

**DIELS-ALDER CYCLOADDITIONS OF DIMETHYL
ACETYLENEDICARBOXYLATE AND DIETHYL
ACETYLENEDICARBOXYLATE WITH SOME DIENES UNDER
MICROWAVE IRRADIATION USING $\text{AlCl}_3/\text{CH}_2\text{Cl}_2$**

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Abstract

Microwave enhanced Diels-Alder reactions of furan, 2,5-dimethylfuran, 1,3-cyclohexadiene and anthracene with dimethyl acetylenedicarboxylate (DMAD) and diethyl acetylenedicarboxylate (DEAD) give [4+2]-cycloadducts in high yields in domestic microwave oven. Aluminum(III) chloride and dichloromethane in combination with microwave irradiation increased the reaction rate.

Key words: microwave, Diels-Alder reaction, aluminum(III) chloride, solvent effect

Introduction

Microwave enhancement of organic reactions has interested the chemists recently.¹ Microwave heating is very useful in organic synthesis as the reactions can be performed efficiently with high reaction rates, low by-products, high yields and ease of experimental manipulations.² Due to all these factors more focus is being paid nowadays to microwave enhanced chemical reactions.

Diels-Alder cycloaddition is the most useful and widely extended method in organic synthesis and is a crucial step in a wide variety of natural products skeleton constructions. Since this is a thermal reaction, the influence of microwave irradiation should be significant. Solvents that possess high dielectric constants such as dichloromethane superheat rapidly in microwave while those with low dielectric constants heat slowly.³ Other efforts to increase the rate and yield of thermal reactions have been the use of Lewis acid catalysts⁴ and high pressure.⁵

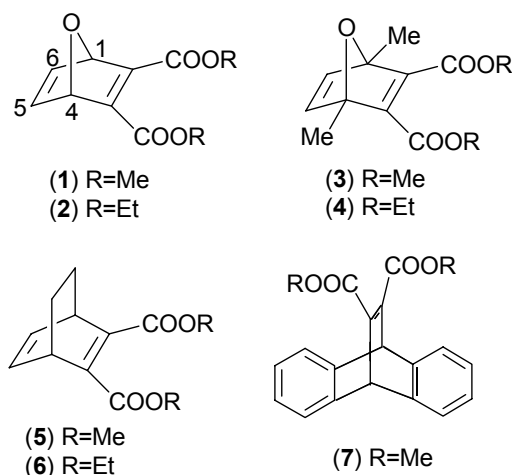
Herein we present the results of the reactions of dimethyl acetylenedicarboxylate (DMAD) and diethyl acetylenedicarboxylate (DEAD) with furan, 2,5-dimethyl furan, 1,3-cyclohexadiene and anthracene in a teflon container under microwave irradiation.

These reactions proceed efficiently in the presence of AlCl_3 as catalyst and in CH_2Cl_2 as solvent. To the best of our knowledge there have been no previous studies of these applications of microwave ovens.

Results and discussion

In this article we describe some [4+2]-cycloaddition reactions by using the dienophilic substrates, such as substituted acetylenedicarboxylates with dienic substrates as furan, 2,5-dimethylfuran, 1,3-cyclohexadiene and anthracene. The classical method for these Diels-Alder reactions requires long heating times at high temperatures (Table).⁶⁻¹⁴ In our hands all reactions proceeded in the presence of polar solvent and catalyst in about one to two minutes (with the power regulation of domestic microwave oven). DMAD and DEAD were allowed to react successively with cyclic dienes in the minimum amount of solvent (CH_2Cl_2) and catalytic amount of AlCl_3 . A continuous MW-irradiation with incident 650 W power during 80-120 s gave the adducts **1-7** in excellent yields (90-95%). Reaction conditions for cycloadditions have been optimized to obtain the best yields. Dichloromethane was used because it superheats rapidly due to its high dielectric constant.³ AlCl_3 was used as catalyst to accelerate the rate of reaction because of the complexation of carbonyl group in dienophile with catalyst. This complexation accentuates both the energy and orbital distortion effects of the carbonyl group and therefore enhance the reactivity of the dienophile, relative to the uncomplexed compound.¹⁵

Cycloadducts



Otherwise, we observed that adducts, upon more powerful irradiation or longer times with low power were decomposed by a retro Diels-Alder reaction and produced 1,2-substituted benzenes and 3,4-substituted furans.¹⁶

Table. Comparison of experimental conditions for Diels-Alder reactions of DMAD and DEAD.

Adduct	Microwave irradiation		Conventional heating	
	Conditions ^a	Yield (%) ^b	Conditions	Yield (%)
1	10 s × 10	95	Neat, 100 °C, 16 h ⁶	>95
			Ether, 20 h ⁷	81
2	10 s × 10	95	Neat, 100 °C, 4 h ⁸ , 18 h ⁹	>95
3	10 s × 10	95	Neat, 100 °C, 10 h ¹⁰	>95
4	10 s × 10	95	Neat, 100 °C, 4 h ⁸	>95
5	10 s × 8	95	Neat, room temperature, 48 h ¹¹	>95
			Neat, reflux, 1 h ¹²	
6	10 s × 8	95	Neat, 200 °C, 1 h ¹³	>95
7	10 s × 12	90	Neat, 180 °C, 15 min ¹⁴	84

^a Reactants used in equimolar amounts or in excess of dienophile for 7 (1.4 : 1).

^b Isolated product.

As Table shows, microwave irradiation allowed cycloadducts to be obtained in 80-120 s with good yields, avoiding the preparation of 1,2-substituted benzenes and 3,4-substituted furans which occur usually by classical heating.⁹ Thus in Diels-Alder reactions the control of irradiation time and microwave power is very important. All prepared compounds conformed to the literature data (see Table).

Conclusions

In summary, the microwave irradiation enhances Diels-Alder reactions of DMAD and DEAD with furan, 2,5-dimethylfuran, 1,3-cyclohexadiene and anthracene. The cycloadducts can be synthesized in high yield within minutes. AlCl₃ as catalyst with CH₂Cl₂ as solvent reduced the reaction times and increased the yields

Experimental

The microwave oven used for this study was a domestic microwave oven (National, Model NN-C988W) with six power settings. All reactions were carried out in medium high mode (600 W) in PFA teflon containers manufactured by Savillex corporation. To prevent the danger of explosion of closed vessels under MW irradiation

the amount of the starting material was adapted by capacity of the vessel and the power of microwave was adjusted for control of the pressure and temperature. In addition, all reactions were conducted in a safe hood. All NMR spectra were measured in CDCl_3 solution. Chemical shifts are reported in ppm downfield from tetramethylsilane (TMS) as an internal reference at 0 ppm. Proton and carbon spectra were recorded on 300 MHz (Bruker Germany Spectrospin), 500 MHz (Bruker DRX- 500, AVANCE) and 90 MHz (FTNMR Geol, GNM-Ex 90A) spectrometers. Some products were characterized also by GC/MS (Agilent, 5973N mass selective detector, Agilent 6890 series G.C. system, Hewlett-Packard). Riedel-de Haën plates coated with silica gel 60F₂₅₄ were used for thin-layer chromatography (TLC). Flash column chromatography was performed on silica gel (spectrum SIL 58, 230-400 mesh, grade 60). The melting points were determined on a Kofler block.

Diels-Alder reaction under microwave irradiation; typical procedure.

Dimethyl 7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (1). A mixture of DMAD (0.37 g, 3.0 mmol), furan (0.20 g, 3.0 mmol) and AlCl_3 (0.026 g, 0.2 mmol) was suspended into a minimum amount of solvent (1 mL CH_2Cl_2). The reaction mixture was placed in the MW reactor and was irradiated 100 s with a power 600 W-IP. After cooling, aluminum chloride was separated by filtration through celite and washed with CH_2Cl_2 . The combined filtrates were concentrated. The crude product was purified by flash column chromatography on silica gel using ethyl acetate/hexane (1:3) as eluent. The yellowish oil adduct (0.60 g, 95%) was identified as (1) by a comparison with the literature data:^{6,7} ^1H NMR (300 MHz, CDCl_3) δ 7.20 (m, 2H, H5 and H6), 5.66 (m, 2H, H1 and H4), 3.80 (s, 6H, 2 CH_3); ^{13}C NMR (90 MHz, CDCl_3) δ 163.2 (C=O), 152.9, 143.2, 85.0, 53.1. MS m/z (relative intensity) (EI): 210 (3.2%, M^+), 184 (10), 153 (56.6), 119 (73.3), 111 (12.3), 68 (100), 59 (17.3), 39 (20).

Diethyl 7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (2). Yellowish oil (0.68 g, 95%); ^1H NMR (90 MHz; CDCl_3) δ 7.22 (m, 2H, H5 and H6), 5.66 (m, 2H, H1 and H4), 4.26 (q, J 7 Hz, 4H, 2 CH_2CH_3), 1.31 (t, J 7 Hz, 6H, 2 CH_2CH_3); ^{13}C NMR (90 MHz, CDCl_3) δ 164.0 (C=O), 152.1, 140.2, 83.6, 60.1, 13.6.

Dimethyl 1,4-dimethyl-7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (3). Yellowish oil (0.68 g, 95%); ^1H NMR (90 MHz; CDCl_3) δ 6.95 (m, 2H, H5 and H6), 3.80 (s, 6H, 2 OCH_3), 1.81 (s, 6H, 2 CH_3); ^{13}C NMR (90 MHz; CDCl_3) δ 164.4 (C=O), 154.8, 147.2, 92.02, 52.1, 15.4.

Diethyl 1,4-dimethyl-7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (4). Yellowish oil (0.76 g, 95%); ^1H NMR (90 MHz; CDCl_3) δ 6.95 (s, 2H, H5 and H6), 4.26 (q, J 7 Hz, 4H, 2 CH_2CH_3), 1.80 (s, 6H, 2 CH_3), 1.32 (t, J 7 Hz, 6H, 2 CH_2CH_3); ^{13}C NMR (90 MHz; CDCl_3) δ 165.3 (C=O), 151.8, 147.0, 90.1, 60.6, 23.6, 13.6.

Dimethyl bicyclo[2.2.2]octa-2,5-diene-2,3-dicarboxylate (5). Yellowish oil (0.63 g, 95%); ^1H NMR (500 MHz; CDCl_3) δ 6.36 (m, 2H, H5 and H6), 4.02 (m, 2H, H1 and H4), 3.76 (s, 6H, 2 OCH_3), 1.43 (m, 4H, 2 H7 and 2 H8); ^{13}C NMR (500 MHz; CDCl_3) δ 165.1 (C=O), 140.9, 125.5, 52.3, 47.0, 28.9. MS m/z (relative intensity) (EI): 222 (2%, M^+), 195 (6.6), 163 (100), 104 (5), 92 (8.3), 77 (17.3), 50 (6.3), 28 (3.3).

Diethyl bicyclo[2.2.2]octa-2,5-diene-2,3-dicarboxylate (6). Yellowish oil (0.71 g, 95%); ^1H NMR (90 MHz; CDCl_3) δ 6.38 (m, 2H, H5 and H6), 4.27 (q, J 7 Hz, 4H, 2 CH_2CH_3), 4.02 (m, 2H, H1 and H4), 1.43 (m, 4H, 2 H7 and 2 H8), 1.31 (t, J 7 Hz, 6H, 2 CH_2CH_3); ^{13}C NMR (90 MHz; CDCl_3) δ 168.0 (C=O), 138.6, 122.0, 60.9, 47.1, 28.8, 13.6.

Diethyl tetracyclo[6.6.2.0^{2,7}.0^{9,14}]hexadeca-2,4,6,9(14),10,12,15-heptaene-15,16-dicarboxylate (7). 0.34 g, 90%; mp 160–161 °C; ^1H NMR (500 MHz; CDCl_3) δ 7.31–7.10 (m, 8H, ArH), 4.87 (s, 2H, 2 CH-Ar), 3.77 (s, 6H, 2 CH_3); ^{13}C NMR (90 MHz; CDCl_3) δ 164.0 (C=O), 155.0, 136.1, 128.4, 126.6, 52.3, 49.9. MS m/z (relative intensity) (EI): 320 (1.6%, M^+), 202 (6.6), 179 (12), 178 (75), 44 (65), 28 (100).

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Povzetek

Z mikrovalovi pospešene Diels-Alderjeve reakcije med furanom, 2,5-dimetilfuranom, 1,3-cikloheksadienom in antracenom z dimetil acetilendikarboksilatom (DMAD) oz. dietil acetilendikarboksilatom (DEAD) v običajni kuhinjski mikrovalovni pečici dajejo [4+2] cikloadukte z visokimi izkoristki. Aluminijev(III) klorid v diklorometanu ob učinkovanju mikrovalov poveča reakcijske hitrosti.