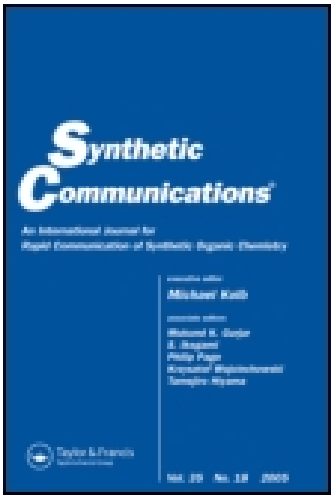

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Aluminosilicate Catalysis of Chalcone Diels–Alder Reactions

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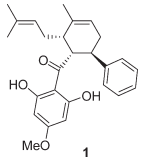
Abstract: Previously unreported Diels–Alder adducts of substituted chalcones with isoprene and myrcene have been formed at less than 0°C by employing a nanoporous aluminosilicate catalyst. This catalyst eliminates problems with diene polymerization that are encountered with many other Lewis acids. The chalcone component has some size restrictions.

Keywords: aluminosilicate catalyst, chalcone, Diels–Alder, isoprene, myrcene

Panduratin A (**1**), a natural anti-inflammatory compound isolated from *Boesenbergia pandurata* (finger root ginger),[1] is regarded as being formally derived from a Diels–Alder reaction between a chalcone and the monoterpene, ocimene. Our interest was to synthesize analogs of **1** for assessment as potential anti-inflammatories. Literature reports of uncatalyzed Diels–Alder reactions of chalcones are relatively few in number, and those that have been successful[2] have required forcing conditions.



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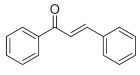

3a

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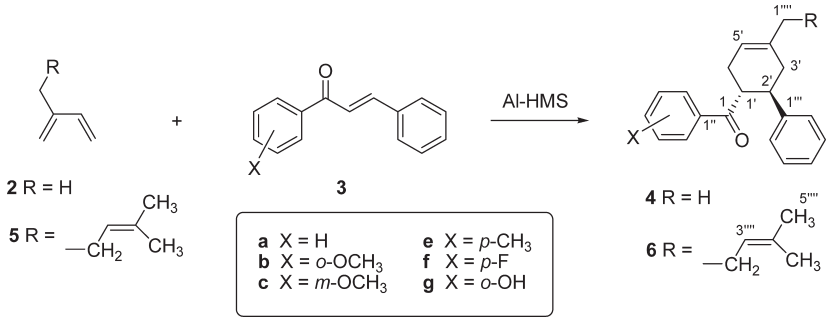
Trial studies were conducted, employing isoprene (**2**) as the diene and either cinnamaldehyde or chalcone (**3a**) as the dienophile. In both cases, heating the two compounds for an extended period at 80°C in the absence of solvent resulted in no reaction. Use of the Lewis acid catalysts $FeCl_3$ on silica, $BF_3 \cdot Et_2O$, or $EtAlCl_2$ resulted in extensive polymerization of the isoprene with no significant adduct formation.

An aluminium hexagonal molecular silica (Al-HMS), prepared by reaction of tetraethyl orthosilicate and aluminium isopropoxide in the presence of hexadecylamine, has been reported to catalyze the Diels–Alder reaction between isoprene and methyl acrylate.[3] Reaction proceeded at −1°C to give a 95% yield of the adduct. We have now employed this catalyst to prepare some new adducts of isoprene and myrcene with various substituted chalcones (Scheme 1, Table 1).

Reaction of chalcone **3a** with **2** at −1°C and at room temperature gave similar yields, but the NMR spectrum of the crude mixture at the higher temperature showed a small but significant increase in the levels of minor by-products. These NMR spectra revealed that the product was almost entirely one regioisomer.

Further NMR spectral studies revealed the orientation of the cycloaddition; in particular the homonuclear correlation spectroscopy (COSY) and heteronuclear multiple bond correlation (HMBC) experiments (Fig. 1). The COSY spectrum of the purified product showed the separation of the phenyl ^{1}H NMR resonances into a deshielded (H-2″-H-6″) and a shielded set (H2‴-H-6‴). Heteronuclear single-quantum coherence (HSQC) and HMBC correlations to these allowed assignment of all phenyl carbon signals. The HMBC spectrum linked H-2‴/6‴ (δ 7.20) to a methine carbon signal (δ 42.8) that could be assigned to C-2′. Correlation was also observed between H-2′ (δ 3.33) and C-2‴/6‴ (δ 127.5). A COSY correlation to H-2′ established the H-1′ signal (δ 3.93). The two allylic methylene groups (C-3′ and C-6′) could be distinguished by a COSY correlation between the olefinic proton, H-5′ (δ 5.50), and the H-6′ signals (δ 2.31, 2.36), along with the facts that the H-6′ peaks were broader than



Scheme 1. Diels–Alder reactions of chalcones.

Table 1. Reaction of isoprene (**2**) with chalcones at $-1^{\circ}C$ catalyzed by Al-HMS

Diene	Dienophile	X =	Time (h)	Product (% yield)
2	**3a**	H	46	**4a** (61)
2	**3b**	*o*-OCH_3	70	**4b** (76)
2	**3c**	*m*-OCH_3	94	**4c** (43)
2	**3d**	*p*-OCH_3	69	No reaction
2	**3e**	*p*-CH_3	75	**4e** (28)
2	**3f**	*p*-F	75	**4f** (78)
2	**3g**	*o*-OH	73	No reaction
5	**3a**	H	70	**6a** (73)
5	**3b**	*o*-OCH_3	70	**6b** (76)
5	**3c**	*m*-OCH_3	47	**6c** (23)
5	**3d**	*p*-OCH_3	69	No reaction
5	**3e**	*p*-CH_3	74	No reaction
5	**3f**	*p*-F	75	**6f** (78)
5	**3g**	*o*-OH	73	No reaction

those of H-3′ and there was an HMBC correlation from the methyl proton resonance (δ 1.74) to the C-3′ carbon signal (δ 39.0). COSY correlations linked H-3′ to H-2′ and H-6′ to H-1′ establishing **3a** as the regioisomer that had been formed. HMBC correlation between H-5′ and C-1′ (δ 46.6) gave further support for this conclusion. The ^{1}H NMR coupling constants measured for H-1′ ($J = 5.5$, 10, 11 Hz) and H-2′ ($J = 7$, 10, 10 Hz) were consistent with a diaxial relationship between H-1′ and H-2′, in accordance with the anticipated *trans* stereochemistry.

Reaction with isoprene was attempted with a variety of substituted chalcones (Scheme 1, Table 1). Successful synthesis of adducts was achieved with *o*- and *m*-methoxychalcone, but the *p*-isomer did not react either at $-1^{\circ}C$ or at room temperature. However, the *p*-methyl and fluoro derivatives did produce Diels–Alder adducts. *o*-Hydroxy chalcone also yielded no adduct.

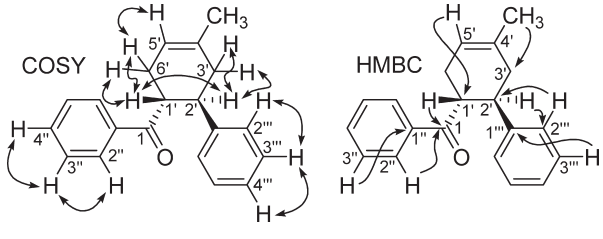


Figure 1. Key COSY and HMBC correlations in **3b**.

The fact that the *o*- and *m*-methoxy chalcones reacted but the *p*-isomer did not suggested that the controlling feature was a size factor rather than an electronic one. Molecular modeling was carried out in an effort to establish structural limits for a successful reaction. Conformational searching on chalcone **3a** yielded five low-energy conformations within a 2 kJ mol^{-1} energy window. These forms had either transoid or cisoid conformations of the enone system. Analysis of the other chalcones yielded similar sets of structures. The lowest-energy conformation for chalcone **3a** had a transoid geometry, and for size comparison, the conformation matching was used for each of the substituted chalcones, even in cases (**3b**, **3d**, and **3g**) where this was not the lowest-energy form. In each case, examination of the constructed surface for the lowest-energy conformation revealed that all the reactants used, with the exception of the unreactive *p*-methoxychalcone, extended no further than 7.5Å from the center of the reacting double bond. This gives some indication of the size of the catalytic site. The lack of reactivity of *o*-hydroxychalcone, which does not have an apparent size constraint, implies that strong polar interactions may interfere with appropriate orientation of the dienophile within the catalyst.

The catalyst proved to be capable of accommodating a larger diene. Reaction of the same set of dienophiles with myrcene (**5**) also yielded some adducts (Scheme 1, Table 1).

Quite good yields were obtained in three cases, but with a larger diene there appeared to be a little less tolerance for a larger dienophile, as *p*-methylchalcone did not react under the conditions used.

This catalyst system provides simple access to some otherwise inaccessible Diels–Alder adducts. NMR studies reveal that the regioselectivity is the same in all cases. Similar catalyst systems with larger pore size may allow successful reaction with bulkier substituted chalcones.

EXPERIMENTAL

With the exception of **3g**, which was synthesized using the method outlined in Ref. [4], the substituted chalcones were synthesized from the corresponding substituted acetophenone and benzaldehyde using $NaOH_{aq}$ in dioxane.[5] Compounds **3b**–**3g** were characterized by comparison of ^{1}H, ^{13}C, and ^{19}F (compound **3f**) NMR spectra with published data.[6] Melting points were obtained on a Mettler Toledo FP62 instrument calibrated with benzoic acid (mp 122.4°C). IR spectra were recorded on a Perkin-Elmer Spectrum BX FTIR system as KBr disks or as neat films. NMR spectra were recorded at 500 MHz (^{1}H) and 125 MHz (^{13}C) on a Varian Inova-500 spectrometer or at 282 MHz (^{19}F) on a Varian Inova-300 spectrometer. Spectra were recorded in $CDCl_3$ and are referenced to residual $CHCl_3$ for ^{1}H (δ 7.26), $CDCl_3$ for ^{13}C (δ 77.1), and external CF_3COOH for ^{19}F (δ 77.0). High-resolution electrospray mass spectra were recorded on a Bruker Daltonics

MicroTOF spectrometer. Microanalyses were performed by the Campbell Microanalytical Laboratory, University of Otago. Molecular mechanics conformational searches were performed with the aid of PCModel version 9 using the MMX forcefield with the mixed Monte Carlo coordinate movements/bond rotations strategy for the generation of initial structures.[7] The default cutoff criteria were employed. Molecular surfaces and distances were calculated using the UCSF Chimera package.[8]

Aluminum Hexagonal Molecular Silica (Al-HMS)

A homogenous solution of tetraethyl orthosilicate (10.6 g, 51.1 mmol) and aluminum isopropoxide (1.45 g, 7110 mmol) was added to a vigorously stirred solution of hexadecylamine (3.53 g, 14.6 mmol) in ethanol (45.0 ml, 766 mmol) and deionized water (23.3 g, 1290 mmol) at room temperature. The mixture was vigorously stirred for 96 h. The white gel was collected by filtration, dried at room temperature under an N_2 flow, and then calcined in dry air in an electric furnace at 500°C for 5 h.

General Procedure for Al-HMS-Catalyzed Diels–Alder Reaction

Al-HMS was predried for 2 h at 400°C/0.5 mm prior to reaction. Al-HMS (0.304 g) was added to a mixture of dienophile (1.0 mmol) and diene (3.0 mmol) in dry petroleum ether (6.00 mL) at room temperature. The mixture was then stirred vigorously at −1°C for the designated time. The catalyst was removed by filtration, and the solvent was evaporated. The crude material was chromatographed on silica gel, eluting with a dichloromethane/petroleum ether gradient. Reactions are reported according to this convention: dienophile (mass, amount), diene, reaction time, product (mass, percent yield).

Data

(4-Methyl-6-phenylcyclohex-3-enyl)(phenyl)methanone (**4a**)

Compound **3a** (0.224 g, 1.08 mmol), **2**, 46 h, **4a** (off-white crystals, 0.182 g, 61%). Recrystallized petroleum ether. Mp = 101.0°C. IR ν_{max} (KBr)/cm^{-1} 3058, 3001, 2976, 2925, 2896, 2827, 1672, 1592, 1578, 1497, 1447, 1380, 1280, 1235, 1200, 1180, 1002, 863, 773, 751, 703, 539. ^{1}H NMR δ 1.74 (3H, br. s, H-1‴′), 2.29 (2H, m, H-3′), 2.31 (1H, m, H-6′), 2.36 (1H, m, H-6′), 3.33 (1H, ddd, J = 10, 10, 7 Hz, H-2′), 3.93 (1H, ddd, J =11, 10, 5.5 Hz, H-1′), 5.50 (1H, br. s, H-5′), 7.05 (1H, tt, J = 7, 1.5 Hz, H-4‴), 7.16 (2H, ddm, J = 8, 8 Hz, H-3‴, 5‴), 7.20 (2H, dd, J = 7, 1.5 Hz,

H-2‴, 6‴), 7.36 (2H, ddm, $J = 8$, 8 Hz, H-3″, 5″), 7.47 (1H, dd, $J = 7.5$, 1.5 Hz, H-4″), 7.80 (2H, dd, $J = 8$, 1.5 Hz, H-2″, 6″). ^{13}C NMR δ 23.2 (C-1⁗), 30.9 (C-6′), 39.0 (C-3′), 42.8 (C-2′), 46.6 (C-1′), 119.3 (C-5′), 126.2 (C-4‴), 127.5 (C-2‴, 6‴), 128.0 (C-2″, 6″), 128.4 (C-3‴, 5‴), 128.5 (C-3″, 5″), 132.8 (C-4″), 134.1 (C-4′), 137.4 (C-1″), 144.7 (C-1‴), 203.7 (C-1). Anal. calcd. for $C_{20}H_{20}O$: C, 86.92; H, 7.29. Found: C, 86.83; H, 7.04.

(2-Methoxyphenyl)(4-methyl-6-phenylcyclohex-3-enyl)methanone (**4b**)

Compound **3b** (0.249 g, 1.04 mmol), **2**, 70 h, **4b** (pale yellow crystals, 0.243 g, 76%). Recrystallized petroleum ether. Mp = 83°C. IR ν_{max} (KBr)/cm^{-1} 3060, 3043, 3015, 2955, 2929, 2889, 2840, 1670, 1600, 1578, 1483, 1436, 1400. ^{1}H NMR δ 1.71 (3H, br. s, H-1⁗), 2.21 (2H, d, $J = 8$ Hz, H-3′), 2.36 (1H, m, H-6′), 2.41 (1H, dm, $J = 17$ Hz, H-6′), 3.19 (1H, ddd, $J = 11$, 8, 8 Hz, H-2′), 3.79 (1H, ddd, $J = 11$, 11, 5 Hz, H-1′), 3.85 (3H, s, H-2″-OMe), 5.51 (1H, br. s, H-5′), 6.73 (1H, ddd, $J = 7.5$, 7.5, 1 Hz, H-5″), 6.81 (1H, dd, $J = 7.5$, 1.5 Hz, H-6″), 6.84 (1H, d, $J = 8$ Hz, H-3″), 7.08 (1H, m, H-4‴), 7.13 (2H, dd, $J = 7.5$, 7.5 Hz, H-3‴, 5‴), 7.14 (2H, dd, $J = 7.5$, 1.5 Hz, H-2‴, 6‴), 7.29 (1H, td, $J = 7.5$, 1.5 Hz, H-4″). ^{13}C NMR 23.3 (C-1⁗), 29.3 (C-6′), 38.6 (C-3′), 43.7 (C-2′), 51.8 (C-1′), 55.5 (C-2″-OMe), 110.9 (C-3″), 120.0 (C-5′), 120.5 (C-5″), 126.1 (C-4‴), 127.9 (C-2‴, 6‴), 128.1 (C-3‴, 5‴), 129.4 (C-6″), 130.8 (C-1″), 132.3 (C-4″), 133.4 (C-4′), 144.6 (C-1‴), 157.4 (C-2″), 207.9 (C-1). Anal. calcd. for $C_{21}H_{22}O_2$: C, 82.32; H, 7.24. Found: C, 82.23; H, 7.39.

(3-Methoxyphenyl)(4-methyl-6-phenylcyclohex-3-enyl)methanone (**4c**)

Compound **3c** (0.138 g, 0.58 mmol), **2**, 94 h, **4c** (colorless oil, 0.077 g, 43%). IR ν_{max} (KBr)/cm^{-1} 3424, 2926, 1677, 1596, 1488, 1453, 1430, 1259. ^{1}H NMR δ 1.74 (3H, br. s, H-1⁗), 2.28 (2H, br. d, $J = 6$ Hz, H-3′), 2.31 (1H, m, H-6′), 2.40 (1H, dm, $J = 16.5$ Hz, H-6′), 3.33 (1H, ddd, $J = 11$, 10, 6.5 Hz, H-2′), 3.78 (3H, s, H-3″-OMe), 3.90 (1H, ddd, $J = 11$, 10, 5.5 Hz, H-1′), 5.50 (1H, br. s, H-5′), 7.03 (1H, dd, $J = 8$, 1 Hz, H-4″), 7.07 (2H, tt, $J = 7$, 1.5 Hz, H-4‴), 7.17 (1H, ddm, $J = 7.5$, 7.5 Hz, H-3‴, 5‴), 7.20 (2H, dd, $J = 8$, 1.5 Hz, H-2‴, 6‴), 7.29 (1H, d, $J = 1.5$ Hz, H-2″), 7.29 (1H, dd, $J = 8$, 8 Hz, H-5″), 7.44 (1H, br. ddd, I = 7.5, 1.5, 1.5 Hz, H-6″). ^{13}C NMR δ 23.2 (C-1⁗), 31.0 (C-6′), 39.0 (C-3′), 42.8 (C-2′), 46.8 (C-1′), 55.4 (C-3″-OMe), 112.3 (C-2″), 119.3 (C-5′), 119.4 (C-4″), 120.6 (C-6″), 126.2 (C-4‴), 127.5 (C-2‴, 6‴), 128.4 (C-3‴, 5‴), 129.4 (C-5″), 134.1 (C-4′), 138.8 (C-1″), 144.7 (C-1‴), 159.8 (C-3″), 203.5 (C-1). HRMS calcd. $C_{21}H_{22}NaO_2$ [$M^+ + Na$] 329.1512; found 329.1516.

(4-Methylphenyl)(4-methyl-6-phenylcyclohex-3-enyl)methanone (**4e**)

Compound **3e** (0.223 g, 1.00 mmol), **2**, 75 h, **4e** (colorless oil. 0.081 g, 28%). IR ν_{max} (film)/cm^{-1} 3060, 3028, 2912, 1673, 1606, 1453, 1408, 1285, 1233, 1180. ^{1}H NMR δ 1.74 (3H, br. s, H-1‴′), 2.28 (1H, br. d, $J = 6$ Hz, H-3′), 2.31 (1H, m, H-6′), 2.35 (3H, s, H-4″-Me), 2.35 (1H, m, H-), 3.33 (1H, ddd, $J = 10$, 10, 6.5 Hz, H-2′), 3.92 (1H, ddd, $J = 11$, 10, 5.5 Hz, H-1′), 5.51 (1H, br.s, H-5′), 7.06 (1H, tt, $J = 7$, 1.5 Hz, H-4‴), 7.16 (2H, dd, $J = 8$, 8 Hz, H-3‴, 5‴), 7.16 (2H, d, $J = 7.5$ Hz, H-3″, 5″), 7.20 (2H, dd, $J = 8$, 1.5 Hz, H-2‴, 6‴), 7.73 (2H, d, $J = 8$ Hz, H-2″, 6″). ^{13}C NMR δ 21.6 (C-4″-Me), 23.2 (C-1‴′), 31.0 (C-6′), 39.0 (C-3′), 42.7 (C-2′), 46.3 (C-1′), 119.4 (C-5′), 126.2 (C-4‴), 127.4 (C-2‴, 6‴), 128.2 (C-2″, 6″), 128.4 (C-3‴, 5‴), 129.2 (C-3″, 5″), 134.1 (C-4′), 134.8 (C-1″), 143.5 (C-4″), 144.9 (C-1‴), 203.2 (C-1). HRMS calcd. $C_{21}H_{22}NaO_1$ [$M^+ + Na$] 313.1563; found 313.1563.

(4-Fluorophenyl)(4-methyl-6-phenylcyclohex-3-enyl)methanone (**4f**)

Compound **3f** (0.237 g, 1.05 mmol), **2**, 75 h, **4f** (pale yellow oil. 0.269 g, 78%). IR ν_{max} (KBr)/cm^{-1} 3064, 3028, 2929, 1681, 1598, 1506, 1453, 1266, 1231, 1157. ^{1}H NMR δ 1.74 (3H, s, H-s), 2.29 (1H, dm, $J = 9.5$ Hz, H-s), 2.34 (1H, m, H-s), 2.36 (1H, m, H-), 3.30 (1H, ddd, $J = 11$, 9, 7.5 Hz, H-s), 3.87 (1H, ddd, $J = 11$, 10, 6 Hz, H-s), 5.50 (1H, br. s, H-s), 7.02 (2H, dd, $J = 8$,8.5 Hz, H-d), 7.06 (1H, m, H-s), 7.15 (2H, ddm, $J = 8$, 8 Hz, H-s), 7.16 (2H, dm, $J = 8$ Hz, H-s), 7.81 (2H, dd, $J = 5.5$, 8.5 Hz, H-d). ^{13}C NMR δ 23.2 (C-1‴′), 30.8 (C-6′), 38.9 (C-3′), 43.0 (C-2′), 46.6 (C-1′), 115.5 (d, $J = 22$ Hz, C-3″, 5″), 119.2 (C-5′), 126.3 (C-4‴), 127.5 (C-2‴, 6‴), 128.4 (C-3‴, 5‴), 130.6 (d, $J = 9.5$ Hz, C-2″, 6″), 133.8 (d, $J = 2.5$ Hz, C-1″), 134.1 (C-4′), 144.5 (C-1‴), 165.6 (d, $J = 254$ Hz, C-4″), 202.2 (C-1). ^{19}F NMR δ 106.3, tt, $J = 5.5$,8.5 Hz. HRMS calcd. $C_{20}H_{19}FNaO_1$ [$M^+ + Na$] 317.1312; found 317.1312.

(4-(4-Methylpent-3-enyl)-6-phenylcyclohex-3-enyl)(phenyl)methanone (**6a**)

Compound **3a** (0.273 g, 1.30 mmol), **5**, 70 h, **6a** (white crystals. 0.331 g, 73%). Recrystallized petroleum ether. Mp = 80.6°C. IR ν_{max} (KBr)/cm^{-1} 2969, 2907, 2833, 1666, 1448, 1234, 1198, 756, 701. ^{1}H NMR δ 1.62 (3H, br. s, H-4‴′-Me), 1.70 (3H, br. d, $J = 1$ Hz, H-5‴′), 2.12 (2H, m, H-2‴′), 2.30 (2H, m, H-3′), 2.34 (1H, m, H-6′), 2.41 (1H, br. ddd, $J = 17$, 5, 5 Hz, H-6′), 3.31 (1H, ddd, $J = 10.5$, 10.5, 6 Hz, H-2′), 3.94 (1H, ddd, $J = 10.5$, 10.5, 5 Hz, H-1′), 5.13 (1H, tm, $J = 7$ Hz, H-3‴′), 5.52 (1H, br. s, H-5′), 7.06 (1H, tt, $J = 7$, 1.5 Hz, H-4‴), 7.16 (2H, ddm, $J = 7.5$, 7.5 Hz, H-3‴, 5‴), 7.19 (2H, dm, $J = 7.5$ Hz, H-2‴, 6‴), 7.37 (2H, ddm, $J = 8$, 8 Hz, H-3″, 5″), 7.48 (1H, tt, $J = 7.5$, 1 Hz, H-4″), 7.81 (2H, dd, $J = 8.5$, 1 Hz, H-2″, 6″). ^{13}C NMR δ 17.8 (C-4‴′-Me), 25.8 (C-5‴′), 26.5 (C-2‴′), 30.9 (C-6′), 37.4 (C-1‴′), 37.4 (C-3′), 42.9 (C-2′), 46.8 (C-1′), 118.9 (C-5′),

124.1 (C-3‴′), 126.2 (C-4‴), 127.5 (C-2‴, 6‴), 128.1 (C-3″, 5″), 128.4 (C-2″, 6″), 128.5 (C-3‴, 5‴), 131.7 (C-4‴′), 132.8 (C-4″), 137.4 (C-1″), 137.8 (C-4′), 144.8 (C-1‴), 203.7 (C-1). Anal. calcd. for $C_{25}H_{28}O$: C, 87.16; H, 8.19. Found: C, 87.06; H, 8.37.

(2-Methoxyphenyl)(4-(4-methylpent-3-enyl)-phenylcyclohex-3-enyl)methanone (**6b**)

Compound **3b** (0. 225 g, 0.94 mmol), **5**, 70 h, **6b** (yellow oil. 0.117 g, 33%). IR ν_{max} (film)/cm^{-1} 2955, 2930, 2887, 1670, 1598, 1455, 1377, 1245, 1163, 911. ^{1}H NMR δ 1.62 (3H, br. s, H-4‴′-Me), 1.70 (3H, br. d, $J = 1$ Hz, H-5‴′), 2.02 (2H, br. t, $J = 8$ Hz, H-1‴′), 2.11 (2H, br dt, $J = 8$, 8 Hz, H-2‴′), 2.23 (2H, m, H-3′), 2.47 (, ddd, $J = 17.5$, 5, 5 Hz, H-6′), 3.18 (1H, ddd, $J = 11$, 10, 6.5 Hz, H-2′), 3.80 (1H, ddd, $J = 11$, 10, 5.5 Hz, H-1′), 3.85 (3H, s, H-2″-OMe), 5.12 (1H, tm, $J = 7$ Hz, H-3‴′), 5.53 (1H, br. s, H-5′), 6.73 (1H, ddd, $J = 7.5$, 7.5, 1 Hz, H-5″), 6.80 (1H, dd, $J = 7.5$, 2 Hz, H-6″), 6.84 (1H, br. d, $J = 8$ Hz, H-3″), 7.08 (1H, m, H-4‴), 7.13 (2H, m, H-3‴, 5‴), 7.14 (2H, m, H-2‴, 6‴), 7.30 (1H, ddd, $J = 8.5$, 7.5, 1.5 Hz, H-4″). ^{13}C NMR δ 17.8 (C-4‴′-Me), 25.8 (C-5‴′), 26.5 (C-2‴′), 29.4 (C-6′), 37.0 (C-3′), 37.4 (C-1‴′), 43.8 (C-2′), 51.9 (C-1′), 55.5 (C-2″-OMe), 110.9 (C-3″), 119.6 (C-5′), 120.5 (C-5″), 124.3 (C-3‴′), 126.1 (C-4‴), 127.9 (C-2‴, 6‴), 128.1 (C-3‴, 5‴), 129.4 (C-6″), 130.8 (C-1″), 131.6 (C-4‴′), 132.2 (C-4″), 137.1 (C-4′), 144.7 (C-1‴), 157.4 (C-2″), 208.0 (C-1). HRMS calcd. $C_{26}H_{30}NaO_2$ [$M^+ + Na$] 397.2138; found 397.2130.

(3-Methoxyphenyl)(4-(4-methylpent-3-enyl)-phenylcyclohex-3-enyl)methanone (**6c**)

Compound **3c** (0. 307 g, 1.29 mmol), **5**, 70 h, **6c** (colorless oil. 0.111 g, 23%). IR ν_{max} (film)/cm^{-1} 3417, 3028, 2926, 1720, 1677, 1596, 1582, 1452, 1430, 1258. ^{1}H NMR δ 1.61 (3H, br. s, H-4‴′-Me), 1.69 (3H, br. d, $J = 1$ Hz, H-5‴′), 2.02 (2H, br. t, $J = 7$ Hz, H-1‴′), 2.12 (2H, br. dt, $J = 7$, 7 Hz, H-2‴′), 2.30 (2H, m, H-3′), 2.43 (1H, dm, $J = 17$ Hz, H-6′), 3.30 (1H, ddd, $J = 11$, 11, 6 Hz, H-2′), 3.78 (3H, s, H-3″-OMe), 3.91 (1H, ddd, $J = 11$, 11, 5.5 Hz, H-1′), 5.12 (1H, tm, $J = 7$ Hz, H-3‴′), 5.51 (1H, br. d, $J = 5$ Hz, H-5′), 7.03 (1H, ddd, $J = 8$, 2.5, 1 Hz, H-4″), 7.07 (1H, tt, $J = 7$, 1, H-4‴), 7.17 (2H, br. dd, $J = 7$, 7 Hz, H-3‴, 5‴), 7.19 (2H, dd, $J = 7.5$, 1.5 Hz, H-2‴, 6‴), 7.28 (1H, d, $J = 2$ Hz, H-2″), 7.29 (1H, dd, $J = 7.5$, 7.5 Hz, H-5″), 7.44 (1H, d, $J = 7.5$ Hz, H-6″). ^{13}C NMR δ 17.8 (C-4‴′-Me), 25.8 (C-5‴′), 26.5 (C-2‴′), 31.0 (C-6′), 37.4 (C-1‴′), 37.5 (C-3′), 42.9 (C-2′), 47.0 (C-1′), 55.4 (C-3″-OMe), 112.3 (C-2″), 118.9 (C-5′), 119.4 (C-4″), 120.7 (C-6″), 124.1 (C-3‴′), 126.2 (C-4‴), 127.5 (C-2‴, 6‴), 128.4 (C-3‴, 5‴), 129.4 (C-5″), 131.7 (C-4‴′), 137.8 (C-4′), 138.8 (C-1″), 144.8 (C-1‴), 159.8 (C-3″), 203.5 (C-1). HRMS calcd. $C_{26}H_{30}NaO_2$ [$M^+ + Na$] 397.2138; found 397.2153.

(4-Fluorophenyl)(4-(4-methylpent-3-enyl)-phenylcyclohex-3-enyl)methanone (**6f**)

Compound **3f** (0. 237 g, 1.05 mmol), **5**, 75 h, **6f** (colorless oil. 0.269 g, 78%). IR ν_{max} (film)/cm^{-1} 3422, 3028, 2925, 1678, 1597, 1376, 1230, 1156. ^{1}H NMR δ 1.62 (3H, br. s, H-4‴′-Me), 1.70 (3H, br. d, $J = 1$ Hz, H-5‴′), 2.05 (2H, br. t, $J = 7.5$ Hz, H-1‴′), 2.12 (2H, m, H-2‴′), 2.31 (2H, br. d, $J = 6$ Hz, H-3′), 2.36 (1H, m, H-6′), 2.38 (1H, m, H-6′), 3.28 (1H, ddd, $J = 10$, 10, 6.5 Hz, H-2′), 3.88 (1H, ddd, $J = 10$, 10, 5.5 Hz, H-1′), 5.13 (1H, tm, $J = 7$ Hz, H-3‴′), 5.52 (1H, br. s, H-5′), 7.02 (2H, dd, $J = 8.5$, 8.5 Hz, H-3″, 5″), 7.06 (1H, br. tt, $J = 7$, 2 Hz, H-4‴), 7.16 (2H, dd, $J = 7.5$, 7.5 Hz, H-3‴, 5‴), 7.19 (2H, dd, $J = 7.5$, 2 Hz, H-2‴, 6‴), 7.82 (2H, dd, $J = 8.5$, 5.5 Hz, H-2″, 6″). ^{13}C NMR δ 17.8 (C-4‴′-Me), 25.8 (C-5‴′), 26.5 (C-2‴′), 30.9 (C-6′), 37.3 (C-1‴′), 37.4 (C-3′), 43.0 (C-2′), 46.8 (C-1′), 115.5 (d, $J = 22$ Hz, C-3″, 5″), 118.8 (C-5′), 124.1 (C-3‴′), 126.3 (C-4‴), 127.5 (C-2‴, 6‴), 128.4 (C-3‴, 5‴), 130.6 (d, $J = 9$ Hz, C-2″, 6″), 131.8 (C-4‴′), 133.8 (d, $J = 2.5$ Hz, C-1″), 137.9 (C-4′), 144.6 (C-1‴), 165.5 (d, $J = 254$ Hz, C-4″), 202.2 (C-1). ^{19}F NMR δ − 106.2, tt, $J = 5.5$, 8.5 Hz. HRMS calcd. $C_{50}H_{54}F_2NaO_2$ [2M$^+$ + Na] 747.3984; found 747.4026.

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