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Enantioselective Michael reaction of anthrone catalyzed by chiral tetraoxacalix[2]arene[2]triazine derivatives†

Hayriye Nevin Genc *

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A highly enantioselective Michael addition reaction of anthrone with nitroalkenes by chiral tetraoxacalix[2]arene[2]triazine catalysts was investigated as a novel topic. The stereoselective conversion progressed smoothly by employing 10 mol% of the catalyst and afforded the corresponding Michael adducts with acceptable to high enantioselectivities (up to 97% ee) and very high yields (up to 96%).

1. Introduction

The chemical properties of anthrone and compounds containing the anthrone skeleton are significant in organic chemistry. Anthrones and their enol tautomers, *i.e.*, 9-anthrols form a vital part of anthracenes since the oxidation of the central rings yields 9,10-anthraquinones, while their reduction affords anthracenes, which are useful intermediates.[1,2] However, naturally occurring compounds bearing the anthrone platform are isolated either as O- or C-glycosides or in a free form from a broad diversity of plants and shrubs such as rhubarb, cassia, and cascara sagrada.[3,4] Several such substances have noteworthy biological characteristics and are utilized as antimicrobial, emetic, antipsoriatic or androgen receptors and telomerase blockers.[5,6] Recent studies have demonstrated that some anthrone- or anthraquinone-based naturally occurring compounds show strong and distinctive antitumor behaviours.[7–11]

The Michael reaction of carbon-centered nucleophiles with different Michael acceptors provides a straightforward and robust technique for the formation of C–C bonds and has received prevalent preference in the production of organic materials. As a result, substantial works have been carried out for the development of the enantioselective forms of this conversion.[12–14] Although remarkable developments have emerged in the catalytic asymmetric Michael reaction, developing a new Michael reaction for the effective production of different novel materials remains a significant target for studies conducted in both academic and industrial contexts. In this field of study, similar to the case of a Michael donor, various carbon-centered nucleophiles such as aldehydes and ketones,[15–19] malonate esters,[20–22] ketoesters,[23] and 1,3-diketones[24–26] have been comprehensively studied; in contrast, not much development has taken place in the improvement of the usage of anthrone as a nucleophile for the Michael addition reaction.[27–33]

Calixarenes and macromolecules bearing one or more calixarene platforms are known as efficient supramolecular materials. Heteroatom-bridged calixaromatics, also called heteroaromatic calixarenes, are a novel group of macrocyclic host compounds in supramolecular chemistry.[34,35] Despite their exceptional physical and bonding characteristics that come from the electronic and steric influences of heteroatom bridges, heteroaromatic calixarenes are far rarer in usage.[36,37] The self-tuning and fine-tuning cavities of their electronic characteristics make heteroaromatic calixarenes strong macrocyclic hosts regarding their interactions with neutral organic guests[38,39] and with positively[40] and negatively charged compounds.[41–43] Oxygen- and nitrogen-bridged calix[2]arene[2]triazines are noteworthy heterocalixaromatics.[44–47] Based on the characteristics of the heteroatoms in the bridging units, calix[2]arene[2]triazines use adaptable conformational constructs and may provide a diverse set of cavity sizes. Not limited to interactions of inclusion,[48] these materials may also show π–π interactions of aromatic rings and hydrogen bonding interactions on the triazine nitrogen atoms as chiral host compounds.

In the past decade, we have reported the synthesis and applications of lower-rim-substituted calix[4]arene-based macromolecules with different functional groups as multiple H-bond donor chiral catalysts for stereoselective conversions.[49–51] Likewise, we have recently reported substituted tetraoxacalix[2]arene[2]triazine derivatives with different purposes as chiral catalysts in the stereoselective Michael additions of isobutyraldehyde using different substituted and

Department of Science Education, A. K. Education Faculty, Necmettin Erbakan University, Konya 42090, Turkey. E-mail: hngenc@erbakan.edu.tr; Fax: +90 332 3238225; Tel: +90 332 3238220/5534

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unsubstituted aromatic *trans*-β-nitrostyrenes.[52] Here, we described an efficient one-pot process to synthesize optically active tetraoxacalix[2]arene[2]triazine derivatives and their possible applications as organic catalysts in the Michael addition of anthrone to β-nitroolefins under mild conditions. As far as we know, this study is the first implementation of tetraoxacalix[2]arene[2]triazine catalysts in the enantioselective reactions of anthrone.

2. Experimental

2.1. Synthesis

2.1.1. Procedure for the synthesis of compounds 4a-4b. Tetraoxa-bridged calix[2]arene[2]triazine was prepared following a procedure described by Wang *et al.*[53,54] A mixture of (*R*)-2-amino-1-((*S*)-2-benzhydrylpyrrolidin-1-yl)-2-phenylethanone **1** or (1*S*,2*S*)–*N*,*N*-bis(3-phenylpropyl)cyclohexane-1,2-diamine **2** (1.1 mmol) and DIPEA (2.2 mmol) in THF (20 mL) was added to a solution of tetraoxa-bridged calix[2]arene[2]triazine **3** (0.5 mmol) in THF (20 mL) at room temperature. The mixture was refluxed for 48–56 h, after which the solvent was evaporated under vacuum, giving off a solid residue. The crude mixture was purified by column chromatography on silica gel using hexane/EtOAc (10 : 1, v/v) to afford the desired products as crystalline solids. The products were characterized by a combination of ^{1}H NMR, ^{13}C NMR, FTIR,[55,56] and elemental analysis.

*Compound **4a**.* Crystalline solid; 75% yield; $\alpha_D^{25} = -205.00$ (c 1, $CHCl_3$); mp 220–222 °C; IR (cm^{-1}): 1358, 1479, 1563, 1708, 3261; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.21–1.40 (m, 8H), 2.98–3.17 (m, 4H), 4.72 (d, 2H, J = 6.7 Hz), 5.04 (d, J = 6.8 Hz, 2H), 6.18 (s, 2H), 7.16–7.38 (m, 32H), 7.82–7.87 (m, 6H), NH-signals not found; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.34, 29.47, 46.29, 51.17, 58.64, 65.80, 124.74, 127.33, 127.63, 128.00, 128.23, 128.43, 128.60, 128.73, 129.05, 129.68, 130.00, 138.20, 140.53, 140.68, 158.20, 162.20, 166.00, 169.10; anal. calcd. for $C_{68}H_{58}N_{10}O_6$ (1111.25): C, 73.49; H, 5.26; N, 12.60%; found: C, 73.51; H, 5.31; N, 12.48%.

*Compound **4b**.* Crystalline solid; 78% yield; α_D^{25} = +218.00 (c 1, $CHCl_3$); mp 326–328 °C; IR (cm^{-1}): 1365, 1483, 1569, 1705, 3281; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.19–1.35 (m, 8H), 1.82–2.12 (m, 16H), 2.60–2.75 (m, 10H), 2.85–2.90 (m, 8H), 4.13 (q, J = 2.7 Hz, 2H), 7.01–7.15 (m, 20H), 7.20 (t, J = 8.4, 0.5 Hz, 2H), 7.25–7.30 (m, 4H), 7.37–7.42 (m, 2H), NH-signals not found; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.16, 21.03, 27.51, 32.04, 32.50, 34.14, 57.00, 60.47, 62.33, 102.86, 116.90, 128.41, 128.90, 128.96, 130.28, 140.40, 157.07, 158.21, 166.00; anal. calcd. for $C_{66}H_{74}N_{10}O_4$ (1071.35): C, 73.99; H, 6.96; N, 13.07%; found: C, 74.15; H, 7.12; N, 12.98%.

2.1.2. Procedure for Michael reaction. A solution of nitroalkenes **6a–k** (0.4 mmol) and the chiral catalyst (0.04 mmol) in toluene (4 mL) was stirred and then, anthrone **5** (0.48 mmol) was added. After being stirred for 36–72 h at room temperature, the reaction mixture was subjected directly to flash column chromatography on silica gel (hexane/EtOAc = 5 : 1) to furnish the corresponding products. The ee% values of the Michael reaction products were determined by chiral HPLC analysis using Daicel Chiralpak OD-H or AS-H columns. The HPLC conditions for products **7a–7k** are shown in Table 1; the ^{1}H NMR, ^{13}C NMR and FTIR spectroscopy values of products **7a–7k** are shown in Table 2.

3. Results and discussion

The chiral tetraoxacalix[2]arene[2]triazine derivatives **4a** and **4b**, which were chosen as chiral catalysts in the model asymmetric Michael reaction, were synthesized in four steps starting from (*R*)-phenylglycine and (1*S*,2*S*)-(+)-1,2-diaminocyclohexane, respectively. The chiral subunits (*R*)-2-amino-1-((*S*)-2-benzhydrylpyrrolidin-1-yl)-2-phenylethanone **1** and (1*S*,2*S*)–*N*,*N*-bis(3-phenylpropyl) cyclohexane-1,2-diamine **2**, which were synthesized in three steps, were prepared according to previously reported procedures,[57,58] as illustrated in Scheme 1. Subsequently, the chiral tetraoxacalix[2]arene[2]triazines **4a** and **4b** were synthesized from **1** and **2**, respectively, in overall good yields (up to 75–78%), as illustrated in Scheme 2.

In the first review of the conditions, having selected the Michael addition of anthrone **5** and *trans*-β-nitrostyrene **6a** as the enantioselective reaction, we found that the tetraoxacalix[2]arene[2]triazine catalysts catalyzed the process effectively, affording the expected adduct **7a** in an optically active form. The reaction progressed successfully in nonpolar solvents including

Table 1 HPLC conditions of products **7a–7k**

Product	Column	Hexane/2-propanol	Flow rate	t_R (minor)	t_R (major)
7a	AS-H	90 : 10	0.7 mL min^{-1}	25.96 min	23.25 min
7b	OD-H	80 : 20	1.0 mL min^{-1}	15.94 min	12.85 min
7c	OD-H	80 : 20	1.0 mL min^{-1}	11.82 min	10.06 min
7d	AS-H	80 : 20	1.0 mL min^{-1}	12.85 min	10.15 min
7e	OD-H	70 : 30	1.0 mL min^{-1}	18.14 min	15.32 min
7f	AS-H	80 : 20	1.0 mL min^{-1}	13.25 min	10.42 min
7g	AS-H	80 : 20	1.0 mL min^{-1}	17.43 min	14.65 min
7h	AS-H	90 : 10	1.0 mL min^{-1}	18.19 min	16.02 min
7i	OD-H	80 : 20	1.0 mL min^{-1}	19.62 min	26.21 min
7j	AS-H	90 : 10	1.0 mL min^{-1}	26.11 min	21.93 min
7k	AS-H	70 : 30	1.0 mL min^{-1}	12.35 min	10.19 min

Table 2 ^{1}H NMR, ^{13}C NMR, and FTIR spectroscopy values of products **7a–7k**

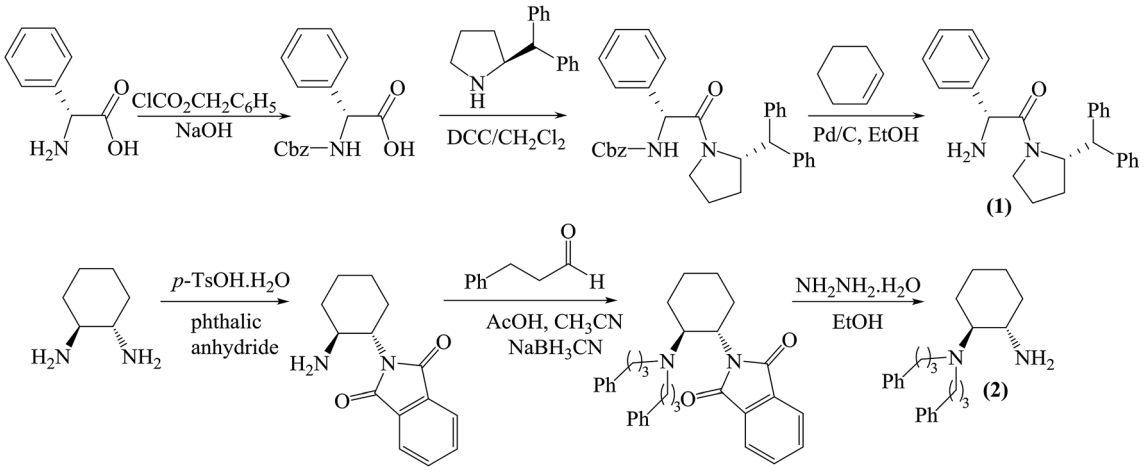
7a	Mp	147–148 °C
	IR (cm^{-1})	928, 1310, 1548, 1600, 1671
	^{1}H NMR (400 MHz, $CDCl_3$)	4.03–4.06 (m, 1H), 4.53 (d, J = 3.7 Hz, 1H), 4.60 (dd, J = 13.3, 7.0 Hz, 1H), 4.88–4.91 (dd, J = 13.3, 9.1 Hz, 1H), 6.07 (d, J = 7.6 Hz, 2H), 6.91 (t, J = 7.8 Hz, 2H), 7.14–7.17 (m, 1H), 7.39–7.43 (m, 2H), 7.50 (d, J = 8.5 Hz, 2H), 7.60–7.68 (m, 2H), 7.94 (d, J = 7.8 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H)
	^{13}C NMR (100 MHz, $CDCl_3$)	45.9, 52.8, 76.4, 126.1, 126.9, 127.8, 128.0, 128.1, 128.2, 128.3, 128.7, 131.9, 132.2, 132.9, 133.4, 134.6, 139.8, 142.3, 183.1
7b	Mp	65–67 °C
	IR (cm^{-1})	929, 1317, 1552, 1598, 1671
	^{1}H NMR (400 MHz, $CDCl_3$)	4.31–4.39 (m, 2H), 4.59–4.69 (m, 2H), 6.18 (d, J = 8.5 Hz, 1H), 6.80 (d, J = 6.7 Hz, 1H), 7.00 (d, J = 7.1 Hz, 1H), 7.40–7.61 (m, 4H), 7.63 (s, 2H), 8.13 (t, J = 7.8 Hz, 2H)
	^{13}C NMR (100 MHz, $CDCl_3$)	45.0, 48.0, 74.0, 126.3, 127.1, 127.3, 127.9, 128.3, 128.5, 128.6, 129.8, 130.3, 131.7, 132.5, 133.0, 133.3, 133.6, 134.9, 136.0, 138.9, 140.2, 183.4
7c	Mp	141–143 °C
	IR (cm^{-1})	935, 1322, 1551, 1600, 1671
	^{1}H NMR (400 MHz, $CDCl_3$)	4.18–4.24 (m, 1H), 4.37 (dd, J = 13.3, 8.4 Hz, 1H), 4.50 (dd, J = 13.6, 6.9 Hz, 1H), 4.68 (d, J = 3.6 Hz, 1H), 5.57 (d, J = 3.3 Hz, 1H), 6.20–6.22 (m, 1H), 7.00 (d, J = 7.5 Hz, 1H), 7.19 (d, J = 1.1 Hz, 1H), 7.49–7.54 (m, 4H), 7.60–7.63 (m, 1H), 8.20 (t, J = 6.1 Hz, 2H)
	^{13}C NMR (100 MHz, $CDCl_3$)	44.8, 46.9, 73.9, 109.3, 110.1, 126.0, 127.3, 127.8, 128.2, 128.3, 128.5, 133.0, 133.2, 133.5, 133.7, 139.9, 140.5, 142.7, 148.4, 183.2
7d	Mp	63–65 °C
	IR (cm^{-1})	938, 1320, 1555, 1601, 1659
	^{1}H NMR (400 MHz, $CDCl_3$)	4.00–4.03 (m, 1H), 4.81 (d, J = 5.4 Hz, 1H), 4.89–5.01 (m, 1H), 5.12 (dd, J = 13.9, 5.5 Hz, 1H), 6.60–6.62 (m, 1H), 7.10–7.13 (m, 2H), 7.29–7.36 (m, 2H), 7.51–7.65 (m, 5H), 7.96 (d, J = 7.6 Hz, 1H)
	^{13}C NMR (100 MHz, $CDCl_3$)	45.0, 49.9, 77.1, 126.0, 126.1, 126.9, 127.8, 128.2, 129.0, 129.4, 130.0, 131.9, 132.2, 132.4, 133.1, 135.0, 139.8, 140.3, 181.3
7e	Mp	69–72 °C
	IR (cm^{-1})	936, 1313, 1529, 1551, 1604, 1670
	^{1}H NMR (400 MHz, $CDCl_3$)	4.69–4.74 (m, 1H), 4.83 (d, J = 5.2 Hz, 1H), 5.09 (dd, J = 13.6, 10.3 Hz, 1H), 5.30 (dd, J = 13.9, 5.5 Hz, 1H), 6.69–6.72 (m, 1H), 7.29–7.38 (m, 3H), 7.48–7.62 (m, 6H), 7.90 (dd, J = 13.9, 7.6 Hz, 2H)
	^{13}C NMR (100 MHz, $CDCl_3$)	44.9, 45.5, 76.8, 123.9, 125.8, 126.1, 127.6, 127.8, 128,2, 128.9, 129.1, 129.2, 129.5, 131.9, 132.0, 132.5, 132.9, 134.0, 140.0, 140.9, 150.0, 183.1
7f	Mp	129–131 °C
	IR (cm^{-1})	929, 1320, 1509, 1555, 1600, 1661
	^{1}H NMR (400 MHz, $CDCl_3$)	3.19 (s, 1H), 4.39–4.43 (m, 1H), 4.69 (d, J = 3.9 Hz, 1H), 4.79 (dd, J = 13.1, 10.1 Hz, 1H), 5.09 (dd, J = 13.4, 5.9 Hz, 1H), 6.03 (d, J = 6.5 Hz, 1H), 6.50 (t, J = 7.4 Hz, 1H), 6.70 (d, J = 8.0 Hz, 1H), 7.10 (t, J = 7.3 Hz, 1H), 7.39–7.50 (m, 4H), 7.59–7.62 (t, J = 7.4 Hz, 2H), 7.82 (d, J = 7.4 Hz, 1H), 7.89 (m, J = 7.9 Hz, 1H)
	^{13}C NMR (100 MHz, $CDCl_3$)	44.9, 45.0, 54.8, 76.7, 109.9, 120.4, 121.3, 124.6, 125.8, 126.2, 127.5, 128.0, 128.4, 129.0, 129.4, 131.9, 132.9, 141.0, 142.6, 156.9, 183.0
7g	Mp	115–117 °C
	IR (cm^{-1})	934, 1313, 1549, 1600, 1661
	^{1}H NMR (400 MHz, $CDCl_3$)	4.01–4.06 (m, 1H), 4.56–4.62 (m, 2H), 4.89 (dd, J = 13.3, 8.8 Hz, 1H), 5.99 (d, J = 7.3 Hz, 1H), 6.17 (s, 1H), 6.86 (t, J = 7.9 Hz, 1H), 7.32 (d, J = 9.1 Hz, 1H), 7.42–7.59 (m, 4H), 7.65–7.71 (m, 2H), 8.05 (d, J = 7.6 Hz, 1H), 8.15 (d, J = 7.7 Hz, 1H)
	^{13}C NMR (100 MHz, $CDCl_3$)	45.9, 53.0, 76.1, 121.9, 126.6, 127.2, 127.6, 128.3, 128.4, 128.5, 128.7, 129.6, 131.6, 131.9, 132.7, 133.0, 133.5, 134.6, 135.7, 139.0, 141.6, 183.0
7h	Mp	156–158 °C
	IR (cm^{-1})	929, 1315, 1548, 1600, 1659
	^{1}H NMR (400 MHz, $CDCl_3$)	2.09 (s, 3H), 4.00–4.04 (m, 1H), 4.49 (d, J = 3.5 Hz, 1H), 4.54 (dd, J = 13.1, 7.1 Hz, 1H), 4.82 (dd, J = 13.1, 8.9 Hz, 1H), 5.99 (d, J = 8.0 Hz, 2H), 6.74 (d, J = 7.7 Hz, 2H), 7.35–7.45 (m, 2H), 7.49 (d, J = 7.4 Hz, 2H), 7.56–7.61 (m, 2H), 8.03 (d, J = 7.7 Hz, 1H), 8.10 (d, J = 7.3 Hz, 1H)

Table 2 (*Contd.*)

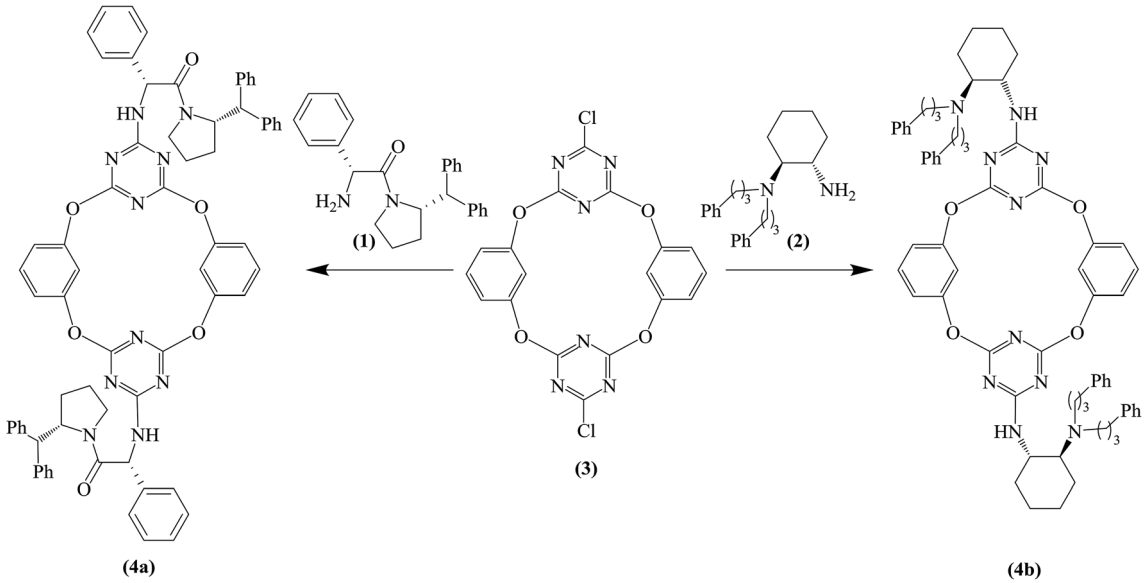
	^{13}C NMR (100 MHz, $CDCl_3$)	20.9, 45.9, 53.1, 75.8, 126.4, 126.9, 127.4, 127.9, 128.3, 128.5, 128.6, 129.9, 132.4, 132.8, 133.4, 134.3, 138.1, 139.3, 142.0, 182.9
7i	Mp	119–121 °C
	IR (cm^{-1})	929, 1312, 1511, 1548, 1599, 1671
	^{1}H NMR (400 MHz, $CDCl_3$)	3.71 (s, 3H), 3.99–4.01 (m, 1H), 4.49 (d, J = 3.8 Hz, 1H), 4.57 (dd, J = 13.3, 7.4 Hz, 1H), 4.82 (dd, J = 13.3, 9.1 Hz, 1H), 6.00 (d, J = 8.8 Hz, 2H), 6.50 (d, J = 8.8 Hz, 2H), 7.40–7.54 (m, 4H), 7.60–7.67 (m, 2H), 8.02 (d, J = 7.9 Hz, 1H), 8.10 (d, J = 7.3 Hz, 1H)
	^{13}C NMR (100 MHz, $CDCl_3$)	45.9, 52.4, 54.9, 76.9, 113.2, 125.0, 127.1, 127.5, 127.8, 128.0, 128.2, 128.3, 129.4, 132.6, 132.8, 133.9, 134.8, 139.0, 141.9, 160.0, 182.9
7j	Mp	168–171 °C
	IR (cm^{-1})	929, 1321, 1549, 1600, 1659
	^{1}H NMR (400 MHz, $CDCl_3$)	4.01–4.04 (m, 1H), 4.49 (d, J = 3.4 Hz, 1H), 4.60 (dd, J = 13.3, 7.6 Hz, 1H), 4.87 (dd, J = 13.3, 8.5 Hz, 1H), 5.99 (d, J = 8.5 Hz, 2H), 6.92 (d, J = 8.5 Hz, 2H), 7.40–7.55 (m, 4H), 7.61–7.67 (m, 2H), 8.03 (d, J = 7.9 Hz, 1H), 8.09 (d, J = 7.6 Hz, 1H)
	^{13}C NMR (100 MHz, $CDCl_3$)	45.8, 52.5, 76.4, 126.8, 127.0, 127.2, 127.6, 127.9, 128.1, 128.2, 128.4, 130.0, 131.9, 132.2, 132.9, 133.1, 134.0, 134.5, 138.9, 141.7, 182.9
7k	Mp	171–172 °C
	IR (cm^{-1})	929, 1323, 1511, 1548, 1605, 1658
	^{1}H NMR (400 MHz, $CDCl_3$)	4.01–4.06 (m, 1H), 4.55 (d, J = 3.7 Hz, 1H), 4.60 (dd, J = 13.3, 7.3 Hz, 1H), 4.90 (dd, J = 13.3, 9.1 Hz, 1H), 5.99 (dd, J = 8.8, 5.2 Hz, 2H), 6.67 (t, J = 8.8 Hz, 2H), 7.45–7.58 (m, 4H), 7.64–7.68 (m, 2H), 7.98 (d, J = 7.3 Hz, 1H), 8.07 (d, J = 7.9 Hz, 1H)
	^{13}C NMR (100 MHz, $CDCl_3$)	46.3, 52.8, 76.6, 114.8, 115.2, 127.1, 127.6, 127.9, 128.0, 128.2, 128.5, 128.9, 129.5, 130.8, 131.9, 132.8, 133.6, 134.5, 138.9, 142.1, 161.9, 182.9

hexane, $CHCl_3$, CH_2Cl_2 or toluene (Table 3, entries 1–8); however, when we used a polar solvent, such as ethyl acetate, diethyl ether or acetone, significant decrease was observed in chemical yield and enantioselectivity (Table 3, entries 15–20). This may be due to the fact that the polar solvents interacted with the organocatalysts through hydrogen bonding to weaken the activation ability of **4a** and **4b** towards the reaction. As projected by our tentative hypothesis, the best yield (96%) and enantioselectivity (97% ee) were obtained using the less polar solvent, *i.e.*, toluene.

Other aspects of this reaction such as temperature, use of the recycled catalyst, and catalyst loading were investigated (Table 4). When the same reaction was performed at 0 °C with 10 mol% of **4a** and **4b** as catalysts, the desired adduct **7a** was obtained with low to 88–89% ee in 83–85% yield, with further extension of the reaction time (72 h, Table 4, entries 3 and 4). In addition, similar to the reaction conducted at 0 °C, the reaction carried out at −20 °C showed less desired yields and enantioselectivities than the reaction at room temperature (Table 4, entries 1 and 2). Additionally, we conducted recycling analysis of the chiral catalysts **4a** and **4b** in the Michael



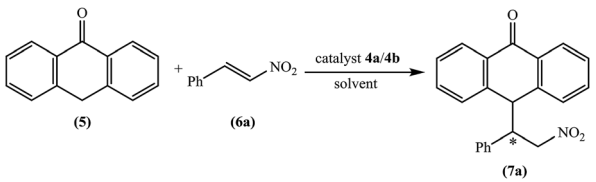
Scheme 1 The synthetic routes for starting materials **1** and **2**.



Scheme 2 The synthetic route for tetraoxa-bridged calix[2]arene[2]triazine derivatives **4a**/**4b**.

reaction of **5** and **6a**. Thus, the compounds **4a** and **4b** could be easily recycled by flash chromatography alongside Michael adducts. However, by prolonging the reaction time, low enantioselectivity and yield values were found at room temperature, as seen in Table 4 (entries 7 and 8). In the presence of 10 mol% catalysts, **4a** and **4b** showed similar enantioselectivities, but **4b** showed slightly higher catalytic activity than **4a** (Table 4, entries 5 and 6). When the loading of the catalysts **4a** and **4b** went up to 15 mol%, *trans*-β-nitrostyrene gave Michael products in low yields with 93–95% and 93–95% enantiomeric excess, respectively (Table 4, entries 9 and 10). These results were better than that for the use of 5 mol% of catalyst, in which case the yields of the Michael products were 88% for catalyst **4a** and 90% for catalyst **4b** and the enantiomeric excesses of the Michael products were 89% for catalyst **4a** and 90% for catalyst **4b** (Table 4, entries 11 and 12). These findings led us to choose the reaction conditions using toluene as a solvent at room temperature in the presence of 10 mol% of **4b** to probe the scope of nitroolefins.

Table 3 Michael addition between anthrone **5** and *trans*-β-nitrostyrene **6a** catalysed by **4a–4b** in various solvents



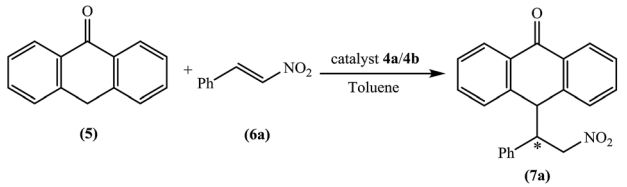
Entry[a]	Catalyst	Solvent	Time (h)	Yield[b] (%)	ee[c,d] (%)
1	**4a**	Hexane	72	88	93
2	**4b**	Hexane	72	90	95
3	**4a**	$CHCl_3$	48	85	90
4	**4b**	$CHCl_3$	48	89	91
5	**4a**	CH_2Cl_2	48	81	92
6	**4b**	CH_2Cl_2	48	83	93
7	**4a**	Toluene	48	95	96
8	**4b**	Toluene	48	96	97
9	**4a**	CH_3CN	72	92	80
10	**4b**	CH_3CN	72	95	81
11	**4a**	Xylene	72	87	91
12	**4b**	Xylene	72	90	95
13	**4a**	THF	72	82	84
14	**4b**	THF	72	85	87
15	**4a**	EtOAc	48	87	80
16	**4b**	EtOAc	48	91	85
17	**4a**	Et_2O	72	83	88
18	**4b**	Et_2O	72	86	89
19	**4a**	Acetone	48	85	82
20	**4b**	Acetone	48	88	85

[a] Conditions: anthrone (0.48 mmol), *trans*-β-nitrostyrene (0.40 mmol) and **4a**/**4b** (10 mol%) in solvents (4.0 mL). [b] Isolated yield after flash chromatograpy. [c] Determined by HPLC. [d] Determined by comparing reported data.

As we enhanced the reaction details for the Michael addition of anthrone **5** to *trans*-β-nitrostyrene **6a** (catalyst **4b** 10 mol% in toluene at room temperature), a set of different nitrostyrenes with various substituent groups were analyzed, and the results are summarized in Table 5. These nitrostyrenes reacted with anthrone to afford the corresponding adducts **7a–7k** in moderate to excellent yields with excellent enantioselectivities (Table 5, entries 1–11). As demonstrated in Table 5, anthrone reacts smoothly with a wide range of *ortho*-, *meta*- or *para*-substituted nitrostyrenes with electron-releasing or electron-withdrawing groups and the corresponding Michael adducts in good to excellent yields (86–96%) and enantioselectivities (81–97%) are obtained. To our satisfaction, *trans*-β-nitrostyrene and 4-Me-nitrostyrene as Michael acceptors gave good yields and enantioselectivities (Table 5, entries 1 and 8).

In conclusion, we developed highly efficient asymmetric Michael addition of anthrone to nitroalkenes catalyzed by

Table 4 Screening of various reaction conditions

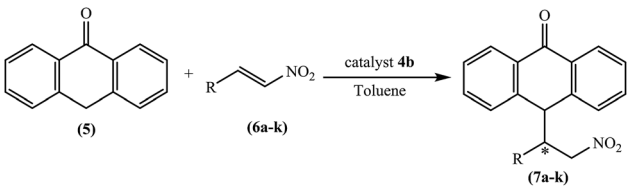


Entry[a]	Catalyst	Temp. (°C)	Time (h)	Yield[b] (%)	ee[c,d] (%)
1	**4a**	−20	72	80	85
2	**4b**	−20	72	81	86
3	**4a**	0	72	83	88
4	**4b**	0	72	85	89
5	**4a**	r.t.	48	95	96
6	**4b**	r.t.	48	96	97
7[e]	**4a**	r.t.	72	75	86
8[e]	**4b**	r.t.	72	78	90
9[f]	**4a**	r.t.	48	93	93
10[f]	**4b**	r.t.	48	95	95
11[g]	**4a**	r.t.	48	88	89
12[g]	**4b**	r.t.	48	90	90

[a] Conditions: anthrone (0.48 mmol), *trans*-β-nitrostyrene (0.40 mmol), and **4a**/**4b** (10 mol%) in toluene (4.0 mL). [b] Isolated yield. [c] Determined by HPLC. [d] Determined by comparing reported data. [e] Reaction was performed with recycled catalyst. [f] 15 mol% of catalyst was used. [g] 5 mol% of catalyst was used.

tetraoxa-bridged calix[2]arene[2]triazine organocatalysts. The results of our study were similar to the literatures which were used thiourea-tertiary amine,[32] cinchona alkaloids,[33] cinchona-based chiral polyesters,[59] and Ar-BINMOLs[60] catalysts for the reaction of anthrone to a series of nitroalkenes. The steric bulkiness and carbonyl groups were crucial in this reaction to give the corresponding adducts in lower ee than that for the catalyst without carbonyl groups. Efforts to elucidate the mechanistic details of this catalytic system and to further extend the scope and limitations of these kinds of organocatalysts are currently in progress.

Table 5 Scope of the Michael addition with anthrone **5** and nitroalkenes **6a–k**



Entry[a]	Ar	Time (h)	Product	Yield[b] (%)	ee[c,d] (%)
1	C_6H_5	48	**7a**	96	97
2	2,4-Cl_2–C_6H_4	36	**7b**	88	82
3	2-Furyl-C_6H_4	48	**7c**	94	88
4	2-Br–C_6H_4	36	**7d**	94	81
5	2-NO_2–C_6H_4	48	**7e**	91	89
6	2-OMe–C_6H_4	48	**7f**	86	95
7	3-Br–C_6H_4	36	**7g**	93	96
8	4-Me–C_6H_4	48	**7h**	95	97
9	4-OMe–C_6H_4	48	**7i**	95	91
10	4-Cl–C_6H_4	36	**7j**	91	82
11	4-F–C_6H_4	36	**7k**	91	92

[a] Conditions: anthrone (0.48 mmol), *trans*-β-nitrostyrene (0.40 mmol), and **4b** (10 mol%) in toluene (4.0 mL). [b] Isolated yield after flash chromatography. [c] Determined by HPLC. [d] The configurations were determined by comparing reported data.

4. Conclusions

In conclusion, in this work, a new class of chiral tetraoxa-bridged calix[2]arene[2]triazine derivatives described as effective organocatalysts for the Michael reaction of anthrone to various nitrostyrenes was reported for the first time. The addition reactions were carried out smoothly in toluene at room temperature by utilizing 10 mol% of **4a** and **4b** to give Michael products with high yields (up to 96%) and ee values (up to 97%).

Conflicts of interest

There are no conflicts to declare.

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