5-FORMYLIMIDAZO[2,1-*b*]THIAZOLES AND DERIVATIVES WITH HERBICIDAL ACTIVITY

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Dedicated to Dr Miroslav Protiva on the occasion of his 70th birthday.

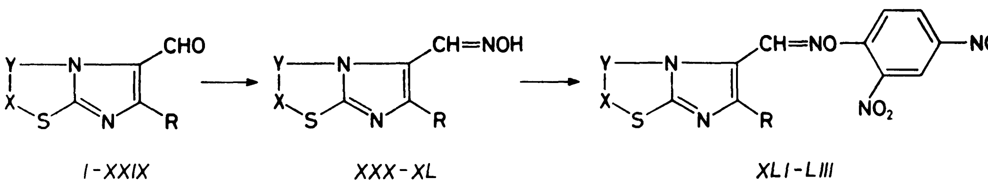
A series of imidazo[2,1-*b*]thiazole derivatives including aldehydes (*I*—*XXIX*), oximes (*XXX*—*XL*) and 2,4-dinitrophenyloximes (*XLI*—*LIII*) were prepared and tested as potential herbicides. Many compounds were active in paddy field treatment, sand and in water culture. In upland condition, a number of dinitrophenyloximes proved herbicides in postemergence treatment, whereas in pre-emergence only compounds *XVI*, *XXV* and *XLVIII* showed some degree of activity.

In 1979 we published[1] the synthesis of 5-formyl-6-phenylimidazo[2,1-*b*]thiazole *I* and we had the opportunity of preparing it again as an intermediate for the synthesis of potential antitumor[2] and antiinflammatory[3] agents. As far as we knew it had never been tested as agrochemical, so we decided to send a sample to SDS Biotech – Tokyo for a general screening. The result of biological testing was beyond our expectation, in fact it showed herbicidal activity on different species of plants. On this basis we planned the synthesis of a series of analogous 5-formyl derivatives differing at the position 2, 3 or 6 of the imidazo[2,1-*b*]thiazole moiety. Furthermore, as in our experience some indole dinitrophenyloximes were much more active as herbicides than the corresponding aldehydes[4], we decided to attempt this kind of derivatization even on the imidazo[2,1-*b*]thiazole skeleton.

RESULTS AND DISCUSSION

The aldehydes *I*–*XXIX* (Scheme 1) were prepared by means of the Vilsmeier reaction on the 6-substituted imidazo[2,1-*b*]thiazoles. Tables I–III report the reference for the known derivatives and the starting material reference for the still unknown ones. The aldehydes *I*–*XXIX* (Tab. I), treated with hydroxylamine hydrochloride afforded the oximes *XXX*–*XL* (Tab. II), which in turn, were the starting material for the synthesis of the 2,4-dinitrophenyloximes *XLI*–*LIII* (Tab. III). As a result of this work we obtained 53 compounds which were subjected to the biological tests. The IR and ^{1}H NMR data of the new compounds are in agreement with the assigned structures (Table IV).

The herbicidal activity of compounds *I*–*LIII* was evaluated according to the methods reported in the experimental section. In Experimental part we report the derivatives which showed a level of activity starting from, at least, 5. A great number of compounds were active in sand and water culture; many oximes and dinitrophenyloximes were also active against *Monochoria vaginalis* whereas only some dinitrophenyloximes could control even the growth of *Chrysanthemum coronarium*: in particular, among these derivatives, the behaviour of compound *XLVIII* is noteworthy because it was active even against two species in the preemergence test in upland condition. The activity against *Scirpus juncoides* in paddy field treatment seems peculiar of the parent compound *I*, since none of the derivatives could control this species.



X,Y,R see Tables I-III

SCHEME 1

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 EM390 (90 MHz) and signals are given in δ ppm relative to TMS as internal standard (J in Hz); the solvents employed are reported in Table IV.

Synthesis of the Aldehydes *VI*–*XI*, *XV*–*XIX*, *XXII*–*XXIV*, *XXVI*–*XXIX*

The Vilsmeier reagent was prepared at 0–5°C by dropping 0·1 mol of $POCl_3$ into a stirred solution of DMF (0·1 mol) in $CHCl_3$ (10 ml). The appropriate imidazo[2,1-*b*]thiazole (0·05 mol), dissolved in 100–200 ml of $CHCl_3$ and 0·1 mol of pyridine, was added dropwise, under stirring at 0–5°C, to the Vilsmeier reagent. After 3 h at room temperature, the reaction mixture was refluxed for 12 h and the solvent was evaporated under reduced pressure. The oily residue was poured onto ice and the resulting precipitate was collected and crystallized from ethanol with a yield of 60–70% (Table I).

TABLE I
Characterization of aldehydes *I*—*XXIX*

Compd.	X	Y	R	Start. mat. or ref.	Formula (M.w.)	M.p., °C	Calculated/Found % C	% H	% N
I[a]	CH	CH	C_6H_5						
II[b]	CH	CH	Cl						
III[a]	CH	CH	CH_3						
IV[c]	CH	CH	4-ClC_6H_4						
V[c]	CH	CH	4-$CH_3C_6H_4$						
VI	CH	CH	2-$CH_3OC_6H_4$	7	$C_{13}H_{10}N_2O_2S$ (258·3)	137—141	60·45 60·17	3·90 3·85	10·85 10·98
VII	CH	CH	4-$CH_3OC_6H_4$	8	$C_{13}H_{10}N_2O_2S$ (258·3)	143—146	60·45 60·85	3·90 3·90	10·85 10·80
VIII	CH	CH	3-$CF_3C_6H_4$	*LIV*	$C_{13}H_7F_3N_2OS$ (296·3)	140—144	52·70 52·55	2·38 2·27	9·46 9·54
IX	CH	CH	4-FC_6H_4	13	$C_{12}H_7FN_2OS$ (246·3)	172—175	58·52 58·75	2·87 2·94	11·38 11·22
X	CH	CH	2-pyridyl	9	$C_{11}H_7N_3OS$ (229·3)	194—198	57·63 57·47	3·08 3·25	18·33 18·35
XI	CH	CH	3-pyridyl	9	$C_{11}H_7N_3OS$ (229·3)	208—212	57·63 57·75	3·08 3·29	18·33 18·06
XII[d]	CH_2	CH_2	CH_3						
XIII[d]	CH_2	CH_2	C_6H_5						
XIV[c]	CH_2	CH_2	4-$CH_3C_6H_4$						

XV	CH_2	CH_2	2-$CH_3OC_6H_4$	7	$C_{13}H_{12}N_2O_2S$ (260·3)	140—142	59·98 60·12	4·65 4·53	10·76 10·87
XVI	CH_2	CH_2	4-$CH_3OC_6H_4$	7	$C_{13}H_{12}N_2O_2S$ (260·3)	148—152	59·98 60·00	4·65 4·74	10·76 10·58
XVII	CH_2	CH_2	3-$CF_3C_6H_4$	*LV*	$C_{13}H_9F_3N_2OS$ (298·3)	93—95	52·34 52·15	3·04 3·12	9·39 9·39
XVIII	CH_2	CH_2	4-FC_6H_4	*LVI*	$C_{12}H_9FN_2OS$ (248·3)	195—198	58·05 58·16	3·65 3·48	11·29 11·33
XIX	CH_2	CH_2	2-pyridyl	9	$C_{11}H_9N_3OS$ (231·3)	185—188	57·12 57·37	3·92 4·05	18·17 18·29
XX[e]	CCH_3	CH	C_6H_5						
XXI[f]	CCH_3	CH	4-ClC_6H_4						
XXII	CCH_3	CH	4-$CH_3C_6H_4$	11	$C_{14}H_{12}N_2OS$ (256·3)	145—147	65·60 65·48	4·72 4·63	10·93 10·88
XXIII	CCH_3	CH	3-$CF_3C_6H_4$	*LVII*	$C_{14}H_9F_3N_2OS$ (310·3)	110—112	54·19 54·22	2·92 2·75	9·03 9·12
XXIV	CCH_3	CH	4-FC_6H_4	*LVIII*	$C_{13}H_9FN_2OS$ (260·3)	163—165	59·98 60·10	3·49 3·55	10·76 10·98
XXV[e]	CH	CCH_3	C_6H_5						
XXVI	CH	CCH_3	3-$CF_3C_6H_4$	*LIX*	$C_{14}H_9F_3N_2OS$ (310·3)	124—125	54·19 54·50	2·92 2·83	9·03 8·98
XXVII	CH	CCH_3	4-FC_6H_4	*LX*	$C_{13}H_9FN_2OS$ (260·3)	188—191	59·98 59·84	3·49 3·38	10·76 10·66
XXVIII	CCH_3	CCH_3	C_6H_5	14	$C_{14}H_{12}N_2OS$ (256·3)	156—159	65·60 65·93	4·72 4·75	10·93 10·88
XXIX	CCl	CH	C_6H_5	15	$C_{12}H_7ClN_2OS$ (262·7)	130—131	54·86 54·92	2·68 2·63	10·66 10·46

For details see [a] ref.[1]; [b] ref.[5]; [c] ref.[6]; [d] ref.[2]; [e] ref.[10]; [f] ref.[12].

TABLE II
Characterization of oximes *XXX*—*XL*

Compd.	X	Y	R	Start. mat. or ref.	Formula (M.w.)	M.p., °C	Calculated/Found % C	% H	% N
XXX	CH	CH	4-ClC_6H_4	*IV*	$C_{12}H_8ClN_3OS$ (277·7)	226—230	51·89 52·09	2·90 2·87	15·13 15·02
XXXI	CH	CH	4-$CH_3C_6H_4$	*V*	$C_{13}H_{11}N_3OS$ (257·3)	205—209	60·68 60·77	4·31 4·52	16·33 16·30
XXXII	CH	CH	4-$CH_3OC_6H_4$	*VII*	$C_{13}H_{11}N_3O_2S$ (273·3)	202—205	57·13 57·41	4·06 4·12	15·37 15·34
XXXIII[a]	CH_2	CH_2	C_6H_5						
XXXIV	CH_2	CH_2	4-ClC_6H_4	6	$C_{12}H_{10}ClN_3OS$ (279·8)	262—266	51·52 51·45	3·60 3·53	15·02 15·21
XXXV	CH_2	CH_2	4-$CH_3C_6H_4$	*XIV*	$C_{13}H_{13}N_3OS$ (259·3)	238—242	60·21 60·34	5·05 5·25	16·20 16·20
XXXVI	CCH_3	CH	Cl	12	$C_7H_6ClN_3OS$ (215·7)	224—225	38·98 38·75	2·80 2·72	19·48 19·63
XXXVII	CCH_3	CH	CH_3	10	$C_8H_9N_3OS$ (195·2)	257—260	49·21 49·38	4·65 4·64	21·52 21·65
XXXVIII	CCH_3	CH	C_6H_5	*XX*	$C_{13}H_{11}N_3OS$ (257·3)	238—240	60·68 60·37	4·31 4·25	16·33 16·12
XXXIX	CCH_3	CH	4-ClC_6H_4	*XXI*	$C_{13}H_{10}ClN_3OS$ (291·8)	240—244	53·51 53·51	3·45 3·28	14·40 14·57
XL	CCH_3	CH	4-$CH_3C_6H_4$	*XXII*	$C_{14}H_{13}N_3OS$ (271·3)	208—210	61·97 61·79	4·83 4·87	15·49 15·36

[a] For details see ref.[3].

Table III

Characterization of O-(2,4-dinitrophenyl)oximes *XLI*–*LIII*

Compd.	X	Y	R	Start. mat. or ref.	Formula (M.w.)	M.p., °C	Calculated/Found % C	Calculated/Found % H	Calculated/Found % N
XLI	CH	CH	Cl	5	$C_{12}H_6ClN_5O_5S$ (367·7)	194–195	39·19 39·48	1·64 1·77	19·05 19·22
XLII	CH	CH	CH_3	3	$C_{13}H_9N_5O_5S$ (347·3)	201–203	44·95 44·64	2·61 2·60	20·17 20·40
XLIII	CH	CH	C_6H_5	3	$C_{18}H_{11}N_5O_5S$ (409·4)	195–197	52·81 52·88	2·71 2·75	17·11 17·34
XLIV	CH	CH	4-ClC_6H_4	*XXX*	$C_{18}H_{10}ClN_5O_5S$ (443·8)	220–222	48·71 48·92	2·27 2·25	15·78 15·71
XLV	CH	CH	4-$CH_3C_6H_4$	*XXXI*	$C_{19}H_{13}N_5O_5S$ (423·4)	205–209	53·89 53·99	3·09 3·03	16·54 16·22
XLVI	CH_2	CH_2	Cl	3	$C_{12}H_8ClN_5O_5S$ (369·7)	181–182	38·98 38·70	2·18 2·28	18·94 19·13
XLVII	CH_2	CH_2	CH_3	3	$C_{13}H_{11}N_5O_5S$ (349·3)	179–180	44·69 44·66	3·17 3·24	20·05 20·35
XLVIII	CH_2	CH_2	C_6H_5	3	$C_{18}H_{13}N_5O_5S$ (411·4)	194–195	52·55 52·17	3·18 3·14	17·02 17·06
XLIX	CH_2	CH_2	4-$CH_3C_6H_4$	*XXXV*	$C_{19}H_{15}N_5O_5S$ (425·4)	199–200	53·64 53·76	3·55 3·47	16·46 16·23
L	CCH_3	CH	Cl	*XXXVI*	$C_{13}H_8ClN_5O_5S$ (381·8)	181–183	40·90 40·86	2·11 2·31	18·35 18·51
LI	CCH_3	CH	C_6H_5	*XXXVIII*	$C_{19}H_{13}N_5O_5S$ (423·4)	188–189	53·89 54·12	3·09 3·17	16·54 16·32
LII	CCH_3	CH	4-ClC_6H_4	*XXXIX*	$C_{19}H_{12}ClN_5O_5S$ (457·9)	188–191	49·84 49·87	2·64 2·52	15·30 15·46
LIII	CCH_3	CH	4-$CH_3C_6H_4$	*XL*	$C_{20}H_{15}N_5O_5S$ (437·4)	191–193	54·91 55·11	3·46 3·34	16·01 16·23

TABLE IV

IR and ^{1}H NMR of the new compounds reported in Tables I—III

Compound	ν_{max}, cm^{-1}	^{1}H NMR
VI[a]	1 640, 1 340, 1 320, 1 240	3·80 s, 3 H (OCH_3); 7·2 m, 2 H (ar); 7·6 m, 2 H (ar); 7·65 d, 1 H (th, J = 4·4); 8·44 d, 1 H (th, J = 4·4); 9·75 s, 1 H (CHO)
VII[a]	1 630, 1 605 1 340, 1 250	3·82 s, 3 H (OCH_3); 7·07 d, 2 H (ar, J = 9); 7·55 d, 1 H (th, J = 4·4); 7·83 d, 2 H (ar, J = 9); 8·38 d, 1 H (th, J = 4·4); 9·85 s, 1 H (CHO)
VIII[a]	1 650, 1 630 1 520, 1 340	7·70 d, 1 H (th, J = 4·4); 7·8 m, 2 H (ar); 8·2 m, 2 H (ar); 8·50 d, 1 H (th, J = 4·4); 10·0 s, 1 H (CHO)
IX[a]	1 645, 1 340 1 320, 1 080	7·3 m, 2 H (ar); 7·64 d, 1 H (th, J = 4·4); 8·0 m, 2 H (ar); 8·45 d, 1 H (th, J = 4·4); 9·95 s, 1 H (CHO)
X[b]	1 630, 1 590 1 330, 1 260	7·08 d, 1 H (th, J = 4·4); 7·3 m, 1 H (py); 7·8 m, 1 H (py); 8·2 m, 1 H (py); 8·50 d, 1 H (th, J = 4·4); 8·7 m, 1 H (py); 10·90 s, 1 H (CHO)
XI[b]	1 635, 1 320 1 260, 1 080	7·12 d, 1 H (th, J = 4·4); 7·5 m, 1 H (py); 8·2 m, 1 H (py); 8·45 d, 1 H (th, J = 4·4); 8·8 m, 1 H (py); 9·1 m, 1 H (py); 10·0 s, 1 H (CHO)
XV[a]	1 645, 1 490 1 235, 1 085	3·76 s, 3 H (OCH_3); 4·0 m, 2 H (thn); 4·5 m, 2 H (thn); 7·1 m, 2 H (ar); 7·4 m, 2 H (ar); 9·52 s, 1 H (CHO)
XVI[a]	1 635, 1 600 1 320, 1 250	3·80 s, 3 H (OCH_3); 4·0 m, 2 H (thn); 4·5 m, 2 H (thn); 7·05 d, 2 H (ar, J = 9); 7·75 d, 2 H (ar, J = 9); 9·73 s, 1 H (CHO)
XVII[a]	1 655, 1 335 1 295, 1 110	4·0 m, 2 H (thn); 4·5 m, 2 H (thn); 7·8 m, 2 H (ar); 8·1 m, 2 H (ar); 9·80 s, 1 H (CHO)
XVIII[a]	1 640, 1 490 1 320, 1 215	4·0 m, 2 H (thn); 4·5 m, 2 H (thn); 7·3 m, 2 H (ar); 7·9 m, 2 H (ar); 9·75 s, 1 H (CHO)
XIX[b]	1 640, 1 590, 1 325, 1 255	3·9 m, 2 H (thn); 4·6 m, 2 H (thn); 7·3 m, 1 H (py); 7·8 m, 1 H (py); 8·1 m, 1 H (py); 8·6 m, 1 H (py); 10·80 s, 1 H (CHO)
XXII[c]	1 640, 1 320, 860, 815	2·38 s, 3 H ($C_6H_4CH_3$); 2·53 d, 3 H (CH_3 th, J = 1·4); 7·40 d, 2 H (ar, J = 9); 7·70 d, 2 H (ar, J = 9); 8·32 q, 1 H (th, J = 1·4); 9·95 s, 1 H (CHO)
XXIII[a]	1 645, 1 630, 1 310, 1 110	2·50 d, 3 H (CH_3, J = 1·4); 7·8 m, 2 H (ar); 8·2 m, 2 H (ar); 8·30 q, 1 H (th, J = 1·4); 10·0 s, 1 H (CHO)
XXIV[b]	1 650, 1 530, 1 490, 1 330	2·50 d, 3 H (CH_3, J = 1·4); 7·2 m, 2 H (ar); 7·8 m, 2 H (ar); 8·13 q, 1 H (th, J = 1·4); 9·90 s, 1 H (CHO)
XXVI[a]	1 660, 1 260, 1 180, 1 115	2·73 d, 3 H (CH_3, J = 1·4); 7·22 q, 1 H (th, J = 1·4); 7·9 m, 2 H (ar); 8·2 m, 2 H (ar); 9·90 s, 1 H (CHO)

TABLE IV
(*Continued*)

Compound	ν_{max}, cm^{-1}	^{1}H NMR
XXVII[b]	1 660, 1 525, 1 220, 830	2·78 d, 3 H (CH_3, *J* = 1·4); 6·54 q, 1 H (th, *J* = 1·4); 7·2 m, 2 H (ar); 7·7 m, 2 H (ar); 9·76 s, 1 H (CHO)
XXVIII[d]	1 660, 1 340, 1 315, 850	2·54 s, 3 H (CH_3); 2·84 s, 3 H (CH_3); 7·75 s, 5 H (ar); 9·82 s, 1 H (CHO)
XXIX[a]	1 635, 1 340, 1 315, 1 300	7·5 m, 3 H (ar); 7·9 m, 2 H (ar); 8·62 s, 1 H (th); 9·98 s, 1 H (CHO)
XXX[a]	3 150, 980, 880, 840	7·50 d, 1 H (th, *J* = 4·4); 7·55 d, 2 H (ar, *J* = 9); 7·75 d, 2 H (ar, *J* = 9); 8·15 d, 1 H (th, *J* = 4·4); 8·40 s, 1 H (CH=N); 11·40 s, 1 H (NOH)
XXXI[a]	3 430, 3 110, 1 610, 960	2·32 s, 3 H (CH_3); 7·30 d, 2 H (ar, *J* = 9); 7·45 d, 1 H (th, *J* = 4·4); 7·60 d, 2 H (ar, *J* = 9); 8·13 d, 1 H (th, *J* = 4·4); 8·40 s, 1 H (CH=N); 11·40 s, 1 H (NOH)
XXXII[a]	3 120, 1 610, 1 245, 835	3·84 s, 3 H (OCH_3); 7·10 d, 2 H (ar, *J* = 9); 7·48 d, 1 H (th, *J* = 4·4); 7·70 d, 2 H (ar, *J* = 9); 8·18 d, 1 H (th, *J* = 4·4); 8·40 s, 1 H (CH=N); 11·40 s, 1 H (NOH)
XXXIV[a]	3 120, 1 330, 980, 845	3·9 m, 2 H (thn); 4·4 m, 2 H (thn); 7·4 m, 2 H (ar, *J* = 9); 7·6 m, 2 H (ar, *J* = 9); 8·15 s, 1 H (CH=N); 11·40 s, 1 H (NOH)
XXXV[a]	3 440, 3 120, 1 335, 950	2·32 s, 3 H (CH_3); 3·9 m, 2 H (thn); 4·4 m, 2 H (thn); 7·2 m, 2 H (ar, *J* = 9); 7·4 m, 2 H (ar, *J* = 9); 8·13 s, 1 H (CH=N); 11·40 s, 1 H (NOH)
XXXVI[a]	3 180, 1 300 1 230, 865	2·45 d, 3 H (CH_3, *J* = 1·4); 7·81 q, 1 H (th, *J* = 1·4); 8·14 s, 1 H (CH=N); 11·40 s, 1 H (NOH)
XXXVII[a]	3 120, 1 620 970, 890	2·28 s, 3 H (CH_3, im); 2·42 d, 3 H (CH_3, th, *J* = 1·4); 7·78 q, 1 H (th, *J* = 1·4); 8·30 s, 1 H (CH=N); 11·10 s, 1 H (NOH)
XXXVIII[a]	3 110, 1 335, 975, 865	2·48 d, 3 H (CH_3, *J* = 1·4); 7·5 m, 3 H (ar); 7·7 m, 2 H (ar); 7·90 q, 1 H (th, *J* = 1·4); 8·35 s, 1 H (CH=N); 11·40 s, 1 H (NOH)
XXXIX[a]	3 110, 1 330, 975, 830	2·45 d, 3 H (CH_3, *J* = 1·4); 7·52 d, 2 H (ar, *J* = 9); 7·70 d, 2 H (ar, *J* = 9); 7·90 q, 1 H (th, *J* = 1·4); 8·36 s, 1 H (CH=N); 11·40 s, 1 H (NOH)
XL[a]	3 110, 1 335, 980, 870	2·34 s, 3 H ($C_6H_4CH_3$); 2·48 d, 3 H (CH_3, th, *J* = 1·4); 7·30 d, 2 H (ar, *J* = 9); 7·60 d, 2 H (ar, *J* = 9); 7·92 q, 1 H (th, *J* = 1·4); 8·38 s, 1 H (CH=N); 11·40 s, 1 H (NOH)
XLI[d]	1 605, 1 340, 1 240, 885	8·02 d, 1 H (th, *J* = 4·4); 8·18 d, 1 H (ar, *J* = 9); 8·70 d, 1 H (th, *J* = 4·4); 8·82 dd, 1 H (ar, *J* = 9, *J* = 3); 9·15 s, 1 H (CH=N); 9·20 d, 1 H (ar, *J* = 3)

TABLE IV
(*Continued*)

Compound	ν_{max}, cm^{-1}	^{1}H NMR
XLII[e]	1 590, 1 510, 1 340, 1 245	2·40 s, 3 H (CH_3); 7·63 d, 1 H (th, *J* = 4·4); 8·38 d, 1 H (ar, *J* = 9); 8·46 d, 1 H (th, *J* = 4·4); 8·65 dd, 1 H (ar, *J* = 9, *J* = 3); 8·98 d, 1 H (ar, *J* = 3); 9·33 s, 1 H (CH=N)
XLIII[d]	1 605, 1 585, 1 530, 1 310	7·83 s, 5 H (C_6H_5); 7·95 d, 1 H (th, *J* = 4·4); 8·17 d, 1 H (ar, *J* = 9); 8·8 d, 1 H (th, *J* = 4·4); 8·8 dd, 1 H (ar, *J* = 9, *J* = 3); 9·1 s, 1 H (CH=N); 9·1 d, 1 H (ar, *J* = 3)
XLIV[d]	1 605, 1 340, 1 315, 1 240	7·80 s, 4 H (clph); 7·92 d, 1 H (th, *J* = 4·4); 8·13 d, 1 H (ar, *J* = 9); 8·72 d, 1 H (th, *J* = 4·4); 8·90 dd, 1 H (ar, *J* = 9, *J* = 3); 9·05 s, 1 H (CH=N); 9·12 d, 1 H (ar, *J* = 3)
XLV[d]	1 605, 1 525, 1 340, 1 240	2·48 s, 3 H (CH_3); 7·52 d, 2 H (tol, *J* = 9); 7·64 d, 2 H (tol, *J* = 9); 7·82 d, 1 H (th, *J* = 4·4); 8·07 d, 1 H (ar, *J* = 9); 8·63 d, 1 H (th, *J* = 4·4); 8·70 dd, 1 H (ar, *J* = 9, *J* = 3); 9·0 s, 1 H (CH=N); 9·03 d, 1 H (ar, *J* = 3)
XLVI[a]	1 600, 1 525, 1 340, 1 235	4·0 m, 2 H (thn); 4·5 m, 2 H (thn); 8·05 d, 1 H (ar, *J* = 9); 8·58 dd, 1 H (ar, *J* = 9, *J* = 3); 8·68 s, 1 H (CH=N); 8·98 d, 1 H (ar, *J* = 3)
XLVII[a]	1 590, 1 340, 1 270, 1 250	2·26 s, 3 H (CH_3); 4·0 m, 2 H (thn); 4·5 m, 2 H (thn); 8·06 d, 1 H (ar, *J* = 9); 8·58 dd, 1 H (ar, *J* = 9, *J* = 3); 8·9 d, 1 H (ar, *J* = 3); 8·9 s, 1 H (CH=N)
XLVIII[a]	1 605, 1 510, 1 340, 1 245	4·1 m, 2 H (thn); 4·6 m, 2 H (thn); 7·6 m, 5 H (C_6H_5); 8·04 d, 1 H (ar, *J* = 9); 8·55 dd, 1 H (ar, *J* = 9, *J* = 3); 8·70 s, 1 H (CH=N); 8·88 d, 1 H (ar, *J* = 3)
XLIX[c]	1 600, 1 520, 1 330, 1 240	2·47 s, 3 H (CH_3); 4·4 m, 2 H (thn); 5·0 m, 2 H (thn); 7·42 d, 2 H (tol, *J* = 9); 7·62 d, 2 H (tol, *J* = 9); 7·96 d, 1 H (ar, *J* = 9); 8·60 dd, 1 H (ar, *J* = 9, *J* = 3); 8·71 s, 1 H (CH=N); 8·91 d, 1 H (ar, *J* = 3)
L[d]	1 605, 1 525, 1 340, 1 245	2·76 d, 3 H (CH_3, *J* = 1·4); 8·03 d, 1 H (ar, *J* = 9); 8·30 q, 1 H (th, *J* = 1·4); 8·72 dd, 1 H (ar, *J* = 9, *J* = 3); 8·98 s, 1 H (CH=N); 9·06 d, 1 H (ar, *J* = 3)
LI[d]	1 595, 1 520, 1 330, 1 230	2·75 d, 3 H (CH_3, *J* = 1·4); 7·77 s, 5 H (C_6H_5); 8·10 d, 1 H (ar, *J* = 9); 8·38 q, 1 H (th, *J* = 1·4); 8·75 dd, 1 H (ar, *J* = 9, *J* = 3); 8·99 s, 1 H (CH=N); 9·10 d, 1 H (ar, *J* = 3)

TABLE IV
(*Continued*)

Compound	ν_{max}, cm^{-1}	^1H NMR
LII[d]	1 605, 1 525, 1 335, 1 265	2·85 d, 3 H (CH_3, J = 1·4); 7·80 s, 4 H (clph); 8·13 d, 1 H (ar, J = 9); 8·43 q, 1 H (th, J = 1·4); 8·80 dd, 1 H (ar, J = 9, J = 3); 9·02 s, 1 H (CH=N); 9·11 d, 1 H (ar, J = 3)
LIII[d]	1 605, 1 530, 1 340, 1 260	2·59 s, 3 H ($C_6H_4CH_3$); 2·80 d, 3 H (CH_3, th, J = 1·4); 7·55 d, 2 H (tol, J = 9); 7·72 d, 2 H (tol, J = 9); 8·10 d, 1 H (ar, J = 9); 8·38 q, 1 H (th, J = 1·4); 8·78 dd, 1 H (ar, J = 9, J = 3); 9·0 s, 1 H (CH=N); 9·11 d, 1 H (ar, J = 3)

Ar aromatic; th thiazole; thn thiazoline; im imidazole; py pyridine; tol -$C_6H_4CH_3$; clph -C_6H_4Cl. Solvents for NMR measurements: [a] $(CD_3)_2SO$; [b] $CDCl_3$; [c] $(CD_3)_2SO + CF_3CO_2D$; [d] CF_3CO_2.D; [e] N,N′-dimethylpropyleneurea.

Synthesis of the Oximes *XXX*–*XXXII*, *XXXIV*–*XL*

The aldehyde (10 mmol) was dissolved in 50–100 ml of ethanol and treated with a solution of hydroxylamine hydrochloride (10 mmol) in H_2O (10 ml). The reaction mixture was treated with few drops of 15% NH_4OH (pH ≃ 6) and refluxed for 1 h. After cooling, the crude oxime was collected (yield 90%) and crystallized from ethanol (Table II).

Synthesis of O-2,4-Dinitrophenyloximes *XLI*–*LIII*

The oxime (20 mmol) was treated with sodium ethoxide (prepared from 22 mmol of Na and 50 ml of absolute ethanol) and 2,4-dinitrochlorobenzene (20 mmol). The mixture was stirred at room temperature for 3 h and the resulting precipitate was filtered and washed with hot ethanol (yield 80%) (see Table III).

6-(*m*-Trifluoromethylphenyl)imidazo[2,1-*b*]thiazole *LIV*

2-Aminothiazole (60 mmol) was dissolved in 80 ml of acetone and treated with the equivalent of α-bromo-*m*-trifluoromethylacetophenone. The mixture was refluxed for 2 h and the resulting precipitate, collected by filtration, was refluxed for 1 h with 300 ml of 2M-HBr. In order to obtain the free base, the solution was treated with 15% NH_4OH until became basic. The precipitate thus formed was collected and crystallized from petroleum ether with a yield of 75%; m.p. 77–79°C; IR (ν_{max}): 1 320, 1 110, 1 055, 640 cm^{-1}; ^1H NMR ($(CD_3)_2SO$): 7·30 d, 1 H (th, J = 4·4), 7·6 m, 2 H (ar), 8·0 d, 1 H (th, J = 4·4), 8·2 m, 2 H (ar), 8·45 s, 1 H (im). For $C_{12}H_7F_3N_2S$ (268·3) calculated: 53·72% C, 2·63% H, 10·44% N; found: 53·65% C, 2·77% H, 10·52% N.

With the same procedure and yield described for compound *LIV* the following derivatives were also prepared: *LV* (from 2-amino-2-thiazoline), *LVII* (from 2-amino-5-methylthiazole), *LIX* (from 2-amino-4-methylthiazole).

2,3-Dihydro-6-(*m*-trifluoromethylphenyl)imidazo[2,1-*b*]thiazole *LV*

M.p. 90–92°C (petroleum ether); IR (ν_{max}): 1 320, 1 280, 1 105, 1 070 cm^{-1}; ^1H NMR ($(CD_3)_2$.SO): 3·9 m, 2 H (thn), 4·3 m, 2 H (thn), 7·6 m, 2 H (thn), 8·0 s, 1 H (im), 8·0 m, 2 H (ar). For $C_{12}H_9F_3N_2S$ (270·3) calculated: 53·32% C, 3·36% H, 10·37% N; found: 53·55% C, 3·18% H, 10·32% N.

2-Methyl-6-(*m*-trifluoromethylphenyl)imidazo[2,1-*b*]thiazole *LVII*

M.p. 119–122°C (ethanol): IR (ν_{max}): 1 325, 1 285, 1 180, 1 105 cm^{-1}; ^1H NMR $(CD_3)_2SO$): 2·38 d, 3 H (CH_3, J = 1·4), 7·6 m, 2 H (ar), 7·6 q, 1 H (th, J = 1·4), 8·2 m, 2 H (ar), 8·36 s, 1 H (im). For $C_{13}H_9F_3N_2S$ (282·3) calculated: 55·31% C, 3·21% H, 9·93% N; found: 55·12% C, 2·98% H, 10·05% N.

3-Methyl-6-(*m*-trifluoromethylphenyl)imidazo[2,1-*b*]thiazole *LIX*

M.p. 110–113°C (ethanol): IR (ν_{max}): 1 330, 1 290, 1 150, 1 110 cm^{-1}; ^1H NMR ($(CD_3)_2SO$): 2·45 d, 3 H (CH_3, J = 1·4), 6·96 q, 1 H (th, J = 1·4), 7·6 m, 2 H (ar), 8·2 m, 2 H (ar), 8·50 s, 1 H (im). For $C_{13}H_9F_3N_2S$ (282·3) calculated: 55·31% C, 3·21% H, 9·93% N; found: 55·43% C, 3·52% H, 9·87% N.

With a procedure analogous to that described for compound *LIV*, but starting from α-bromo-*p*-fluoroacetophenone, the following derivatives were prepared (yield 60%): *LVI* (from 2-amino-2-thiazoline), *LVIII* (from 2-amino-5-methylthiazole), *LX* (from 2-amino-4-methylthiazole).

2,3-Dihydro-6-(*p*-fluorophenyl)imidazo[2,1-*b*]thiazole *LVI*

M.p. 155–156°C (ethanol): IR (ν_{max}): 1 540, 1 205, 830, 750 cm^{-1}; ^1H NMR ($(CD_3)_2SO$): 3·9 m, 2 H (thn), 4·2 m, 2 H (thn), 7·2 m, 2 H (ar), 7·7 s, 1 H (im), 7·7 m, 2 H (ar). For $C_{11}H_9F$.N_2S (220·3) calculated: 59·98% C, 4·12% H, 12·72% N; found: 60·15% C, 4·00% H, 12·94% N.

2-Methyl-6-(*p*-fluorophenyl)imidazo[2,1-*b*]thiazole *LVIII*

M.p. 203–208°C (ethanol): IR (ν_{max}): 1 540, 1 210, 835, 730 cm^{-1}; ^1H NMR ($(CD_3)_2SO$ + CF_3COOD): 2·50 d, 3 H (CH_3, J = 1·4), 7·3 m, 2 H (ar), 7·9 m, 2 H (ar), 7·9 q, 1 H (th, J = 1·4), 8·44 s, 1 H (im). For $C_{12}H_9FN_2S$ (232·3) calculated: 62·05% C, 3·91% H, 12·06% N; found: 62·15% C, 3·78% H, 11·87% N.

3-Methyl-6-(*p*-fluorophenyl)imidazo[2,1-*b*]thiazole *LX*

M.p. 116–118°C (ethanol): IR (ν_{max}): 1 540, 1 220, 1 145, 825 cm^{-1}; ^1H NMR ($(CD_3)_2SO$), 2·42 d, 3 H (CH_3, J = 1·4), 6·90 q, 1 H (th, J = 1·4), 7·3 m, 2 H (ar), 7·9 m, 2 H (ar), 8·25 s, 1 H (im). For $C_{12}H_9FN_2S$ (232·3) calculated: 62·05% C, 3·91% H, 12·06% N; found: 61·88% C 3·90% H, 12·26% N.

b) Biology

The herbicidal activity was evaluated in five tests. Two weeks after the treatment, the effectiveness and plant response were rated from 0 (no effect) to 10 (complete kill). Only values from 5 to 10 are reported bellow.

(i) Upland, preemergence (1 kg/ha): immediately after the plants were seeded, a suspension of the compound under test was sprayed on the surface soil. *Digitaria ciliaris*: *XXV* (5). *Brassica napus*: *XVI* (8), *XLVIII* (8). *Chrysanthemum coronarium*: *XLVIII* (8).

(ii) Upland, postemergence (1 kg/ha): a suspension of the test compound was sprayed on the plants at one leaf stage of *Digitaria ciliaris*: *XXX* (5). *Chrysanthemum coronarium*: *XXV* (5), *XLI* (8), *XLII* (5), *XLVI* (6), *XLVII* (7), *XLVIII* (5), *LIII* (6).

(iii) Paddy (1 kg/ha): a suspension of the test compound was applied by means of a pipet at one leaf stage of *Echinochloa crus-galli*: *I* (10), *XII* (8), *XV* (7). *Scirpus juncoides*: *I* (9). *Monochoria vaginalis*: *XXI* (5), *XXX* (6), *XXXI* (5), *XXXII* (8), *XXXIII* (7), *XXXV* (8), *XXXVIII* (5), *XL* (7), *XLI* (5), *XLVII* (8), *XLVIII* (5), *L* (9). *Ammania multiflora*: *XII* (5), *XXXII* (8), *XXXV* (5), *XLI* (8), *L* (8).

(iv) Sand culture (50 ppm): the plants were seeded on quarz sand containing a suspension of the test compound. *Echinochloa crus-galli*: *VII* (5), *X* (9), *XIX* (9), *XLI* (6), *XLII* (6), *XLV* (7), *XLVI* (6), *XLVII* (6), *XLVIII* (6), *L* (6). *Lactuca sativa*: *I* (5), *IX* (9), *X* (10), *XIX* (9), *XXIV* (10), *XXXII* (9), *XXXIII* (10), *XXXV* (10), *XXXIX* (8), *XLI* (7), *XLII* (5), *XLVI* (5), *XLVIII* (7), *L* (8).

(v) Water culture (50 ppm): the plant was transferred into a suspension of the compound under test. *Lemna minor*: *I* (10), *VIII* (8), *IX* (5), *XVIII* (5), *XXVI* (7), *XXX* (9), *XXXII* (10), *XXXIII* (10), *XXXV* (10), *LI* (7).

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