Materials Physics and Chemistry(2018)

Original Research Article

Synthesis of Novel Chalcone Derivatives by Organic Catalysis

Junlong Li,Ruocan Zhuang,Yinan Qian

College of Chemistry and Chemical Engineering, Anyang University of Technology, Henan, China

ABSTRACT

Chalcone compounds have a wide range of biological activities. In this paper, nine kinds of novel chalcone compounds were synthesized by using transacrylone derivatives and anthrone as raw materials. The effects of different catalysts and solvents on the yield of the products were investigated. The optimal catalyst was DABCO. The optimum solvent was dichloromethane with the highest yield of 71.6%. On this basis, the effect of the co - catalyst on the yield was investigated. The yield was increased to 89.9%.

1. Introduction

Diphenyl ketone, also known as chalcone. Chalcone compounds are a class of natural organic compounds present in many medicinal plants, such as natural organic compounds [1] in medicinal plants such as licorice and safflower, with a basic skeleton structure of 1,3-diphenyl Acrylone, due to its molecular structure with greater flexibility can be combined with different receptors [2]. Modern pharmacological studies have shown that chalcone derivatives have a variety of biological activities, including: anti-tumor, anti-oxidation, platelet aggregation, antiparasitic, anti-virus, anti-ulcer, anti-bacterial, anti-inflammatory, and inhibition, Liver and other effects [3]. In recent years, the study of the biological activity of chalcone derivatives has been favored.

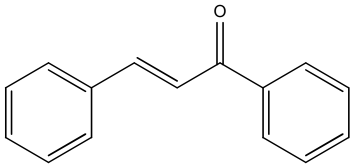


Figure 1. Chalcone structure

9,10-dihydro-9-oxoanthracene (anthrone) is widely reported that anthrone colorimetric determination of the content of sugar in food because of its high sensitivity, good reproducibility, saving reagents and other advantages of domestic. The anthrone colorimetric method is classified as one of the standard analytical methods for sugar content in food. There are also many reports of anthrone and its derivatives can inhibit acetylcholinesterase, butyrylcholinesterase and acetylcholinesterase-induced Aβ aggregation activity, and anti-tumor activity [5-6]. Preparation of anthrone and diketene synthesis of chalcone has a broader, stronger biological activity. In this paper, nine novel chalcone derivatives were synthesized by organic catalysis.

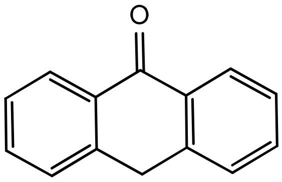


Figure 2. Structure of 9,10-dihydro-9-oxoanthracene (anthrone)

1, 5-diaryl-1, 4-pentadiene-3-keto (diketene) ketone ketone or ketene dimer is a highly active unsaturated aldehydes and ketones that can be used in multiple positions (Figure 3) nucleophilic addition reaction. In this paper, 1,4-nucleophilic addition products were obtained by organic catalysis.

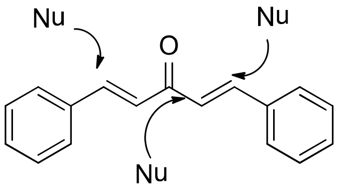


Figure 3. Reaction sites for diketene

Since 1989, List and others began to use organic small molecules catalyzed, scientists are its easy to operate, the air, water and other insensitive and it is friendly to the characteristics of the environment [7]. Organic catalysis refers to the use of metal-free organic molecules as a catalyst for catalytic mode. Organic molecular catalyst does not contain metal, which is mainly composed of hydrogen, nitrogen, carbon, sulfur, phosphorus and other elements [8]. The use of organic molecules as a catalyst generally has a wide range of applications, high catalytic efficiency, non-toxic cheap, good selectivity, simple structure, easy loading, recycling and easy operation, environmentally friendly and so on. However the organic catalytic substrate to adapt to a narrow range, the reaction is relatively slow, the amount is relatively large and its activity is relatively difficult to adjust [9]. Subsequently, a variety of synergistic catalytic models have been reported, the catalytic efficiency of different organic catalysts and the catalytic substrate range, catalyst activity, species richness and catalytic selectivity have their own characteristics. It has also been reported that two different organic catalysts are used in combination. In the catalytic series reaction [10-11], both can play the advantages of these two catalytic models and they also meet the requirements of green chemistry, may achieve a good catalytic effect.

In this paper, the effects of solvents, catalysts and organic synergistic catalysts on the synthesis of novel chalcone derivatives were investigated by using a variety of diketene derivatives and anthrone as raw materials.

2. Experimental method

2.1. Experimental reagents and instruments

Triethylenediamine (DABCO), anthrone, diketene, anthrone, proline, diketene, aladdine reagent Co., Ltd., benzoic acid, 2-naphthol, p-nitrobenzoic acid, acetic acid, Sodium, petroleum ether, ethyl acetate, ethyl ether, toluene, methanol, chloroform, dichloromethane, tetrahydrofuran, ethanol, N, N-dimethylformamide, trimethylamine aqueous solution, dimethylamine aqueous solution Company, all reagents are of analytical grade.

AR1140 electronic analytical balance, OHAUS; ZF-I-type three-use UV analyzer, Shanghai Gu Village electro-optical instrument factory; 101 type electric blast oven, Tianjin Tai Site Instrument Co., Ltd.; DF-1 collector thermostatic magnetic stirring Device; NOVA single-mode microwave synthesizer, Shanghai Yi Yi Yao Instrument Technology Development Co., Ltd. SHB-B95-type circulating water-type multi-purpose vacuum pump.

2.2. Synthesis of Chalcone Derivatives

2.2.1. Synthesis of Diketene Derivatives

A solution of 1.3647 g o-methoxybenzaldehyde and 0.2884 g of acetone was charged to a 50 ml round bottom flask, and then 5 ml of absolute ethanol was added. The mixture was stirred at room temperature and 6 ml of 10% NaOH was added slowly. As the NaOH was added with a large amount of pale yellow solids. After completion of the reaction, the filtrate was decompressed under reduced pressure and washed several times with distilled water, and 1.3628 g was weighed in a yield of 82.4% (Fig. 4)

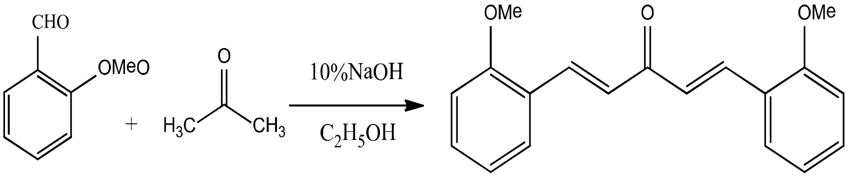


Figure 4. Reaction of o-methoxybenzaldehyde with acetone

2.2.2. Synthesis of Chalcone Derivatives

(Fig. 5) was synthesized by using anthrone, diketene as raw material, dichloromethane as solvent and DABCO as catalyst.

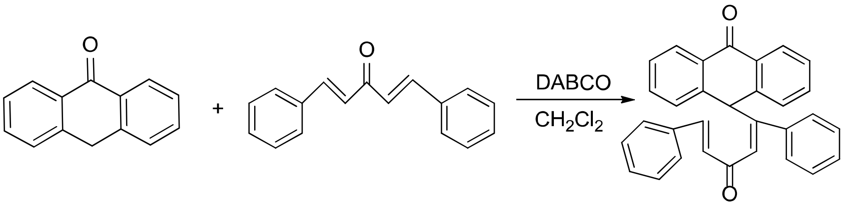


Figure 5.

(0.7 mmol), 1.2 mg (0.01 mmoL) of DABCO in 8 mL of the reaction flask, and then 1 mL of methylene chloride was added and the reaction was started by the addition of a stirrer to give 9.7 mg (0.05 mmol) of anthrone, 11.7 mg (0.05 mmol) After 12 hours of reaction, the column (the filler was silica gel, the developing solvent was 1: 5 ethyl acetate: petroleum ether) in a yield of 71.6%

3. Results and discussion

The effects of different solvents and catalysts on the yield were investigated under normal temperature, the amount of solvent was 1mL, the reaction time was 12 hours, and the ratio of anthrone and diketene was 1: 1.

3.1. Effect of catalyst on yield

The effects of different catalysts on the yield were investigated under normal conditions, the solvent was 1 mL of dichloromethane, the reaction time was 12 hours, and the ratio of anthrone to dienone was 1: 1 (Table 1). The experimental results show that the catalytic yield of DABCO catalyst is 66.6%, the yield of pyridine is 59.3%, 56.7%, inorganic sodium carbonate and sodium hydroxide. The catalytic effect of less than organic base, neutral 4A molecular sieve, silica, quinoline catalytic effect of the worst yield of less than 30%. This reaction is a nucleophilic substitution reaction, and the alkaline solution favors the attack of the nucleophile.

Table 1. Effect of catalyst on yield

No	Catalyst	Yield/%
1	DABCO	66.6
2	Triethylamine	29.8
3	Sodium carbonate	41.1
4	Quinoline	23.7
5	Pyridine	56.7
6	Sodium hydroxide	39.8
7	Dimethyl Ammonia Solution	59.3
8	Trimethylamine aqueous solution	30.0
9	4AMolecular sieve	22.3
10	Silica gel	27.4

3.2. Effect of Solvent on Yield

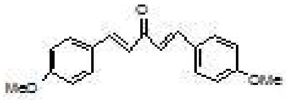
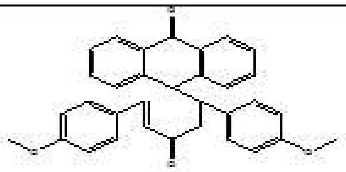
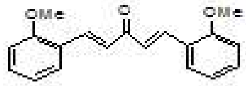
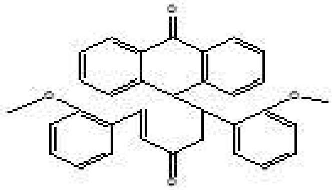
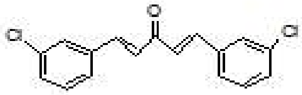
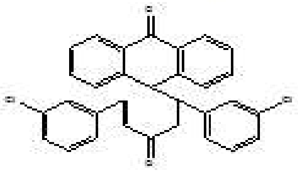
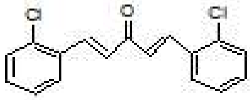
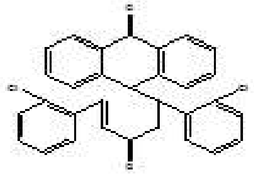
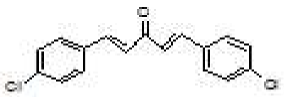
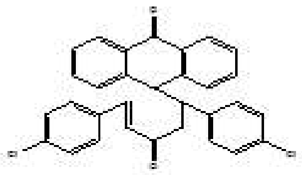
The effect of different solvents on the yield was investigated when the solvent was 1 mL of dichloromethane, the reaction time was 12 hours, the ratio of anthrone to diketene was 1: 1, and the catalyst was DABCO. The experimental results show that the yield of petroleum ether with non-polarity is 39.8%, the yield of ethanol and ether is lower, and the yield of medium polarity is 71.6%. This reaction is a nucleophilic reaction, medium polar solvent is conducive to the formation of carbon positive ions.

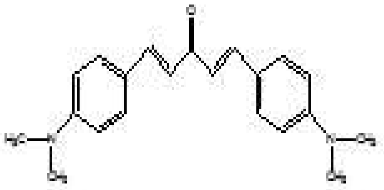
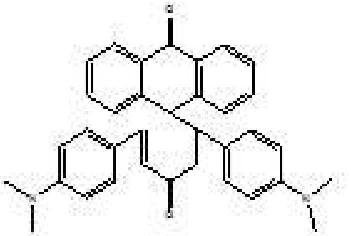
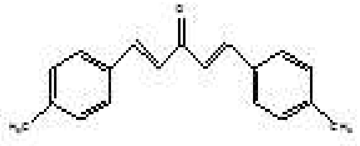
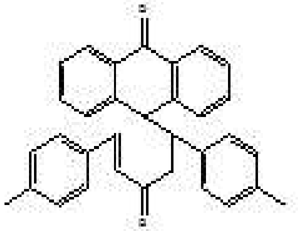
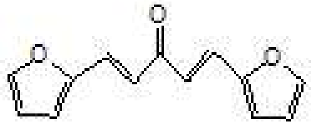
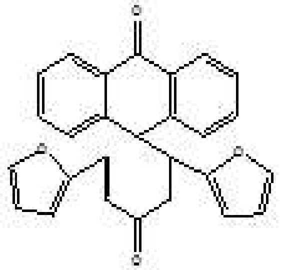
Table 2. Effect of solvent on yield

No	Solvent	Yield/%
1	Toluene	46.7
2	Ether	25.6
3	Ethanol	48.5
4	Trichloromethane	45.0
5	THF	51.1
6	Ethyl acetate	64.5
7	Dichloromethane	71.6
8	Petroleum ether	39.8

3.3. Substrate expansion

Under the condition of normal temperature, the amount of solvent was 1mL, the reaction time was 12 hours, and the catalyst was DABCO. The optimum reaction conditions were as follows: solvent dichloromethane, catalyst as DABCO, Yield up to 71.6%. Substrate development under optimal synthesis conditions (Table 3). The experimental results show that the yield of chlorine is 71.3% when the substituents are chlorine, the highest is 87.3% and the substituents are nitrogen and nitrogen dimethyl is 83.6%.

No.	Diphenone Derivative	Product	Yield/%
1		 (Product number 5.1)	56.1%
2		 (Product number 5.2)	60.7%
3		 (Product number 5.3)	71.1%
4		 (Product number 5.4)	72.4%
5		 (Product number 5.5)	87.3%

6		 (Product number 5. 6)	83. 6%
7		 (Product number 5. 7)	68. 3%
8		 (Product number 5. 8)	61. 8%

Substrate expansion

3.4. Effect of Double Catalyst on Yield

Table 3. Effect of double catalyst on yield

No.	Catalysy	Yield/%
1	Quinine amine proline	62.0
2	Quinine 2-naphthol	78.0
3	Quinineamine Acetic acid	28.1
4	Quinine p-toluenesulfonic acid	43.4
5	Quinineamine benzoic acid	89.9

The experimental data in Table 2 show that DABCO has the best catalytic effect, but the yield is only 71.6%. In order to further improve the yield, this paper attempts to explore the catalytic effect of the double catalyst (Table 4). The experimental results show that the catalytic effect is improved when the quinolinamine and benzoic acid are used for catalysis. The yield is as high as 89.9%.

4. Conclusion

(1) In this paper, a series of novel chalcone derivatives were synthesized from anthrone, diketene and its derivatives as raw materials. The effects of different catalysts and solvents on the yield were investigated. The optimal catalyst was DABCO, The solvent was dichloromethane in a yield of 71.6%.

(2) Under the optimal synthesis conditions, the effect of the synergistic effect of the double catalyst on the yield was improved from 71.6% to 89.9%, which provided a better method for the synthesis of chalcone compounds.

(3) Chalcone compounds have a wide range of biological activities. In this paper, nine novel chalcone compounds are synthesized, which provides a more perfect data base for the further study of chalcone compounds.

5. Product characterization

5.1. Compound 1 (p-methoxy): white crystals, m.p .: 50.7-56.5, 1H NMR (400 MHz, CDCl3) δ 8.08 (dd, J = 25.0, 7.5 Hz, 2H), 7.66-7.34 (m, (D, J = 8.6 Hz, 2H), 6.63 (d, J = 16.0 Hz, 1H), 6.53 (d, J = 8.6 Hz, 2H), 6.18 (d, J = 8.6 Hz, 2H), 4.65 (D, J = 3.6 Hz, 1H), 3.89-3.82 (m, 3H), 3.72 (s, 3H), 3.08 (dd, J = 16.9, 8.1 Hz, 1H), 2.83 (dd, J = 16.9, 6.9 Hz, 1H).

5.2. (M, 2H), 7.84-6.61 (m, 18H), 6.21 (d, \u0026 lt; RTI ID = 0.0 \u0026 gt; J = 6.9 Hz, 1H), 5.99 (d, J = 12.6 Hz, 0H), 4.74 (d, J = 3.4 Hz, 1H), 4.53-4.40 (m, 1H), 3.88 (s, 3H) S, 3H), 2.73 (qd, J = 16.9, 7.7 Hz, 2H).

5.3. (T, J = 8.8 Hz, 2H), 7.90-7.75 (m, 1H), 7.69 (dd, 1H) J = 14.6, 7.1 Hz, 2H), 7.56 - 7.16 (m, 10H), 7.03 (t, J = 7.5 Hz, 1H), 6.64 (d, J = 7.6 Hz, 1H), 6.50 (d, (D, J = 3.4 Hz, 1H), 2.68 (d, J = 7.6 Hz, 2H), 4.64 (d, J = 3.7 Hz, 1H) The

5.4. Compound 4 (o-chloro), white crystals, melting point: 37.1-44.5, 1H NMR (400 MHz, CDCl3)? 8.32 - 8.18 (m, 2H), 7.86 - 7.63 (m, 3H), 7.58 - 7.11 (m, (D, J = 16.1 Hz, 1H), 6.32 (dd, J = 11.0, 4.2 Hz, 1H), 6.63 (d, J = 7.6 Hz, 1H), 6.50 Hz, 1H), 4.74 (d, J = 3.7 Hz, 1H), 4.56 (d, J = 3.5 Hz, 1H), 2.68 (d, J = 7.6 Hz, 2H).

5.5. Compound 5 (p-Chloro Substitution): white crystals, melting point: 146.1-154.3, 1H NMR (400 MHz, CDCl3)? 8.16 - 8.10 (m, 1H), 8.08 (d, J = 7.5 Hz, 1H), 7.67 - (D, J = 8.4 Hz, 2H), 6.66 (d, J = 16.1 Hz, 1H), 6.26 (d, J = 8.4 Hz, 2H), 4.63 (d, J = 3.7 Hz (Dd, J = 17.3, 7.5 Hz, 1H), 2.84 (dd, J = 17.3, 7.4 Hz, 1H), 3.93 (td, J = 7.4, 3.9 Hz, 1H)

5.6. Compound 6 (p-dimethylamine): white crystals, melting point: 123.8-128.5, 1H NMR (400 MHz, CDCl3) δ 7.96 (dd, J = 5.9, 3.2 Hz, 2H), 7.61-7.41 (m, 6H) (D, J = 16.1 Hz, 1H), 4.80 (s, 1H), 3.06 (s, 5H), 2.37 (m, 1H), 6.71 (d, J = 8.8 Hz, 2H) S, 3H).

5.7. (M, 2H), 7.69 - 7.18 (m, 11H), 6.81 (d, J = \u0026 lt; RTI ID = 0.0 \u0026 gt; (D, J = 3.6 Hz, 1H), 3.91 (dd, J = 7.6, 2H), 6.70 (d, J = 16.1 Hz, 1H), 6.18 (d, J = 8.0 Hz, 2H) (Dd, J = 17.0, 6.9 Hz, 1H), 2.39 (d, J = 9.4 Hz, 3H), 2.25 (s, \u0026 lt; RTI ID = 0.0 \u0026 gt; 3H).

5.8. Compound 8 (furan): white crystals, m.p. 108.5-118.4, 1H NMR (400 MHz, CDCl3) δ 8.37 - 8.10 (m, 2H), 7.74 - 7.34 (m, 6H), 7.15 (d, J = 15.8 Hz (2H, J = 3.0, 1.9 Hz, 1H), 5.54 (m, 1H), 6.64 (d, J = 3.4 Hz, 1H), 6.55-6.47 (m, 2H) D, J = 3.2 Hz, 1H), 4.80 (d, J = 3.5 Hz, 1H), 4.14 - 3.98 (m, 1H), 2.58 (t, J = 6.8 Hz, 2H).

References

1. Zhang ZJ. Therapeutic effects of herbal extracts and const ituents in an -imalmodels of psych iatric d isorders [j]. Life Sci, 2004, 75: 1659.
2. Go M L, Wu X, Liu X L. Chalcones: an update on cytotoxic and chemo protective propert ies [J]. CurrMed Chem, 2005, 12 (4): 481-499.
3. Zheng Hongwei, Niu Xinwen, Zhu Jun and so on. Studies on the biological activity of chalcone compounds [J]. Chinese Journal of New Drugs, 2007,16 (18): 1445-1449.
4. UEDA T, ABLIZ Z, SATO M, et al. Structural determination by MS, NMR, and UV spectra of bromo and nitroderivatives of 1-azabenzanthrone [J]. JM olStruc, 1990, 224: 313-322.
5. Synthesis and Biological Activity of 6- (Alkylhydrazide) -1-Azabenzanthraquinone Derivatives [J]. Chinese Journal of Organic Chemistry, 2012,32 (6) 4): 1-14
6. (B) Melchiorre, P .; Marigo, M .; Carlone, A .; Bartoli, G. Angew. Chem. Int. Edit. [6] (a) MacMillan, DWCNature 2008, 455 (7211), 304-308; . 2008, 47 (33), 6138-6171; (c) Bertelsen, S .; Jorgensen, KA, Chem. Soc. Rev. 2009, 38 (8), 2178-2189.
7. (B) List, B .; Lerner, RA; Barbas (1) (a) Ahrendt, KA; Borths, CJ; MacMillan, DWC, J. Am. Chem. Soc. 2000, 122 (17), 4243-4244; , CF, J. Am. Chem. Soc. 2000, 122 (10), 2395-2396.
8. Anastas, P.T., Chem. Rev. 2007, 107 (6), 2167-2168.
9. Jellerichs, B.G .; Kong, J.-R .; Krische, M.J., J. Am. Chem. Soc. 2003, 125 (26), 7758-7759.

10. (a) Rios, R .; Sundén, H .; Vesely, J .; Zhao, G.-L .; Dziedzic, P .; Córdova, A. Adv. Synt. Catal. 2007, 349 (7), 1028-1032; (b) Lu, L.-Q .; Cao, Y.-J .; Liu, X. -P .; An, J .; Yao, C.-J .; Ming, Z. (C) Lu, L.-Q .; Li, F .; An, J, Am. Chem. Soc. 2008, 130 (22), 6946-6948; Zhang, J.-J .; An, X. -L .; Hua, Q. -L .; Xiao, W.-J., Angew. Chem. Int. Edit. 2009, 48 (50), 9542 (5) Lu, L.-Q .; Zhang, J.-J .; Li, F .; Cheng, Y .; An, J .; Chen, J.-R .; Xiao, W.- J., Angew. Chem. Int. Edit. 2010, 49 (26), 4495-4498; (e) Riches, SL; Saha, C .; Filgueira, NFn; Grange, E .; McGarrigle, EM; Aggarwal, VK (Manufactured by J. Am. Chem. Soc. 2010, 132 (22), 7626-7630; (f) Hashimoto, T .; Omote, M .; Maruoka, K., Angew. Chem. Int. Edit. 2011, 15), 3489-3492.
11. (a) Erb, J .; Paull, DH; Dudding, T .; Belding, L .; Lectka, T., J. Am. Chem. Soc. 2011, 133 (19), 7536-7546; B) Kim, HY; Oh, K., Org. Lett. 2011, 13 (6), 1306-1309; (c) Hrdina, R .; Müller, CE; Wende, RC; Lippert, KM; Benassi, M. (50), 7624-7627; (d) Iwata, M .; Yazaki, R .; Chen, IH; Sureshkumar, D., \u0026 lt; RTI ID = 0.0 \u0026 gt; ; Kumagai, N .; Shibasaki, M., J. Am. Chem. Soc. 2011, 133 (14), 5554-5560; (e) Belot, S .; Vogt, KA; Besnard, C .; Krause, (F) Zhou, S .; Fleischer, S .; Junge, K .; Beller, M., Angew, \u0026 lt; RTI ID = 0.0 \u0026 gt; Chem. Int. Edit. 2011, 50 (22), 5120-5124.