N-Substituted 2,4,5-Tribromoimidazole Derivatives

M. VEVERKA and A. DOVIČIČOVÁ

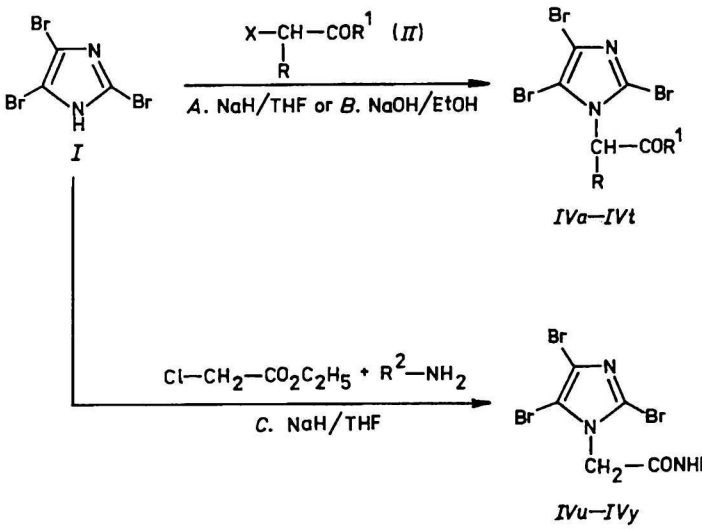
Institute of Biotechnology, Slovak Technical University, CS-812 37 Bratislava

Received 3 May 1991
Accepted for publication 20 January 1992

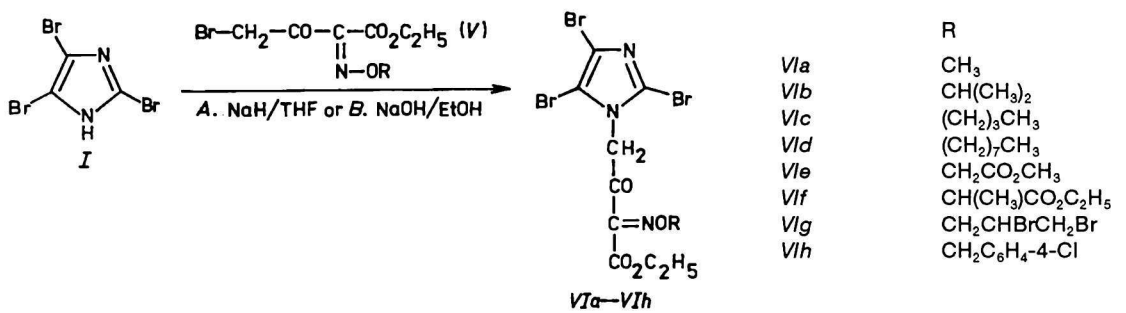
Synthesis of *N*-substituted 2,4,5-tribromoimidazole derivatives with potential pesticide activity is described.

As known [1], 1-substituted trihaloimidazoles and 2-(hydroxyimino)-3-oxobutanoates [2, 3] reveal pesticide activities. Relationship between the structure and biological activity of *N*-substituted tribromoimidazoles was also reported [4, 5]. Because the derivatives of 1-imidazolylacetic acid have been relatively little investigated [6—8] with respect to their 1-carboxy analogues [4, 5, 9—11], we prepared a series of (2,4,5-tribromo-1-imidazolyl)-acetates *IV* (Scheme 1) and 4-(2,4,5-tribromo-1-imidazolyl)-2-(alkoxyimino)-3-oxobutanoates *VI* (Scheme 2).

The *N*-substituted tribromoimidazoles *IVa—IVt* were prepared either from 2,4,5-tribromoimidazole [12] and sodium hydride in tetrahydrofuran and alkylation of the intermediate with α-haloacetic acid



Scheme 1



Scheme 2

II (method *A*), or from sodium salt of tribromoimidazole obtained with sodium hydroxide in ethanol and an alkylation reagent *II* in toluene or benzene (method *B*), or from ethyl (2,4,5-tribromo-1-

imidazolyl)acetate [7] and the respective substituted aniline (amides *IVu—IVy*, method *C*).

The starting α-haloacetates were obtained from α-haloacetyl chlorides or their analogues and the respective alcohols or substituted anilines in the presence of organic or inorganic bases [13]. Elemental analyses, yields, and melting points are listed in Tables 1 (compounds *IVa—IVt*) and 2 (*IVu—IVy*).

The starting 4-bromo-2-alkoxyimino-3-oxobutanoates *V*, synthesized from ethyl acetoacetate according to [14, 15], were reacted with 2,4,5-tribromoimidazole to give the required α-alkoxyimino-3-oxobutanoates *VIa—VIh*. Separation of the products by column chromatography yielded, in addition to the starting material, pure compounds *VIa—VIh* (monitored by thin-layer chromatography in various solvents — Table 3).

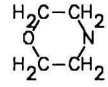
The IR spectra of compounds *IV* revealed strong absorption bands at $\tilde{\nu}$ = 1650—1780 cm^{-1} (ν(CO)) and 1600—1610 cm^{-1} (ν(C=N)). Also the IR spectra of compounds *VIa—VIh* disclosed strong stretching vibrations at $\tilde{\nu}$ = 1720—1780 cm^{-1} (ν(CO) – carbonyl of the ester and 3-oxo group).

The ^{1}H NMR spectra of 2,4,5-tribromoimidazoles *IVa—IVy* showed singlets of CH_2 protons at nitrogen at δ = 4.57—5.13 (Table 4), while those of 3-oxobutanoates *VI* at δ = 5.23—5.47 (due to the absence of acetyl group – Table 3).

EXPERIMENTAL

The melting points are corrected, the ^{1}H NMR spectra of deuterochloroform solutions, contain-

Table 1. Characteristic Data for *N*-Substituted (2,4,5-Tribromo-1-imidazolyl)acetates *IVa—IVt*

Compound	R	R[1]	Formula	w_i(calc.)/% w_i(found)/%			Yield/%	M.p./°C	$\tilde{\nu}$/cm^{-1}
			M_r	C	H	N	Method		ν(C=O)
IVa	H	C_2H_5O	$C_7H_7Br_3N_2O_2$	21.50	1.80	7.16	79	96—98	1710
			390.9	21.64	1.92	6.98	*A*		
IVb	H		$C_9H_{10}Br_3N_3O_2$	25.03	2.33	6.49	73	106—108	1650
			431.9	24.88	2.41	6.52	*A, B*		
IVc	H	2-Cl-5-NO_2—C_6H_3NH	$C_{11}H_6Br_3ClN_4O_3$	25.53	1.16	10.82	64	256—258	1680
			517.4	25.62	1.19	10.91	*A*		
IVd	H	3-CH_3—C_6H_4NH	$C_{12}H_{10}Br_3N_3O$	31.88	2.23	9.29	81	198—202	1660
			452.0	31.88	2.25	9.31	*B*		
IVe	H	3-CF_3—C_6H_4NH	$C_{12}H_7Br_3F_3N_3O$	28.48	1.39	8.30	36	192—193	1660
			505.9	28.49	1.59	8.42	*B*		
IVf	H	2-Cl-4-NO_2—C_6H_3NH	$C_{11}H_6Br_3ClN_4O_3$	25.53	1.16	10.82	72	257—260	1680
			517.4	25.67	1.10	10.95	*A*		
IVg	H	$Cl(CH_2)_3O$	$C_8H_8Br_3ClN_2O_2$	21.86	1.83	6.37	65	Oil	1750
			439.4	21.91	1.79	6.42	*A*		
IVh	H	CH_3OCHCH_2O (CH$_3$)	$C_9H_{11}Br_3N_2O_3$	24.85	2.54	6.44	48	Oil[a]	1735
			434.9	24.97	2.59	6.50	*A*		
IVi	H	CH_3CHO (CH_2OCH_3)	$C_9H_{11}Br_3N_2O_3$	24.36	2.55	6.44	75	Oil	1735
			434.9	25.00	2.62	6.39	*A*		
IVj	H	$NCCH_2CH_2O$	$C_8H_6Br_3N_3O_2$	23.10	1.45	10.10	79	Oil	1740
			415.9	23.19	1.48	11.00	*A*		
IVk	H	2,6-diCH_3—C_6H_3O	$C_{13}H_{11}Br_3N_2O_2$	33.43	2.37	6.00	71	179—181	1760
			467.0	33.59	2.41	6.11	*A*		
IVl	H	2-CH_3—C_6H_4O	$C_{12}H_9Br_3N_2O_2$	31.81	2.00	6.18	54	114—116	1755
			453.0	31.79	2.11	6.27	*A*		
IVm	H	2-Cl-4-NO_2—C_6H_3O	$C_{11}H_5Br_3ClN_3O_4$	25.48	0.97	8.10	32	43	1745
			518.4	25.55	0.89	8.12	*A*		
IVn	H	2-CH_3-4-Cl—C_6H_3O	$C_{12}H_8Br_3ClN_2O_2$	29.56	1.65	5.75	79	119—121	1770
			487.4	29.49	1.49	5.67	*A*		
IVo	H	HO	$C_5H_3Br_3N_2O_2$	16.54	0.83	7.72	75	186—188	1710
			362.8	16.59	0.80	7.96	*A*		
IVp	H	2-CH_3-4-NO_2—C_6H_3O	$C_{12}H_8Br_3N_3O_4$	28.94	1.61	8.43	63	155—157	1780
			498.0	28.75	1.79	8.52	*A*		
IVr	H	$(CH_2{=}CH{-}CH_2)_2N$	$C_{11}H_{12}Br_3N_3$	29.89	2.74	9.51	67	106—107	–
			442.0	29.71	2.79	9.52	*A*		
IVs	CH_3CO	C_2H_5O	$C_9H_9Br_3N_2O_3$	24.97	2.10	6.47	62	76—79	1755
			433.0	24.85	2.15	6.32	*A*		
IVt	CH_3	C_2H_5O	$C_8H_9Br_3N_2O_2$	23.72	2.24	6.91	72	79—81	1740
			404.9	23.86	2.29	6.83	*A*		

a) B.p.(9.33 Pa) = 170 °C.

Table 2. Characteristic Data for *N*-Substituted (2,4,5-Tribromo-1-imidazolyl)acetates *IVu—IVy*

Compound	R^2	Formula M_r	w_i(calc.)/% w_i(found)/% C	H	N	Yield/% Method	M.p./°C	$\tilde{\nu}$/cm^{-1} ν(C=O)
IVu	C_6H_5	$C_{11}H_8Br_3N_3O$ 437.9	30.16 30.22	1.84 1.96	9.54 9.49	82 *C*	228—230	1660
IVv	2-C_2H_5-6-CH_3—C_6H_3	$C_{14}H_{14}Br_3N_3O$ 480.0	35.02 35.08	2.93 2.99	8.75 8.68	68 *C*	242—245	1665
IVw	2-F-3-Cl—C_6H_3	$C_{11}H_6Br_3ClFN_3O$ 490.4	26.94 27.05	1.23 1.33	8.57 8.61	42 *C*	218—221	–
IVx	C_2H_5	$C_9H_{12}Br_3N_3O$ 418.0	25.86 25.81	2.89 2.92	10.05 10.18	54 *C*	Oil	–
IVy	4-F-C_6H_4	$C_{11}H_7Br_3FN_3O$ 455.9	28.98 29.02	1.55 1.67	9.22 5.24	35 *C*	200—203	–

Table 3. Characteristic Data for 4-(2,4,5-Tribromo-1-imidazolyl)-2-(alkoxyimino)-3-oxobutanoates *VIa—VIh*

Compound	Formula M_r	w_i(calc.)/% w_i(found)/% C	H	N	Yield/% Method	M.p./°C	^{1}H NMR chemical shifts for =N—OR; N—CH_2
VIa	$C_{10}H_{10}Br_3N_3O_4$ 476.0	25.23 25.82	2.11 2.28	8.82 8.71	28 *A*	116—118	4.19 (s, 3H, CH_3), 5.47 (s, 2H, N—CH_2)
VIb	$C_{12}H_{14}Br_3N_3O_4$ 504.0	26.21 27.00	2.79 2.71	8.33 8.15	22 *A*	132—135	4.50 (m, 1H, CH), 1.39 (d, 6H, 2 × CH_3), 5.23 (s, 2H, N—CH_2)
VIc	$C_{13}H_{16}Br_3N_3O_4$ 518.0	30.13 30.80	3.11 3.19	8.11 8.21	24 *A*	81—82	4.37 (br s, 2H, CH_2), 1.76 (m, 2H, CH_2), 1.42 (m, 2H, CH_2), 0.97 (m, 3H, CH_3), 5.23 (s, 2H, N—CH_2)
VId	$C_{17}H_{24}Br_3N_3O_4$ 574.1	35.57 35.62	4.21 4.18	7.32 7.47	51 *B*	69—73	4.30 (br s, 2H, CH_2), 1.3—1.7 (m, 12H, CH_2), 0.89 (m, 3H, CH_3), 5.24 (s, 2H, N—CH_2)
VIe	$C_{12}H_{12}Br_3N_3O_6$ 534.0	26.98 26.71	2.26 2.41	7.86 7.89	21 *B*	Solidifying oil	4.87 (s, 2H, CH_2), 3.80 (s, 3H, CH_3), 5.19 (s, 2H, N—CH_2)
VIf	$C_{14}H_{16}Br_3N_3O_6$ 562.0	29.91 28.86	2.86 2.72	7.47 7.41	26 *B*	Solidifying oil	4.97 (q, 1H, CH), 1.63 (d, 3H, CH_3), 4.27 (q, 2H, CH_2O), 1.32 (t, 3H, CH_3), 5.20 (s, 2H, N—CH_2)
VIg	$C_{12}H_{12}Br_5N_3O_4$ 661.8	21.77 21.59	1.82 1.75	6.34 6.28	34 *A*	Solidifying oil	4.80 (d, 1H, CH), 4.40 (m, 2H, CH_2), 3.80 (d, 2H, CH_2), 5.25 (s, 2H, N—CH_2)
VIh	$C_{16}H_{13}Br_3ClN_3O_4$ 586.5	32.77	2.23	7.17	64 *B*	179—182	5.35 (s, 2H, CH_2), 7.33 (m, 4H, H_{arom}), 5.18 (s, 2H, N—CH_2)

ing tetramethylsilane as internal reference, were measured with an instrument IX-100 (Jeol), the IR spectra were recorded with a spectrophotometer PU 9800 FTIR (Philips Analytical) in KBr pellets. Samples of products were dried over phosphorus pentaoxide at 60 Pa and room temperature, or in air. The reaction course was monitored on Silufol (Kavalier) sheets, detection was performed with UV (254 nm) light or by iodine vapours. The products were purified by column chromatography on silica gel (30 g, grain size 60—120 μm per 1 g of the substance), solvent system benzene—acetone (φ_r = 10 : 1). Products *IVa—IVy* and *VIa—VIh* were crystallized from ethanol and toluene, respectively.

(2,4,5-Tribromo-1-imidazolyl)acetates *IVa—IVy* and 4-(2,4,5-Tribromo-1-imidazolyl)-2-(alkoxyimino)-3-oxobutanoates *VIa—VIh*

Method A. 2,4,5-Tribromoimidazole (10 g; 30 mmol) was added to a suspension of sodium hydride (0.83 g; 35 mmol) in dry tetrahydrofuran (50 cm^3). The respective α-halogen derivative of acid *II*, or 4-bromo-2-alkoxyimino-3-oxobutanoate *V* (30 mmol) was added to the stirred mixture at room temperature. After 12 h stirring acetic acid was dripped into acid reaction, the suspension was filtered, the filtrate was concentrated under reduced pressure and crystallized or distilled under diminished pressure. Compounds *VIa—VIc*, *VIg* were purified by column chromatography. Characteristic data are presented in Tables 1—3.

Method B. 2,4,5-Tribromoimidazole (10 g; 30 mmol) was poured into the solution of sodium hydroxide (1.4 g; 35 mmol) in ethanol (50 cm^3). Toluene (70 cm^3) and the respective α-halogen derivative of acid *II*, or 4-bromo-2-alkoxyimino-3-oxobutanoate *V* (30 mmol) was added to the dried sodium salt, the mixture was refluxed for 6 h and acidified with acetic acid. The suspension was fil-

Table 4. ^{1}H NMR Chemical Shift Values of Selected (2,4,5-Tribromo-1-imidazolyl)acetates

Compound	δ
IVb	5.04 (s, 2H, CH_2—N), 3.50—3.61 t
IVc	5.13 (s, 2H, CH_2—N), 7.78—8.70 (m, 3H, H_{arom}), 10.55 (s, 1H, N—H_{amide})
IVd	4.90 (s, 2H, CH_2—N), 6.87—7.43 (m, 4H, H_{arom}), 10.48 (s, 1H, N—H_{amide}), 2.27 (s, 3H, CH_3)
IVe	4.96 (s, 2H, CH_2—N), 7.35—8.06 (m, 4H, H_{arom}), 10.92 (s, 1H, N—H_{amide})
IVg	4.99 (s, 2H, CH_2—N), 4.29 (t, 2H, CH_2), 2.06 (m, 2H, CH_2), 3.69 (t, 2H, CH_2)
IVh	4.97 (s, 2H, CH_2—N), 1.07 (d, 3H, CH_3), 3.51 (q, 2H, OCH_2), 3.48 (m, 1H, CH), 3.24 (s, 3H, CH_3)
IVi	4.93 (s, 2H, CH_2—N), 1.18 (d, 3H, CH_3), 3.25 (s, 3H, CH_3), 3.24 (m, 5H), 3.27 (m, 1H, CH)
IVj	4.88 (s, 2H, CH_2—N), 4.49 (t, 2H, CH_2), 2.81 (t, 2H, CH_2)
IVk	5.39 (s, 2H, CH_2—N), 2.11 (s, 6H, 2 × CH_3)
IVl	5.02 (s, 2H, CH_2—N), 2.19 (s, 3H, CH_3)
IVn	5.02 (s, 2H, CH_2—N), 2.16 (s, 3H, CH_3)
IVu	4.91 (s, 2H, CH_2—N), 7.03—7.06 (m, 5H, H_{arom}), 10.52 (s, 1H, N—H_{amide})
IVv	4.87 (s, 2H, CH_2—N), 7.18—7.26 (m, 3H, H_{arom}), 2.17 (s, 3H, CH_3), 3.61 (q, 2H, CH_2), 1.03 (t, 3H, CH_3)

tered, the solvent was removed *in vacuo* and the products were purified either by crystallization or distillation. Derivatives *IVe*, *VId*, *VIe*, *VIf*, *VIh* were purified by chromatography. Characteristic data of these compounds are listed in Tables 1, 3, 4.

Method C. Ethyl (2,4,5-tribromo-1-imidazolyl)-acetate (3.9 g; 10 mmol) and the substituted aniline (10 mmol) were refluxed in toluene (70 cm^3). The mixture was then concentrated under reduced pressure and the compounds *IVu—IVy* were purified by column chromatography. Characteristic data of the above-mentioned compounds are shown in Table 2.

(2,4,5-Tribromo-1-imidazolyl)acetic Acid (*IVo*)

2,4,5-Tribromoimidazole (0.6 g) and bromoacetic acid (0.3 g) were stirred in sodium hydroxide (0.15 g) in water (15 cm^3) for 24 h. Product *IVo*, precipitated by addition of acetic acid, was filtered off and crystallized from benzene.

REFERENCES

1. Brookes, R. F., Goodson, D. H., Greenwood, D., Johns, M., and Leafe, E. L., *Neth.* 6609596; *Chem. Abstr. 67,* 64398b (1967).
2. Budai, Z., Jurak, F., Kis-Tamas, A., Lay Konya, A., Mezei, T., Vig, Z., and Zubovits, K., *Ger. Offen.* 2933405; *Chem. Abstr. 93,* 46065y (1980).
3. Ciba-Geigy, A.-G., *Fr.* 2434572; *Chem. Abstr. 94,* 65137k (1981).
4. Leone-Bay, A., Timony, P. E., Green, L., and Glaser, L., *J. Agric. Food Chem. 34,* 733 (1986).
5. Copping, L. G., Birchmore, R. J., Wright, K., and Godson, D. H., *Pestic. Sci. 5,* 280 (1984).
6. Elitropi, G., Panto, E., and Tricerri, S., *J. Heterocycl. Chem. 16,* 1545 (1979).
7. Iddon, B. and Lim, B. Z., *J. Chem. Soc., Perkin Trans. 1 1983,* 735.
8. Iddon, B., Khan, N., and Lim, B. L., *J. Chem. Soc., Perkin Trans. 1 1987,* 1437.
9. Leone-Bay, A., Timony, P. E., Tomko, J., and Weil, E. D., *U.S.* 4596598; *Chem. Abstr. 105,* 92927v (1986).
10. Iizuja, K. and Abahane, L., *J. Med. Chem. 9,* 1643 (1986).
11. Tolkmith, H. and Mussell, D. R., *World Rev. Pest. Control 1967,* 74—79.
12. Balaban, E. and Pyman, F. L. J., *J. Chem. Soc. 121,* 947 (1922).
13. Sandler, R. S. and Karo, W., *Organic Functional Group Preparation,* Vol. *12,* p. 270. Academic Press, New York, 1963.
14. Veverka, M. and Motacek, T., *Czech.* 240399; *Chem. Abstr. 110,* 153750j (1989).
15. Veverka, M. and Motacek, T., *Czech.* 243578; *Chem. Abstr. 111,* 114963g (1989).

Translated by Z. Votický