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Thiocarbamates as non-nucleoside HIV-1 reverse transcriptase inhibitors. Part 2: Parallel synthesis, molecular modelling and structure–activity relationship studies on analogues of *O*-(2-phenylethyl)-*N*-phenylthiocarbamate

Sara Cesarini,[a,*] Andrea Spallarossa,[a] Angelo Ranise,[a] Olga Bruno,[a] Paolo La Colla,[b,*] Barbara Secci,[b] Gabriella Collu[b] and Roberta Loddo[b]

[a]*Dipartimento di Scienze Farmaceutiche, Università di Genova, Viale Benedetto XV 3, I-16132 Genova, Italy*
[b]*Dipartimento di Scienze e Tecnologie Biomediche, Università di Cagliari, Cittadella Universitaria, S.S. 554, Km 4,500, I-09042 Monserrato (Cagliari), Italy*

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Abstract—To acquire further insight into the structure–activity relationship (SAR) of the thiocarbamates (TCs) described in the preceding work, 57 analogues of the lead compound *O*-(2-phenylethyl)-*N*-phenylthiocarbamate **I** were prepared by parallel solution-phase synthesis. We varied the 2-phenylethyl moiety (mono-substitution on the phenyl ring and modification of the ethyl linker), keeping constant the *N*-phenyl ring substitutions which have given the best results in the previous series. Most of the new TCs inhibited wild-type HIV-1 at micro- and nanomolar concentrations in MT-4 cell-based assays. Some TCs were also active at micromolar concentrations against the Y181C and/or K103N/Y181C resistant mutants. The SARs were rationalized by docking simulations.

1. Introduction

In the preceding study,[1] we described new thiocarbamate (TC) non-nucleoside reverse transcriptase inhibitors (NNRTIs), close isosteres of *N*-phenethyl-*N*′-thiazolylthiourea (PETT) derivatives (Fig. 1a).[2–17]

Among the new TCs, compound **I** and its congeners **II**–**V** (Fig. 1b)[1] were selected for further modifications, as the simplicity and easy synthetic accessibility of the structures made them an attractive target for potential optimization.

The SAR strategy was focused on variations of the phenyl (ring A, Fig. 1b) and the ethyl spacer, whereas the *N*-phenyl (ring B, Fig. 1b) was kept unsubstituted, 4-monosubstituted (CH_3, F, Cl, NO_2 and OCH_3) and 3,4-disubstituted (CH_3,Cl; Cl,Cl; Cl,NO_2), according to the SARs developed for the 2-(2-pyridyl)ethyl TC series.[1] We investigated the effects of the monosubstitution at ring A *ortho*, *meta* and *para* position with functional groups featured by various electronic, steric and lipophilic properties (CH_3, Cl, Br, OH and OCH_3) (**1**–**19**, Table 1). The ethyl linker was branched (**20**–**27**, Table 2), lengthened with a methylene or a sulfur or oxygen atom (**28**–**30**, Table 3 and **35**–**48**, Table 4), conformationally constrained (**31**–**34**, Table 3) and shortened (**49**–**57**, Table 5).

2. Chemistry

TC **1**–**57** were prepared by a convergent solution-phase parallel synthesis (Scheme 1), by using ordered arrays of spatially separated reaction vessels (Carousel reaction station™). This two-step procedure combines two building blocks (alcohols and isothiocyanates, functionalised according to the planned SARs). Starting alcohols $\mathbf{A_{1–37}}$ (Fig. 2a) were first transformed into their corresponding

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* Corresponding authors. Tel.: +39 010 353 8370; fax: +39 010 353 8358 (S.C.); tel.: +39 070 675 4148; fax: +39 070 675 4210 (P.L.C.); e-mail addresses: sara.cesarini@unige.it; placolla@unica.it

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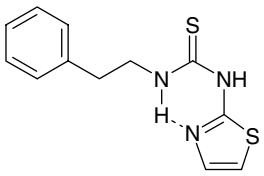
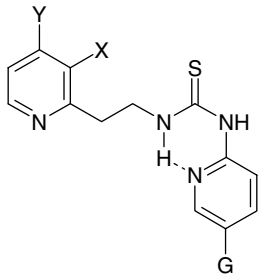
a) PETT derivatives

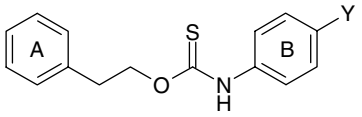


PETT



Trovirdine (X = Y = H, G = Br)
PETT-1 (X = F, Y = OC_2H_5, G = CN)

b) TCs

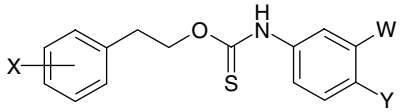


I-V

TC	Y	EC_{50} (μM)	CC_{50} (μM)
I	H	6.0	100
II	Cl	0.5	>100
III	NO_2	0.9	>100
IV	CH_3	4.3	>100
V	OCH_3	17	36

Figure 1. Chemical structure of PETT, Trovirdine and PETT-1; chemical structure, anti-HIV-1 activity and cyitotoxicity of TCs previously synthesized (**I-V**).

Table 1. Cytotoxicity and anti-HIV-1 activity of TC **1**–**19**[a]

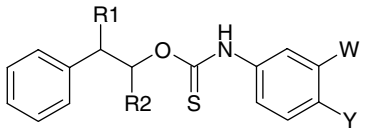


Compound	X	Y	W	CC_{50}[b]	EC_{50}[c]	SI[d]
1	2-CH_3	NO_2	H	>100	0.7	>143
2	2-Cl	NO_2	H	>100	0.4	>250
3	2-OH	NO_2	H	36	10	3.6
4	2-OCH_3	Cl	H	43	0.07	614
5	2-OCH_3	NO_2	H	>100	0.1	>1000
6	2-OCH_3	Cl	Cl	45	0.3	150
7	2-OCH_3	Cl	NO_2	44	0.9	49
8	3-CH_3	NO_2	H	96	0.5	192
9	3-Cl	NO_2	H	>100	1.5	>67
10	3-OH	NO_2	H	24	3.7	6.5
11	3-OCH_3	Cl	H	94	0.08	1175
12	3-OCH_3	NO_2	H	>100	0.2	>500
13	3-OCH_3	Cl	Cl	44	1.0	44
14	3-OCH_3	Cl	NO_2	43	2.0	22
15	4-CH_3	NO_2	H	>100	0.3	>333
16	4-Cl	NO_2	H	>100	13	>7.7
17	4-Br	NO_2	H	>100	7.9	>13
18	4-OH	NO_2	H	41	>41	<1.0
19	4-OCH_3	NO_2	H	>100	1.4	>71
Trovirdine				60	0.02	3000

[a] Data mean values for three separate experiments. Variation among triplicate samples was less than 10%.
[b] Compound concentration [μM] required to reduce the viability of mock-infected cells by 50%, as determined by the MTT method.
[c] Compound concentration [μM] required to achieve 50% protection of MT-4 cell from HIV-1 induced cytopathogenicity, as determined by the MTT method.
[d] Selectivity index: CC_{50}/EC_{50} ratio.

salts in the presence of sodium hydride in dry THF or DMF, depending on the different building block solubility and reactivity. Then, the alcoholates (**B_{1-57}**) condensed in situ with the proper isothiocyanate (**I_{1-9}**, Fig. 2b) to afford the corresponding thiocarbamate sodium salts, which were converted into the desired products by treatment with a 2 N HCl or aqueous NH_4Cl solution. The work-up simply required filtrations or extractions and the final products were purified by crystallization. The yields (not optimized) ranged from 13% to 99%.

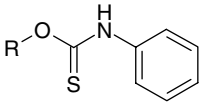
Table 2. Cytotoxicity and anti-HIV-1 activity of TC **20**–**27**[a]

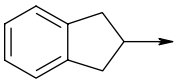
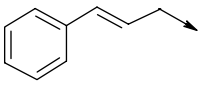
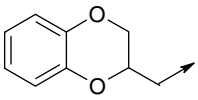


Compound	R_1	R_2	Y	W	CC_{50}[b]	EC_{50}[c]	SI[d]
20[e]	CH_3	H	Cl	H	30	0.2	150
21[e]	CH_3	H	NO_2	H	>100	0.6	>167
22[e]	CH_3	H	Cl	Cl	44	0.3	147
23[e]	CH_3	H	Cl	NO_2	41	0.5	82
24	$-CH_2CH_2-$	H	H	H	51	7.0	7.3
25[e]	C_6H_5	H	H	H	>100	>100	—
26[e]	H	CH_3	H	H	>100	9.0	>11
27[e]	H	CH_3	NO_2	H	39	1.3	30
Trovirdine					60	0.02	3000

[a,b,c,d] See legend to Table 1.
[e] Assayed as racemic mixtures.

Table 3. Cytotoxicity and anti-HIV-1 activity of TC **28**–**33**[a]



Compound	R	CC_{50}[b]	EC_{50}[c]	SI[d]
28	3-Phenylpropyl	>100	67	>1.5
29	2-Phenoxyethyl	>100	5.8	>17
30	2-Phenylthioethyl	>100	38	>2.6
31		>100	12	>8.3
32		>100	67	>1.5
33		>100	52	>1.9
Trovirdine		60	0.02	3000

[a,b,c,d] See legend to Table 1.

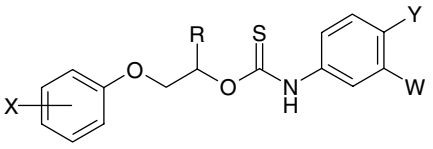
Scheme 2 describes the hypothetical intramolecular SN2-mechanism leading to TC **34**. The not-isolable *N*-phenyl thiocarbamic anion $\mathbf{B_{34}}$ would cause the displacement of acrylate and the consequent cyclization to form the oxazolidine ring.

3. Biological results and discussion

TC **1**–**57** were evaluated for their cytotoxicity and anti-HIV-1 activity in MT-4 cells using Trovirdine as reference compound (Tables 1–5). The most potent derivatives were also tested against the clinically relevant K103R, Y181C and K103N/Y181C resistant mutants,[18,19] employing Efavirenz as reference molecule (Table 6).

All the analogues bearing a substituent on ring A (**1**–**19**, Table 1), with the exception of **18**, showed anti-HIV activity ranging from nanomolar to micromolar concentrations (EC_{50} = 0.07–13 μM). TC potency was affected by the ring A substitution pattern as well as the nature of the substituent. When X was a methoxy group or a chlorine atom, the potency trend was: *ortho* > *meta* >

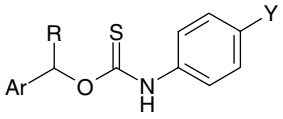
Table 4. Cytotoxicity and anti-HIV-1 activity of TC **35–48**[a]



Compound	X	R	Y	W	CC_{50}[b]	EC_{50}[c]	SI[d]
35	H	H	CH_3	H	74	10	7.4
36	H	H	Cl	H	34	2.9	12
37	H	H	NO_2	H	>100	8.5	>12
38	H	H	OCH_3	H	48	17	2.8
39	2-OH	H	H	H	>100	19	>5.2
40	4-Br	H	NO_2	H	>100	>100	—
41	4-NO_2	H	Cl	H	72	>72	<1.0
42[e]	H	CH_3	H	H	>100	2.0	>50
43[e]	H	CH_3	CH_3	H	24	1.2	20
44[e]	H	CH_3	F	H	>100	11	>9
45[e]	H	CH_3	Cl	H	>100	1.6	>63
46[e]	H	CH_3	NO_2	H	>100	2.6	>38
47[e]	H	CH_3	OCH_3	H	>100	>100	—
48[e]	H	CH_3	CH_3	Cl	>100	4.0	>25
Trovirdine					60	0.02	3000

[a,b,c,d] See legend to Table 1.
[e] Assayed as racemic mixtures.

Table 5. Cytotoxicity and anti-HIV-1 activity of TC **49–57**[a]

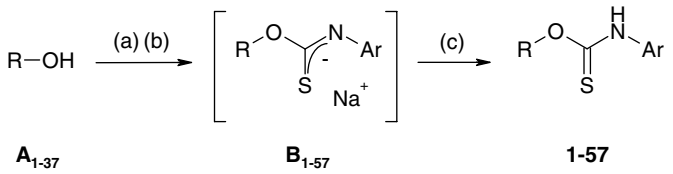


Compound	Ar	R	Y	CC_{50}[b]	EC_{50}[c]	SI[d]
49	2-Thienyl	H	H	38	>38	<1.0
50	2,6-Dichlorophenyl	H	H	>100	>100	—
51	3-Phenoxyphenyl	H	H	>100	>100	—
52[e]	4-Chlorophenyl	CH_3	H	>100	5.3	>19
53[e]	4-Chlorophenyl	CH_3	NO_2	>100	7.0	>14
54[e]	4-Biphenyl	CH_3	Cl	>100	57	>1.8
55[e]	1-Naphthyl	CH_3	Cl	>100	82	>1.2
56[e]	2-Naphthyl	CH_3	Cl	>100	26	>3.8
57[e]	Phenyl	C_2H_5	H	>100	>100	—
Trovirdine				60	0.02	3000

[a,b,c,d] See legend to Table 1.
[e] Assayed as racemic mixtures.

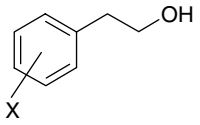
para (**5** > **12** > **19**; **2** > **9** > **16**; **4** > **11**; **6** > **13**; **7** > **14**). This is in accordance with the SARs of PETT derivatives substituted with polar groups, indicating that *ortho* and *meta* substitution were preferred over the *para* substitution.[2] Conversely, for the methyl-substituted compounds (**1**, **8**, **15**) the potency trend was *para* > *meta* > *ortho*, with the EC_{50} values falling in the concentration range of 0.3–0.7 μM. Maximal activity was observed for the *ortho*-methoxy derivatives **4** and **5** and the *meta*-methoxy congeners **11** and **12** (EC_{50} = 70, 100, 80 and 200 nM, respectively), which turned out to be 7- to 4.5-fold more potent than the corresponding unsubstituted TCs **II** and **III**, and 30- to 86-fold more potent than the lead compound **I**. The series of *ortho*- and *meta*-methoxy derivatives highlighted also the influence of the ring B substitution on the activity trend, which was chloro > nitro > 3,4-dichloro > 4-chloro-3-nitro (see the EC_{50} values of TC **4–7**, and **11–14**). Among the chloro-derivatives, only the *ortho*-substituted TC **2** displayed a sub-micromolar activity. The presence of a hydrophobic group at *para* position was favourable, as found in PETT SARs.[5] The activity order was methyl **15** > methoxy **19** > bromo **17** > chlorine **16**. TC **15** (EC_{50} = 0.3 μM) resulted as 3-fold more potent than the corresponding unsubstituted TC **III** and 20-fold more potent than the lead **I**. The presence of a hydrophilic hydroxyl group (added to enhance TC water solubility) at ring A *ortho* (**3**), *meta* (**10**) and *para* (**18**) position was little tolerated, probably because of the highly hydrophobic nature of the NNRTI binding pocket.

Regarding the modifications of the ethyl linker, Table 2 indicates that a methyl substituent in the benzilic posi-

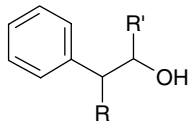


Scheme 1. Reagents and conditions: (a) NaH, dry THF (for $\mathbf{A_{1–24}}$, $\mathbf{A_{27–29}}$, $\mathbf{A_{36}}$ and $\mathbf{A_{37}}$) or DMF (for $\mathbf{A_{25}}$, $\mathbf{A_{26}}$, $\mathbf{A_{30–35}}$), rt, 30 min; (b) Ar–N=C=S ($\mathbf{I_{1–9}}$), rt, 18 h; (c) 2 N HCl (for **1**–**30**, **32**, **33**, **35**–**41** and **49**–**51**) or $NH_4Cl_{(aq)}$ (for **31**, **34**, **42**–**48** and **52**–**57**). For the structure list of alcohols $\mathbf{A_{1–37}}$ and isothiocyanates $\mathbf{I_{1–9}}$, see Figure 2.

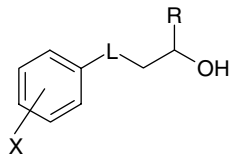
a) Alcohols $\mathbf{A_{1-37}}$



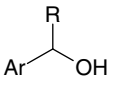
$\mathbf{A_1}$: X = H
$\mathbf{A_2}$: X = 2-CH_3
$\mathbf{A_3}$: X = 2-Cl
$\mathbf{A_4}$: X = 2-OH
$\mathbf{A_5}$: X = 2-OCH_3
$\mathbf{A_6}$: X = 3-CH_3
$\mathbf{A_7}$: X = 3-Cl
$\mathbf{A_8}$: X = 3-OH
$\mathbf{A_9}$: X = 3-OCH_3
$\mathbf{A_{10}}$: X = 4-CH_3
$\mathbf{A_{11}}$: X = 4-Cl
$\mathbf{A_{12}}$: X = 4-Br
$\mathbf{A_{13}}$: X = 4-OH
$\mathbf{A_{14}}$: X = 4-OCH_3



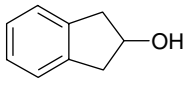
$\mathbf{A_{15}}$: R = CH_3; R' = H
$\mathbf{A_{16}}$: R = CH_2CH_2; R' =H
$\mathbf{A_{17}}$: R = Ph; R' = H
$\mathbf{A_{18}}$: R = H; R' = CH_3



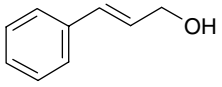
$\mathbf{A_{19}}$: X = H; L = CH_2; R = H
$\mathbf{A_{20}}$: X = H; L = O; R = H
$\mathbf{A_{21}}$: X = 2-OH; L = O; R = H
$\mathbf{A_{22}}$: X = 4-Br; L = O; R = H
$\mathbf{A_{23}}$: X = 4-NO_2; L = O; R = H
$\mathbf{A_{24}}$: X = H; L = S; R = H
$\mathbf{A_{25}}$: X = H; L = O; R = CH_3
$\mathbf{A_{26}}$: X = H; L = O;
R = $CH_2OCOCH{=}CH_2$



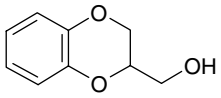
$\mathbf{A_{27}}$: Ar = 3-phenoxyphenyl; R = H
$\mathbf{A_{28}}$: Ar = 2,6-dichlorophenyl; R = H
$\mathbf{A_{29}}$: Ar = 2-thienyl; R = H
$\mathbf{A_{30}}$: Ar = 4-chlorophenyl; R = CH_3
$\mathbf{A_{31}}$: Ar = biphenyl; R = CH_3
$\mathbf{A_{32}}$: Ar = 1-naphthyl; R = CH_3
$\mathbf{A_{33}}$: Ar = 2-naphthyl; R = CH_3
$\mathbf{A_{34}}$: Ar = phenyl; R = C_2H_5



$\mathbf{A_{35}}$



$\mathbf{A_{36}}$



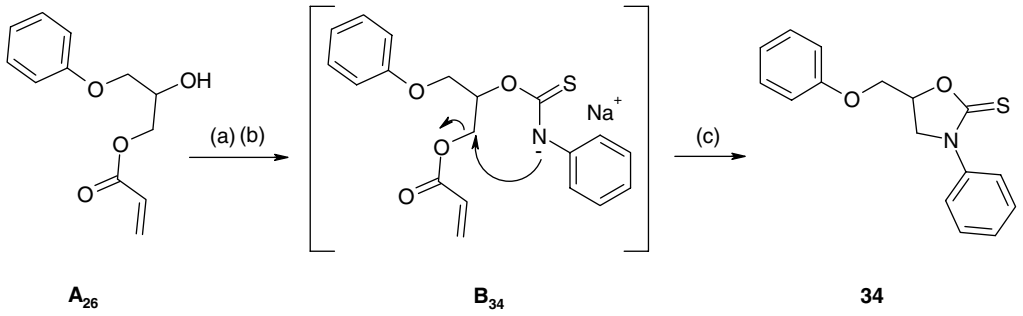
$\mathbf{A_{37}}$

b) Isothiocyanates Ar-NCS ($\mathbf{I_{1-9}}$)

	Ar
$\mathbf{I_1}$	phenyl
$\mathbf{I_2}$	4-tolyl
$\mathbf{I_3}$	4-fluorophenyl
$\mathbf{I_4}$	4-chlorophenyl
$\mathbf{I_5}$	4-nitrophenyl
$\mathbf{I_6}$	4-methoxyphenyl
$\mathbf{I_7}$	3,4-dichlorophenyl
$\mathbf{I_8}$	3-chloro-4-methylphenyl
$\mathbf{I_9}$	4-chloro-3-nitrophenyl

Figure 2. Building blocks used.

tion (**20**–**23**, EC_{50} = 0.2–0.6 μM) slightly enhanced activity (compare **20** with **II** and **21** with **III**), whereas the same group in the phenethyl position (**26**, **27**) diminished activity (**26** vs **I** and **27** vs **III**). Interestingly, this is not in accordance with the SARs of *O*-(2-phthalimidoethyl)-*N*-phenylthiocarbamates (C-TCs),[20] but it agrees with PETT SARs.[2] The fusion of the benzylic methylene into a cyclopropane ring did not affect remarkably the activity, whereas the addition of a phenyl ring at the benzylic position was detrimental (com-



Scheme 2. Synthesis of compound **34**, cyclic analogue of **29**, and hypothetical reaction mechanism for its formation. Reagents and conditions: (a) NaH, dry DMF, rt, 30 min; (b) $\mathbf{I}_1$, rt, 18 h; (c) $NH_4Cl_{(aq)}$.

Table 6. Anti-HIV-1 activity of **4**, **8**, **11**, **12**, **15** and **20** against the Y181C and K103N/Y181C resistant mutants

Compound	EC_{50} (μM)[c]	
	Y181C	K103N/Y181C
4	8.9	n.a.[e]
8	8.9	69
11	12	86
12	8.3	n.a.[e]
15	8.6	92
20	12	n.a.[e]
Efavirenz	0.01	0.04

[c] See legend to Table 1.
[e] Not active.

pare **24** and **25** with **I**). As reported for PETT[2] and C-TC SARs,[20] a propyl linker caused a dramatic decrease in activity (Table 3, **28** vs **I**). In this respect, the isosteric replacement of the methylene adjacent to ring A with oxygen (**29**) or sulfur (**30**) led to the following trend: O > S > CH_2. The rigidification of the propyl linker did not cause any activity variation (**32** vs **28**), while semirigid cyclic analogues **31** and **33** were less active than the corresponding unconstrained TC **I** and **29**, respectively. In addition, embodying the thiocarbamic function into the oxazolidine-2-thione ring led to the inactive compound **34**.

The significant activity detected for TC **29** prompted us to expand the SARs by synthesizing a number of its analogues (**35**–**48**, Table 4). TC **35**–**38** displayed an EC_{50} value in the concentration range of 2.9–17 μM, being in general less active than the corresponding phenylethyl derivatives (compare **35** with **IV**, **36** with **II** and **37** with **III**). The substitution on ring A (X = 2-OH, 4-Br, 4-NO_2) led to weakly active (**39**) or inactive (**40**, **41**) products. The methyl-branched derivatives (**42**–**48**), with the exception of **47**, exhibited anti-HIV activity in the low micromolar concentration range. In contrast with the SARs of the phenylethyl TCs, a methyl at the position adjacent to the thiocarbamic function generally enhanced the potency (compare **42** with **29**, **43** with **35**, **45** with **36** and **46** with **37**).

Table 5 reports the activity data of the inferior homologues of **I**. The linker shortening (**49**–**51**) was detrimental, in accordance with PETT[2] and C-TC SARs.[20] However, the introduction of a methyl on the methylene spacer allowed to obtain TCs approximately as active as **I** (**52**, **53**). Rings that are more sterically demanding than A (**54**–**56**) produced a significant decrease in activity.

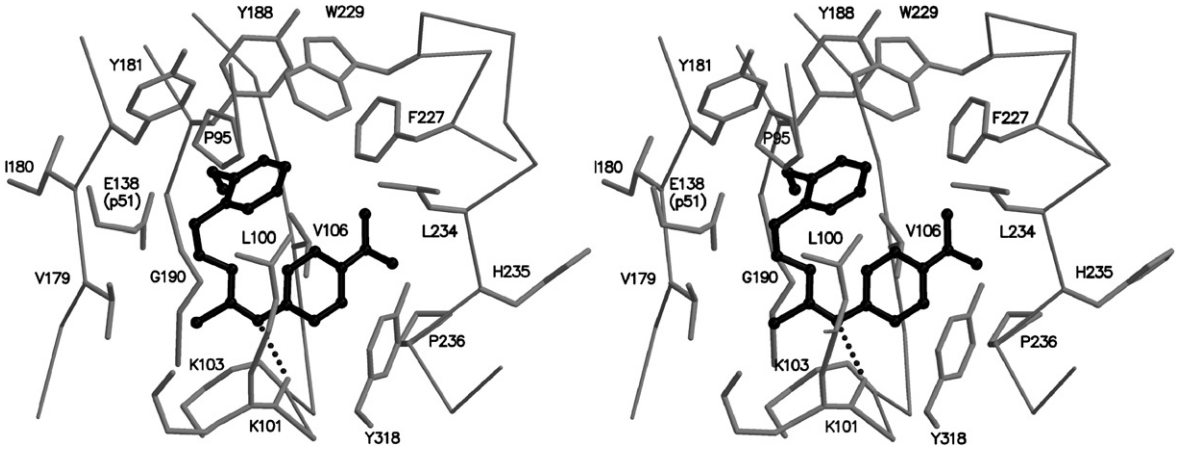


Figure 3. Stereoview showing the position and orientation of TC 5, the most potent among the *N-para*-nitrophenyl derivatives. The ligand is represented as black balls-and-sticks, while the residues lining RT non-nucleoside binding site are shown as grey sticks. Hydrogen bonds are depicted as dotted lines. The drawing was realized by the programs MolScript[22] and Raster 3D.[23]

The replacement of the methyl with an ethyl group afforded an inactive compound (**57**).

The activity of TC **21** was confirmed also by means of the determination of the dose required to reduce HIV-1 p24 antigen levels by 90% in virus infected C8166 cultures (EC_{90} = 0.6 μM) in comparison with Trovirdine (EC_{90} = 0.015 μM). TC **42** and **43**, tested in enzyme assays against recombinant wild type RT (rRT), showed an IC_{50} (dose required to inhibit the rRT activity by 50%) of 1.0 μM and 1.4 μM, respectively, comparable with that of Trovirdine (IC_{50} = 1.03 μM), used as reference compounds with Efavirenz (IC_{50} = 0.014 μM).

Finally, TC **4**, **8**, **11**, **12**, **15** and **20** significantly reduced the multiplication of the Y181C resistant strain and also of the K103N + Y181C mutant in the case of **8**, **11** and **15** (Table 6). The K103R mutated strain proved to be unsusceptible to the tested TCs.

All compounds except **18**, **41** and **49** showed values of CC_{50} higher than EC_{50} (CC_{50} in many cases superior to 100 μM).

4. Molecular modelling

To rationalize the most relevant SARs, computational studies were performed using the docking model of phenylethyl-TCs bound into the HIV-1 RT NNBS, previously constructed for **III**.[1] Briefly, TC **2**, **5**, **12**, **15**, **21** and **27** were docked (Autodock 3.05) into the NNBS using the X-ray coordinates of RT-PETT-1 complex (PDB code 1DTQ)[11] as template structure. The resulting RT-TC complexes were energy-minimized by a combined protocol of simulated annealing and Powell minimization.

The potency increase of **2** and, even more, of **5** (Fig. 3) in comparison with **III** would be ascribed to the hydrophobic contacts established between the chlorine atom (**2**) or the methoxy group (**5**) at the *ortho* position of ring A with the Leu 100, Glu138(p51) and Tyr181 side chains. Additionally, the methoxy substituent is engaged in a polar interaction with the Glu138(p51) carboxyl. The shift of the methoxy functionality from *ortho* (**5**) to *meta* (**12**) position did not affect the potency, as the methoxy group of **12** is involved in van der Waals contacts with the His96 backbone and the Pro95, Leu100 and Trp229 side chains. The docking model calculated for **15** explains the beneficial effects on activity due to the methyl group at the ring A *para*-position. This substituent is orientated towards the ring plane of the nearby Trp229 side chain, with which it establishes extensive hydrophobic contacts. The complexes of RT and **21** and **27**, modelled as single enantiomers, would rationalize why a methyl substituent in the benzilic position slightly enhances activity, whereas a methyl group in the phenethyl position is detrimental. In the former case, in both enantiomers the methyl group provides further stabilization to the complex by interacting with the Val179, Ile180 and Tyr188 main chains and the Tyr181 side chain (enantiomer S) or the Val179 and Gly190 main chains (enantiomer R). In the latter case, the methyl in the enantiomer S is engaged in hydrophobic contacts with the Glu138(p51) and Val 179 side chains, but in the enantiomer R a steric clash between the methyl and the Val179 side chain destabilizes the complex.

5. Conclusions

Our SAR expansion on *O*-(2-phenylethyl)-*N*-phenylthiocarbamate led to TCs with improved activity against wild-type HIV-1 compared to the TCs of the preceding work.[1] Moreover, a few TCs turned out to be significantly effective against the Y181C and K103N + Y181C mutant strains, but a further optimization is still needed to improve their resistance profile. However, the SAR data collected will be useful to design and synthesize second generation TCs with improved broad anti-HIV properties. Besides, additional studies will be done to explore the potential use of the most potent TCs so far synthesized, as vaginal and rectal microbicides preventing HIV transmission[14,15] and as antioxidants on analogy of PETT derivatives.[10]

6. Experimental protocols

6.1. Chemistry

6.1.1. General. All chemicals were purchased by Chiminord and Aldrich Chemical, Milan, Italy. The synthesis of Trovirdine was accomplished according to the published procedure.[2]

Solvents were reagent grade. THF was distilled in the presence of sodium. DMF was dried on molecular sieves (5 Å 1/16″ pellets). Unless otherwise stated, all commercial reagents were used without further purification. Organic solutions were dried over anhydrous sodium sulfate.

Thin-layer chromatography (TLC) system for routine monitoring the course of reactions and confirming the purity of analytical samples employed aluminium-backed silica gel plates (Merck DC-Alufolien Kieselgel 60 F_{254}): $CHCl_3$ or $CHCl_3$/methanol were used as developing solvents and detection of spots was made by UV light and/or by iodine vapours. Merck silica gel, 230–400 mesh, was used for chromatography.

The parallel solution-phase chemistry was performed by using a Carousel Reaction Station™ (Radleys Discovery Technologies, Italian distributor: StepBio, Bologna). The evaporation of solutions in parallel fashion was performed with an Evaposel™ apparatus (Radleys Discovery Technologies, Italian distributor: StepBio, Bologna) operating at reduced pressure of about 15–20 torr. Yields were not optimized. Melting points were determined on a Fisher-Johns apparatus and are uncorrected.

IR spectra were recorded on a Perkin-Elmer 398 spectrometer as KBr discs. ^{1}H NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 on a Varian Gemini 200 instrument. Chemical shifts were reported in δ (ppm) units rel-

ative to the internal standard tetramethylsilane, and the splitting patterns were described as follows: s (singlet), d (doublet), t (triplet), m (multiplet) and br s (broad singlet). The first order values reported for coupling constants *J* were given in Hz. Elemental analyses were performed by an EA1110 Elemental Analyser (Fison-Instruments, Milan) and were within ±0.4% of the theoretical values.

6.1.2. Parallel synthesis of *O*-(2-phenylethyl)*N*-phenylthiocarbamates 1–27; *N*-phenylthiocarbamates 28–30, 32, 33 and 49–51; *O*-(2-phenoxylethyl)*N*-phenylthiocarbamates 35–41. Sixty percent of sodium hydride dispersion in mineral oil (0.40 g, 10 mmol; for **3**, **10**, **18** and **39**, 0.80 g, 20 mmol) was added in a single portion at rt to each numbered reaction tube of a 12-Carousel Reaction Station™, containing a stirred solution of the starting alcohol (10 mmol) in dry THF (30 mL). After stirring for 30 min, the proper isothiocyanate (10 mmol) was added to each reaction mixture, which was then stirred for 18 h at rt. Two different types of work-up were carried out. Work-up (i) (**1**–**6**, **8**–**10**, **12**, **13**, **15**–**20**, **35**–**38**, **40** and **41**): after parallel evaporation of THF in vacuo using an Evaposel™ apparatus, a 2 N HCl solution (45 mL) was added into each tube. The contents of the tubes were then transferred into a set of beakers. Further 2 N HCl solution (120 mL) was added into each beaker. The precipitates obtained were filtered in parallel by an in-house device and dissolved in CH_2Cl_2. The solutions were washed with water, dried over anhydrous Na_2SO_4 and filtered in parallel through pads of Florisil (diameter 5 × 2 cm) by an in-house device. Parallel evaporating in vacuo using an Evaposel™ apparatus gave residues which were purified by crystallization from the suitable solvent mixtures. Work-up (ii) (**7**, **11**, **14**, **21**–**30**, **32**, **33**, **39** and **49**–**51**): after parallel evaporation of THF in vacuo using an Evaposel™ apparatus, a 2 N HCl solution (45 mL) was added into each tube. The contents of the tubes were then transferred into a set of separating funnels. Further 2 N HCl solution (120 mL) was added into each funnel. After parallel extraction with diethyl ether (CH_2Cl_2 for **27**), the combined extracts of each reaction were washed with water, dried over anhydrous Na_2SO_4 and filtered in parallel through pads of Florisil (diameter 5 × 2 cm) by an in-house device. Parallel evaporating in vacuo using an Evaposel™ apparatus gave residues which were purified by crystallization from the suitable solvent mixtures.

6.1.2.1. *O*-[2-(2-Methylphenyl)ethyl]*N*-(4-nitrophenyl) thiocarbamate (1). Mp 162–164 °C; yield: 68% from CH_2Cl_2/ethanol. IR (KBr) cm^{-1}: 3267, 2984. ^1H NMR ($CDCl_3$) δ: 2.36 (s, 3H, CH_3), 3.14 (t, J = 6.6 Hz, 2H, CH_2Ph), 4.85 (t, J = 6.6 Hz, 2H, CH_2O), 7.01–7.33 (m, 4H, arom. H), 7.48–7.81 (m, 2H, arom. H), 7.99–8.30 (m, 2H, arom. H), 10.83 (br s, 1H, NH, exchangeable). Calcd for $C_{16}H_{16}N_2O_3S$: C, 60.74; H, 5.1; N, 8.85; S, 10.13. Found: C, 60.91; H, 5.14; N, 8.99; S, 10.15.

6.1.2.2. *O*-[2-(2-Chlorophenyl)ethyl]*N*-(4-nitrophenyl) thiocarbamate (2). Mp 148–150 °C; yield: 98% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3268, 1553, 1332. ^1H NMR ($CDCl_3$) δ: 3.22 (t, J = 6.6 Hz, 2H, CH_2Ph), 4.82 (t, J = 6.6 Hz, 2H, CH_2O), 7.09–7.44 (m, 6H, arom. H), 8.03–8.15 (m, 2H, arom. H), 8.43 (br s, 1H, NH, exchangeable). Calcd for $C_{15}H_{13}ClN_2O_3S$: C, 53.49; H, 3.89; N, 8.32; S, 9.52. Found: C, 53.39; H, 4.00; N, 8.31; S, 9.50.

6.1.2.3. *O*-[2-(2-Hydroxyphenyl)ethyl]*N*-(4-nitrophenyl) thiocarbamate (3). Mp 181–184 °C; yield: 99% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3496, 3242, 1552, 1334. ^1H NMR (DMSO-d_6) δ: 2.88–3.08 (m, 2H, CH_2Ph), 4.53–4.73 (m, 2H, CH_2O), 6.58–7.15 (m, 4H, arom. H), 7.46–7.73 (m, 2H, arom. H), 7.97–8.16 (m, 2H, arom. H), 9.49 (s, 1H, OH, exchangeable), 11.53 (s, 1H, NH, exchangeable). Anal. Calcd for $C_{15}H_{14}N_2O_4S$: C, 56.59; H, 4.43; N, 8.8; S, 10.07. Found: C, 56.62; H, 4.43; N, 8.74; S, 10.02.

6.1.2.4. *O*-[2-(2-Methoxyphenyl)ethyl]*N*-(4-chlorophenyl) thiocarbamate (4). Mp 108–110°C; yield: 88% from diethyl ether/methanol. IR (KBr) cm^{-1}: 3219, 2938. ^1H NMR ($CDCl_3$) δ: 3.09 (t, J = 6.4 Hz, 2H, CH_2Ph), 3.80 (s, 3H, CH_3), 4.80 (t, J = 6.6 Hz, 2H, CH_2O), 6.66–7.50 (m, 8H, arom. H), 8.84 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{16}H_{16}ClNO_2S$: C, 59.72; H, 5.01; N, 4.35; S, 9.96. Found: C, 59.73; H, 4.93; N, 4.15; S, 9.98.

6.1.2.5. *O*-[2-(2-Methoxyphenyl)ethyl]*N*-(4-nitrophenyl) thiocarbamate (5). Mp 178–179 °C; yield: 98% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3266, 2959, 1551, 1332. ^1H NMR (DMSO-d_6) δ: 3.11 (t, J = 6.6 Hz, 2H, CH_2Ph), 3.83 (s, 3H, CH_3), 4.72 (t, J = 6.6 Hz, 2H, CH_2O), 6.77–7.45 (m, 4H, arom. H), 7.56–7.88 (m, 2H, arom. H), 8.01–8.39 (m, 2H, arom. H), 10.92 (br s, 1H, NH, exchangeable). Calcd for $C_{16}H_{16}N_2O_4S$: C, 57.82; H, 4.85; N, 8.43; S, 9.65. Found: C, 57.79; H, 4.95; N, 8.40; S, 9.67.

6.1.2.6. *O*-[2-(2-Methoxyphenyl)ethyl]*N*-(3,4-dichlorophenyl)thiocarbamate (6). Mp 115–117 °C; yield: 84% from CH_2Cl_2/ethanol. IR (KBr) cm^{-1}: 3226. ^1H NMR ($CDCl_3$) δ: 3.11 (t, J = 6.6 Hz, 2H, CH_2Ph), 3.81 (s, 3H, CH_3), 4.82 (t, J = 6.6 Hz, 2H, CH_2O), 6.56–7.62 (m, 7H, arom. H), 8.95 (br s, 1H, NH, exchangeable). Calcd for $C_{16}H_{15}Cl_2NO_2S$: C, 53.94; H, 4.24; N, 3.93; S, 9.0. Found: C, 54.10; H, 4.38; N, 4.04; S, 9.03.

6.1.2.7. *O*-[2-(2-Methoxyphenyl)ethyl]*N*-(4-chloro-3-nitrophenyl)thiocarbamate (7). Mp 139–140 °C; yield: 45% from diethyl ether/ethanol. IR (KBr) cm^{-1}: 3217, 2954, 1543, 1340. ^1H NMR ($CDCl_3$) δ: 3.13 (t, J = 6.6 Hz, 2H, CH_2Ph), 3.83 (s, 3H, CH_3), 4.85 (t, J = 6.6 Hz, 2H, CH_2O), 6.73–7.56 (m, 6H, arom. H), 7.79–7.97 (m, 1H, arom. H), 8.80 (br s, 1H, NH, exchangeable). Calcd for $C_{16}H_{15}ClN_2O_4S$: C, 52.39; H, 4.12; N, 7.64; S, 8.74. Found: C, 52.49; H, 4.34; N, 7.68; S, 8.72.

6.1.2.8. *O*-[2-(3-Methylphenyl)ethyl]*N*-(4-nitrophenyl) thiocarbamate (8). Mp 113–115 °C; yield: 84% from CH_2Cl_2/ethanol. IR (KBr) cm^{-1}: 3250, 2914. ^1H NMR ($CDCl_3$) δ: 2.34 (s, 3H, CH_3), 3.10 (t, J = 6.6 Hz, 2H, CH_2Ph), 4.88 (t, J = 6.6 Hz, 2H, CH_2O), 6.95–7.61 (m, 6H, arom. H), 7.97–8.31 (m, 2H, arom. H), 9.14 (br s,

1H, NH, exchangeable). Calcd for $C_{16}H_{16}N_2O_3S$: C, 60.74; H, 5.1; N, 8.85; S, 10.13. Found: C, 61.03; H, 5.17; N, 9.03; S, 10.19.

6.1.2.9. *O*-[2-(3-Chlorophenyl)ethyl]*N*-(4-nitrophenyl)thiocarbamate (9). Mp 137–138 °C; yield: 98% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3264, 1552, 1336. ^1H NMR ($CDCl_3$) δ: 3.12 (t, $J = 6.6$ Hz, 2H, CH_2Ph), 4.85 (t, $J = 6.6$ Hz, 2H, CH_2O), 7.08–7.80 (m, 6H, arom. H), 7.98-8.37 (m, 2H, arom. H), 10.87 (br s, 1H, NH, exchangeable). Calcd for $C_{15}H_{13}ClN_2O_3S$: C, 53.49; H, 3.89; N, 8.32; S, 9.52. Found: C, 53.41; H, 4.02; N, 8.29; S, 9.55.

6.1.2.10. *O*-[2-(3-Hydroxyphenyl)ethyl]*N*-(4-nitrophenyl)thiocarbamate (10). Mp 143–145 °C; yield: 97% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3391, 3256, 1551, 1335. ^1H NMR (DMSO-d_6) δ: 2.93 (t, $J = 6.6$ Hz, 2H, CH_2Ph), 4.63 (t, $J = 6.6$ Hz, 2H, CH_2O), 6.44–6.70 (m, 3H, arom. H), 6.92–7.10 (m, 1H, arom. H), 7.39–7.68 (m, 2H, arom. H), 7.96–8.16 (m, 2H, arom. H), 9.31 (br s, 1H, OH, exchangeable), 11.54 (s, 1H, NH, exchangeable). Anal. Calcd for $C_{15}H_{14}N_2O_4S$: C, 56.59; H, 4.43; N, 8.8; S, 10.07. Found: C, 56.57; H, 4.53; N, 8.51; S, 10.08.

6.1.2.11. *O*-[2-(3-Methoxyphenyl)ethyl]*N*-(4-chlorophenyl)thiocarbamate (11). Mp 84–86 °C; yield: 41% from diethyl ether/methanol. IR (KBr) cm^{-1}: 3208, 2965. ^1H NMR ($CDCl_3$) δ: 3.03 (t, $J = 6.6$ Hz, 2H, CH_2Ph), 3.77 (s, 3H, CH_3), 4.79 (t, $J = 6.6$ Hz, 2H, CH_2O), 6.63–7.46 (m, 8H, arom. H), 8.85 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{16}H_{16}ClNO_2S$: C, 59.72; H, 5.01; N, 4.35; S, 9.96. Found: C, 59.61; H, 4.99; N, 4.12; S, 9.95.

6.1.2.12. *O*-[2-(3-Methoxyphenyl)ethyl]*N*-(4-nitrophenyl)thiocarbamate (12). Mp 135–136 °C; yield: 98% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3272, 2921, 1551, 1336. ^1H NMR (DMSO-d_6) δ: 2.99 (t, $J = 6.6$ Hz, 2H, CH_2Ph), 3.63 (s, 3H, CH_3), 4.66 (t, $J = 6.6$ Hz, 2H, CH_2O), 6.68–6.87 (m, 3H, arom. H), 7.0–7.22 (m, 1H, arom. H), 7.44–7.64 (m, 2H, arom. H), 8.00–8.12 (m, 1H, arom. H), 11.55 (s, 1H, NH, exchangeable). Calcd for $C_{16}H_{16}N_2O_4S$: C, 57.82; H, 4.85; N, 8.43; S, 9.65. Found: C, 57.81; H, 5.13; N, 8.14; S, 9.86.

6.1.2.13. *O*-[2-(3-Methoxyphenyl)ethyl]*N*-(3,4-dichlorophenyl)thiocarbamate (13). Mp 60–62 °C; yield: 75% from diethyl ether/ethanol. IR (KBr) cm^{-1}: 3192, 2924. ^1H NMR ($CDCl_3$) δ: 3.05 (t, $J = 6.6$ Hz, 2H, CH_2Ph), 3.77 (s, 3H, CH_3), 4.80 (t, $J = 6.6$ Hz, 2H, CH_2O), 6.60–7.55 (m, 7H, arom. H), 8.73 (br s, 1H, NH, exchangeable). Calcd for $C_{16}H_{15}Cl_2NO_2S$: C, 53.94; H, 4.24; N, 3.93; S, 9.00. Found: C, 54.10; H, 4.55; N, 3.83; S, 9.22.

6.1.2.14. *O*-[2-(3-Methoxyphenyl)ethyl]*N*-(4-chloro-3-nitrophenyl)thiocarbamate (14). Mp 51–53 °C; yield: 22% from diethyl ether/petroleum ether. IR (KBr) cm^{-1}: 3353, 1538, 1343. ^1H NMR (DMSO-d_6) δ: 2.86–3.04 (m, 2H, CH_2Ph), 3.62 (s, 3H, CH_3), 4.50–4.70 (m, 2H, CH_2O), 6.62–6.84 (m, 3H, arom. H), 7.04–7.19 (m, 2H, arom. H), 7.48–7.67 (m, 2H, arom. H), 11.44 (s, 1H, NH, exchangeable). Calcd for $C_{16}H_{15}ClN_2O_4S$: C, 52.39; H, 4.12; N, 7.64; S, 8.74. Found: C, 52.50; H, 3.88; N, 7.53; S, 8.67.

6.1.2.15. *O*-[2-(4-Methylphenyl)ethyl]*N*-(4-nitrophenyl)thiocarbamate (15). Mp 130–132 °C; yield: 79% from CH_2Cl_2/diethyl ether. IR (KBr) cm^{-1}: 3212. ^1H NMR ($CDCl_3$) δ: 2.35 (s, 3H, CH_3), 3.10 (t, $J = 6.6$ Hz, 2H, CH_2Ph), 4.85 (t, $J = 6.6$ Hz, 2H, CH_2O), 7.00–7.64 (m, 6H, arom. H), 7.96–8.30 (m, 2H, arom. H), 9.01 (br s, 1H, NH, exchangeable). Calcd for $C_{16}H_{16}N_2O_3S$: C, 60.74; H, 5.1; N, 8.85; S, 10.13. Found: C, 60.73; H, 5.10; N, 8.87; S, 10.10.

6.1.2.16. *O*-[2-(4-Chlorophenyl)ethyl]*N*-(4-nitrophenyl)thiocarbamate (16). Mp 151–153 °C; yield: 98% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3263, 1552, 1337. ^1H NMR ($CDCl_3$) δ: 3.11 (t, $J = 6.6$ Hz, 2H, CH_2Ph), 4.83 (t, $J = 6.6$ Hz, 2H, CH_2O), 7.08–7.76 (m, 6H, arom. H), 7.94–8.32 (m, Hz, 2H, arom. H), 10.43 (br s, 1H, NH, exchangeable). Calcd for $C_{15}H_{13}ClN_2O_3S$: C, 53.49; H, 3.89; N, 8.32; S, 9.52. Found: C, 53.61; H, 4.19; N, 7.97; S, 9.50.

6.1.2.17. *O*-[2-(4-Bromophenyl)ethyl]*N*-(4-nitrophenyl)thiocarbamate (17). Mp 145–146 °C; yield: 96% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3256, 1552, 1337. ^1H NMR (DMSO-d_6) δ: 3.12 (t, $J = 6.6$ Hz, 2H, CH_2Ph), 4.78 (t, $J = 6.6$ Hz, 2H, CH_2O), 7.16–7.90 (m, 6H, arom. H), 8.05–8.38 (m, 2H, arom. H), 11.73 (br s, 1H, NH, exchangeable). Calcd for $C_{15}H_{13}BrN_2O_3S$: C, 47.26; H, 3.44; N, 7.35; S, 8.41. Found: C, 47.32; H, 3.69; N, 7.10; S, 8.38.

6.1.2.18. *O*-[2-(4-Hydroxyphenyl)ethyl]*N*-(4-nitrophenyl)thiocarbamate (18). Mp 195–197 °C; yield: 99% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3459, 3267, 1550, 1334. ^1H NMR (DMS*O*-d_6) δ: 2.89 (t, $J = 6.6$ Hz, 2H, CH_2Ph), 4.59 (t, $J = 6.6$ Hz, 2H, CH_2O), 6.47–6.69 (m, 2H, arom. H), 6.87–7.07 (m, 2H, arom. H), 7.34–7.70 (m, 2H, arom. H), 7.93–8.12 (m, 2H, arom. H), 9.22 (s, 1H, OH, exchangeable), 11.54 (s, 1H, NH, exchangeable). Anal. Calcd for $C_{15}H_{14}N_2O_4S$: C, 56.59; H, 4.43; N, 8.8; S, 10.07. Found: C, 56.56; H, 4.60; N, 8.77; S, 10.06.

6.1.2.19. *O*-[2-(4-Methoxyphenyl)ethyl]*N*-(4-nitrophenyl)thiocarbamate (19). Mp 145–146 °C; yield: 77% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3264, 1553, 1335. ^1H NMR ($CDCl_3$) δ: 3.09 (t, $J = 6.6$ Hz, 2H, CH_2Ph), 3.83 (s, 3H, CH_3), 4.85 (t, $J = 6.6$ Hz, 2H, CH_2O), 6.78–7.58 (m, 6H, arom. H), 8.07–8.34 (m, 2H, arom. H), 8.85 (br s, 1H, NH, exchangeable). $C_{16}H_{16}N_2O_4S$: C, 57.82; H, 4.85; N, 8.43; S, 9.65. Found: C, 57.89; H, 4.95; N, 8.41; S, 9.51.

6.1.2.20. (±) *O*-(2-Methyl-2-phenylethyl)*N*-(4-chlorophenyl)thiocarbamate (20). Mp 68–69 °C; yield: 58% from diethyl ether/methanol. IR (KBr) cm^{-1}: 3220, 3104, 2925. ^1H NMR ($CDCl_3$) δ: 1.26 (d, $J = 7.2$ Hz, 3H, CH_3), 3.10–3.30 (m, 1H, CH), 4.53–4.74 (m, 2H, CH_2O), 6.68–7.45 (m, 9H, arom. H), 8.76 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{16}H_{16}ClNOS$: C,

62.84; H, 5.27; N, 4.58; S, 10.48. Found: C, 62.85; H, 5.33; N, 4.52; S, 10.45.

6.1.2.21. (±) *O*-(2-Methyl-2-phenylethyl)*N*-(4-nitrophenyl)thiocarbamate (21). Mp 148–150 °C; yield: 40% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3250. ^1H NMR ($CDCl_3$) δ: 1.37 (d, $J = 6.0$ Hz, 3H, CH_3), 3.10–3.39 (m, 1H, CH), 4.69 (d, $J = 6.0$ Hz, 2H, CH_2O), 7.09–7.60 and 7.90–8.24 (m, 9H, arom. H), 10.61 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{16}H_{16}N_2O_3S$: C, 60.74; H, 5.10; N, 8.85; S, 10.13. Found: C, 60.84; H, 5.06; N, 8.92; S, 10.17.

6.1.2.22. (±) *O*-(2-Methyl-2-phenylethyl)*N*-(3,4-dichlorophenyl)thiocarbamate (22). Mp 74–76 °C; yield: 49% from diethyl ether/ethanol. IR (KBr) cm^{-1}: 3248, 2966. ^1H NMR ($CDCl_3$) δ: 1.33 (d, $J = 7.2$ Hz, 3H, CH_3), 3.06–3.55 (m, 1H, CHPh), 4.74 (d, $J = 7.2$ Hz, 2H, CH_2O), 7.13–7.54 (m, 8H, arom. H), 9.53 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{16}H_{15}Cl_2NOS$: C, 56.48; H, 4.44; N, 4.12; S, 9.42. Found: C, 56.67; H, 4.74; N, 4.00; S, 9.46.

6.1.2.23. (±) *O*-(2-Methyl-2-phenylethyl)*N*-(4-chloro-3-nitrophenyl)thiocarbamate (23). Mp 90–92 °C; yield: 14% from diethyl ether/petroleum ether. IR (KBr) cm^{-1}: 3238, 1534, 1343. ^1H NMR ($CDCl_3$) δ: 1.34 (d, $J = 7.2$ Hz, 3H, CH_3), 2.98–3.56 (m, 1H, CHPh), 4.84 (d, $J = 7.2$ Hz, 2H, CH_2O), 7.11–7.91 (m, 8H, arom. H), 8.98 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{16}H_{15}ClN_2O_3S$: C, 54.78; H, 4.31; N, 7.99; S, 9.14. Found: C, 54.50; H, 4.57; N, 8.04; S, 9.12.

6.1.2.24. *O*-[(1-Phenylcyclopropyl)methyl]*N*-phenylthiocarbamate (24). Mp 99–100 °C; yield: 85% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3230. ^1H NMR ($CDCl_3$) δ: 1.00 (qs, 4H, $2CH_2$), 4.67 (s, 2H, CH_2O), 6.99–7.94 (m, 10H, arom. H), 8.53 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{17}H_{17}NOS$: C, 72.05; H, 6.05; N, 4.94; S, 11.31. Found: C, 72.35; H, 6.08; N, 5.07; S, 11.58.

6.1.2.25. (±) *O*-(2,2-Diphenylethyl)*N*-phenylthiocarbamate (25). Mp 112–113 °C; yield: 93% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3210. ^1H NMR ($CDCl_3$) δ: 4.55 (t, $J = 7.2$ Hz, 1H, CH), 5.14 (d, $J = 7.2$ Hz, 2H, CH_2O), 6.95–7.83 (m, 15H, arom. H), 8.66 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{21}H_{19}NOS$: C, 75.64; H, 5.74; N, 4.20; S, 9.60. Found: C, 75.70; H, 5.87; N, 4.20; S, 9.43.

6.1.2.26. (±) *O*-(1-Methyl-2-phenylethyl)*N*-phenylthiocarbamate (26). Mp 81–83 °C; yield: 81% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3260. ^1H NMR ($CDCl_3$) δ: 1.35 (d, $J = 6.0$ Hz, 3H, CH_3), 2.83–3.20 (m, 2H, CH_2Ph), 5.65–6.08 (m, 1H, OCH), 6.80–7.70 (m, 10H, arom. H), 8.61 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{16}H_{17}NOS$: C, 70.82; H, 6.31; N, 5.16; S, 11.81. Found: C, 70.78; H, 6.65; N, 4.99; S, 11.83.

6.1.2.27. (±) *O*-(1-Methyl-2-phenylethyl)*N*-(4-nitrophenyl)thiocarbamate (27). Mp 111–112 °C; yield: 45% from diethyl ether/methanol. IR (KBr) cm^{-1}: 3236, 3133, 1554, 1331. ^1H NMR ($CDCl_3$) δ: 1.37 (d, $J = 6.2$ Hz, 3H, CH_3), 2.84–3.20 (m, 2H, CH_2Ph), 5.75–5.94 (m, 1H, OCH), 7.09–7.46 (m, 7H, arom. H), 8.04–8.16 (m, 2H, arom. H), 8.84 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{16}H_{16}N_2O_3S$: C, 60.74; H, 5.10; N, 8.85; S, 10.13. Found: C, 60.87; H, 5.18; N, 8.85; S, 10.10.

6.1.2.28. *O*-(3-Phenylpropyl)*N*-phenylthiocarbamate (28). Mp 73–75 °C; yield: 87% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3200. ^1H NMR ($CDCl_3$) δ: 1.89–2.41 (m, 2H, CH_2Bn), 2.73 (t, $J = 7.2$ Hz, 2H, CH_2Ph), 4.60 (t, $J = 6.6$ Hz, 2H, CH_2O), 6.72–7.85 (m, 10H, arom. H), 8.79 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{16}H_{17}NOS$: C, 70.82; H, 6.31; N, 5.16; S, 11.81. Found: C, 71.18; H, 6.38; N, 5.18; S, 12.04.

6.1.2.29. *O*-(2-Phenoxyethyl)*N*-phenylthiocarbamate (29). Mp 104–106 °C; yield: 75% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3170. ^1H NMR ($CDCl_3$) δ: 4.27 (t, $J = 5.0$ Hz, 2H, CH_2OPh), 4.91 (t, $J = 5.0$ Hz, 2H, CH_2OCS), 6.68–7.55 (m, 10H, arom. H), 8.82 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{15}H_{15}NO_2S$: C, 65.91; H, 5.53; N, 5.12; S, 11.73. Found: C, 65.88; H, 5.56; N, 5.05; S, 11.68.

6.1.2.30. *O*-(2-Phenylthioethyl)*N*-phenylthiocarbamate (30). Mp 102–103 °C; yield: 35% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3208. ^1H NMR ($CDCl_3$) δ: 3.30 (t, $J = 6.6$ Hz, 2H, CH_2S), 4.77 (t, $J = 6.6$ Hz, 2H, CH_2O), 6.54–8.05 (m, 10H, arom. H), 8.62 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{15}H_{15}NOS_2$: C, 62.25; H, 5.22; N, 4.84; S, 22.16. Found: C, 62.45; H, 5.14; N, 5.08; S, 21.98.

6.1.2.31. *O*-[(*E*)-3-Phenylprop-2-en-yl]*N*-phenylthiocarbamate (32). Mp 110-112 °C; yield: 56% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3220, 1657. ^1H NMR ($CDCl_3$) δ: 5.25 (d, $J = 6.5$ Hz, 2H, CH_2), 6.30–6.70 (m, 2H, CH=CH), 6.87–7.65 (m, 10H, arom. H), 8.50 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{16}H_{15}NOS$: C, 71.35; H, 5.60; N, 5.20; S, 11.90. Found: C, 71.63; H, 5.68; N, 5.28; S, 12.24.

6.1.2.32. *O*-[(2,3-Dihydro-1,4-benzodioxin-2-yl)methyl]*N*-phenylthiocarbamate (33). Mp 88–90 °C; yield: 68% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3240. ^1H NMR ($CDCl_3$) δ: 0.79–1.41 (m, 1H, CH), 3.83–4.95 (m, 4H, $2CH_2$), 6.71–7.64 (m, 9H, arom. H), 8.75 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{16}H_{15}NO_3S$: C, 63.77; H, 5.02; N, 4.65; S, 10.64. Found: C, 64.02; H, 5.14; N, 4.68; S, 10.46.

6.1.2.33. *O*-(2-Phenoxyethyl)*N*-(4-tolyl)thiocarbamate (35). Mp 88–89 °C; yield: 87% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3229. ^1H NMR ($CDCl_3$) δ: 2.27 (s, 3H, CH_3), 4.09–4.42 (m, 2H, CH_2OPh), 4.73–5.04 (m, 2H, CH_2OCS), 6.67–7.51 (m, 9H, arom. H), 6.67–7.51 (m, 9H, arom. H), 8.80 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{16}H_{17}NO_2S$: C, 66.87; H, 5.96; N, 4.87; S, 11.16. Found: C, 66.89; H, 6.14; N, 4.84; S, 11.25.

6.1.2.34. *O*-(2-Phenoxyethyl)*N*-(4-chlorophenyl)thiocarbamate (36). Mp 84–86 °C; yield: 63% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3228. ^1H NMR ($CDCl_3$) δ: 4.16–4.44 (m, 2H, CH_2OPh), 4.74–5.09 (m, 2H, CH_2OCS), 6.78–7.59 (m, 9H, arom. H), 8.75 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{15}H_{14}ClNO_2S$: C, 58.53; H, 4.58; N, 4.55; S, 10.42. Found: C, 58.67; H, 4.84; N, 4.24; S, 10.44.

6.1.2.35. *O*-(2-Phenoxyethyl)*N*-(4-nitrophenyl)thiocarbamate (37). Mp 122–124 °C; yield: 99% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3295, 1552, 1337. ^1H NMR (DMSO-d_6) δ: 4.27–4.63 (m, 2H, CH_2OPh), 4.73–5.08 (m, 2H, CH_2OCS), 6.84–8.45 (m, 9H, arom. H), 11.84 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{15}H_{14}N_2O_4S$: C, 56.59; H, 4.43; N, 8.80; S, 10.07. Found: C, 56.68; H, 4.55; N, 8.79; S, 10.05.

6.1.2.36. *O*-(2-Phenoxyethyl)*N*-(4-methoxyphenyl) thiocarbamate (38). Mp 84–85 °C; yield: 98% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3226. ^1H NMR ($CDCl_3$) δ: 3.71 (s, 3H, CH_3), 4.17–4.28 (m, 2H, CH_2OPh), 4.75–4.90 (m, 2H, CH_2OCS), 6.65–7.42 (m, 9H, arom. H), 8.63 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{16}H_{17}NO_3S$: C, 63.35; H, 5.65; N, 4.62; S, 10.57. Found: C, 63.38; H, 5.67; N, 4.85; S, 10.64.

6.1.2.37. *O*-[2-(2-Hydroxyphenoxy)ethyl]*N*-phenylthiocarbamate (39). Mp 79–80 °C; yield: 74% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3380, 3280. ^1H NMR ($CDCl_3$) δ: 4.33 (t, $J = 6.0$ Hz, 2H, CH_2OPh), 4.98 (t, $J = 6.0$ Hz, 2H, CH_2O), 5.76 (s, 1H, OH, exchangeable), 6.77–7.58 (m, 9H, arom. H), 8.44 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{15}H_{15}NO_3S$: C, 62.26; H, 5.23; N, 4.84; S, 11.08. Found: C, 62.33; H, 5.26; N, 4.96; S, 11.10.

6.1.2.38. *O*-[2-(4-Bromophenoxy)ethyl]*N*-(4-nitrophenyl) thiocarbamate (40). Mp 167–168 °C; yield: 89% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3274, 1555, 1333. ^1H NMR (DMSO-d_6) δ: 4.23–4.36 (m, 2H, CH_2OPh), 4.67–4.78 (m, 2H, CH_2OCS), 6.83–6.98 (m, 2H, arom. H), 7.31–7.45 (m, 2H, arom. H), 7.64–7.87 (m, 2H, arom. H), 8.11 (d, $J = 9.0$ Hz, 2H, arom. H), 11.72 (s, 1H, NH, exchangeable). Anal. Calcd for $C_{15}H_{13}BrN_2O_4S$: C, 45.35; H, 3.30; N, 7.05; S, 8.07. Found: C, 45.65; H, 3.43; N, 6.99; S, 8.06.

6.1.2.39. *O*-[2-(4-Nitrophenoxy)ethyl]*N*-(4-chlorophenyl) thiocarbamate (41). Mp 153–154 °C; yield: 84% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3214, 1541, 1340. ^1H NMR (DMSO-d_6) δ: 4.37–4.47 (m, 2H, CH_2OPh), 4.63–4.82 (m, 2H, CH_2OCS), 7.04–7.72 (m, 6H, arom. H), 8.05 (d, $J = 9.0$ Hz, 2H, arom. H), 9.16 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{15}H_{13}ClN_2O_4S$: C, 51.07; H, 3.71; N, 7.94; S, 9.09. Found: C, 51.11; H, 3.78; N, 7.89; S, 9.02.

6.1.2.40. *O*-(2-Thienylmethyl)*N*-phenylthiocarbamate (49). Mp 165–167 °C; yield: 82% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3238. ^1H NMR ($CDCl_3$) δ: 5.79 (s, 2H, CH_2), 6.70–7.25 (m, 8H, arom H), 8.77 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{12}H_{11}NOS_2$: C, 57.80; H, 4.45; N, 5.62; S, 25.72. Found: C, 58.03; H, 4.40; N, 5.76; S, 25.82.

6.1.2.41. *O*-(2,6-Dichlorobenzyl)*N*-phenylthiocarbamate (50). Mp 155–157 °C; yield: 13% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3200. ^1H NMR ($CDCl_3$) δ: 5.84 (s, 2H, CH_2), 6.86–7.10 (m, 8H, arom H), 8.36 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{14}H_{11}Cl_2NOS$: C, 53.86; H, 3.55; N, 4.49; S, 10.27. Found: C, 54.09; H, 3.85; N, 4.48; S, 9.99.

6.1.2.42. *O*-(3-Phenoxybenzyl)*N*-phenylthiocarbamate (51). Mp 84–86 °C; yield: 73% from CH_2Cl_2/methanol. IR (KBr) cm^{-1}: 3180. ^1H NMR ($CDCl_3$) δ: 5.56 (s, 2H, CH_2), 6.53–7.52 (m, 14H, arom H), 9.09 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{20}H_{17}NO_2S$: C, 71.62; H, 5.11; N, 4.18; S, 9.56. Found: C, 71.93; H, 5.22; N, 4.23; S, 9.54.

6.1.3. Parallel synthesis of *N*-phenylthiocarbamates 31, 34, 52–57 and *O*-(1-methyl-2-phenoxylethyl)*N*-phenylthiocarbamates 42–48. Sixty percent sodium hydride dispersion in mineral oil (0.40 g, 10 mmol) was added in a single portion at rt to each numbered reaction tube of a 12-Carousel Reaction Station™, containing a stirred solution of the starting alcohol (10 mmol) in dry DMF (30 mL). After stirring for 30 min, the proper isothiocyanate (10 mmol) was added to each reaction mixture, which was then stirred for 18 h at rt. Work-up was carried out by adding a solution of NH_4Cl (1 g in 40 mL of water) into each tube. The contents of the tubes were then transferred into a set of separating funnels. Further solution of NH_4Cl (3 g in 120 mL of water) was added into each funnel. After parallel extraction with diethyl ether, the combined extracts of each reaction were washed with water (4×30 mL), dried over anhydrous Na_2SO_4 and filtered in parallel through pads of Florisil (diameter 5×2 cm) by an in-house device. Parallel evaporating in vacuo using an Evaposel™ apparatus gave residues which were purified by crystallization from CH_2Cl_2/methanol.

6.1.3.1. *O*-(Indan-2-yl)*N*-phenylthiocarbamate (31). Mp 125–126 °C; yield: 55%. IR (KBr) cm^{-1}: 3250. ^1H NMR ($CDCl_3$) δ: 3.16–3.50 (m, 4H, $2CH_2$), 5.97–6.40 (m, 1H, CH), 7.02–7.78 (m, 9H, arom. H), 8.64 (br s, 1H, NH, exchangeable). Calcd for $C_{16}H_{15}NOS$: C, 71.35; H, 5.60; N, 5.20; S, 11.90. Found: C, 71.63; H, 5.68; N, 5.28; S, 12.24.

6.1.3.2. (±) 5-(Phenoxymethyl)-3-phenyl-1,3-oxazolidine-2-thione (34). Mp 142–143 °C; yield: 51%. IR (KBr) cm^{-1}: 1492. ^1H NMR ($CDCl_3$) δ: 4.09–4.53 (m, 4H, CH_2N and CH_2O), 5.92–5.40 (m, 1H, CH), 6.76–7.82 (m, 10H, arom. H). Calcd for $C_{16}H_{15}NO_2S$: C, 67.34; H, 5.30; N, 4.91; S, 11.23. Found: C, 67.27; H, 5.28; N, 4.97; S, 10.98.

6.1.3.3. (±) *O*-(1-Methyl-2-phenoxyethyl)*N*-phenylthiocarbamate (42). Mp 56–58 °C; yield: 88%. IR (KBr) cm^{-1}: 3218. ^1H NMR ($CDCl_3$) δ: 1.48 (d, $J = 6.0$ Hz, 3H, CH_3), 4.19 (d, $J = 6.0$ Hz, 2H, CH_2), 5.66–6.19 (m, 1H, CH), 6.79–7.73 (m, 10H, arom. H),

9.03 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{16}H_{17}NO_2S$: C, 68.87; H, 5.96; N, 4.87; S, 11.16. Found: C, 66.72; H, 6.14; N, 4.95; S, 11.14.

6.1.3.4. (±) *O*-(1-Methyl-2-phenoxyethyl)*N*-(4-tolyl)thiocarbamate (43). Mp 69–71 °C; yield: 55%. IR (KBr) cm^{-1}: 3225. ^1H NMR ($CDCl_3$) δ: 1.50 (d, $J = 6.0$ Hz, 3H, CH_3), 2.29 (s, 3H, CH_3Ph), 4.17 (d, $J = 6.0$ Hz, 2H, CH_2), 5.54–6.21 (m, 1H, CH), 6.72–7.72 (m, 9H, arom. H), 8.78 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{17}H_{19}NO_2S$: C, 59.72; H, 5.01; N, 4.35; S, 9.96. Found: C, 60.01; H, 5.10; N, 4.45; S, 9.84.

6.1.3.5. (±) *O*-(1-Methyl-2-phenoxyethyl)*N*-(4-fluorophenyl)thiocarbamate (44). Mp 82–84 °C; yield: 33%. IR (KBr) cm^{-1}: 3190. ^1H NMR ($CDCl_3$) δ: 1.48 (d, $J = 6.0$ Hz, 3H, CH_3), 4.15 (d, $J = 6.0$ Hz, 2H, CH_2), 5.65–6.15 (m, 1H, CH), 6.68–7.61 (m, 9H, arom. H), 8.95 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{16}H_{16}FNO_2S$: C, 62.93; H, 5.28; N, 4.59; S, 10.50. Found: C, 63.20; H, 5.21; N, 4.64; S, 10.32.

6.1.3.6. (±) *O*-(1-Methyl-2-phenoxyethyl)*N*-(4-chlorophenyl)thiocarbamate (45). Mp 84–86 °C; yield: 33%. IR (KBr) cm^{-1}: 3190. ^1H NMR ($CDCl_3$) δ: 1.51 (d, $J = 6.0$ Hz, 3H, CH_3), 4.18 (d, $J = 6.0$ Hz, 2H, CH_2), 5.57–6.12 (m, 1H, CH), 6.78–7.56 (m, 9H, arom. H), 8.64 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{16}H_{16}ClNO_2S$: C, 59.72; H, 5.01; N, 4.35; S, 9.96. Found: C, 60.01; H, 5.10; N, 4.45; S, 9.84.

6.1.3.7. (±) *O*-(1-Methyl-2-phenoxyethyl)*N*-(4-nitrophenyl)thiocarbamate (46). Mp 118–120 °C; yield: 68%. IR (KBr) cm^{-1}: 3240. ^1H NMR ($CDCl_3$) δ: 1.57 (d, $J = 6.0$ Hz, 3H, CH_3), 4.25 (d, $J = 6.0$ Hz, 2H, CH_2), 5.70–6.20 (m, 1H, CH), 6.79–7.84 and 8.03–8.30 (m, 9H, arom. H), 8.35 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{16}H_{16}N_2O_4S$: C, 57.82; H, 4.85; N, 8.43; S, 9.65. Found: C, 58.09; H, 4.94; N, 8.48; S, 9.47.

6.1.3.8. (±) *O*-(1-Methyl-2-phenoxyethyl)*N*-(4-methoxyphenyl)thiocarbamate (47). Mp 73–74 °C; yield: 42%. IR (KBr) cm^{-1}: 3180. ^1H NMR ($CDCl_3$) δ: 1.49 (d, $J = 6.0$ Hz, 3H, CH_3), 3.79 (s, 3H, CH_3O), 4.16 (d, $J = 6.0$ Hz, 2H, CH_2), 5.67–6.14 (m, 1H, CH), 6.68–7.54 (m, 9H, arom. H), 8.55 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{17}H_{19}NO_3S$: C, 64.33; H, 6.03; N, 4.41; S, 10.01. Found: C, 65.23; H, 6.19; N, 4.48; S, 10.03.

6.1.3.9. (±) *O*-(1-Methyl-2-phenoxyethyl)*N*-(3-chloro-4-methylphenyl)thiocarbamate (48). Mp 86–87 °C; yield: 21%. IR (KBr) cm^{-1}: 3180. ^1H NMR ($CDCl_3$) δ: 1.10 (d, $J = 6.0$ Hz, 3H, CH_3), 2.30 (s, 3H, $PhCH_3$), 4.16 (d, $J = 6.0$ Hz, 2H, CH_2), 5.72–6.10 (m, 1H, CH), 6.73–7.71 (m, 8H, arom. H), 8.67 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{17}H_{18}ClNO_2S$: C, 60.80; H, 5.40; N, 4.17; S, 9.55. Found: C, 60.70; H, 5.39; N, 4.36; S, 9.76.

6.1.3.10. (±) *O*-(4-Chlorobenzyl-α-methyl)*N*-phenylthiocarbamate (52). Mp 94–96 °C; yield: 72%. IR (KBr) cm^{-1}: 3218. ^1H NMR ($CDCl_3$) δ: 1.66 (d, $J = 6.6$ Hz, 3H, CH_3), 6.39–6.76 (m, 1H, CH), 6.96–7.79 (m, 9H, arom. H), 8.66 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{15}H_{14}ClNOS$: C, 61.74; H, 4.84; N, 4.80; S, 10.99. Found: C, 62.24; H, 4.99; N, 4.77; S, 11.05.

6.1.3.11. (±) *O*-(4-Chlorobenzyl-α-methyl)*N*-(4-nitrophenyl)thiocarbamate (53). Mp 102–103 °C; yield: 61%. IR (KBr) cm^{-1}: 3362. ^1H NMR ($CDCl_3$) δ: 1.74 (d, $J = 6.6$ Hz, 3H, CH_3), 6.51–6.73 (m, 1H, CH), 7.27–7.83 and 8.08–8.39 (m, 8H, arom. H), 9.73 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{15}H_{13}ClN_2O_3S$: C, 53.48; H, 3.89; N, 8.32; S, 9.52. Found: C, 53.75; H, 4.10; N, 8.52; S, 9.36.

6.1.3.12. (±) *O*-(4-Phenylbenzyl-α-methyl)*N*-(4-chlorophenyl)thiocarbamate (54). Mp 126–128 °C; yield: 54%. IR (KBr) cm^{-1}: 3220. ^1H NMR ($CDCl_3$) δ: 1.72 (d, $J = 6.0$ Hz, 3H, CH_3), 6.40–6.91 (m, 1H, CH), 7.15–8.90 (m, 13H, arom. H), 9.36 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{21}H_{18}ClNOS$: C, 68.56; H, 4.93; N, 3.81; S, 8.71. Found: C, 68.38; H, 4.77; N, 3.85; S, 8.35.

6.1.3.13. (±) *O*-[1-(1-Naphthyl)ethyl]*N*-(4-chlorophenyl) thiocarbamate (55). Mp 106–108 °C; yield: 84%. IR (KBr) cm^{-1}: 3200. ^1H NMR ($CDCl_3$) δ: 1.85 (d, $J = 6.0$ Hz, 3H, CH_3), 6.73–7.03 (m, 1H, CH), 7.12–8.32 (m, 11H, arom. H), 8.75 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{19}H_{16}ClNOS$: C, 66.76; H, 4.79; N, 4.10; S, 9.38. Found: C, 67.01; H, 4.79; N, 4.11; S, 9.08.

6.1.3.14. (±) *O*-[1-(2-Naphthyl)ethyl]*N*-(4-chlorophenyl) thiocarbamate (56). Mp 121–122 °C; yield: 88%. IR (KBr) cm^{-1}: 3200. ^1H NMR ($CDCl_3$) δ: 1.35 (d, $J = 6.0$ Hz, 3H, CH_3), 6.57–7.05 (m, 1H, CH), 7.10–8.04 (m, 11H, arom. H), 8.68 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{19}H_{16}ClNOS$: C, 66.76; H, 4.79; N, 4.10; S, 9.38. Found: C, 66.85; H, 4.86; N, 4.17; S, 9.00.

6.1.3.15. (±) *O*-(Benzyl-α-ethyl)*N*-phenylthiocarbamate (57). Mp 82–84 °C; yield: 37%. IR (KBr) cm^{-1}: 3180. ^1H NMR ($CDCl_3$) δ: 1.41 (t, 3H, CH_3), 1.89–2.38 (m, 2H, CH_2), 6.42 (t, $J = 5.6$ Hz, 1H, CH), 7.12–7.94 (m, 10H, arom. H), 8.62 (br s, 1H, NH, exchangeable). Anal. Calcd for $C_{16}H_{17}NOS$: C, 70.82; H, 6.31; N, 5.16; S, 11.81. Found: C, 71.01; H, 6.34; N, 5.36; S, 11.83.

6.2. Virology: materials and methods

The biological evaluation of the synthesized compounds was performed according to the previously reported procedures.[20,21]

6.3. Molecular modelling

Docking models for compounds for compounds **2**, **5**, **12**, **15**, **21** and **27** have been obtained according to the procedure previously described.[1]

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