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# MICROWAVE ASSISTED ENANTIOSELECTIVE MICHAEL ADDITION REACTION USING BINOL-AI-LI CATALYST

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### MICROWAVE ASSISTED ENANTIOSELECTIVE MICHAEL ADDITION REACTION USING BINOL-AI-LI CATALYST

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#### ABSTRACT

Enantioselective (S)-BINOL-Al-Li catalyzed Michael reaction of malonates and thiols with cyclic enones are achieved with high enantioselectivity in a remarkably lesser reaction time using microwaves.

*Key Words:* Microwave irradiation; Michael reaction; Enantioselectivity; Heterobimetallic catalyst

#### **INTRODUCTION**

Conjugate addition reactions of carbon nucleophiles to  $\alpha,\beta$ -unsaturated carbonyl compounds are among the most widely used methods for C–C bond formation in organic syntheses.<sup>[1]</sup> Recently Shibasaki<sup>[2]</sup> and his co-workers introduced a new class of aluminium based BINOL complexes as effective catalysts for Michael addition reactions of malonate esters

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to cyclic enones. But the reactions require long reaction times for completion (72 h).

In recent years, microwave mediated organic reactions<sup>[3]</sup> have gained importance providing the advantages of short reaction times, reduced amount of solvent and eco-friendly nature of the process. This, coupled with the significance of Michael reaction in asymmetric C–C bond formation, prompted us to study enantioselective Michael addition reaction under microwave irradiation.

#### **RESULTS AND DISCUSSION**

We describe here the use of microwave technology in asymmetric Michael addition of malonates to cyclic  $\alpha,\beta$ -unsaturated ketones in the presence of S-BINOL–Al–Li catalyst<sup>[4]</sup> (Sch. 1).

We adopted a similar procedure reported by Shibasaki<sup>[4]</sup> for preparing the heterobimetallic catalyst (which contains two different metal ions, Al and Li for coordinating with the reactants after each catalytic cycle). Typically a mixture of cyclohexenone and diethylmalonate was irradiated with microwaves in a domestic microwave oven (IFB model 750 W). After cooling to room temperature, the product was isolated (See Experimental). The experiment was performed with a number of different substrates and the results are presented in the table. Interestingly the reaction was complete within a short period of time (2–15 min) retaining high enantioselectivity (>98%). Although many reports are available on the catalytic asymmetric Michael addition using malonate derivatives, the same using thiols as substrates has not been explored in detail. The only catalyst that has shown reasonably good enantioselectivity in the asymmetric C–S bond formation was made from Lanthanum–sodium–BINOL (LSB).<sup>[5]</sup> However, the reaction required longer reaction times (from 20 min to 43 h). Hence we explored



MWI = Microwave irradiation

Scheme 1.

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#### **BINOL-Al-Li CATALYST REACTION**

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Table 1. Asymmetric Michael Adducts of Malonates and Thiols with Cyclic Enones Using S-BINOL-AI-Li Under MWI

		с ·	Time	Yield	1 (%)	eec	(%)	
Enone	Malonate (R)	Ctrl <sup>a</sup> (h)	MWI <sup>b</sup> (min)	Ctrl	IWM	Ctrl	IWM	$[\alpha]_{D}^{0}$ $(c=5$ in CHCl <sub>3</sub> ) <sup>d</sup>
n = 1	Ethyl	72	9	84	82	91	88	-29.75 (+24.2, $c = 1.89$ in CHCl <sub>3</sub> 82% ee for
n = 1	Isopropyl	I	12	I	80	I	I	the R-isomer -3.1 (-) <sup>e</sup>
n = 1	Benzyl	72	10	93	90	91	90	-3.0 (+28.35, c = 1.89, CHCl3 82% ee for the
		i	G		0		0	R-isomer)
n = 2	Ethyl	72	×	87	90	95	98	$-3.50 (+2.9, c = 2.56, CHCl_3 81\%$ ee for the
								R-isomer)
n = 2	Isopropyl	$46^{f}$	15	72	75	49	52	$-2.78 (+2.3, c = 1.0, CHCl_3, 49\%$ ee for the
								R-isomer)
n = 2	Benzyl	72	10	88	90	66	90	-1.1 (+ 1.10, $c = 2.21$ , CHCl <sub>3</sub> , 88% ee for the
								R-isomer)
	Thiols							
n=2	R=H	30	2	82	88	29	31	-22.5 (-16.4, c = 1.0, benzene, 22.5% ee for
								the S-isomer)
n=2	R=CH <sub>3</sub>	25	2	83	85	30	28	-19.6 (+70.00, c = 2.0, benzene, 100% ee for
								the S-isomer)
a.C+1		of another to						
b MWT	was carried out	i at room to in milee of	amperature sunt 1 min duration	mg. with 3	0 ser int	امسم		
CAA WING	determined base	in puise of	ntical rotation	, aerilor	and otions	viv tha	literatu	a caa Daf [/]
CC Was	nerei IIIIIten Dase		pucal rotation v	alues e			ווכומוח	16 266 INCI. [4].

<sup>d</sup>Values in the parentheses indicate the reported [ $\alpha$ ]<sub>D</sub> values. See Ref. [4].

<sup>e</sup>Literature  $[\alpha]_D$  was not available. <sup>f</sup>See Ref. [6].

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the reaction using BINOL-Al-Li under microwave conditions. It was gratifying to note that the addition was complete in a remarkably less time (2 min) with moderate enantioseletivity (31%). The results are presented in Table 1 (Sch. 2).

In conclusion, the BINOL-Al-Li catalyst can be effectively used to promote the asymmetric Michael addition of malonates and thiols under microwave activation in short reaction times and with high enantioselectivity.

#### **EXPERIMENTAL**

Reactions were conducted under nitrogen atmosphere in an ovendried flask closed with a septum. BINOL–Al–Li catalyst was prepared from S-BINOL and LiAlH<sub>4</sub> by the literature procedure.<sup>[4]</sup> To 0.5 mmol of BINOL–Al–Li catalyst generated in situ, 5 mmol of 2-cyclohexenone (490 mg, 5 mmol) and diethyl malonate (800 mg, 5 mmol) were added. The reaction mixture was kept under microwave irradiation for the stipulated period of time (See Table 1). The progress of the reaction was monitored by tlc. When all of the malonate had reacted, the reaction mixture was quenched with 1N HCl and extracted with ethyl acetate. The organic layer was washed successively with saturated NaHCO<sub>3</sub> solution, brine and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. Removal of the solvent under reduced pressure gave a syrupy mass, which on flash column chromatography (using 230–400 mesh type silica gel, Hexane : ethyl acetate (98 : 2) as eluant) gave the product as a colorless oil (1.1 g, 90% yield,  $[\alpha]_D^0 = -3.5^\circ$  ee = 98%).

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