, 2H (im), 3.78 m, 2H (im), 4.31 q, 2H (CH_2, J = 7.5), 7.08 s, 1H (NH), 7.30 m, 2H (ind), 7.60 m, 1H (ind), 7.78 s, 1H (CH), 8.44 m, 1H (ind)	292 (M+2, 15), 290 (M+, 42), 204 (M-im, 100), 189 (39), 176 (18), 150 (19)
4d	C_6H_5	$C_{18}H_{15}ClN_4O$ (338.8)	233-236	63.81 64.08	4.46 4.42	16.54 16.73	3290, 1740, 1700, 1270, 1225, 740	3.48 m, 2H (im), 3.80 m, 2H (im), 7.09 m, 1H, (ar), 7.16 s, 1H (NH), 7.26 m, 2H (ind), 7.54 m, 2H (ar), 7.61 m, 1H (ind), 7.66 m, 2H (ar), 7.75 s, 1H (CH), 8.43 m, 1H (ind)	340 (M+2, 35), 338 (M+, 100), 252 (M-im, 86), 217 (14), 86 (14), 77 (16)
4e	$CH_2C_6H_4Cl(p)$	$C_{19}H_{16}Cl_2N_4O$ (387.3)	278-280 dec	58.93 58.69	4.16 3.98	14.47 14.24	3225, 3125, 1725, 1265, 1240, 750	3.48 m, 2H (im), 3.81 m, 2H (im), 5.57 s, 2H (CH_2), 7.14 s, 1H (NH), 7.16 d, 2H (ar, J = 8.5), 7.26 m, 2H (ind), 7.42 d, 2H (ar, J = 8.5), 7.59 m, 1H (ind), 7.73 s, 1H (CH), 8.39 m, 1H (ind)	388 (M+2, 24), 386 (M+, 26), 300 (M-im, 7), 150 (22), 125 (100), 101 (8), 89 (10), 86 (15)

[a] J given in Hz, im = 2-imidazolidinone, ind = indole, ar = aromatic.

Table II

Herbicidal Activity of Compounds **4a-e**

	A [a]	B	C	D
4a	CH, GD [b] (p) [c]	GR (P)	CB (P)	-
4b	CH (p), CB (P)	GR (p, P)	-	CB (P)
4d	-	-	CB (P)	CB (P)
4e	-	-	CB (P)	CB (P)

[a] Weeds: A = *Ipomoea hederacea*; B = *Abutilon theophrasti*; C = *Digitaria sanguinalis*; D = *Echinochloa crus-galli*. [b] Activity: CH = chlorosis; GD = growth distortion effect; GR = growth retarded; CB = contact burn. [c] Procedure: (p) = preemergence, 2 Kg/ha; (P) = postemergence, 1 Kg/ha.

The Authors found that some linkages (*e.g.* -N=CH-) produced inactive compounds, whereas compounds bearing other linkages (*e.g.* -CH=N-) were highly active. Moreover maximum activity was associated with five membered ring derivatives where **a** was NH. As a result of this study, compounds **3**, among others, proved to possess potent herbicide activity.

In the light of these findings and in connection with our previous paper on the synthesis of 2-chloroindole herbicides [9], we planned to synthesize a series of 1-substituted 2-chloro-3-(2-oxo-1-imidazolidinyliminomethyl)-indoles **4a-e** in order to evaluate their herbicidal activity.

Chemistry.

Compounds **4a-e** were prepared by reaction of the appropriate 1-substituted 2-chloroindole-3-carboxaldehyde with 1-amino-2-imidazolidinone: the spectroscopic data are in agreement with the assigned structures (Table I). In the ^{1}H-nmr spectra it is easy to recognize the 2-imidazolidinone ring from two bands of the methylene groups (~3.4 and 3.8 ppm) and the singlet of the NH group (~7.1 ppm); the methine group gives a sharp singlet at ~7.7 ppm. In the mass spectra, the molecular ion peak is always prominent (in compound **4d** it is the base peak): as expected, in compounds **4a-d** the M+2 peak is about 40% of the molecular ion peak and in compound **4e**, where two chlorine atoms are present, it is about 90%. In all the compounds, a peak is evident (indicated in Table I as M-im) from loss of 2-imidazolidinone (86): this is the base peak in compounds **4b-c**.

Biological Results.

Compounds **4a-e** were tested on four species of weeds according to the procedures reported in the experimental part. Compound **4c** was inactive; the other ones provided slight control in particular with postemergence application (see Table II). Nevertheless the level of activity, compared to that of commercially available herbicides, does not merit additional biological follow-up.

EXPERIMENTAL

a) Chemistry.

Melting points are uncorrected. Bakerflex plates (Silica gel IB2-F) were used for tlc; the eluent was a mixture of petroleum ether/acetone in various proportions. The ir spectra were recorded in Nujol on a Perkin-Elmer 298. The ^{1}H-nmr spectra were recorded on a Varian EM-390 (90 MHz) using TMS as an internal standard. The ms (EI) were recorded at 70 eV on a VG 7070 E.

General Procedure for the Synthesis of Compounds **4a-e**.

The appropriate 1-substituted 2-chloroindole-3-carboxaldehyde [10-13] (30 mmoles) was dissolved in ethanol (100 ml) and treated with the equivalent of 1-amino-2-imidazolidinone [14]. The mixture was refluxed for 1 hour and concentrated under reduced pressure. The precipitate thus formed was collected by filtration (90-95%) and crystallized from ethanol.

b) Biology (Herbicidal Activity).

Postemergence Procedure.

The species considered were grown in Matapeke silt loam soil (*p*H 6.5 and 1.2% organic matter) to which sand had been added at a level of 20%. Plants were grown 7-16 days prior to treatment. The test sample was dissolved in 90% aqueous acetone and sprayed on the foliage of the plants at a volume of 420 l/ha. Postemergence and preemergence applications were made at the same time. Treated and control plants were maintained in their respective greenhouse environments for 12 to 14 days before evaluation of phytotoxicity.

Preemergence Procedure.

The species considered were planted in Matapeke silt loam soil one day prior to treatment. The test compound was sprayed onto the soil surface of the pots (simultaneously with the foliar treatment, see above). The surface of the pots were lightly sprinkled with water to activate the test compound and the pots were placed in a greenhouse. Plants were grown in the greenhouse for 12 to 14 days before evaluation of phytotoxicity.

Acknowledgment.

We are grateful to du Pont, Agricultural Products Department, Wilmington, DE, for the evaluation of the herbicidal activity.

REFERENCES AND NOTES

[1] D. L. Shaner, K. Umeda, D. R. Ciarlante and M. Los, Proc. 1982 Brit. Crop Prot. Conf. Weeds, Vol **1**, 1982, p 25-31.

[2] M. Los, in Pesticide Synthesis through Rational Approaches, ACS Symposium Series 255, P. S. Magee, G. K. Kohn and J. J Menn, eds, 1984, p 29-44.

[3] M. Los, 6th Pestic. Sci. Biotechnol. Proc. Int. Congr. Pestic. Chem., 1986, R. Greenhalgh and T. R. Roberts, eds, 1987, p 35-42.

[4] M. A. Guaciaro, M. Los, R. K. Russel, P. J. Wepplo, B. L. Lences, P. C. Lauro, P. L. Orwick, K. Umeda and A. M. Pierre, in Synthesis and Chemistry of Agrochemicals, ACS Symposium Series, 355, D. R. Baker, J. G. Fenyes, W. K. Moberg and B. Cross, eds, 1987,

p 87-99.

[5] J. Finn, N. Quinn and B. Buckman, in Synthesis and Chemistry of Agrochemicals II, ACS Symposium Series, 443, D. R. Baker, J. G. Fenyes and W. K. Moberg, eds, 1991, p 133-143.

[6] M. A. Guaciaro, M. Los, D. L. Little, P. A. Marc and L. Quakenbush, in Synthesis and Chemistry of Agrochemicals III, ACS Symposium Series, 504, D. R. Baker, J. G. Fenyes and J. J. Steffens, eds, 1992, p 56-74.

[7] D. L. Shaner, P. C. Anderson and M. A. Stidham, *Plant Physiol.*, **76**, 545 (1984).

[8] K. H. Pilgram, W. D. Kollmeyer, R. D. Skiles and L. E. Wittsell, in Synthesis and Chemistry of Agrochemicals, ACS Symposium Series, 355, D. R. Baker, J. G. Fenyes, W. K. Moberg and B. Cross, eds, p 36-53.

[9] A. Andreani and M. Rambaldi, *J. Heterocyclic Chem.*, **25**, 1519 (1988).

[10] K. E. Schulte, J. Reisch and U. Stoess, *Angew. Chem., Int. Ed. Engl.*, **4**, 1081 (1965).

[11] A. Andreani, D. Bonazzi, V. Cavrini, R. Gatti, G. Giovanninetti, L. Franchi and A. Nanetti, *Farmaco, Ed. Sci.*, **32**, 703 (1977).

[12] A. Andreani, D. Bonazzi, M. Rambaldi, A. Guarnieri, F. Andreani, P. Strocchi and N. Montanaro, *J. Med. Chem.*, **20**, 1344 (1977).

[13] A. Andreani, M. Rambaldi, D. Bonazzi, F. Andreani, R. Bossa and I. Galatulas, *Arch. Pharm. (Weinheim)*, **317**, 847 (1984).

[14] J. G. Michels and G. Gever, *J. Am. Chem. Soc.*, **78**, 5349 (1956).