

Rajendra K. Singh\* and Michael D. Rogers

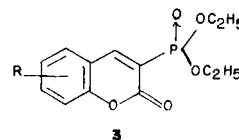
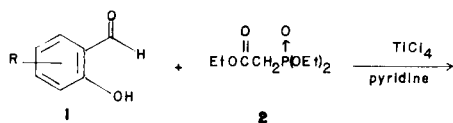
Monsanto Agricultural Products Company, 800 North Lindbergh Blvd.,  
St. Louis, Missouri 63167  
Received March 22, 1985

A general synthesis of a number of diethyl coumarin-3-phosphonates (**3**) has been achieved using titanium tetrachloride-pyridine as the condensing agent.

*J. Heterocyclic Chem.*, **22**, 1713 (1985).

There are numerous references in literature [1-5] on the synthesis of 3-substituted coumarins. However, the isolation of diethyl coumarin-3-phosphonates (**3**) has not been successful [6]. Thus Robinson and Addison [6] have attempted the condensation of salicylaldehyde (**1**) with triethyl phosphonoacetate (**2**), under basic conditions [7]. The resulting product (presumably **3a**) could not be purified. Robinson confirmed the structure by hydrolysis of the product to the free phosphonic acid. In 1974, Lehnert [8] reported that by using titanium tetrachloride *N*-methylmorpholine catalysis, aromatic aldehydes could be condensed with triethyl phosphonoacetate to give benzylidene phosphonic esters.

We have condensed triethyl phosphonoacetate (**2**) with a number of salicylaldehydes **1** using titanium tetrachloride and pyridine as catalysts to give diethyl coumarin-3-phosphonates **3**. The reaction was conveniently carried out at 0° to room temperature.



In the case of salicylaldehyde ( $\text{R} = \text{H}$ ) **1a**, the product was distilled while in other cases, the products were crystallized using ethanol-water mixture. Table 1 shows examples synthesized in this area. Further reactions using these compounds will be reported in the near future. In summary, the above method provides an efficient synthesis of diethyl coumarin-3-phosphonates.

#### EXPERIMENTAL

Melting points were determined using a Thomas-Hoover capillary melting point apparatus and are uncorrected. The  $^1\text{H}$  nmr spectra were recorded on Varian T-60 and  $^{31}\text{P}$  nmr on FX-100 spectrometers. Elemental analyses were performed by Atlantic Microlabs, Inc., Knoxville, Tennessee.

General Method for the Preparation of Diethyl Coumarin-3-phosphonates **3**.

To 1 liter of anhydrous tetrahydrofuran stirred at  $-10^\circ$  under nitrogen atmosphere, a solution of 66 ml (0.6 mole) of titanium tetrachloride

Table 1

Physical Data for Diethyl Coumarin-3-phosphonates **3**

No.	R	Mp °C (Bp)	Yield, %	Molecular Formula	$^{31}\text{P}$ NMR $\delta$	Analysis (%)		
						Calcd./Found	C	H
<b>3a</b>	H	65-66 (203-205/0.1 mm)	67	$\text{C}_{13}\text{H}_{15}\text{O}_5\text{P}$	10.78	55.32	5.36	—
						55.35	5.39	—
<b>3b</b>	6-Br	110-111	67	$\text{C}_{13}\text{H}_{14}\text{BrO}_5\text{P}$	5.12	43.24	3.91	22.13
						43.13	3.95	22.08
<b>3c</b>	6-Cl	70-75	61	$\text{C}_{13}\text{H}_{14}\text{ClO}_5\text{P}$	10.26	49.31	4.46	11.20
						49.33	4.49	11.20
<b>3d</b>	6,8-Di-Cl	118-122	83	$\text{C}_{13}\text{H}_{13}\text{Cl}_2\text{O}_5\text{P}$	9.63	44.47	3.73	20.19
						44.36	3.76	20.09
<b>3e</b>	7- $\text{OCH}_3$	86-88	23	$\text{C}_{14}\text{H}_{17}\text{O}_6\text{P}$	21.84	53.85	5.49	—
						54.23	5.45	—
<b>3f</b>	5,6-Benzo	138-140	47	$\text{C}_{17}\text{H}_{17}\text{O}_5\text{P}$	11.24	61.45	5.16	—
						61.36	5.20	—

in 150 ml of carbon tetrachloride was added dropwise. Then a solution of 60.3 g (0.3 mole) of 5-bromosalicylaldehyde (**1b**) and 67.2 g (0.3 mole) of triethyl phosphonoacetate in 150 ml of tetrahydrofuran was added dropwise. It was then followed by addition of 96 ml (1.2 moles) of pyridine in 200 ml of tetrahydrofuran. The reaction mixture was stirred overnight (~ 18 hours) at room temperature followed by addition of 300 ml of water and 300 ml of ether. The organic layer was separated and washed with water ( $\times 2$ ), brine, then dried over magnesium sulfate. The solvent was removed to give a light yellow semisolid. This was triturated with ether and filtered to give 72.8 g of **3b** (67%), mp 110-111°;  $^1\text{H}$  nmr (deuteriochloroform):  $\delta$  ppm 1.4 (t, 6H, J = 7 Hz), 4.28 (2 sets of quart, 4H, J = 7 Hz), 7.1-7.7 (m, 3H, Ar), 8.4 (d, 1H, H-3, J = 18 Hz).

In the case of **3a**, the product was distilled, bp 203-205° (0.1 mm) while in other examples, the products were recrystallized using ethanol-water.

## REFERENCES AND NOTES

- [1] A. Fujimoto and A. Sakurai, *Synthesis*, 871 (1977).
- [2] A. Sakurai and H. Midorikawa, *J. Org. Chem.*, **34**, 3612 (1969).
- [3] R. O. Clinton and S. C. Laskowski, *J. Am. Chem. Soc.*, **71**, 3602 (1949).
- [4] A. A. Avetisyan, Z. V. Vanyan and M. T. Dangyan, *Khim. Gheterotsikl. Soedin.*, 1181 (1979); *Chem. Abstr.*, **92**, 146544b (1980).
- [5] G. Jones, *Org. React.*, **15**, 204 (1967).
- [6] C. N. Robinson and J. F. Addison, *J. Org. Chem.*, **31**, 4325 (1966).
- [7] See also S. Patai and A. Schwartz, *J. Org. Chem.*, **25**, 1232 (1960).
- [8] W. Lehnert, *Tetrahedron*, **30**, 301 (1974).