SHORT PAPER

J. Chem. Research (S), 2003, 418–419

Microwave irradiation for the oxidative 1, 3-dipolar cycloaddition of aldehyde phenylhydrazones and methyl acrylate by (diacetoxy)iobenzene†

Min Xia*

Department of Applied Chemistry, Zhejiang Institute of Science and Technology, Hangzhou 310033, P. R. China

Methyl 1-phenyl-3-aryl-2-pyrazolinyl-5-carboxylates were rapidly synthesised by a 1,3-dipolar cycloaddition in good to excellent yields with complete regioselectivity under microwave irradiation.

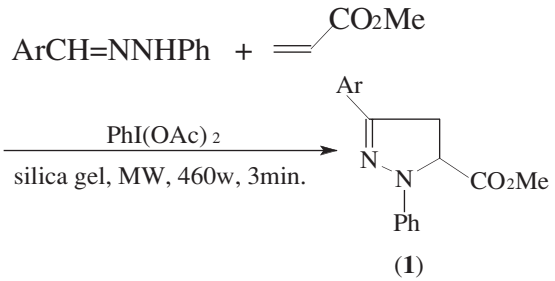
Keywords: pyrazoline derivatives, 1, 3-dipolar cycloadditon

It is known that pyrazoline derivatives are significant compounds not only as intermediates and agricultural pesticides, but also as effective luminescent and fluorescent substances.[1] Although there have been many approaches to their synthesis, 1,3-dipolar cycloaddition through nitrilimines generated *in situ* is the most powerful and versatile route to the five-membered heterocycles.[2]

A number of methods have been reported for the generation *in situ* of nitrilimines, *e.g.* the base-induced dehydrochlorination of hydrazonyl halides,[3] the thermal decomposition of 2,5-disubstituted tetrazoles [4] or sodium salts of 2-nitrohydrazones,[5] the photolysis of 3,4-disubstituted sydones[6] or 2,5-disubstituted tetrazoles,[7] the oxidation of aldehyde arylhydrazones with lead tetraacetate,[8] *etc*. All of them have shortcomings with difficulty in operation, harsh conditions, difficulty in preparation of starting substrates, low yields of nitrilimines or the use of potentially fatal reagents. It is well known that (diacetoxy)iodobenzene is the most useful and promising reagent among the hypervalent iodine compounds. It can be prepared easily with little toxicity and is an effective oxidant, especially for the oxidation of compounds containing N atoms in good yields under mild conditions.[9] Herein, we provide an alternative formation of nitrilimines *in situ* by using (diacetoxy)iodobenzene to oxidse aldehyde phenylhydrazones.

Microwave (MW)-assisted organic synthesis has become an increasingly used technique for the generation of new molecules.[10] Many solvent-free reactions using microwaves have been developed since the risks of hazards by pressure build-up in the reaction vessel are reduced and scale-up is made easier. Recently, solvent-free 1,3-dipolar cycloadditions under microwave (MW) irradiation have appeared to be attractive for the synthesis of heterocyclic compounds.[11] We herein report that methyl 1-phenyl-3-aryl-2-pyrazolinyl-5-carboxylates (**1**) can be prepared through the solvent-free 1,3-dipolar cycloaddition of methyl acrylate and nitrilimines generated *in situ* by the oxidation of aldehyde phenylhydrazones with (diacetoxy)iodobenzene under microwave irradiation (Scheme 1). To our knowledge, this is the first report that (diacetoxy)iodobenzene can be employed in solvent-free 1,3-dipolar cycloadditions under MW.

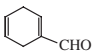
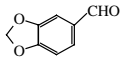
The reaction took place in 3 minutes at 460W in good to excellent yields under MW on a silica gel support. The results are shown in Table 1. It is clear that the reaction is affected by substituent electronic effects. When the aldehydes had electron-donating groups, the yields were excellent. However,



Scheme 1

when there existed electron-withdrawing groups, the yields were low, especially for the strongly electron-withdrawing NO_2 group where the expected product could not be obtained. Not only aromatic hydrazones but also heterocyclic and α, β-unsaturated hydrazones were effective substrates.

Table 1 1,3-dipolar cycloaddition of nitrilimines with methyl acrylate

Entry	ArCHO	Yield/%	Entry	ArCHO	Yield/%
a	PhCHO	86	**e**	*o*-ClC_6H_4CHO	56
b	*p*-$CH_3C_6H_4CHO$	83	**f**	PhCH=CHCHO	91
c	*p*-$CH_3OC_6H_4CHO$	94	**g**	*m*-$O_2NC_6H_4CHO$	0
d		71	**h**		96

The reaction was completely regioselective, since we only obtained the 1-phenyl-3-aryl-2-pyrazolinyl-5-carboxylate. The regioselectivity could be determined by ^{1}H NMR by the fact that the chemical shifts of C_5–H were at 4.8 ppm, at relatively low field.

In conclusion, we report an efficient solvent-free method of synthesising pyrazoline derivatives rapidly and regioselectively in good to excellent yields under microwave irradiation.

Experimental

Melting points were uncorrected. ^{1}H NMR spectra were recorded on a Bruker 500MHz instrument in $CDCl_3$ solutions using TMS as internal standard. FT-IR spectra were recorded using KBr disks on a Bruker Vector-22 infrared spectrometer. Elemental analyses were performed on an EA-1110 instrument. MS were carried out on HP5989B mass spectrometer. Microwave irradiation was carried out on WP800J-823 domestic microwave oven.

* To receive any correspondence. E-mail: chchxm@21cn.com

† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

General procedure for the preparation of methyl 1-phenyl-3-aryl-2-pyrazolinyl-5-carboxylates (l) by microwave irradiation: At room temperature, silica gel (3g) was added to the solution of the corresponding aldehyde phenylhydrazone (1mmol) in methyl acrylate (10ml). The resulting mixture was stirred completely and then evaporated under reduced pressure until it turned to slurry. A solution of (dicaetoxy)iodobenzene (1mmol) in CH_2Cl_2 (5ml) was added to the slurry and the CH_2Cl_2 was removed under reduced pressure. After the slurry was irradiated in an open vessel at 460W for 3 minutes and cooled to room temperature, Et_2O (2×10ml) was added, followed by filtration and the filtrate was evaporated to give the residue which was purified on a chromatographic column (silica gel) using hexane/Et_2O (4:1) as the eluent.

Compound ***1a****:* m.p. 107° (Lit . 106–107°), δ (ppm) 3.42 (dd, *J*=17Hz, *J*=6.5Hz, 1H), 3.68(dd, *J*=17Hz, *J*=12.5Hz,1H), 3.75(s, 3H), 4.83(dd, *J*=12.5Hz, *J*=6.5Hz, 1H), 6.88(t, *J*=7Hz, 1H), 7.12(d, *J*=8Hz, 2H), 7.25–7.41(m, 5H), 7.72 (d, *J*=7.5Hz, 2H); ν (cm^{-1}) 3029, 2952, 1737, 1596, 1504, 1493, 1397, 1336, 1263, 1135, 1016, 889, 745, 686; *m*/*z* (%) 280(M^+, 33.34), 221(100), 118(14.79), 104(18.45), 91(28.05), 77(53.97), 51(30.91); Anal. calcd. for $C_{17}H_{16}N_2O_2$: C 72.86, H 5.71, N 10.00; found C 72.83, H5.63, N 10.08%

Compound ***1b****:* m.p. 104°, δ (ppm) 2.37(s, 3H), 3.40 (dd, *J*=17Hz, *J*=7Hz, 1H), 3.67(dd, *J*=13Hz, *J*=17Hz, 1H), 3.75(s, 3H), 4.81(dd, *J*=13Hz,*J*=7Hz, 1H), 6.87(t, *J*=7.5Hz, 1H), 7.11(d, *J*=8Hz, 2H), 7.20(t, *J*=8Hz, 2H), 7.25–7.30 (m, 2H), 7.60(d, *J*=8Hz, 2H); ν (cm^{-1}) 3027, 2950, 1740, 1597, 1497, 1378, 1321, 1268, 1200, 1122, 1031, 880, 821, 753, 692; *m*/*z* (%) 294(M^+, 38.29), 235(100), 117(10.44), 104(9.56), 91(22.54), 77(28.18), 51(13.71);Anal. calcd. for $C_{18}H_{18}N_2O_2$: C 73.47, H 6.12, N 9.52; Found C 73.42, H 6.33, N 9.67%

Compound ***1c****:* m.p. 121° (Lit .114–115°), δ (ppm) 3.38 (dd, *J*=7Hz, *J*=17Hz, 1H), 3.64(dd, *J*=17Hz, *J*=13Hz, 1H), 3.74(s, 3H), 3.83(s, 3H), 4.79(dd, *J*=13Hz, *J*=7Hz, 1H), 6.86(t, *J*=7.5Hz, 1H), 6.92(d, *J*=9Hz, 2H), 7.10(d, *J*=8Hz, 2H), 7.25–7.33(m, 2H), 7.66 (d, *J*=8.5Hz, 2H); ν (cm^{-1}) 3043, 2958, 1735, 1596, 1501, 1392, 1250, 1132, 1034, 879, 826, 743, 691; *m*/*z*(%) 310(M^+, 48.45), 251(100), 162(18.10), 135(25.38), 117(14.70), 104(14.23), 91(68.32), 77(61.24), 57(33.13), 51(27.65), 43(33.31);Anal. calcd. for $C_{18}H_{18}N_2O_3$: C 69.68, H 5.81, N 9.03; found C 69.66, H 5.91, N 9.11%

Compound ***1d****:* m.p. 84°, δ (ppm) 3.39(dd, *J*=6.5Hz, *J*=17Hz, 1H), 3.62(DD, *J*=13Hz, *J*=17Hz, 1H), 3.73(s, 3H), 4.81(dd, *J*=13Hz, *J*=6.5Hz,1H), 6.48(dd, *J*=2Hz, *J*=3.5Hz, 1H), 6.63(d, *J*=3Hz, 1H), 6.87(t, *J*=7Hz, 1H), 7.09(d, *J*=8Hz, 2H), 7.25–7.29(m, 2H), 7.49(d, *J*=2Hz, 1H); ν (cm^{-1}) 3136, 2954, 1735, 1595, 1503, 1373, 1264, 1133, 1002, 922, 887, 804, 746, 690; *m*/*z* (%) 270 (M^+, 58.45), 211(100), 183(18.37), 117(8.83), 104(8.89), 91(13.05), 77(42.28), 51(27.00); Anal. calcd. for $C_{15}H_{14}N_2O_3$: C 66.67, H 5.18, N 10.37; found C 66.61, H 5.02, N 10.46%

Compound ***1e****:* m.p. 142°, δ (ppm) 3.63(dd, *J*=6.5Hz, *J*=17Hz, 1H), 3.74(s,3H), 3.92(dd, *J*=13Hz, *J*=17.5Hz, 1H), 4.84(dd, *J*=6.5Hz, *J*=13Hz, 1H), 6.89(t, *J*=7Hz, 1H), 7.11 (d, *J*=8Hz, 2H), 7.25–7.30(m, 4H), 7.38~7.40(m,1H), 7.84–7.86(m,1H); ν (cm^{-1}) 3064, 2952, 1739, 1599, 1502, 1435, 1389, 1322, 1265, 1204, 1141, 1036, 879, 750, 691, 666; *m*/*z* (%) 314(M^+, 41.92), 255(100), 117(13.83), 104(9.31), 91(23.88), 77(49.44), 51(27.25); Anal. calcd. for $C_{17}H_{15}N_2O_2Cl$: C 64.97, H 4.77, N 8.92; found C 64.93, H 4.68, N 9.09%

Compound ***1f****:* m.p. 124°, δ (ppm) 3.32(dd, *J*=6.5Hz, *J*=17Hz, 1H), 3.56(dd, *J*=13Hz, *J*=17Hz, 1H), 3.75(s, 3H), 4.82(dd, *J*=6.5Hz, *J*=13Hz, 1H), 6.62(d, *J*=16.5Hz, 1H), 6.88(t, *J*=7Hz, 1H), 7.06(d, *J*=7.5Hz, 2H), 7.19(d, *J*=16.5, 1H), 7.26–7.30(m, 3H), 7.36(t, *J*=7Hz, 2H), 7.47(d, *J*=7.5Hz, 2H); ν (cm^{-1}) 2950, 1741, 1599, 1501, 1324, 1200, 1122, 1038, 958, 882, 748, 691; *m*/*z* (%) 306(M^+, 58.42), 247(100), 115(15.11), 104(17.99), 91(19.36), 77(76.95), 51 33.04); Anal. calcd. for $C_{19}H_{18}N_2O_2$: C 74.51, H 5.88, N 9.15; found C 74.55, H 5.80, N 9.11%

Compond ***1h****:* m.p. 137°, δ (ppm) 3.38(dd, *J*=7Hz, *J*=17Hz, 1H), 3.62(dd, *J*=13Hz, *J*=17Hz, 1H), 3.75(s, 3H), 4.78(dd, *J*=13Hz, *J*=7Hz, 1H), 5.99(s, 2H), 6.80(d, *J*=8Hz, 1H), 6.86(t, *J*=7Hz, 1H), 7.02(dd, *J*=1.5Hz, *J*=8Hz, 1H), 7.09(d, *J*=8Hz, 2H), 7.25–7.29(m, 2H), 7.38(d, *J*=1.5Hz, 1H); ν (cm^{-1}) 3042, 2921, 1732, 1599, 1500, 1454, 1351, 1318, 1220, 1039, 936, 876, 812, 747, 694, 669, 619; *m*/*z* (%) 324(M^+, 51.86), 265(100), 235(10.85), 207(24.05), 104(9.44), 91(9.86), 77(34.16), 51(16.19); Anal. calcd. for $C_{18}H_{16}N_2O_4$: C 66.67, H 4.94, N 8.64; found C 66.62, H 5.06, N 8.57%

Received 14 August 2002; accepted 3 December 2002
Paper 02/1512

References:

1. A.N. Kost and I.I. Grandberg, *Advances in Heterocyclic Chemistry*, A.R. Katritzky and A.J. Boulton, Academic Press, New York and London, 1966, Vol.**6**, 347.
2. (a) A.S. Shawli, *Chem. Rev*., 1993, **93**, 2731; (b) G. Bertrand and C. Wentrup, *Angew. Chem. Int. Ed. Engl*., 1994, **33**, 529.
3. (a) R. Huisgen, H. Seidel, G. Wallibillich and H. Knupfer, *Tetrahedron*, 1962, **17**, 3; (b) J.S. Clovis, A. Eckell, R. Huisgen and R. Sustamann, *Chem. Ber*., 1967, **100**, 60.
4. (a) A. Padwa, S. Nahm and E. Satu, *J. Org. Chem.,* 1978, **43**, 1664; (b) A.H. Beckett, A.G.W. Spickett and S.H.B. Wright, *Tetrahedron*, 1968, **24**, 2839.
5. H.M. Hassaneen and A.S. Shawli, *Ind. J. Chem.,* 1992, **28B**, 133.
6. (a) H. Gotthard and F. Reiter, *Chem. Ber*., 1979, **112**, 1206; (b) A. Haneda, T. Imagawa and M. Kawanish, *Bull. Chem. Soc. Jpn*, 1976, **49**, 748.
7. (a) C.S. Angadiyavar and M.V. Geroge, *J. Org. Chem*., 1971, **36**, 1589; (b) P. Scheiner and J.F. Dina, *Tetrahedron*, 1970, **26**, 2619.
8. W.A.F. Gladstone, J.B. Ayiward and R.O.C. Norman, *J. Chem. Soc (C)*., 1969, 2587.
9. (a) L.W. Deady and N.H. Quazi, *Aust. J. Chem*., 1993, **46**, 411; (b) D.W. Chen and Z.C. Chen, *Synthesis*, 1994, 773; (c) R.Y. Yang and L.X. Dai, *J. Org. Chem*., 1993, **58**, 3381.
10. (a) S. Caddick, *Tetrahedron,* 1995, **51,** 10403; (b) A. Loupy, A. Petit, J. Hamelin, F. Texier-Boullet, P. Jacquault and D. Mathe, *Synthesis,* 1998, 1213.
11. (a) A. Arrieta, J.R. Carrillo, F.P. Cossio, A. Diaz-Ortiz, M.J. Gomez-Escalonilla, A.de la Hoz, A. Moreno and F. Langa, *Tetrahedron*, 1998, **54**, 13167; (b) P. de la Cruz, E. Espildora, J.J. Garcia, A de la Hoz, F. Langa, N. Martin and L. Sanchez, *Tetrehedron Lett*., 1999, **40**, 4889.