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Supplementary Information

Partial Rotation of isopropyl Group in the Solid State: Single-Crystal-to-Single-Crystal Phase Transformation in a Carvacrol Derivative

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Synthesis of 1-(benzoyl)-3-[(5'-isopropyl-2'-methylphenoxy)acetamino]thiourea (TACH)

All solvents and reagents were of analytical grade and were dried in advance and redistilled before use. The structures of all synthesized compounds were identified by elemental analysis, LCMS, ^{1}H & ^{13}C NMR. Melting points of all the synthesized compounds were determined by open capillary method. The purity of synthesized compounds was checked by thin layer chromatography (TLC) and the spots were visualized under UV-light. ^{1}H nuclear magnetic resonance (^{1}H NMR) and ^{13}C NMR spectra were scanned at 300 MHz on Varian Mercury YH-300 FT NMR in $CDCl_3$ and DMSO-d_6 using tetramethylsilane (TMS) as an internal reference. Chemical shift values (δ) are given in parts per million (ppm). The APCI +Ve mass spectra were recorded on Shimadzu LCMS-QP8000 LC MS spectrometer. Figure S1 below shows a detail synthetic scheme for TACH.

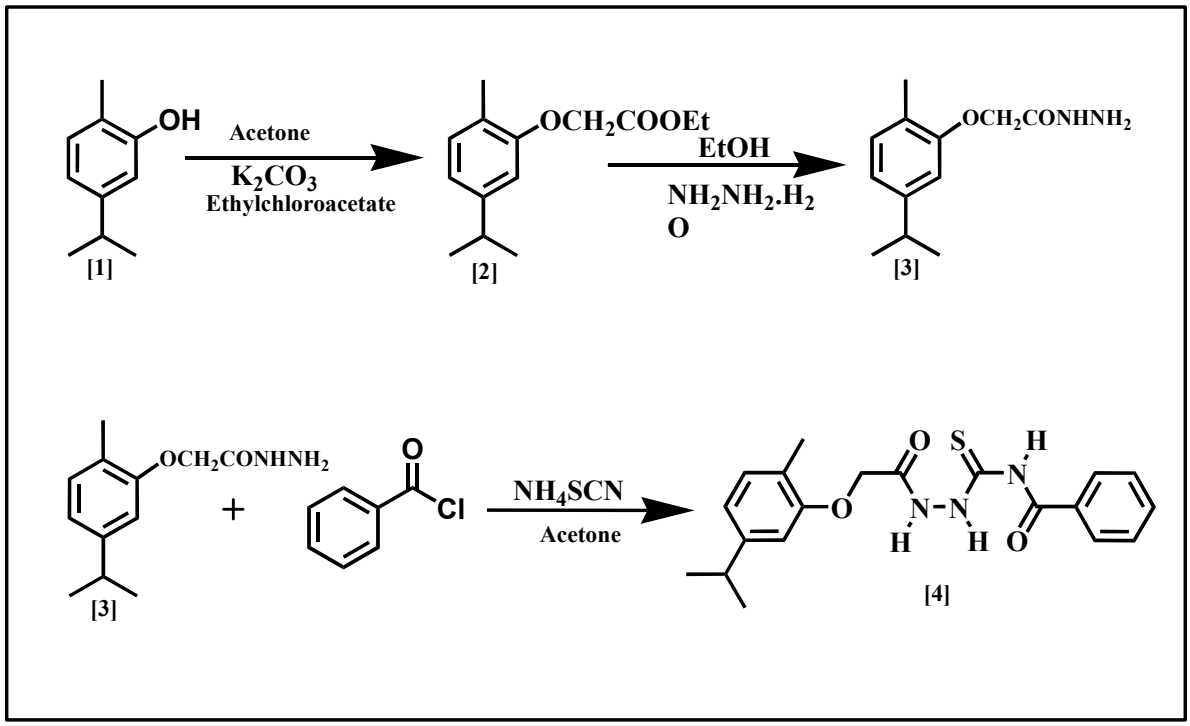

Figure S1 Synthetic scheme for 1-(benzoyl)-3-[(5'-isopropyl-2'-methylphenoxy)acetamino]thiourea (TACH)

Synthesis of ethyl-2-(5-isopropyl-2-methylphenoxy) acetate (2)

A mixture of carvacrol (0.02 moles), dry acetone (50 ml), and anhydrous K_2CO_3 (0.03 moles) in 100 ml round bottom flask was heated to reflux for 6 hrs. Upon cooling to room temperature, ethyl chloroacetate (0.02 moles) was added drop wise (in 1 hr) and the mixture was refluxed for 4 hrs. The

reaction mixture was kept overnight, the excess of solvent was recovered and the residue was quenched onto crushed ice. Further, the contents were stirred for half an hour and extracted with diethyl ether. Organic layer was washed with water and dried with Na_2SO_4. Solvent was recovered under vacuum to obtain yellowish oil, Yield: 79.55%, which was used in the next step without purification.

Synthesis of 2-(5-isopropyl-2-methylphenoxy) acetohydrazide (3)

Ethyl-2-(5-isopropyl-2-methylphenoxy) acetate **(2)** (0.015 moles) and 99 % hydrazine hydrate (0.023 moles) in ethanol (15 ml) were charged to a 50 ml round bottom flask and refluxed for 2 hrs. Progress of the reaction was monitored by TLC. The resulting clear solution was concentrated under vacuum and suspension formed was poured on crushed ice. The product separated was filtered, washed with cold water, dried and recrystallized from ethanol-water, Yield: 84%, m. p. 78-81 °C.

Synthesis of 1-(benzoyl)-3-[(5'-isopropyl-2'-methylphenoxy)acetamino]thiourea (4)

Ammonium thiocyanate (0.011 moles) in dry acetone (20 ml) and benzoyl chloride (0.011 moles) in dry acetone (10 ml) were charged in 100 ml round bottom flask. The reaction mixture was stirred on a hot plate under stirring for 1.5 hrs and then 2-(5-isopropyl-2-methylphenoxy) acetohydrazide (0.01 moles) was charged in small lots. The reaction mixture was refluxed for 5-6 hrs and reaction was monitored by TLC during this course. After completion of reaction, 50% solvent was recovered under vacuum at 35-40°C. Finally the reaction mass was quenched into 20 gm crashed ice, stirred half hour and then filtered and washed with water. The separated solid was purified by recrystallization from hexane-ethyl acetate mixture.

Analytical data

IUPAC Name of Compound	1-(benzoyl)-3-[(5'-isopropyl-2'-methylphenoxy)acetamino]thiourea
Molecular Formula (Weight)	$C_{20}H_{23}N_3O_3S$ (385.49)
Appearance	White Crystalline powder
R_f value	0.14, System – Hexane : Ethylacetate (75:25) [compound was dissolved in Methanol]
Yield (%)	70

IR Data

Bond	N-H	C-H	C=C	C-O	C=O
Characteristic frequency	3163	2949	1603	1055, 1280	1616, 1610

NMR Data

^{1}H NMR:1.25 (6H, d, *J* = 6.89, C-9H), 2.35 (3H, s, C-7H), 2.88 (1H, m, *J* = 6.9, C-8H), 4.72 (2H, s, C-10H), 6.68 (1H, s, C-6H), 6.85 (1H, d, C-4H), 7.11 (1H, d, C-3H), 7.54 (2H, t, C-19 & 21H), 7.65 (1H, t, C-20H) 7.88 (2H, d, C-18 & 22H), 9.03 (1H, s, N-13H), 10.31 (1H, s, N-12H), 13.40 (1H, s, N-15H).

^{13}C NMR: 16.13 (C-9), 24.03 (C-7), 34.02 (C-8), 66.39 (C-10), 109.54 (C-6), 119.88 (C-4), 124.02 (C-3), 127.61 (C-18 & 22), 129.23 (C-19 & 21), 130.96 (C-20), 131.03 (C-2), 133.89 (C-17), 148.38 (C-5), 154.90 (C-1), 163.16 (C-11), 166.61 (C-16) and 171.57 (C-14).

Mass data

m/z	
$[M]^+$	$[M]^-$
--	385

Crystallographic details of TACH structures at 295K (RT), 250K, 200K and 110K

Data were collected on a well defined thick plate shaped colourless crystal (0.3x0.2x0.1 mm^3) crystallized from ethyl acetate/hexane (0.75/0.25) system. Crystal was mounted on a nylon cryoloop with paratone oil (open mounting). X-ray diffraction data were collected on an Oxford Mova diffractometer,[1] equipped with an EoS detector, with MoKα radiation (λ = 0.71073 Å) and desired temperature was maintained using Oxford Instruments N2 cryosystem. All structures were solved by direct methods using SHELXS-97 and refined against F^2 using SHELXL-97.[2] H-atoms were fixed geometrically and refined isotropically. WinGX[3] and OLEX2[4] were used for structure refinement and production of data tables, and ORTEP-3[5] was used for structure visualization. Analysis of the H-bonded and π-interactions was carried out using PLATON.[6] Asymmetric unit and Packing diagrams were generated with MERCURY.[7]

References:

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Table S1 Crystallographic data of TACH at 295K (RT), 250K, 200K and 110K.

Temp (K)	295 (RT)	250	200	110
CCDC number	941953	1060424	1060425	1060426
Crystal system	Monoclinic	Monoclinic	Triclinic	Triclinic
Space group	*C*2/*c*	*C*2/*c*	*P*-1	*P*-1
a (Å)	33.842(3)	33.698(2)	8.291(5)	8.1589(10)
b (Å)	8.1803(9)	8.1286(6)	15.440(5)	15.3909(13)
c (Å)	15.5183(15)	15.4818(9)	16.932(5)	16.8655(18)
α (°)	90	90	67.702(5)	67.525(9)
β (°)	111.285(11)	111.393(7)	77.616(5)	78.145(10)
γ (°)	90	90	89.556(5)	89.508(9)
Volume (Å^3)	4002.9(8)	3948.5(5)	1952.3(15)	1909.5(4)
Z	8	8	4	4
Density (g/cc)	1.279	1.297	1.311	1.341
μ (1/mm)	0.186	0.189	0.191	0.195
F (000)	1632	1632	816	816
θ (min, max)	2.5, 25.0	2.5, 25.0	2.4, 25.0	2.3, 25
No. Unique Reflns	3533	3491	6854	6719
No. of parameters	259	259	494	494
$h_{min,max}$	-40, 40	-40, 40	-9, 9	-9, 9
$k_{min,max}$	-9, 9	-9, 9	-18, 18	-16, 18
$l_{min,max}$	-18, 18	-18, 18	-13, 20	0, 20
$R_{\_obs}$, wR_{2_obs}	0.070, 0.1893	0.055, 0.153	0.099, 0.277	0.099, 0.276
$R_{\_all}$, wR_{2_all}	0.115, 0.2301	0.085, 0.170	0.135, 0.306	0.123, 0.293
$\Delta\rho_{min}$, $\Delta\rho_{max}$ (eÅ^{-3})	-0.264, 0.217	-0.236, 0.308	-0.570, 0.804	-0.657, 1.193
GooF	1.02	1.10	1.05	1.05

Simulated PXRD comparison of TACH structures at 295K (RT), 250K, 200K and 110K

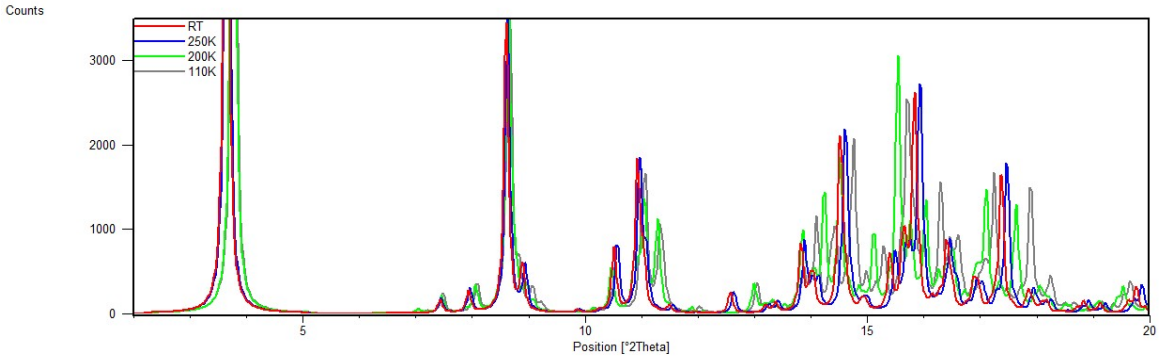

Figure S2 Overlay of simulated PXRD patterns (wavelength, λ = 1 Å) of 295K (RT), 250K, 200K and 110K structures.