Michael–Michael Ring Closure Reaction of Benzyl Cyanides and Chalcones

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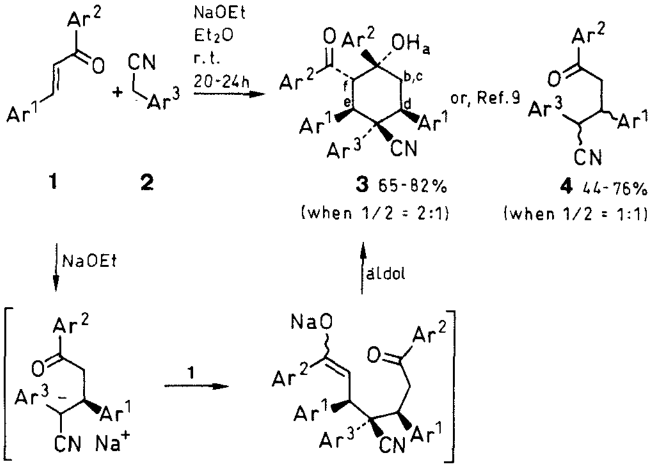
The synthesis of a number of highly substituted cyclohexane derivatives has been accomplished in a single step reaction of benzyl cyanides and chalcones (1:2) using sodium ethoxide in anhydrous diethyl ether at room temperature to give 3-aroyl-1,2,4,6-tetraaryl-4-hydroxycyclohexanecarbonitriles. An unambiguous structural assignment was achieved from the analytical and infrared, ^{1}H NMR and ^{13}C NMR spectroscopic data as well as X-ray crystallography.

Although a fair amount of work has been published on the condensation of chalcones with active methylene compounds, less is known about the reactions with benzyl cyanides using different stoichiometric amounts of starting materials. For example, the reaction of chalcones with malonitrile and ethyl cyanoacetate in the presence of ammonium acetate gives substituted pyridines.[1-2] Chalcones also react with thioacetamide to give 2-pyridinethiones[3] with cyanoacetamide to give 2-pyridones,[4] with ethyl cyanoacetate in the presence of sodium ethoxide to give 8-oxaquinolines[5] and with ethyl phenylacetate to give the corresponding ethyl 3-aryl-2,5-diphenyl-5-oxopentanoates.[6] In addition, chalcones were also condensed with guanidine hydrochloride to give 4,6-diaryl-3,4-dihydropyrimidine-2(1*H*)-thione and 2-amino-4,6-diarylpyrimidine, respectively.[7]

Furthermore, the preparative value of one-pot, multicomponent, sequential Michael–Michael ring-closure reactions followed by aromatization is illustrated by a total synthesis of juncunol, an unusual vinyldihydrophenanthrene.[8] Recently, we reported[9] that the base-catalyzed reaction of chalcones with benzyl cyanides in (1:1) molar ratio using a sodium ethoxide/diethyl ether suspension affords a single diastereomer of 2,3-diaryl-4-aroylbutyronitriles **4**. In view of our continued interest[10-19] in the chemistry of benzyl cyanides and other related cyano compounds, we report herein the synthesis of a series of novel highly substituted cyclohexanol derivatives **3** by a base-catalyzed cyclocondensation reaction of chalcones **1** with benzyl cyanides **2** in (2:1) molar ratio as shown in the Scheme.

This simple one-pot reaction is carried out by stirring a mixture of chalcones **1** and benzyl cyanides **2** for 20–24 hours at room temperature using a suspension of sodium ethoxide in anhydrous diethyl ether as the base. In each condensation, a colored precipitate is formed which upon workup and crystallization from glacial acetic acid provides the cyclohexanol derivatives **3**. The isolated products indicated that the reaction could involve a double Michael addition of benzyl cyanide carbanion to two moles of chalcone followed by cyclization.

A suggested reaction mechanism is also outlined in that Scheme in which the 1,7-diketone undergoes an intramolecular aldol cyclization to give the cyclohexanols **3a–n**.



3	Ar^1	Ar^2	Ar^3
a	Ph	Ph	Ph
b	Ph	Ph	3,4-$Cl_2C_6H_3$
c	4-ClC_6H_4	4-BrC_6H_4	4-BrC_6H_4
d	4-MeC_6H_4	2-naphthyl	4-BrC_6H_4
e	4-$MeOC_6H_4$	Ph	3,4-$Cl_2C_6H_3$
g	4-$MeOC_6H_4$	Ph	4-BrC_6H_4
g	4-ClC_6H_4	Ph	4-BrC_6H_4
h	4-MeC_6H_4	2-naphthyl	4-ClC_6H_4
i	4-ClC_6H_4	2-naphthyl	4-ClC_6H_4
j	4-MeC_6H_4	2-naphthyl	3-MeC_6H_4
k	3-MeC_6H_4	2-naphthyl	4-BrC_6H_4
l	4-MeC_6H_4	2-naphthyl	3,4-$Cl_2C_6H_3$
m	4-$MeOC_6H_4$	2-naphthyl	3,4-$Cl_2C_6H_3$
n	4-ClC_6H_4	2-naphthyl	3,4-$Cl_2C_6H_3$

Scheme

The structure of the products **3** was elucidated on the basis of their elemental analysis, NMR and IR data. The IR spectra of the cyclohexanol derivatives **3** showed a peak at $\nu = 3390-3480\ cm^{-1}$ due to the hydroxy group, in addition to a peak at $\nu = 2230-2250\ cm^{-1}$ characteristic of cyano groups. Another peak at $\nu = 1635-1660\ cm^{-1}$ assigned to the benzoyl stretching frequency was also observed. The NMR spectra were also in agreement with the suggested structure. As a representative example, the ^{1}H NMR spectrum of **3a** showed a doublet of doublets at $\delta = 2.33$ due to H_b, a doublet of triplets at $\delta = 3.20$ due to H_c. An overlapping two pair of doublet of doublets at $\delta = 4.30$ due to H_d and H_e was also observed. Another two separated doublets at $\delta = 5.10$ and 5.45 due to H_f and H_a also appeared. The hydroxylic protons H_a is split by long range W coupling with H_c ($J_{ac} = 2.6$ Hz).

The ^{13}C NMR data showed a signal at $\delta = 203.5$ due to carbonyl carbon and another signal at $\delta = 119.6$ due to the cyano group, in addition to the cyclohexane carbons (Table 1).

Table 1. ^{13}C NMR Data of Compounds **3a–n**, δ

3	C=O	C≡N	Cyclohexane Carbons
a	203.05	119.60	43.00, 47.16, 51.05, 53.38, 56.26, 74.71
b	205.70	120.00	43.41, 47.28, 51.13, 54.10, 56.95, 75.11
c	203.77	119.71	43.02, 47.26, 51.15, 53.47, 56.34, 74.81
d	205.62	120.45	43.57, 47.70, 51.85, 54.13, 56.88, 75.43
e	205.65	120.00	43.40, 47.30, 51.13, 54.09, 56.96, 75.12
f	205.71	120.26	43.37, 47.13, 51.06, 54.11, 57.16, 75.13
g	205.14	119.88	43.34, 47.46, 51.55, 54.12, 56.53, 75.09
h	205.56	120.47	43.53, 47.68, 51.87, 54.07, 56.79, 75.41
i	205.01	122.62	43.19, 47.44, 51.61, 53.67, 56.52, 75.40
j	205.92	120.83	43.48, 47.47, 51.84, 54.19, 57.03, 75.42
k	205.62	120.42	43.86, 48.18, 52.33, 54.12, 56.73, 75.41
l	205.37	120.22	43.72, 47.92, 52.04, 54.38, 56.70, 75.40
m	205.47	120.17	43.62, 47.39, 51.40, 54.35, 57.04, 75.45
n	205.43	119.93	43.65, 48.11, 52.13, 53.73, 56.40, 75.43

Table 2. Bond Lengths (Å) of Compound **3g**

Atoms		Atoms	
Br-C(10)	1.895(4)	Cl(1)-C(17)	1.745(3)
Cl(2)-C(36)	1.740(3)	O(1)-C(20)	1.225(4)
O(2)-C(4)	1.432(3)	N-C(13)	1.139(4)
C(1)-C(2)	1.573(3)	C(1)-C(6)	1.578(3)
C(1)-C(7)	1.532(5)	C(1)-C(13)	1.483(4)
C(2)-C(3)	1.549(5)	C(2)-C(14)	1.516(3)
C(3)-C(4)	1.559(3)	C(3)-C(20)	1.529(3)
C(4)-C(5)	1.529(3)	C(4)-C(27)	1.529(5)
C(5)-C(6)	1.528(5)	C(6)-C(33)	1.515(3)
C(7)-C(8)	1.392(4)	C(7)-C(12)	1.388(4)
C(8)-C(9)	1.382(5)	C(9)-C(10)	1.375(5)
C(10)-C(11)	1.373(5)	C(11)-C(12)	1.385(6)
C(14)-C(15)	1.389(5)	C(14)-C(19)	1.393(4)
C(15)-C(16)	1.387(4)	C(16)-C(17)	1.374(4)
C(17)-C(18)	1.380(5)	C(18)-C(19)	1.389(4)
C(20)-C(21)	1.487(3)	C(21)-C(22)	1.390(4)
C(21)-C(26)	1.383(5)	C(22)-C(23)	1.374(4)
C(23)-C(24)	1.367(6)	C(24)-C(25)	1.374(5)
C(25)-C(26)	1.381(4)	C(27)-C(28)	1.386(5)
C(27)-C(32)	1.395(5)	C(28)-C(29)	1.390(6)
C(29)-C(30)	1.371(6)	C(30)-C(31)	1.371(6)
C(31)-C(32)	1.397(6)	C(33)-C(34)	1.393(5)
C(33)-C(38)	1.391(4)	C(34)-C(35)	1.385(4)
C(35)-C(36)	1.374(4)	C(36)-C(37)	1.376(5)
C(37)-C(38)	1.387(3)	O(3)-C(39)	1.236(5)
O(4)-C(39)	1.283(5)	C(39)-C(40)	1.494(5)

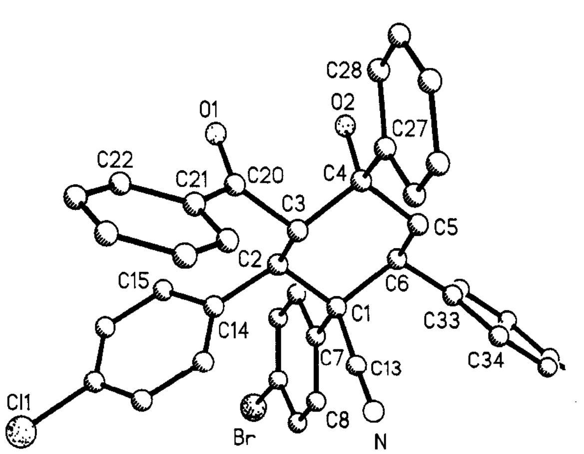


Figure. X-ray plot of **3g**

Table 3. Bond Angles (deg) of Compound **3g**

Atoms		Atoms	
C(2)-C(1)-C(6)	109.2(2)	C(2)-C(1)-C(7)	110.2(2)
C(6)-C(1)-C(7)	111.8(2)	C(2)-C(1)-C(13)	109.2(2)
C(6)-C(1)-C(13)	107.5(2)	C(7)-C(1)-C(13)	108.9(2)
C(1)-C(2)-C(3)	111.0(2)	C(1)-C(2)-C(14)	113.1(2)
C(3)-C(2)-C(14)	112.0(2)	C(2)-C(3)-C(4)	111.5(2)
C(2)-C(3)-C(20)	108.1(2)	C(4)-C(3)-C(20)	110.2(2)
O(2)-C(4)-C(3)	110.1(2)	O(2)-C(4)-C(5)	105.9(2)
C(3)-C(4)-C(5)	109.7(2)	O(2)-C(4)-C(27)	111.3(2)
C(3)-C(4)-C(27)	109.2(2)	C(5)-C(4)-C(27)	110.7(3)
C(4)-C(5)-C(6)	114.3(3)	C(1)-C(6)-C(5)	110.5(2)
C(1)-C(6)-C(33)	112.4(2)	C(5)-C(6)-C(33)	111.9(3)
C(1)-C(7)-C(8)	122.4(3)	C(1)-C(7)-C(12)	119.8(3)
C(8)-C(7)-C(12)	117.9(3)	C(7)-C(8)-C(9)	121.5(3)
C(8)-C(9)-C(10)	119.0(3)	Br-C(10)-C(9)	119.1(3)
Br-C(10)-C(11)	120.0(3)	C(9)-C(10)-C(11)	120.9(3)
C(10)-C(11)-C(12)	119.6(3)	C(7)-C(12)-C(11)	121.0(3)
N-C(13)-C(1)	178.6(2)	C(2)-C(14)-C(15)	119.7(2)
C(2)-C(14)-C(19)	122.1(3)	C(15)-C(14)-C(19)	118.2(2)
C(14)-C(15)-C(16)	121.6(2)	C(15)-C(16)-C(17)	118.8(3)
Cl(1)-C(17)-C(16)	119.6(3)	Cl(1)-C(17)-C(18)	119.2(2)
C(16)-C(17)-C(18)	121.2(3)	C(17)-C(18)-C(19)	119.5(3)
C(14)-C(19)-C(18)	120.7(3)	O(1)-C(20)-C(3)	119.0(2)
O(1)-C(20)-C(21)	119.9(2)	C(3)-C(20)-C(21)	121.0(3)
C(20)-C(21)-C(22)	118.7(3)	C(20)-C(21)-C(26)	122.5(2)
C(22)-C(21)-C(26)	118.8(2)	C(21)-C(22)-C(23)	120.4(3)
C(22)-C(23)-C(24)	120.6(3)	C(23)-C(24)-C(25)	119.7(3)
C(24)-C(25)-C(26)	120.5(4)	C(21)-C(26)-C(25)	120.1(3)
C(4)-C(27)-C(28)	121.2(3)	C(4)-C(27)-C(32)	120.8(3)
C(28)-C(27)-C(32)	118.0(3)	C(27)-C(28)-C(29)	121.1(3)
C(28)-C(29)-C(30)	120.3(4)	C(29)-C(30)-C(31)	119.6(4)
C(30)-C(31)-C(32)	120.5(4)	C(27)-C(32)-C(31)	120.3(3)
C(6)-C(33)-C(34)	121.7(2)	C(6)-C(33)-C(38)	120.8(3)
C(34)-C(33)-C(38)	117.5(2)	C(33)-C(34)-C(35)	121.3(3)
C(34)-C(35)-C(36)	119.6(3)	Cl(2)-C(36)-C(35)	118.8(3)
Cl(2)-C(36)-C(37)	120.4(2)	C(35)-C(36)-C(37)	120.8(2)
C(36)-C(37)-C(38)	119.1(3)	C(33)-C(38)-C(37)	121.7(3)
O(3)-C(39)-O(4)	124.6(3)	O(3)-C(39)-C(39)	119.7(4)
O(4)-C(39)-C(40)	115.7(3)		

All reagents were of commercial quality from freshly opened containers. Benzyl cyanides were purchased from Aldrich Chemical Co. Reagent quality solvents were used without further purification. IR spectra were recorded as a KBr disc using a Pye-Unicam SP3-100 instrument. ^1H and ^{13}C NMR spectra were run on a Bruker WP 80-SY instrument with TMS as internal standard. Compounds were analyzed at M-H-W Laboratories, Phoenix, Arizona, USA. Satisfactory microanalyses obtained: C ± 0.22 (except **3e**: C − 0.51), H ± 0.21, N ± 0.10 (except **3j**: + 0.60); for **3b,e,h,i,l,m,n**: Cl ± 0.49; for **3d,f,k**: Br ± 0.29. Melting points were determined on an Electrothermal melting point apparatus and are uncorrected. R_f values were determined on Silica gel plates using toluene/EtOAc (19:1) as an eluent. All coupling constant values (*J*) are in Hz.

1*R,2*R**,3*S**,4*S**,6*S**-(±)-3-Aroyl-1,2,4,6-tetraaryl-4-hydroxycyclohexanecarbonitriles 3a–n; General Procedure:**

To a suspension of NaOEt (0.01 mol) in anhydr. Et_2O (150 mL) containing benzyl cyanides **2** (0.01 mol) was added chalcone **1** (0.02 mol). The mixture was stirred at r.t. for 20–24 h, the solid formed was filtered and crystallized from glacial AcOH. The filtrate was poured into H_2O (100 mL), the organic layer separated, dried (Na_2SO_4) and evaporated to give the crude unreacted starting materials.

X-ray crystallography of **3g** showed that there was a molecule of AcOH incorporated into the structure of the main molecule. It may interact through some weak hydrogen bonding with the main molecule, but its strongest hydrogen bond was to another molecule of AcOH. The main molecule had one strong intramolecular hydrogen bond between the hydrogen on O(2) and O(1). Thus, the O(2)...O(1) distance is 2.717 Å, the distance H(2A)...O(1) is 1.88 Å and the O(2)-H(2A)...O(1) angle is 144°.

X-ray Analysis of 2,6-Bis(4-chlorophenyl)-3-benzoyl-1-(4-bromophenyl)-4-hydroxy-4-phenylcyclohexanecarbonitrile (3 g):[20]

The summary of crystal data, data collection, solution and refinement for this compound are as follows: empirical formula, $C_{40}H_{32}BrCl_2NO_4$; color and habit, colorless blocks; crystal size (mm), 0.32 × 0.28 × 0.24; crystal system, triclinic; space group, $P\bar{1}$; unit cell dimensions; a (Å), 12.649 (3); b (Å), 12.737 (2); c (Å), 12.988 (3); α (deg), 105.58 (2) β (deg), 96.48 (2); γ (deg), 118.09 (2); volume (Å^3), 1703.7 (9); Z, 2; formula weight, 741.5; density (calc.), 1.445 Mg/m^3; absorption coefficient, 1.407 mm^{-1}; F (000); 760.

The diffractometer used: Siemens R3m/V; radiation, MoKα (λ = 0.71073 Å); temp., 130; monochromator, highly oriented graphite crystal; 2θ range, 0.0 to 55.0°; standard reflections, 2 measured every 198 reflections; reflection collected, 7820; independent reflections, 7820; observed reflections, 5670 [$F > 4.0\sigma(F)$]; absorption correction, XABS.[21] The system used: Siemens SHELXTL;[22,23] final R indices[24] (obs. data), R = 4.39 %, R_w = 4.xx %; goodness-of-fit,[25] 1.44.

The X-ray plot of **3g** is given in the figure, which clearly shows the cyclic structure of product **3g**. Tables 2 and 3 show bond lengths and bond angles of the same molecule.

3-Benzoyl-4-hydroxy-1,2,4,6-tetraphenylcyclohexanecarbonitrile **(3a)**:

Crystallization of the crude product yielded pure crystals of **3a**, 4.54 g (82 %), mp 245–246 °C, R_f: 0.80.

IR (KBr): ν = 3480 (OH), 2245 (C≡N), 1650 cm^{-1} (C=O).

^{1}H NMR (CDCl$_3$): δ = 2.33 (dd, 1 H, J = 13.0, 3.5, H_b), 3.20 (dt, 1 H, J = 14.3, 2.5, 13.2, H_c), 4.30 (dd, 2 H, J = 14.5, 2.6, 13.2, H_d, H_e), 5.10 (d, 1 H, J = 12.4, H_f), 5.45 (d, 1 H, J = 2.6, H_a), 6.70–7.82 (m, 25 H_{arom}).

3-Benzoyl-4-hydroxy-1-(3,4-dichlorophenyl)-2,4,6-triphenylcyclohexanecarbonitrile **(3b)**:

Crystallization of the crude product furnished pure crystals of **3b**, 4.76 g (79 %), mp 251–253 °C, R_f: 0.73.

IR (KBr): ν = 3440 (OH), 2240 (C≡N), 1660 cm^{-1} (C=O).

^{1}H NMR (CDCl$_3$): δ = 2.30 (dd, 1 H, J = 13.1, 3.2, H_b), 3.11 (dt, 1 H, J = 14.2, 2.5, 13.3, H_c), 4.22 (dd, 2 H, J = 14.4, 2.6, 13.0, H_d, H_e), 5.09 (d, 1 H, J = 12.3, H_f), 5.43 (d, 1 H, J = 2.7, H_a), 6.75–7.68 (m, 23 H_{arom}).

1,4-Bis(4-bromophenyl)-2,6-bis(4-chlorophenyl)-3-(4-bromobenzoyl)-4-hydroxycyclohexanecarbonitrile **(3c)**:

Crystallization of the crude product provided analytical sample of **3c**, 6.29 g (75 %), mp 228–230 °C, R_f: 0.59.

IR (KBr): ν = 3435 (OH), 2240 (C≡N), 1650 cm^{-1} (C=O).

^{1}H NMR (CDCl$_3$): δ = 2.21 (dd, 1 H, J = 13.0, 3.3, H_b), 2.96 (dt, 1 H, J = 14.3, 2.6, 13.3, H_c), 4.18 (dd, 2 H, J = 14.3, 2.6, 13.1, H_d, H_e), 4.92 (d, 1 H, J = 13.2, H_f), 5.27 (d, 1 H, J = 2.6, H_a), 6.76–7.45 (m, 20 H_{arom}).

2,6-Bis(4-methylphenyl)-1-(4-bromophenyl)-4-hydroxy-3-(2-naphthoyl)-4-(2-naphthyl)cyclohexanecarbonitrile **(3d)**:

Crystallization of the crude product gave pure crystals of **3d**, 5.56 g (75 %), mp 264–266 °C, R_f: 0.54.

IR (KBr): ν = 3400 (OH), 2230 (C≡N), 1640 cm^{-1} (C=O).

^{1}H NMR (CDCl$_3$): δ = 1.83 (s, 3 H, ArCH$_3$), 2.20 (s, 3 H, ArCH$_3$), 2.25 (dd, 1 H, J = 13.2, 3.0, H_b), 3.24 (dt, 1 H, J = 14.0, 2.6, 13.2, H_c), 4.31 (dd, 2 H, J = 14.3, 2.6, 13.1, H_d, H_e), 5.33 (d, 1 H, J = 12.3, H_f), 5.64 (d, 1 H, J = 5.64, H_a), 6.51–8.09 (m, 26 H_{arom}).

2,4-Bis(4-methoxyphenyl)-3-benzoyl-1-(3,4-dichlorophenyl)-4-hydroxy-4-phenylcyclohexanecarbonitrile **(3e)**:

Crystallization of the crude product furnished pure crystals of **3e**, 5.50 g (83 %), mp 201–203 °C, R_f: 0.60.

IR (KBr): ν = 3420 (OH), 2250 (C≡N), 1640 cm^{-1} (C=O).

^{1}H-NMR (CDCl$_3$): δ = 2.23 (dd, 1 H, J = 13.2, 3.2, H_b), 3.10 (dt, 1 H, J = 14.0, 2.6, 13.2, H_c), 3.46 (s, 3 H, ArOCH$_3$), 3.65 (s, 3 H, ArOCH$_3$), 4.18 (dd, 2 H, J = 14.3, 2.6, 13.2, H_d, H_e), 5.05 (d, 1 H, J = 12.2, H_f), 5.49 (d, 1 H, J = 2.6, H_a), 6.27–7.67 (m, 21 H_{arom}).

2,6-Bis(4-methoxyphenyl)-3-benzoyl-1-(4-bromophenyl)-4-hydroxy-4-phenylcyclohexanecarbonitrile **(3f)**:

Crystallization of the crude product yielded pure sample of **3f**, 5.11 g (76 %), mp 233–235 °C, R_f: 0.61.

IR (KBr): ν = 3420 (OH), 2240 (C≡N), 1640 cm^{-1} (C=O).

^{1}H NMR (CDCl$_3$): δ = 2.24 (dd, 1 H, J = 13.2, 3.0, H_b), 3.06 (dt, 1 H, J = 14.0, 2.6, 13.2, H_c), 3.48 (s, 3 H, ArOCH$_3$), 3.67 (s, 3 H, ArOCH$_3$), 4.20 (dd, 2 H, J = 14.2, 2.5, 13.2, H_d, H_e), 5.04 (d, 1 H, J = 12.2, H_f), 5.67 (d, 1 H, J = 2.5, H_a), 6.25–7.75 (m, 22 H_{arom}).

2,6-Bis(4-chlorophenyl)-3-benzoyl-1-(4-bromophenyl)-4-hydroxy-4-phenylcyclohexanecarbonitrile **(3g)**:

Crystallization of the crude product gives pure crystals of **3g**, 4.43 g (65 %), mp 205–207 °C, R_f: 0.70.

IR (KBr): ν = 3340 (OH), 2250 (C≡N), 1650 cm^{-1} (C=O).

^{1}H NMR (CDCl$_3$): δ = 2.25 (dd, 1 H, J = 13.0, 3.1, H_b), 3.05 (dt, 1 H, J = 14.1, 2.5, 13.1, H_c), 4.23 (dd, 2 H, J = 14.1, 2.6, 13.1, H_d, H_e), 5.03 (d, 1 H, J = 12.3, H_f), 5.67 (d, 1 H, J = 2.6, H_a), 6.71–7.65 (m, 22 H_{arom}).

2,6-Bis(4-methylphenyl)-1-(4-chlorophenyl)-4-hydroxy-3-(2-naphthoyl)-4-(2-naphthyl)cyclohexanecarbonitrile **(3h)**:

Crystallization of the crude product provided analytical sample of **3h**, 5.43 g (78 %), mp 248–250 °C, R_f: 0.55.

IR (KBr): ν = 3390 (OH), 2230 (C≡N), 1640 cm^{-1} (C=O).

^{1}H NMR (CDCl$_3$): δ = 1.84 (s, 3 H, ArCH$_3$), 2.02 (s, 3 H, ArCH$_3$), 2.31 (dd, 1 H, J = 13.1, 3.1, H_b), 3.24 (dt, 1 H, J = 14.1, 2.7, 13.1, H_c). 4.31 (dd, 2 H, J = 14.3, 2.6, 13.0, H_d, H_e), 5.34 (d, 1 H, J = 12.6, H_f), 5.62 (d, 1 H, J = 2.6, H_a), 6.46–8.09 (m, 26 H_{arom}).

4-Hydroxy-3-(2-naphthoyl)-4-(2-naphthyl)-1,2,6-tris(4-chlorophenyl)cyclohexanecarbonitrile **(3i)**:

Crystallization of the crude product yielded pure crystals of **3i**, 5.16 g (70 %), mp 268–270 °C, R_f: 0.65.

IR (KBr): ν = 3400 (OH), 2230 (C≡N), 1640 cm^{-1} (C=O).

^{1}H NMR (CDCl$_3$): δ = 2.33 (dd, 1 H, J = 13.1, 3.2, H_b), 3.21 (dt, 1 H, J = 14.2, 2.5, 13.1, H_c), 4.34 (dd, 2 H, J = 14.3, 2.6, 13.0, H_d, H_e), 5.31 (d, 1 H, J = 12.3, H_f), 5.55 (d, 1 H, J = 2.5, H_a), 6.66–8.08 (m, 26 H_{arom}).

2,6-Bis(4-methylphenyl)-4-hydroxy-1-(3-methylphenyl)-3-(2-naphthoyl)-4-(2-naphthyl)cyclohexanecarbonitrile **(3j)**:

Crystallization of the crude product gave pure sample of **3j**, 4.80 g (71 %), mp 260–262 °C, R_f: 0.63.

IR (KBr): ν = 3410 (OH), 2230 (C≡N), 1640 cm^{-1} (C=O).

^{1}H NMR (CDCl$_3$): δ = 1.82 (s, 3 H, ArCH$_3$), 2.18 (s, 3 H, ArCH$_3$), 2.30 (dd, 1 H, J = 13.1, 3.2, H_b), 3.26 (dt, 1 H, J = 14.1, 2.5, 13.1, H_c), 4.35 (dd, 2 H, J = 14.1, 2.6, 13.0, H_d, H_e), 5.34 (d, 1 H, J = 12.1, H_f), 5.64 (d, 1 H, J = 2.4, H_a), 6.43–8.10 (m, 26 H_{arom}).

2,6-Bis(3-methylphenyl)-1-(4-bromophenyl)-4-hydroxy-3-(2-naphthoyl)-4-(2-naphthyl)cyclohexanecrbonitrile **(3k)**:

Crystallization of the crude product gave analytical sample of **3k**, 4.82 g (65 %), mp 226–228 °C, R_f: 0.69.

IR (KBr): ν = 3400 (OH), 2220 (C≡N), 1635 cm^{-1} (C=O).

^{1}H NMR (CDCl$_3$): δ = 1.76 (s, 3 H, ArCH$_3$), 2.19 (s, 3 H, ArCH$_3$), 2.29 (dd, 1 H, J = 13.0, 3.1, H_b), 3.26 (dt, 1 H, J = 14.2, 2.5, 13.0, H_c), 4.32 (dd, 2 H, J = 14,1, 2.6, 13.1, H_d, H_e), 5.39 (d, 1 H, J = 12.3, H_f), 5.60 (d, 1 H, J = 2.6, H_a), 6.50–8.13 (m, 26 H_{arom}).

2,6-Bis(4-methylphenyl)-1-(3,4-dichlorophenyl)-4-hydroxy-3-(2-naphthoyl)-4-(2-naphthyl)cyclohexanecarbonitrile **(3l)**:

Crystallization of the crude product provided pure crystals of **3l**, 5.92 g (81 %), mp 256–257 °C, R_f: 0.67.

IR (KBr): ν = 3420 (OH), 2260 ($C\equiv N$), 1635 cm^{-1} ($C=O$).

^{1}H NMR ($CDCl_3$): δ = 1.85 (s, 3 H, $ArCH_3$), 2.20 (s, 3 H, $ArCH_3$), 2.31 (dd, 1 H, J = 13.0, 3.2, H_b), 3.24 (dt, 1 H, J = 14.1, 2.5, 13.0, H_c), 4.29 (dd, 2 H, J = 14.1, 2.6, 13.0, H_d, H_e), 5.33 (d, 1 H, J = 12.0, H_f), 5.63 (d, 1 H, J = 2.6, H_a), 6.55–8.10 (m, 25 H_{arom}).

2,6-Bis(4-methoxyphenyl)-1-(3,4-dichlorophenyl)-4-hydroxy-3-(2-naphthoyl)-4-(2-naphthyl)cyclohexanecarbonitrile (**3m**):

Crystallization of the crude product yielded pure crystals of **3m**, 6.25 g (82 %), mp 235–237 °C, R_f: 0.67.

IR (KBr): ν = 3440 (OH), 2225 ($C\equiv N$), 1625 cm^{-1} ($C=O$).

^{1}H NMR ($CDCl_3$): δ = 2.32 (dd, 1 H, J = 13.0, 3.1, H_b), 3.15 (dt, 1 H, J = 14.2, 2.5, 13.1, H_c), 3.37 (s, 3 H, $ArOCH_3$), 3.70 (s, 3 H, $ArOCH_3$), 4.30 (dd, 2 H, J = 14.1, 2.6, 13.0, H_d, H_e), 5.30 (d, 1 H, J = 12.0, H_f), 5.60 (d, 1 H, J = 2.6, H_a), 6.37–8.09 (m, 25 H_{arom}).

2,6-Bis(4-chlorophenyl)-1-(3,4-dichlorophenyl)-4-hydroxy-3-2-naphthoyl)-4-(2-naphthyl)cyclohexanecarbonitrile (**3n**):

Crystallization of the crude product furnished pure sample of **3n**, 5.86 g (76 %), mp 215–217 °C, R_f: 0.58.

IR (KBr): ν = 3415 (OH), 2220 ($C\equiv N$), 1645 cm^{-1} ($C=O$).

^{1}H NMR ($CDCl_3$): δ = 2.33 (dd, 1 H, J = 13.1, 3.2, H_b), 3.19 (dt, 1 H, J = 14.2, 2.5, 3.1, H_c), 4.34 (dd, 2 H, J = 14.1, 2.6, 13.0, H_d, H_e), 5.30 (d, 1 H, J = 12.1, H_f), 5.50 (d, 1 H, J = 2.5, H_a), 6.96–8.07 (m, 25 H_{arom}).

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$Rw = \Sigma \| Fo | - | Fc \| \sqrt{w} / \Sigma | Fo | \sqrt{w}$.

(25) Goodness-of-fit = $[\Sigma(w^0 \| Fo | - | Fc \|^2)/(M\text{-}N)]^{\frac{1}{2}}$ where M is the number of observed reflections and N is the number of parameters refined.