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Preparation of Intermediate of Indoxacarb

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The effective synthesis of indoxacarb is valuable for its application. Several organic bases were used in place of reported N,N-dimethylaniline to prepare (4-trifluoromethoxy)phenylcarbamate, which is an important intermediate for the manufacturing synthesis of indoxacarb. Compared with the method in literature, the new process is convenient and effective, furthermore more friendly to environment.

Key Words: Indoxacarb, Organic base, 4-Trifluoromethoxy phenyl carbamate, Synthesis.

INTRODUCTION

Indoxacarb (DPX-JW062, Fig. 1) is a new oxadiazine insecticide introduced by the E.I. DuPont Company in 1992. It has shown outstanding field activity, low mammalian toxicity, environmental compatibility and a high degree of non-target organism safety. But the synthesis of indoxacarb is rather complicated[1-3].

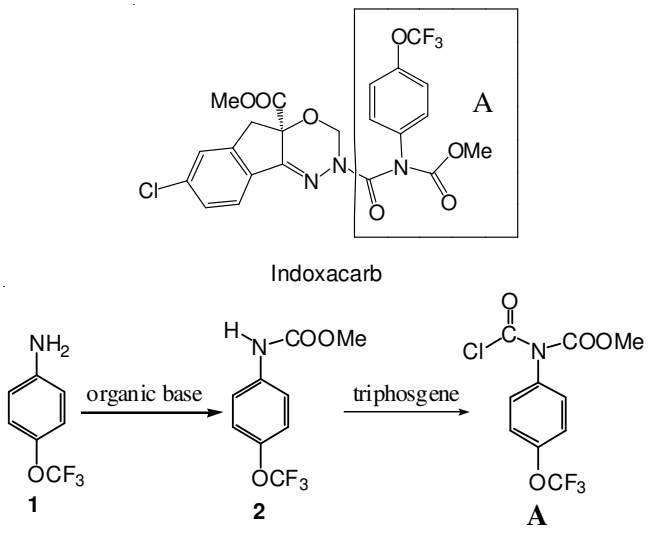

Fig. 1. Synthesis of structure A in indoxacarb

Indoxacarb and its analogues show similar activity. Most of the analogues have an N-alkoxycarbonyl-N-arylcarbamoyl moiety (structure A in Fig. 1) which is an important intermediate to prepare indoxacarb. By employing N,N-dimethylaniline as base, the acylation of *p*-alkyl aniline (**1**) gives N-arylcarbamate (**2**), which subsequently reacts with triphosgene to give the chloroformyl derivative A. The preparation of compound **2** is important in the synthesis of many insecticides of this class[4]. However, N,N-dimethylaniline is one kind of expensive organic bases and could cause environmental pollution[5-7]. To avoid these problems, some other organic bases with low price and low-toxicity was introduced instead of N,N-dimethylaniline. In our previous work, we reported[8] that inorganic base (Na_2CO_3) was used as base to obtain compound **2** in excellent yield. In this paper, other kind bases were employed as base or as catalyst to form compound **2** in good to excellent yields. All these methods could be easily applied in the production of indoxacarb with good yield and safety. Moreover, these organic bases produce less pollution to environment.

EXPERIMENTAL

All reagents were of analytical grade and were used as supplied. The melting point was measured with an XRC-1 microscope melting-point apparatus. ^{1}H NMR spectra were run on Varian-400; 4-trifluoromethoxyaniline and methyl chloroformate were purchased from ACROS. 1,2-Dichloroethane was freshly distilled from CaH_2 before use.

General procedure for preparation of methyl (4-trifluoromethoxy)phenylcarbamate (2): Methyl chloroformate (0.29 g, 3 mmol) was added dropwise to a stirred solution of 4-trifluoromethoxyaniline (0.35 g, 2 mmol) and different organic bases in 1,2-dichloroethane (20 mL) at 0-5 ºC. Then the mixture was warmed to different temperature. After the reaction was completed (showed by TLC). The

reaction mixture was cooled to room temperature and washed with hydrochloric acid (1 mol/L, 15 mL). Then the water solution was extracted with ethyl acetate (5 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated to give the product as white solid, m.p.: 85.8-86.8 ºC (lit.: 86.2-87.7 ºC[9]). ^{1}H NMR ($CDCl_3$, 300 MHz), δ: 3.79 (s, 3H, CH_3); 6.67 (bs, 1H, NH); 7.15-7.18 (m, 2H, ArH); 7.39-7.42 (m, 2H, ArH).

RESULTS AND DISCUSSION

Previous studies[11,12] have showed that the best yield of **2** was only 75.4 % when N,N-diethylaniline was used as acid scavenger. Therefore, it is decided to use other different organic bases in formation of compound **2**. It was found that reaction temperature and time were important factors for the yield and they were optimized in order to give the best yield as showed in following tables. In all tables, entry 1, 2, 3, 4 showed the relationship between yields and reaction temperature and entry 3 and entry 5, 6, 7 indicated the relationship between yields and reaction time.

When the base, for example, triethylamine (1.2 eq) was used only for acid scavenger, the middle yields were achieved (Table-1) and the best yield was just 59.6 % (Table-1, entry 3) under the optimized condition because of low conversion rate of reaction.

TABLE-1
EFFECT OF REACTION TEMPERATURE AND TIME TOWARD YIELD USING TRIETHYLAMINE

Entry	Reaction temperature (ºC)	Reaction time (h)	Yield (%)
1	35	2.0	48.4
2	45	2.0	50.3
3	55	2.0	59.6
4	65	2.0	55.5
5	55	0.5	47.0
6	55	1.0	53.0
7	55	3.0	56.5

To impel the best conversion of reaction, pyridine (Pyr.) and 4-dimethylamino pyridine (DMAP) were used both as acid scavenger and catalysts which can activate ClCOOMe. The yields were reached over 80 % (Table-2) and the best yield was up to 90.5 % (Table-2, entry 2) catalyzed by pyridine. When the reaction was accelerated by 4-dimethylamino pyridine, the best yield was reached to 98.5 % (Table-3, entry 2). In general, 4-dimethylamino pyridine was better acid scavenger and catalyst than pyridine since most of the batches gave yields of over 90 % except entry 5 and 7 in Table-3.

TABLE-2
EFFECT OF THE REACTION TEMPERATURE AND TIME TOWARD YIELD USING PYRIDINE

Entry	Reaction temperature (ºC)	Reaction time (h)	Yield (%)
1	-5	2.0	80.4
2	0	2.0	90.5
3	5	2.0	87.8
4	10	2.0	86.7
5	0	0.5	85.7
6	0	1.5	84.5
7	0	3.0	83.5

TABLE-3
EFFECT OF THE REACTION TEMPERATURE AND TIME TOWARD YIELD USING 4-DIMETHYLAMINO-PYRIDINE

Entry	Reaction temperature (ºC)	Reaction time (h)	Yield (%)
1	30	2	94.5
2	40	2	98.5
3	50	2	98.4
4	60	2	95.5
5	40	1	78.5
6	40	3	93.5
7	40	4	5.7

However, 4-dimethylamino pyridine is much expensive than triethylamine, then triethylamine (1.1 eq)was used as acid scavenger, meanwhile, only 0.1 eq of 4-dimethylamino pyridine or pyridine were employed as catalyst to activate ClCOOMe. The good to excellent yields were obtained (Tables 4 and 5) and the highest yields was reached to 97.4 % (Table-4, entry 3). Generally, 4-dimethylamino pyridine is a much better catalyst than pyridine. since almost all the yields were achieved over 90 % while the yields were obtained lower than 90 % when reaction was catalyzed by pyridine.

TABLE-4
EFFECT OF THE REACTION TEMPERATURE AND TIME TOWARD YIELD USING 4-DIMETHYLAMINO-PYRIDINE AND TRIETHYLAMINE

Entry	Reaction temperature (ºC)	Reaction time (h)	Yield (%)
1	-5	2.0	92.5
2	0	2.0	95.8
3	15	2.0	97.4
4	30	2.0	95.5
5	15	0.5	70.5
6	15	1.5	91.5
7	15	3.0	96.7

TABLE-5
EFFECT OF THE REACTION TEMPERATURE AND TIME TOWARD YIELD USING PYRIDINE AND TRIETHYLAMINE

Entry	Reaction temperature (ºC)	Reaction time (h)	Yield (%)
1	-5	2.0	82.5
2	0	2.0	85.8
3	15	2.0	87.4
4	30	2.0	85.5
5	15	0.5	80.5
6	15	1.5	81.5
7	15	3.0	86.7

Conclusion

The results in all the five Tables 1-5 showed that normally, when the reaction time was shortened or prolonged, the yield was reduced and the best reaction time is 2 h in all case. It was found that triethylamine to be a very good acid scavenger and it was combined with catalytic doses of 4-dimethylamino pyridine to give the excellent yield at 15 ºC (97.4 %, Table-4, entry 3). The current method affords simple experimental procedure, environmental friendliness and high yields. These findings would be valuable for developing practical applications in the manufacture of indoxacarb and other chemicals.

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REFERENCES

1. R. Shapiro, G.D. Annis, C.T. Blaisdell, D.J. Dumas, J. Fuchs, S.M. Griswold, G.W. Higley, Jr., W.C. Hollinsed, J.J. Mrowca, J.A. Sternberg, and P. Wojtkowski, Synthesis and Chemistry of Agrochemicals VI, ACS Symposium Series, Vol. 800, Ch. 17, pp. 178-185 (2001).
2. W. Song, Z. Liu and K. Dong, *Neurotoxicology*, **27**, 237 (2006).
3. A.P. Alves, W.J. Allgeier and B.D. Siegfried, *Pestic. Biochem. Physiol.*, **90**, 26 (2008).
4. Y.H. Zhou, R.J. Gong and W.R. Miao, *Synth. Commun.*, **36**, 2661 (2006).
5. J.P. Niu and X.H. Zhao, *J. Health Toxicol.*, **13**, 160 (1999).
6. G.D. Annis, Arthropodicidal Oxadiazine Intermediate, U.S. Patent 5602251 (1997).
7. Y. Sachem, C.Z. Chao and S. Peng, *J. Xiangtan Normal Univ. (Natural Science Ed.)*, **23**, 60 (2001).
8. J.F. Zhang, L.Z. Zhang and D.Q. Sun, *J. Pestic. Sci.*, **2**, 252 (2011).
9. S. Yu, X.G. Hu, Y.Q. Zhu and F. Chen, *Liaoning Chem. Ind.*, **38**, 77 (2009).
10. G.D. Annis, S.F. Mccann and R. Shapiro, PCT Int. Appl. WO 9529171 (1995).
11. G.D. Annis, W.E. Barnette, S.F. Mccann and K.D. Wind, Arthropodicidal Oxadiazinyl, Thiadiazinyl and Triazinyl Carboxanilides, U.S. Patent 5462938 (1995).
12. D. Dumas, S.K. Sengupta and D.R. Corbin, (DuPont Co., Ltd.), PCT Int. Appl. WO9620151 (1996).