A Convenient Synthesis of Novel 1,3,4-Substituted 2-Pyrazoline-5-ones

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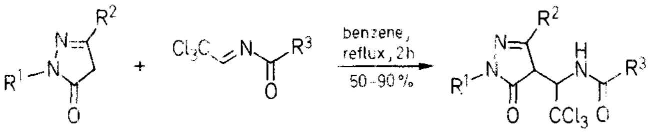
A number of new 1,3,4-substituted 2-pyrazoline-5-ones **3a-i** have been prepared by addition of 1,3-substituted 2-pyrazoline-5-ones **1a-f** to trichloroacetaldimine derivatives **2a-c**.

The 2-pyrazoline-5-one ring system has been extensively studied.[1] However, investigations on 2-pyrazoline-5-ones possessing a substituent, which is attached to the 4-position by a C–C single bond are only a few. Thus, 4-benzyl derivatives were synthesized by reduction of the corresponding 4-arylidene compounds.[2] 4-Benzoyl derivatives, useful for heavy metal extraction and as herbicides arise from acylation with benzoyl chloride.[3,4] The 4-bromo compound was shown to undergo nucleophilic substitution by carbanions.[5,6] Furthermore, 4-C-substituted 2-pyrazoline-5-ones were obtained by condensation with hydroxy compounds,[7] by Mannich reaction.[8] Vilsmeier synthesis[9] and Michael additions to vinylogous carbonyl compounds[10] and to 4-(3-methyl-5-oxo-1-phenyl-2-pyrazoline-4-ylidene)-3-methyl-1-phenyl-2-pyrazoline-5-one (pyrazolone blue) forming trimeric 2-pyrazoline-5-ones.[11]

We have now found that the reaction of 1,3-substituted 2-pyrazoline-5-ones **1a–f** with trichloroacetaldimine derivatives **2a–c** gives the 1,3,4-substituted 2-pyrazoline-5-ones **3a–i** (Table). The 2-pyrazoline-5-ones add as heterocyclic C-nucleophiles to the heterovinylogous carbonyl compounds **2**. The reaction thus proceeds as a Hetero-Michael addition. It is carried out preferably in an absolute apolar aprotic solvent like benzene. It is noteworthy that in contrast to many vinylogous carbonyl compounds the trichloroacetaldimine derivatives **2a–c**, due to the trichloromethyl group as a strong acceptor, show such a tendency for addition to a CH-acidic compound that all reactions could be realized without addition of base for the deprotonation of the 2-pyrazoline-5-ones. This possibility to react pyrazolones under neutral conditions is also of interest in comparison to the results of Weygand and Steglich et al, who reacted acyclic C-nucleophiles in their activated forms like carbanions[12] or Grignard reagents[13,14] with *N*-acylaldimines.



1a-f **2a-c** **3a-i**

1	R^1	R^2
a	C_6H_5	CH_3
b	C_6H_5	C_2H_5
c	C_6H_5	t-C_4H_9
d	C_6H_5	C_6H_5
e	2,4,6-$Cl_3C_6H_2$	CH_3
f	CH_3	CH_3

2	R^3
a	CH_3
b	C_6H_5
c	OC_2H_5

3	R^1	R^2	R^3
a	C_6H_5	CH_3	CH_3
b	C_6H_5	CH_3	C_6H_5
c	C_6H_5	CH_3	OC_2H_5
d	C_6H_5	C_2H_5	CH_3
e	C_6H_5	t-C_4H_9	CH_3
f	C_6H_5	C_6H_5	CH_3
g	C_6H_5	C_6H_5	C_6H_5
h	2,4,6-$Cl_3C_6H_2$	CH_3	CH_3
i	CH_3	CH_3	CH_3

It was ruled out on the basis of spectroscopic data that the compounds **1a–f** reacted in their NH- or OH-tautomeric forms[15] with the imines **2**, which would have resulted in the formation of constitutional isomeric adducts of **3**.

In summary, the procedure described here[16] gives rise to a new class of 4-substituted 2-pyrazoline-5-ones by means of a simple addition reaction of 2-pyrazoline-5-ones to highly reactive trichloroacetaldimine derivatives as azavinylogous carbonyl compounds.

Melting points were determined on a Boetius micro hotstage and are uncorrected. The ^{1}H-NMR spectra were recorded on a TESLA BS 487C spectrometer (80 MHz). The IR spectra were measured on a VEB Carl Zeiss Jena spectrometer UR 20. The mass spectra were recorded on a Varian MAT CH6 spectrometer at an ion source temperature of 200 °C.

The starting 2-pyrazoline-5-ones **1a**,[17] **1b**,[18] **1c**,[19] **1d**,[20] **1e**[21] and **1f**[21] as well as the starting imines *N*-(2,2,2-trichloroethylidene)acetamide **(2a)**,[22] *N*-(2,2,2-trichloroethylidene)benzamide **(2b)**[23] and *N*-(2,2,2-trichloroethylidene)carbamic acid ethyl ester **(2c)**[24] were prepared according to the literature procedures. Compound **2b** after distillation (b.p. 105–107 °C/0.7 mbar) solidified to yellow crystals (m.p. 46–47.5 °C, 55%).

2-Acylamino-1,1,1-trichloro-2-(1,3-substituted-2-pyrazoline-5-on-4-yl)-ethanes 3a–i; General Procedure:

The starting substituted 2-pyrazoline-5-one **1** (Table) (0.01 mol) is dissolved in absolute benzene (50 ml). A solution of the corresponding

Table. Compounds **3** Prepared

Reactants	Product	Yield (%)	m.p. (°C) (solvent)	Molecular Formula[a]	IR (KBr) $\nu_{C=O}$ (cm^{-1})	^{1}H-NMR (solvent/HMDS$_{int}$) δ (ppm)	MS *m/e* (rel.inten., %)
1a + **2a**	**3a**	66	179–180 (acetone)	$C_{14}H_{14}Cl_3N_3O_2$ (362.6)	1705	($CDCl_3$): 1.97 (s, 3H); 2.19 (s, 3H); 5.71 (s, 1H); 6.32 (d, 1H, *J* = 11 Hz); 6.72 (d, 1H, *J* = 11 Hz); 7.1–7.8 (m, 5H)	361 (M$^+$, 0.3); 284 (0.1); 188 (1); 174 (71); 146 (10); 91 (25); 77 (62); 43 (100)
1a + **2b**	**3b**[b]	50	139–140 (hexane/acetone)	$C_{19}H_{16}Cl_3N_3O_2$ (424.6)	1675	(Acetone-d_6): 2.11 (s, 3H); 5.81 (s, 1H); 6.66 (d, 1H, *J* = 10 Hz); 7.0–8.0 (m, 10H); 9.02 (d, 1H, *J* = 10 Hz)	423 (M$^+$, 0.1); 388 (0.1); 250 (1); 215 (0.2); 174 (19); 105 (100)
1a + **2c**	**3c**	53	123–124 (hexane)	$C_{15}H_{16}Cl_3N_3O_3$ (392.6)	1720	(CCl_4): 1.13 (t, 3H, *J* = 7 Hz); 2.15 (s, 3H); 4.12 (q, 2H, *J* = 7 Hz); 5.62 (s, 1H); 5.92 (d, 1H, *J* = 3 Hz); 7.0–7.8 (m, 5H)	391 (M$^+$, 0.2); 346 (0.1); 218 (3); 174 (97); 146 (12); 91 (30); 77 (100)
1b + **2a**	**3d**	90	144–145 (hexane/acetone)	$C_{15}H_{16}Cl_3N_3O_2$ (376.6)	1690	($CDCl_3$): 1.12 (t, 3H, *J* = 8 Hz); 1.95 (s, 3H); 2.51 (q, 2H, *J* = 8 Hz); 5.68 (s, 1H); 6.31 (d, 1H, *J* = 10 Hz); 7.0–7.8 (m, 5H)	375 (M$^+$, 0.1); 316 (0.1); 298 (0.5); 188 (39); 146 (7); 91 (7); 77 (54); 43 (100)
1c + **2a**	**3e**	87	142–143 (hexane/acetone)	$C_{17}H_{20}Cl_3N_3O_2$ (404.7)	1670	(CCl_4): 1.24 (s, 9H); 1.88 (s, 3H); 4.38 (s, 1H); 6.20 (d, 1H, *J* = 10 Hz); 6.59 (d, 1H, *J* = 10 Hz); 6.9–7.8 (m, 5H)	403 (M$^+$, 0.5); 368 (0.1); 326 (0.1); 216 (45); 174 (16); 146 (11); 91 (5); 77 (23); 43 (100)
1d + **2a**	**3f**	61	143–145 (hexane/acetone)	$C_{19}H_{16}Cl_3N_3O_2$ (424.6)	1695	($CDCl_3$): 1.99 (s, 3H); 6.20 (s, 1H); 6.40 (d, 1H, *J* = 10 Hz); 6.63 (d, 1H, *J* = 10 Hz); 7.0–7.9 (m, 10H)	423 (M$^+$, 0.2); 306 (0.1); 236 (20); 146 (28); 91 (13); 77 (36); 43 (100)
1d + **2b**	**3g**[b]	54	137–138 (hexane)	$C_{24}H_{18}Cl_3N_3O_2$ (486.7)	1680	($CDCl_3$): 6.35 (s, 1H); 6.64 (d, 1H); *J* = 10 Hz); 6.95 (d, 1H, *J* = 10 Hz); 7.1–7.8 (m, 15H)	236 (17); 194 (2); 105 (100) 91 (18); 77 (94)
1e + **2a**	**3h**[b]	50	146–147 (hexane/acetone)	$C_{14}H_{11}Cl_6N_3O_2$ (465.9)	1700	($CDCl_3$): 2.05 (s, 3H); 2.20 (s, 3H); 5.65 (s, 1H); 6.24 (d, 1H, *J* = 10 Hz); 6.56 (d, 1H, *J* = 10 Hz); 7.37 (s, 2H)	463 (M$^+$, 0.1); 384 (0.1); 276 (9); 241 (3); 179 (6); 146 (10); 43 (100)
1f + **2a**	**3i**	64	144–145 (hexane/acetone)	$C_9H_{12}Cl_3N_3O_2$ (300.5)	1690	($CDCl_3$): 2.06 (s, 3H); 2.09 (s, 3H); 3.54 (s, 3H); 5.50 (s, 1H); 6.25 (d, 1H, *J* = 10 Hz); 7.04 (d, 1H, *J* = 10 Hz)	299 (M$^+$, 0.7); 188 (4); 146 (17); 112 (100); 97 (5)

[a] Satisfactory microanalyses obtained: C ±0.35, H ±0.25, N ±0.31, Cl ±0.37.

[b] Purified by chromatography over silica gel (0.063–0.200) with toluene/ethyl acetate (1 : 1) as eluent.

imine **2** (see table) (0.01 mol) in absolute benzene (20 ml) is added and the mixture refluxed for 2 h. The solvent is then removed *in vacuo* and the residue recrystallized or purified by column chromatography.

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(1) Elguero, J., in: *Comprehensive Heterocyclic Chemistry*, Katritzky, A.R., Rees, C.W. (eds.), Vol. 5, Pergamon Press, Oxford, 1984, p. 167.
(2) Wreciono, U. *Liebigs Ann. Chem.* **1975**, 2293.
(3) Jensen, S. *Acta Chem. Scand.* **1959**, *13*, 1668.
(4) Soni, H.K., Shah, J.R. *Bull. Soc. Chim. Fr.* **1985**, 147.
(5) Youssef, M.S.K. *Z. Naturforsch. Teil B* **1984**, *39*, 86.
(6) Aziz, S.I., Abd-Allah, S.D., Ibrahim, N.S. *Heterocycles* **1984**, *22*, 2523.
(7) Einhorn, A. *Liebigs Ann. Chem.* **1905**, *343*, 304.
(8) Pathak, I.B., Ghosh, T.N. *J. Indian Chem. Soc.* **1949**, *26*, 371.
(9) Wallace, D.J., Straley, J.H. *J. Org. Chem.* **1961**, *26*, 3825.
(10) Elnagdi, M.H., Nawar, G.A.M., Girgis, N.S., Elgemeie, G.E. *Liebigs Ann. Chem.* **1983**, 1468.
(11) Mann, G., Hauptmann, S., Wilde, H., Hennig, L., Schindler, W. *DDR-Patent* 212737 (1984); *C. A.* **1985**, *102*, 115146.
(12) Weygand, F., Steglich, W. *Chem. Ber.* **1965**, *98*, 487.
(13) Weygand, F., Steglich, W., Oettmeier, W. *Chem. Ber.* **1970**, *103* 818.
(14) Kober, R., Hammes, W., Steglich, W. *Angew. Chem.* **1982**, *94*, 213 *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 203.
(15) Freyer, W., Köppel, H., Radeglia, R., Malewski, G. *J. Prakt Chem.* **1983**, *325*, 238.

(16) Sicker, D., Böhlmann, W., Bendler, D., Mann, G. *DDR-Patent* 285878 (1986).

(17) Knorr, L. *Ber. Dtsch. Chem. Ges.* **1883**, *16*, 2597.

(18) Zoss, A. O., Hennion, G. F. *J. Am. Chem. Soc.* **1941**, *63*, 1151.

(19) Friedmann, H., Hänsel, W. *Arch. Pharm.* **1983**, *316*, 726.

(20) Knorr, L., Klotz, C. *Ber. Dtsch. Chem. Ges.* **1887**, *20*, 2545.

(21) Hänsel, W. *Liebigs Ann. Chem.* **1976**, 1380.

(22) Drach, B.S., Sinitsa, A.D., Kirsanov, A.W. *Zh. Obshch. Khim.* **1969**, *39*, 2193; *C. A.* **1970**, *72*, 42706.

(23) Weygand, F., Steglich, W., Lengyel, I., Fraunberger, F., Maierhofer, A., Oettmeier, W. *Chem. Ber.* **1966**, *99*, 1944.

(24) Ulrich, H., Tucker, B., Sayigh, A.A.R. *J. Org. Chem.* **1968**, *33*, 2887.