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SYNTHESIS AND CHARACTERIZATION OF ACYCLIC 1,3-BIS(2,6-DIISOPROPYLPHENYL)-1,3-DIMETHYLTHIOUREA

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ABSTRACT: Isolation of 1,3-bis(2,6-diisopropylphenyl)-1,3-dimethylthiourea (2) is achieved by treatment of *N,N'*-bis(2,6-di-isopropylphenyl)-*N,N'*-dimethylformamidinium iodide (1) with KHMDS followed by addition of sulfur and structurally characterized. This compound crystallizes in the monoclinic system, space group $P2_1/n$ with cell parameters of a = 10.182(5), b = 19.493(5), c = 12.924(5) Å, β = 92.968(5)˚, V = 2561.7(17) Å^3, and Z = 4. The crystal structure was solved with the SHELXT structure solution program using Intrinsic phasing and refined with the SHELXL refinement package using Least Squares minimisation in the Olex-2 software.

KEYWORDS: Acyclic diaminocarbene (ADC), 2,6-diisopropylaniline, Olex-2 software, *N,N'*-bis(2,6-di-isopropylphenyl)-*N,N'*-dimethylformamidinium iodide.

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1. INTRODUCTION

Urea and its derivatives have exhibits a powerful role in agriculture, chemical industry, laboratory, medical use etc [1-3]. Thiourea and its derivatives are identical to urea, except that sulfur atom is present in place of the oxygen atom [4-7]. Thiourea and its derivatives have various applications in medicinal chemistry, herbicides and synthesis of heterocyclic compounds [8-12]. Apart from this, thiourea and its derivatives have important role in asymmetric organic synthesis and represent a special class of organocatalysts [13-15]. Double hydrogen bond interaction between thiourea and substrates is responsible for its catalytic activity and activate the reacting substrate [8-15]. Synthesis of substituted thiourea from formamidinium salt has not been explored [16-19]. Herein we report the synthesis and characterization of Acyclic 1,3-Bis(2,6-diisopropylphenyl)-1,3-dimethylthiourea from corresponding formamidinium salt.

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2. MATERIALS AND METHODS

2.1. General Procedures

All the reactions and manipulations were carried out under an atmosphere of dry nitrogen using standard Schlenk line techniques unless otherwise mentioned. Solvents were dried according to the standard literature procedures, and they were freshly distilled under nitrogen prior to use. All other reagents were used as received. Glassware was dried in an oven maintained at 140 °C overnight prior to use. Chemicals, such as 2,6-diisopropylaniline was purchased from Sigma-Aldrich and used as received. Sulfur, methyl iodide and triethyl orthoformate were purchased from SD Fine-Chem Limited and used as received. Compound *N,N'*-Bis(2,6-di-isopropylphenyl)-*N,N'*-dimethylformamidinium Iodide (1) was prepared by literature procedures [20-21].

2.2. Instrumentation

^{1}H and ^{13}C NMR spectra were obtained on a JEOL-DELTA 500 MHz spectrometer. The spectra were recorded in $CDCl_3$ as the solvent. ^{1}H and ^{13}C NMR Chemical shifts were referenced with respect to tetramethylsilane (TMS). Infrared spectra (IR) were recorded as KBr pellets on a Perkin Elmer-Spectrum Two. Electrospray ionization mass spectrometry (ESI-MS) spectra were recorded on a Waters-Q-TOF Premier-HAB213 spectrometer. Elemental analyses were performed with a Perkin Elmer-Series-II CHNS/O analyzer 2400. Melting points were determined in Stuart melting point apparatus SMP10 and are uncorrected.

2.3. X-ray Crystallography

The crystal data were collected on a Bruker D8-quest-Photon diffractometer (for compound **2**). Data were collected using graphite-monochromated MoKα radiation (λ = 0.71073 Å) at 100 K. The structure was solved with the SHELXT structure solution program using Intrinsic phasing and refined with the SHELXL refinement package using Least Squares minimisation in the Olex-2 software [22-29]. All the nonhydrogen atoms were refined with anisotropic thermal parameters. All the hydrogen atoms were placed in geometrically calculated positions or found in the Fourier difference map and included in the refinement process using riding model [22-29].

2.4. Synthesis 1,3-bis(2,6-diisopropylphenyl)-1,3-dimethylthiourea (2)

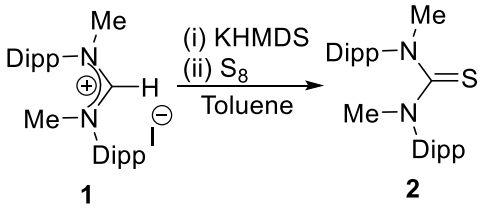
To a stirred solution of *N,N'*-Bis(2,6-di-isopropylphenyl)-*N,N'*-dimethylformamidinium Iodide (**1**) (0.521 g, 1 mmol) in dry toluene (30 mL) was added KHMDS (2.4 mL, 1.2 mmol, 0.5 M in toluene) and stirred for 4 h at room temperature under a nitrogen atmosphere. Resulting reaction mixture was filtered through a pad of celite and to this yellow filtrate, S_8 (0.038 g, 1.2 mmol) was added and stirred for overnight. Removal of the volatiles under vacuum and washing the residue with hexane affords off-white solid. It was purified by column chromatography (silica gel (60−120 mesh) using 1/20 ethyl acetate/ hexane) affords 1,3-bis(2,6-diisopropylphenyl)-1,3-dimethylthiourea (**2**) as off-white solid. Crystals were obtained in dichloromethane solution of **2** by slow evaporation at room temperature. Yield: 0.25 g (59%). Mp: 177−180 °C. Anal. Calcd for $C_{27}H_{40}N_2S$: C, 76.36; H, 9.49;

N, 6.60. Found: C, 75.12; H, 9.36; N, 6.12. ^{1}H NMR ($CDCl_3$, 500 MHz, δ, ppm): 1.12 (d, 6H, CH(C*H*$_3$)$_2$), 1.26 (m, 9H, CH(C*H*$_3$)$_2$), 1.37 (d, 9H, CH(C*H*$_3$)$_2$), 2.61 (s, 3H, N−C*H*$_3$), 2.99 (sept., 2H, C*H*(CH$_3$)$_2$), 3.27 (sept., 2H, C*H*(CH$_3$)$_2$), 3.69 (s, 3H, N−C*H*$_3$), 7.14–7.36 (m, 6H, C$_6$*H*$_3$). ^{13}C NMR ($CDCl_3$, 125 MHz; δ, ppm): 22.8, 24.1, 24.3, 24.6, 24.8, 26.0, 28.6, 28.9, 29.1, 43.1, 44.4, 50.2, 124.3, 124.5, 127.5, 129.1, 142.8, 143.7, 145.4, 146.0, 147.1, 182.1 (C=S). IR (KBr, cm^{-1}): 2962 (s), 2927 (m), 2866 (m), 1644 (w), 1588 (w), 1471 (s), 1425 (m), 1358 (s), 1336 (s), 1314 (m), 1260 (m), 1241 (w), 1228 (w), 1196 (w), 1180 (w), 1126 (m), 1099 (m), 1057 (w), 1009 (w), 932 (w), 810 (m), 795 (m), 774 (m), 764 (m), 718 (w), 637 (w), 594 (w), 571 (w), 554 (w), 486 (w). ESI-MS: calcd 425.2985, found 425.2932 $(M + H^+)^+$.

3. RESULTS AND DISCUSSION

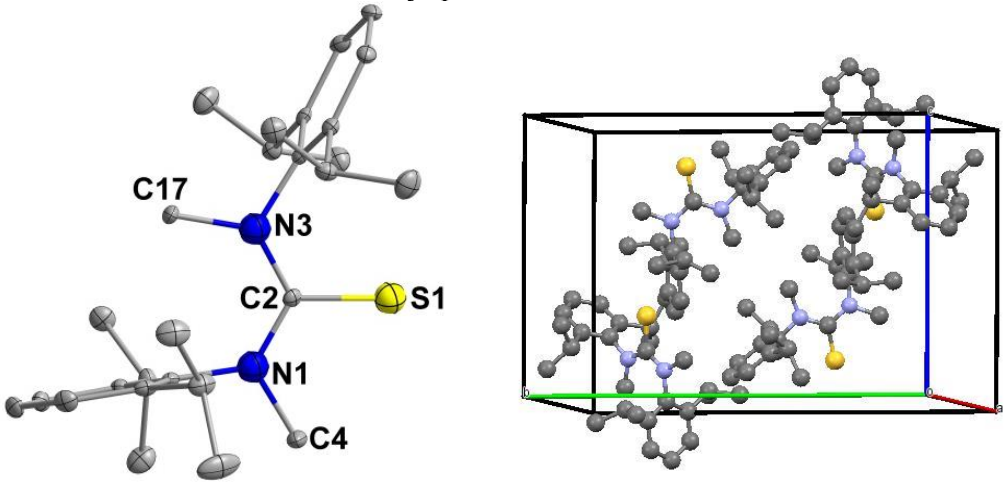
Previously, 1,3-dimethylimidazole-2-thione was obtained by *in situ* generated carbene from corresponding imidazolium salt, potassium *tert*-butoxide and elemental sulfur [30-35]. Similarly, treatment of *N,N'*-bis(2,6-di-isopropylphenyl)-*N,N'*-dimethylformamidinium iodide (**1**) with KHMDS in a toluene afforded *in situ* generated acyclic diaminocarbene (ADC), followed by addition of sulfur lead to the formation of corresponding 1,3-bis(2,6-diisopropylphenyl)-1,3-dimethylthiourea (**2**) in 59% yield as air-stable compounds (Scheme 1). Purification of compound **2** was achieved by column chromatography. In the proton NMR, disappearance of a C2−H signal and appearance of a 182.1 ppm (C=S) signal in ^{13}C NMR of compound **2** authenticate its formation. Further formation of this compound was confirmed by ESI-MS spectra shows the presence of a molecular ion peak 425.2985 $(M + H^+)^+$ for **2**. Additionally, white color crystals were obtained in dichloromethane solution of **2** by the slow evaporation method and were subjected to single crystal X-ray diffraction analysis.

Scheme 1: Synthesis of 1,3-bis(2,6-diisopropylphenyl)-1,3-dimethylthiourea (2)



1 **2**

The molecular structure of **2** and the crystallographic parameters are given in Figure 1 and Table 1 respectively. Solid-state structure of **2** shows that N-aryl substituents are present in a *pseudo-trans* orientation. The NCN bond angle [121.49(18)°] in **2** is smaller as compare with **1** (129.6°) and significant elongation of C−N bond lengths [N1−C2 = 1.357(3), N3−C2 = 1.355(2) Å] are observed [20]. In addition, C2═S1 [1.691(2) Å] bond is similar to five membered 1,3-dimethylimidazole-2-thione [C2═S1 = 1.695 Å] [30-35].



(a) (b)

Figure 1: (a) ORTEP diagram showing 50% probability thermal ellipsoids and selected atom labels for compound **2**. Hydrogen atoms have been omitted for clarity. Selected bond lengths (Å) and angles (deg): S1−C2 = 1.691(2), N1− C2 = 1.357(3), N3−C2 = 1.355(2), N1−C2−N3 = 121.49(18). (b) A packing diagram of compound (**2**). For the sake of clarity, H atoms have been omitted.

Table 1: Crystal data and structure refinement for 2

Compound Number	**2**
Identification code	20octb_0m
Empirical formula	$C_{27}H_{40}N_2S$
Formula weight	424.67
Temperature/K	273(2)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	10.182(5)
b/Å	19.493(5)
c/Å	12.924(5)
α/°	90.000(5)
β/°	92.968(5)
γ/°	90.000(5)
Volume/Å^3	2561.7(17)
Z	4
ρ_{calc}g/cm^3	1.101
μ/mm^{-1}	0.142
F(000)	928.0
Crystal size/mm^3	0.14 × 0.12 × 0.11

Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.518 to 52
Index ranges	-12 ≤ h ≤ 12, -23 ≤ k ≤ 24, -15 ≤ l ≤ 15
Reflections collected	21767
Independent reflections	5012 [R_{int} = 0.0588, R_{sigma} = 0.0607]
Data/restraints/parameters	5012/0/281
Goodness-of-fit on F^2	0.942
Final R indexes [I>=2σ (I)]	R_1 = 0.0494, wR_2 = 0.1259
Final R indexes [all data]	R_1 = 0.0859, wR_2 = 0.1495
Largest diff. peak/hole / e Å^{-3}	0.25/-0.25

Table 2: Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for 20octb_0m. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
S(1)	6570.6(6)	3419.0(3)	1641.5(4)	24.71(18)
N(3)	5368.9(16)	4081.1(8)	3093.6(12)	15.2(4)
N(1)	6334.1(16)	3015.8(8)	3571.1(12)	18.6(4)
C(18)	5081.4(19)	4592.4(10)	2294.2(15)	16.4(4)
C(5)	6034.5(19)	3013.3(10)	4654.4(15)	16.2(4)
C(23)	3877(2)	4558.0(10)	1732.1(15)	17.4(5)
C(6)	4903(2)	2668.4(10)	4937.4(15)	17.3(5)
C(7)	4648(2)	2652.4(11)	5988.4(16)	20.7(5)
C(2)	6054.0(18)	3511.5(10)	2856.6(15)	17.0(4)
C(10)	6917.4(19)	3314.8(10)	5379.4(16)	19.5(5)
C(22)	3574(2)	5090.2(11)	1042.9(16)	22.9(5)
C(19)	5969(2)	5129.7(10)	2186.9(15)	18.9(5)
C(20)	5604(2)	5646.8(11)	1488.0(16)	22.2(5)
C(21)	4423(2)	5629.6(11)	920.2(16)	23.9(5)
C(8)	5479(2)	2968.6(11)	6709.9(16)	24.2(5)
C(24)	7278(2)	5161.1(11)	2792.7(17)	23.3(5)
C(11)	3967(2)	2314.2(11)	4158.2(16)	23.6(5)

C(27)	2935(2)	3960.4(11)	1828.3(16)	21.6(5)
C(9)	6606(2)	3294.6(11)	6412.6(16)	23.9(5)
C(17)	4773(2)	4252.2(11)	4074.3(16)	23.1(5)
C(14)	8187(2)	3648.1(11)	5065.4(19)	29.1(5)
C(25)	7327(2)	5752.3(12)	3562.4(18)	30.4(5)
C(12)	2561(2)	2572.0(12)	4225.0(17)	28.7(5)
C(28)	2712(2)	3592.1(12)	794.5(17)	31.4(6)
C(29)	1631(2)	4183.2(12)	2247(2)	36.1(6)
C(16)	8417(2)	4346.0(12)	5553(2)	39.7(6)
C(13)	4011(2)	1536.9(11)	4304(2)	35.0(6)
C(4)	7051(2)	2403.8(11)	3250.9(18)	32.1(6)
C(26)	8423(2)	5209.3(13)	2076(2)	39.2(6)
C(15)	9357(2)	3180.9(13)	5327(3)	57.6(9)

Table 3: Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for 20octb_0m. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
S(1)	31.9(3)	25.8(3)	17.1(3)	1.5(2)	7.9(2)	11.3(2)
N(3)	16.8(9)	14.8(9)	14.2(8)	-0.6(7)	2.4(7)	4.0(7)
N(1)	22.8(9)	16.3(9)	17.2(9)	2.9(7)	5.5(7)	6.8(8)
C(18)	20.1(11)	15.6(10)	13.8(10)	0.2(8)	3.0(8)	5.6(9)
C(5)	16.7(10)	14.0(10)	18.0(10)	3.5(8)	2.5(8)	5.1(8)
C(23)	19.5(11)	16.8(10)	16.2(10)	-4.4(8)	4.4(8)	4.4(9)
C(6)	17.7(11)	15.4(10)	18.6(11)	1.4(8)	-0.6(8)	3.1(8)
C(7)	17.0(11)	23.6(12)	21.7(11)	4.2(9)	3.9(9)	-0.2(9)
C(2)	11.7(10)	17.7(10)	21.7(11)	-0.2(9)	2.1(8)	-0.5(8)
C(10)	15.1(10)	14.7(10)	28.5(12)	1.2(9)	-0.9(9)	1.9(8)
C(22)	23.4(12)	22.5(12)	22.3(11)	-3.0(9)	-2.6(9)	7.8(10)
C(19)	20.8(11)	18.0(11)	18.2(11)	-1.4(9)	2.9(9)	3.7(9)
C(20)	27.4(12)	16.0(11)	23.8(11)	1.5(9)	6.2(10)	0.5(9)
C(21)	32.3(13)	18.3(11)	21.2(11)	3.8(9)	1.3(10)	8.2(10)
C(8)	26.9(12)	30.8(12)	14.9(10)	1.6(10)	-0.4(9)	5.1(10)
C(24)	22.2(12)	20.3(11)	27.2(12)	4.4(9)	-0.9(10)	-0.4(9)
C(11)	23.2(12)	30.6(12)	17.0(11)	-0.2(9)	1.3(9)	-4.0(10)

C(27)	20.7(11)	21.7(11)	22.2(11)	-1.5(9)	0.1(9)	2.0(9)
C(9)	22.0(12)	27.1(12)	21.7(11)	-3.4(10)	-8.0(9)	0.0(10)
C(17)	29.5(12)	22.0(11)	18.7(11)	1.1(9)	9.3(9)	9.3(10)
C(14)	18.8(12)	24.2(12)	44.2(14)	1.4(11)	1.9(10)	-3.6(10)
C(25)	25.3(13)	33.7(13)	32.0(13)	-1.4(11)	-1.6(10)	-4.4(11)
C(12)	20.8(12)	34.2(13)	30.6(13)	0.7(11)	-5.0(10)	-4.9(10)
C(28)	37.0(14)	27.0(13)	30.1(13)	-4.3(10)	0.1(11)	-6.6(11)
C(29)	24.8(13)	37.7(14)	46.4(15)	-6.7(12)	7.3(11)	-2.3(11)
C(16)	26.9(13)	29.2(14)	62.3(18)	0.2(13)	-3.7(12)	-8.8(11)
C(13)	30.8(13)	30.1(13)	43.8(15)	-11.2(12)	0.0(11)	-6.0(11)
C(4)	43.8(15)	24.3(12)	29.6(13)	7.1(10)	15.4(11)	15.1(11)
C(26)	22.0(13)	50.0(16)	46.0(16)	-4.4(13)	5.6(11)	1.8(12)
C(15)	20.2(14)	32.9(15)	120(3)	5.7(17)	7.6(15)	-1.0(12)

Table 4: Bond Lengths for 20octb_0m

Atom	Atom	Length/Å	Atom	Atom	Length/Å
S(1)	C(2)	1.691(2)	C(10)	C(9)	1.389(3)
N(3)	C(18)	1.454(2)	C(10)	C(14)	1.520(3)
N(3)	C(2)	1.355(2)	C(22)	C(21)	1.376(3)
N(3)	C(17)	1.472(2)	C(19)	C(20)	1.391(3)
N(1)	C(5)	1.448(3)	C(19)	C(24)	1.512(3)
N(1)	C(2)	1.357(3)	C(20)	C(21)	1.376(3)
N(1)	C(4)	1.469(3)	C(8)	C(9)	1.384(3)
C(18)	C(23)	1.394(3)	C(24)	C(25)	1.522(3)
C(18)	C(19)	1.395(3)	C(24)	C(26)	1.529(3)
C(5)	C(6)	1.399(3)	C(11)	C(12)	1.525(3)
C(5)	C(10)	1.394(3)	C(11)	C(13)	1.527(3)
C(23)	C(22)	1.391(3)	C(27)	C(28)	1.523(3)
C(23)	C(27)	1.518(3)	C(27)	C(29)	1.523(3)
C(6)	C(7)	1.396(3)	C(14)	C(16)	1.512(3)
C(6)	C(11)	1.517(3)	C(14)	C(15)	1.523(3)
C(7)	C(8)	1.373(3)			

Table 5: Bond Angles for 20octb_0m

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C(18)	N(3)	C(17)	112.31(15)	C(9)	C(10)	C(5)	117.58(19)
C(2)	N(3)	C(18)	119.22(16)	C(9)	C(10)	C(14)	120.53(19)
C(2)	N(3)	C(17)	128.36(16)	C(21)	C(22)	C(23)	121.6(2)
C(5)	N(1)	C(4)	113.71(15)	C(18)	C(19)	C(24)	122.51(18)
C(2)	N(1)	C(5)	127.82(16)	C(20)	C(19)	C(18)	117.13(19)
C(2)	N(1)	C(4)	118.46(16)	C(20)	C(19)	C(24)	120.37(19)
C(23)	C(18)	N(3)	118.45(17)	C(21)	C(20)	C(19)	121.7(2)
C(23)	C(18)	C(19)	122.76(18)	C(22)	C(21)	C(20)	119.6(2)
C(19)	C(18)	N(3)	118.53(17)	C(7)	C(8)	C(9)	120.59(19)
C(6)	C(5)	N(1)	118.17(17)	C(19)	C(24)	C(25)	111.56(18)
C(10)	C(5)	N(1)	119.17(17)	C(19)	C(24)	C(26)	111.63(19)
C(10)	C(5)	C(6)	122.54(18)	C(25)	C(24)	C(26)	110.43(18)
C(18)	C(23)	C(27)	122.45(18)	C(6)	C(11)	C(12)	111.86(17)
C(22)	C(23)	C(18)	117.22(19)	C(6)	C(11)	C(13)	110.87(18)
C(22)	C(23)	C(27)	120.31(19)	C(12)	C(11)	C(13)	109.97(18)
C(5)	C(6)	C(11)	122.88(18)	C(23)	C(27)	C(28)	110.84(17)
C(7)	C(6)	C(5)	117.56(18)	C(23)	C(27)	C(29)	112.11(18)
C(7)	C(6)	C(11)	119.56(18)	C(29)	C(27)	C(28)	110.67(18)
C(8)	C(7)	C(6)	120.7(2)	C(8)	C(9)	C(10)	120.91(19)
N(3)	C(2)	S(1)	119.06(15)	C(10)	C(14)	C(15)	110.56(19)
N(3)	C(2)	N(1)	121.49(18)	C(16)	C(14)	C(10)	112.86(19)
N(1)	C(2)	S(1)	119.45(14)	C(16)	C(14)	C(15)	110.1(2)
C(5)	C(10)	C(14)	121.89(19)				

Table 6: Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 20octb_0m

Atom	*x*	*y*	*z*	U(eq)
H(7)	3905.68	2425.02	6201.82	25
H(22)	2778.68	5080.98	655.75	27
H(20)	6172.08	6013.61	1402.51	27
H(21)	4200.74	5980.54	456.25	29

H(8)	5282.77	2963.62	7404.67	29
H(24)	7381.4	4733.9	3188.22	28
H(11)	4253.45	2417.52	3462.72	28
H(27)	3344.75	3633.24	2322.16	26
H(9)	7163.48	3503.04	6911.62	29
H(17A)	5451.26	4300.23	4613.26	35
H(17B)	4181.54	3892.47	4253.03	35
H(17C)	4295.87	4675.55	3996.43	35
H(14)	8123.33	3709.77	4311.9	35
H(25A)	7284.4	6179.77	3193.26	46
H(25B)	8133.12	5730.79	3980.8	46
H(25C)	6594.98	5719.42	3998.82	46
H(12A)	2257.55	2474.44	4900.57	43
H(12B)	2002.49	2345.71	3709.75	43
H(12C)	2535.77	3058.11	4106.67	43
H(28A)	2257.59	3891.73	307.43	47
H(28B)	2194.23	3187.69	889.01	47
H(28C)	3545.08	3464.93	535.57	47
H(29A)	1787.2	4390.55	2915.79	54
H(29B)	1072.03	3790.29	2307.76	54
H(29C)	1212.25	4509.23	1781.17	54
H(16A)	7673.23	4635.94	5386.2	60
H(16B)	9192.35	4547.61	5289.8	60
H(16C)	8529.73	4297.48	6290.99	60
H(13A)	4892.79	1376.15	4231.53	52
H(13B)	3433	1322.61	3790.28	52
H(13C)	3735.23	1423.44	4982.3	52
H(4A)	7908.94	2534.97	3047.09	48
H(4B)	6575.95	2189.27	2677.17	48
H(4C)	7136.82	2087.14	3819.38	48
H(26A)	8378.83	4833.62	1595.7	59
H(26B)	9239.5	5190	2481.63	59
H(26C)	8369.93	5634.7	1702.25	59

H(15A)	9439.05	3109.37	6062.09	86
H(15B)	10144.6	3390.91	5099.47	86
H(15C)	9224.09	2747.89	4983.05	86

4. CONCLUSION

In this report, synthesis of 1,3-bis(2,6-diisopropylphenyl)-1,3-dimethylthiourea (**2**) is described. Synthesis of 1,3-bis(2,6-diisopropylphenyl)-1,3-dimethylthiourea (**2**) was achieved by treatment of sulfur to the *in situ* generated acyclic diaminocarbene (ADC) from corresponding formamidinium sat (**1**). This methodology has wide substrate scope for the synthesis of tetrasubstituted thiourea.

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CONFLICT OF INTEREST

The author declares no conflict of interest.

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