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Unexpected Synthesis of 2, 2'-[1-(4-Methoxyphenoxy)propane-2, 2-diyl]bis(5-methoxy-3-methylbenzofuran)

Yu Dong SHEN[1, 2], Hai Qiang WU[1], Lin Kun AN[2], Zhi Shu HUANG[2], Xian Zhang BU[1]*, Lian Quan GU[b]

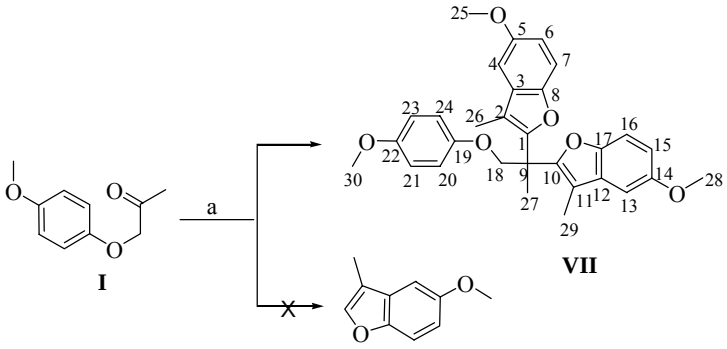
[1]School of Chemistry and Chemical Engineering, Sun Yat-sen University, Guangzhou 510275
[2]School of Pharmaceutical Sciences, Sun Yat-sen University, Guangzhou 510080

Abstract: A new bisbenzofuran analogue **VII** was achieved unexpectedly in one step procedure from 1-(4-methoxyphenoxy)acetone **I** by using Amberlyst 15 resin as catalyst in excellent yield. The structure was elucidated by spectroscopy analysis including ^{1}H-NMR, ^{13}C-NMR, DEPT, ESI-MS, element analysis.

Keywords: Benzofuran, Amberlyst 15 resin, cyclization.

Most of natural and synthetic compounds[1-3] with benzofuran moieties exhibit broad spectrum bioactivities, such as antitumor, antifungal, antivirus activities; 5-lipoxygensase inhibitory activity and 5α-reductase inhibitory activity[4-7]. Moreover, they are also key intermediates for constructing some natural bioactive quinones[8].

Scheme 1 Synthesis of compound **VII**



a: Amberlyst 15 resin, benzene, RT, 24 h, 80 %

As part of our research program focused on novel *ortho*-naphthofuranoquinone derivatives, various 3-substituted benzofurans were required as synthetic intermediates. Synthesis of these kind of intermediates is generally according to the literature[9].

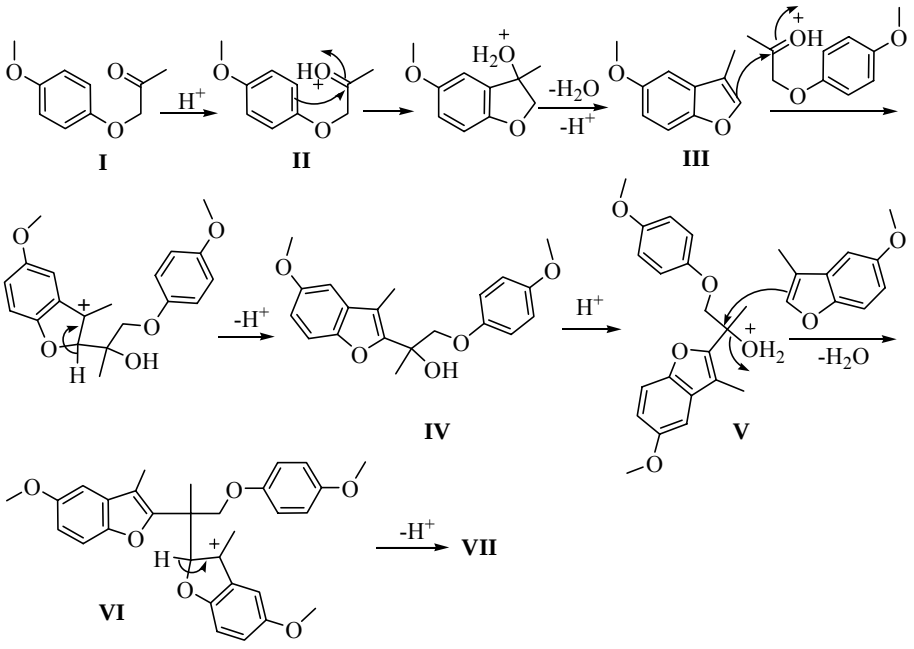
* E-mail: phsbxzh@zsu.edu.cn

2-(4-Methoxyphenoxy)-1-arylethanones was treated in reflux benzene by using Amberlyst 15 resin as catalyst, after purification, the target product 3-arylbenzofurans were obtained smoothly. However, when we use 1-(4-methoxyphenoxy)acetone **I** as starting material in the same condition, only a complex mixture was yielded and no any target product was separated.

We primarily considered that too high reaction temperature would lead to our failure. Therefore, we conduct the reaction under room temperature. Fortunately, a yellow oil was successfully separated in excellent yield. After thoroughly analysis by ESI-MS, ^{1}H-NMR, ^{13}C-NMR and EA[10], it was unexpectedly found that the structure of this oil was not the proposed 5-methoxy-3-methylbenzofuran, but a new bisbenzofuran derivative **VII** (**Scheme 1**) instead.

The formation of **VII** is much interesting. **Scheme 2** described a possible mechanism briefly. Under the catalysis by Amberlyst 15 resin, the ionized intermediate **II** was first cyclized and dehydrated into **III** which attacked another molecular **II** thereon and then formed the ionized intermediate **V**. In succession, the intermediate **V** was attacked again by molecule **III** along with dehydration , to produce **VII** finally.

Scheme 2 Mechanism of cyclization and coupling



It is noticeable that although benzofuran has been reported to react with aldehydes under acidic conditions to give cyclic polymers[11], its reaction with ketone in mild conditions has not been found. The unexpected and interesting result afforded a novel strategy on constructing coupled cyclic or linear polymers of benzofuran.

*Synthesis of compound **VII***

1-(4-Methoxyphenoxy)acetone **I** (0.36 g, 2 mmol), Amberlyst 15 resin (0.5 g) was added into benzene (10 mL) and then stirred at room temperature for 24 h. Then Amberlyst 15 resin was filtered off and solvent was vaporized in vacuum. Finally, silica gel column chromatography (EtOAc/petroleum, 1/20) gave 0.26 g of title compound **VII** (yellow oil) in 80 % yield.

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References and Notes

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10. Selected data for compound **VII**. Yellow oil (EtOAc/petroleum, 1/20), yield 80%. MS(ESI): 487 $[M+H]^+$. Anal. Calcd. for $C_{30}H_{30}O_6$: C, 74.06; H, 6.21; Found: C, 74.01; H, 6.37. ^{1}H NMR(300MHz, $CDCl_3$, TMS, δ ppm): 1.88 (s, 6H, 26-CH_3 and 29-CH_3), 1.99 (s, 3H, 27-CH_3), 3.72 (s, 3H, 30-CH_3), 3.83 (s, 6H, 25-CH_3 and 28-CH_3), 4.54 (s, 2H, 18-CH_2), 6.74-6.86 (m, 8H, 4-CH, 7-CH, 13-CH, 16-CH, 20-CH, 21-CH, 23-CH, 24-CH), 7.29 (dd, 2H, J=0.8, 8.5Hz, 6-CH, 15-CH). ^{13}C NMR(75MHz, $CDCl_3$, TMS, δ ppm): 8.2 (26-C, 29-C), 22.2 (27-C), 44.0 (9-C), 55.7 (30-C), 56.0 (25-C, 28-C), 73.1 (18-C), 101.6 (4-C, 13-C), 111.3 (7-C, 16-C), 111.6 (2-C, 11-C), 112.2 (6-C, 15-C), 114.4 (21-C, 23-C), 115.8 (20-C, 24-C), 131.3 (3-C, 12-C), 147.9 (8-C, 17-C), 153.0 (19-C), 153.7 (1-C, 10-C), 153.8 (22-C), 155.5 (5-C, 14-C).
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