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## SYNTHESIS, CHARACTERIZATION AND INSECTICIDAL EVALUATION OF SOME *p*-*tert*-BUTYLTHIACALIX[4]ARENE DERIVATIVES AGAINST COWPEA APHID (*APHIS CRACCIVORA* KOCH)

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**Abstract** – Herein, we offer a facile synthesis of three novel conformers (*cone*, *partial cone*, and *1,3-alternate*) of thiacalix[4]arene derivatives, comprising 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis{2-oxo-2-[(dimethylamino)methylidene]hydrazino]ethoxy}-2,8,14,20-tetrathiacalix[4]arene, **3a-c** via the thiocarbonylation of their corresponding carbonyl derivatives **2a-c** with Lawesson's reagent (LR) in refluxed chloroform with good yields (80, 95, and 85%, respectively). The new O/S exchanged tetrathiacalix[4]arene products (**3a-c**) were identified by various spectroscopic tools such as FT-IR, <sup>1</sup>H NMR, and <sup>13</sup>C NMR. Importantly, agrochemical efficacy of the as-prepared thionated *p*-*tert*-butylthiacalix[4]arene conformers (**3a-c**) as well as the parent derivatives **2a-c** were investigated against adults and nymphs of Cowpea aphid (*Aphis craccivora*). In view of the calculated IC<sub>50</sub> values, conformers **2c** and **3c** possessed the highest insecticidal potency, with respective values of 5.47 and 3.50 ppm against nymphs, whereas values of 14.38 and 14.04 ppm were recorded against Cowpea aphid adults. The overall finding of this work may give an inspiration and

motivation on the search for new eco-friendly insecticidal agents that have strong toxicological potency but with minimal impact on the environment.

## INTRODUCTION

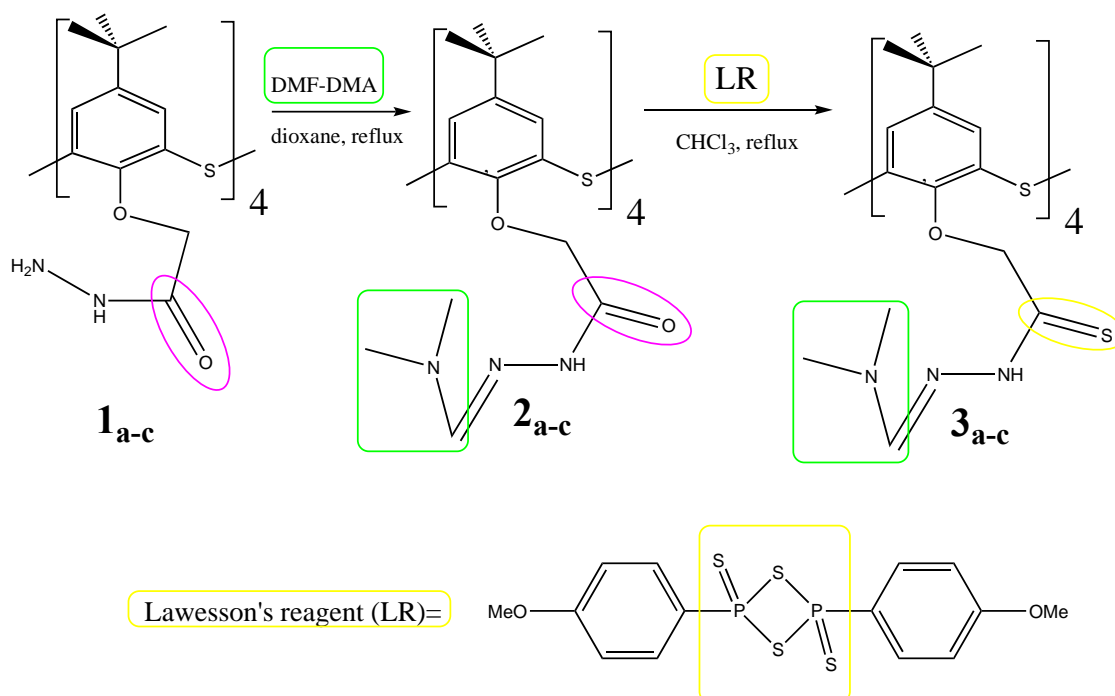
Calix[n]arenes<sup>1-4</sup> and their twins thiacalixarenes<sup>5-7</sup> are interesting cage macrocycles with a plethora of fundamental and practical applications, including catalysis<sup>8</sup> molecular recognition,<sup>9</sup> metal ion receptors,<sup>10</sup> sensors,<sup>11</sup> and a variety of biological activity.<sup>12-15</sup> In particular, thiacalix[4]arenes, simply calixarenes containing sulfur atoms, are considered as the most important members of this class of compounds, owing to their structural diversity, reactivity and promising optical properties. In view of these astonishing applications of both calixarene and thiacalixarenes, large numbers of their derivatives in three conformers (i.e., *cone*, *partial cone* and *1,3-alternate*) have been structurally modified through their upper rims,<sup>16,17</sup> lower rims and bridging methylene or sulfur groups.<sup>18,19</sup> Thus, simple modification in the thiacalixarenes synthesis has been undertaken through the alkylation of their hydroxyl groups in the lower rim by forming *p-tert*-butylthiacalix[4]arene tetraesters,<sup>20</sup> tetraethers,<sup>21</sup> tetraketones,<sup>22</sup> and tetraamides<sup>23</sup> reagents. Among these conformers, *p-tert*-butylthiacalix[4]arene tetra esters are the best starting materials for more functionalization of thiacalixarenes to form tetra-acids,<sup>24</sup> tetrathioesters<sup>25</sup> and tetrahydrazides.<sup>26</sup> In this respect, our laboratory have successfully employed *p-tert*-butylthiacalix[4]arene tetrahydrazides for the synthesis of different thiacalixarene derivatives for their utilization in various environmental and sensing applications.<sup>27-29</sup>

Currently, there is a globally growing interest and high demand to harness the full potential of the biological control offered by most insecticides for aphid pest. However, agricultural industries are dramatically concerned about the escalating of insecticide resistance among a number of pests together with the high toxicity that these insecticides may cause to other useful insects, plants, and the soil. Therefore, the search for new generation of eco-friendly insecticides is the main focus of researchers worldwide.<sup>30-32</sup> Bearing in mind that thiacalixarene derivatives are known to be safe materials; and have been previously implemented for elimination of pesticide residues<sup>33-35</sup> along with the established toxicity against various strains of bacteria and fungi.<sup>12-15</sup>

In view of the aforementioned promising properties, we report, herein, a facile synthesis of *p-tert*-butylthiacalix[4]arene derivatives **2a-c** as well as their thiated derivatives **3a-c** in three different conformers and evaluate their toxicological activity against aphids as a potential candidates for novel and safe insecticides that are comparatively less harmful to the environment.

## RESULTS AND DISCUSSION

Non-thiated *p*-*tert*-butylthiacalix[4]arene compounds **2a-c** (i.e., *cone*, *partial-cone* and *1,3-alternate* conformers), which have been synthesized in our previous work,<sup>36</sup> were prepared through slightly modified method, by reacting of *p*-*tert*-butylthiacalix[4]arene tetrahydrazides **1a-c** in dioxane instead of toluene using dimethylformamide dimethyl acetal (DMF-DMA) (Scheme 1). The obtained *p*-*tert*-butylthiacalix[4]arene compounds **2a-c** were then refluxed with Lawesson's reagent (LR) in chloroform (CHCl<sub>3</sub>) as a solvent to afford the corresponding novel thiated-analogues of *p*-*tert*-butylthiacalix[4]arene derivatives **3a-c** in *cone*, *partial-cone* and *1,3-alternate* conformers, respectively as illustrated in Scheme 1.



**Scheme 1.** Synthesis of **3a-c** from **2a-c** with LR in CHCl<sub>3</sub>

Importantly, the structures of all-prepared thiacalixarene derivatives **3a-c** as proposed in Scheme 2 were deduced based on the data obtained by FT-IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR (Supplementary Materials). The structure determination of the novel thiated thiacalixarenes derivatives **3a-c** was evident by the disappearing of the amidic carbonyl stretching peaks, which were observed in IR analysis, as shown in supplementary data. In addition to the definitive IR spectroscopic evidence, the symmetrical structure of both *cone* **3a** and *1,3-alternate* **3c** conformers are always obtained from their parents' *cone* **2a** and *1,3-alternate* **2c** conformers, respectively. Hence it is anticipated to show the same number of peaks in NMR spectra. However, their structures are differentiated by considering the different chemical shifts that

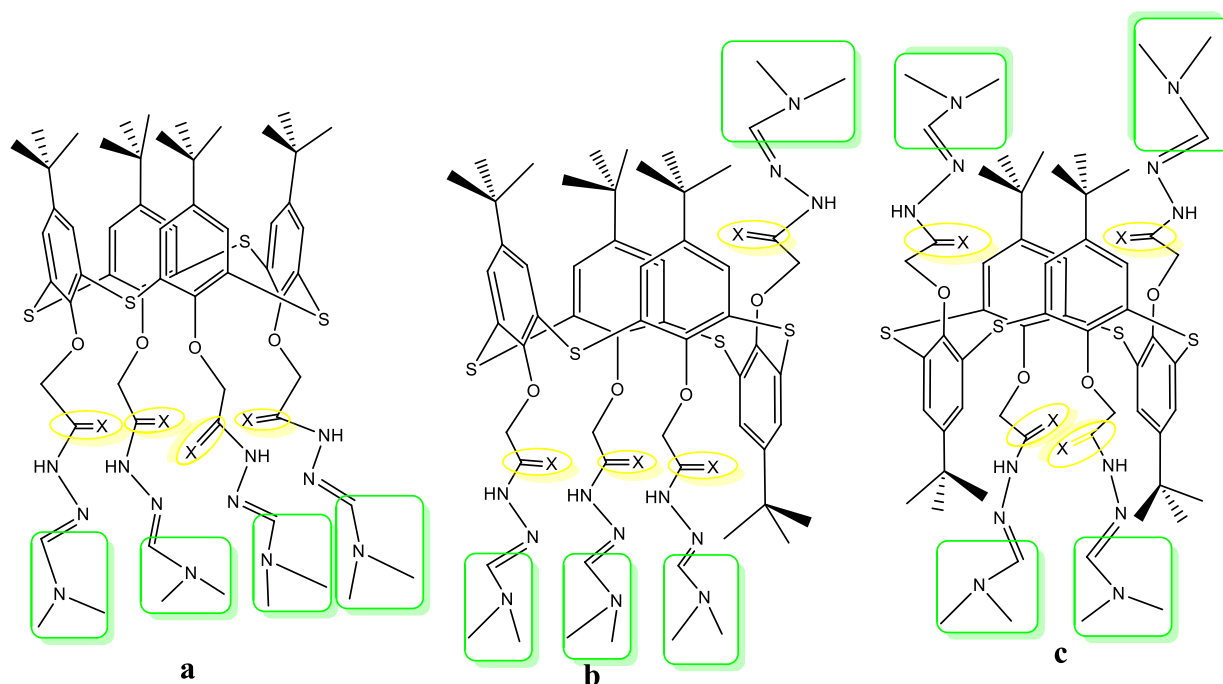
arise from analogous proton groups. Thus, by comparing the thiacalixarene *cone* **3a** with the congener calixarene **2a**, the protons of the  $-\text{OCH}_2\text{C}(\text{S})-$  and  $\text{OCH}_2\text{C}(\text{O})-$  groups are detected at different chemical shifts ( $\delta$ : 4.87 ppm versus  $\delta$ : 5.83 ppm), respectively.

Similarly, the NH protons of  $-\text{C}(\text{S})\text{NH}-$  in **3a** and  $-\text{C}(\text{O})\text{NH}-$  in **2a** are present at different chemical shifts with  $\delta$ : 9.15 and 10.66 ppm, respectively (see provided supplementary data). As for the *1,3-alternate* conformer **3c** and its related congener **2c**, the  $-\text{OCH}_2\text{C}(\text{S})-$  and  $\text{OCH}_2\text{C}(\text{O})-$  groups are detected at different chemical shifts as well ( $\delta$ : 5.42 and 4.21 ppm), respectively. Additionally, the NH protons of  $-\text{C}(\text{S})\text{NH}-$  in **3c** and  $-\text{C}(\text{O})\text{NH}-$  in **2c** exhibited different chemical shift at  $\delta$ : 9.49 and 8.38 ppm, respectively (supplementary data). In addition to the aforementioned results, there are different chemical shifts of all different hydrogen groups (i.e.,  $\text{Bu}^t$ ,  $-\text{N}(\text{Me})$ , Ar-H and  $=\text{NCH}-$ ).

Moreover, the *1,3-alternate* **3c** protons are presented at a shielded area by two adjacent benzene rings, therefore some signals of these protons were noted in a higher field than the signals of the corresponding protons in *cone* **3a**, as the  $\text{Bu}^t$  protons have chemical shifts at 0.94 ppm for **3c** and 1.33 ppm for **3a**, respectively. Given these results, the structures of compounds **3a** and **3c** can be unambiguously assigned to *cone* and *1,3-alternate* conformers, respectively. The unsymmetrical structure of *partial cone* **3b** is similar to *partial cone* **2b** in number of peaks and therefore, the  $^1\text{H}$  NMR showed a significant increase in the splitting and multiplicity of protons for a different group. The obtained  $^1\text{H}$  NMR spectrum of thiacalixarene **3b** showed the presence of three different chemical shifts associated with the *tert*-butyl groups that exhibited a 2:1:1 ratio of resonance patterns in the proton spectrum at 0.97, 1.15, and 1.37 ppm, which differ in their chemical shifts from the analogous *tert*-butyl groups of **2b**, which appeared at  $\delta$ : 1.15, 1.29, and 1.36 ppm. There are three peaks of conformer **3b** for  $\text{OCH}_2\text{C}(\text{S})-$  protons with 2:1:1 ratio of resonance patterns at 5.43, 5.58, and 5.65 ppm, which are different from the chemical shift obtained for the corresponding  $\text{OCH}_2\text{C}(\text{O})-$  group of **2b** at 4.62, 4.72, and 4.82 ppm. Similar splitting and multiplicity peaks are evident for Ar-H and  $-\text{NH}$  protons.

Consistence with the results of  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR spectra of both **3a** (*cone*) and **3c** (*1,3-alternate*) also confirmed the symmetrical structure via the appearance of only 10 different peaks in their spectra. In view of the well-known isotropic de-shielding of the carbon nucleus in the  $\text{C}=\text{S}$  group relative to  $\text{C}=\text{O}$ , which is mainly due to the decreased energy associated with the  $\sigma \leftrightarrow \pi^*$  excitation within the thiocarbonyl moiety, we expect distinctive chemical shifts in  $^{13}\text{C}$  NMR spectra between all conformers of **2** and **3**. For instance, the reported  $^{13}\text{C}$  NMR signal of the  $\text{C}=\text{O}$  group in compound **2c** (162.9 ppm)<sup>36</sup> has changed to de-shielded  $^{13}\text{C}$  NMR signal of  $\text{C}=\text{S}$  to appear at 166 ppm in compound **3c**.

$^{13}\text{C}$  NMR spectra of the unsymmetrical structure **3b** (*partial cone*) showed similar splitting and multiplicity in number of peaks as shown in its  $^1\text{H}$  NMR spectra (see experimental part and supplementary data).



**Scheme 2.** Structures of stereoisomers **2a-c** (X= O) and **3a-c** (X= S)

### Insecticidal bio-efficacy screening

Thiocalixarene compounds have a wide variety of applications especially in separation, purification and pollution control. Hence, thiocalixarenes are classified as eco-friendly compounds that exhibit also toxicity against some bacterial and fungal strains. In this work, we offer a new attempt to illustrate the toxicity of the prepared thiocalixarene derivatives **3a-c** as eco-friendly insecticidal agents against Cowpea aphids, thereby avoiding the ecologically unfriendly insecticides. All toxicological data of aphid's mortality were analyzed with probity analysis via a statistic (LDP-line) package to calculate the LC<sub>50</sub> values, and the obtained data of LC<sub>50</sub> values, slope and toxic ratio are summarized in Table 1 and depicted in Figure 1.

### Toxicological activity against nymphs of *Aphis craccivora*.

Both Table 1 and Figure 1 revealed that all tested six thiocalixarene derivatives, namely **2a-c** and **3a-c**, have a reasonable toxicological activity against the nymphs of *A. craccivora* with LC<sub>50</sub> values varied from 3.50 to 38.32 ppm after 24 h of treatment. Importantly, among all tested derivatives, compounds **3c** and **2c** showed the highest potency with LC<sub>50</sub> value of **3.50** and **5.47** ppm, respectively.

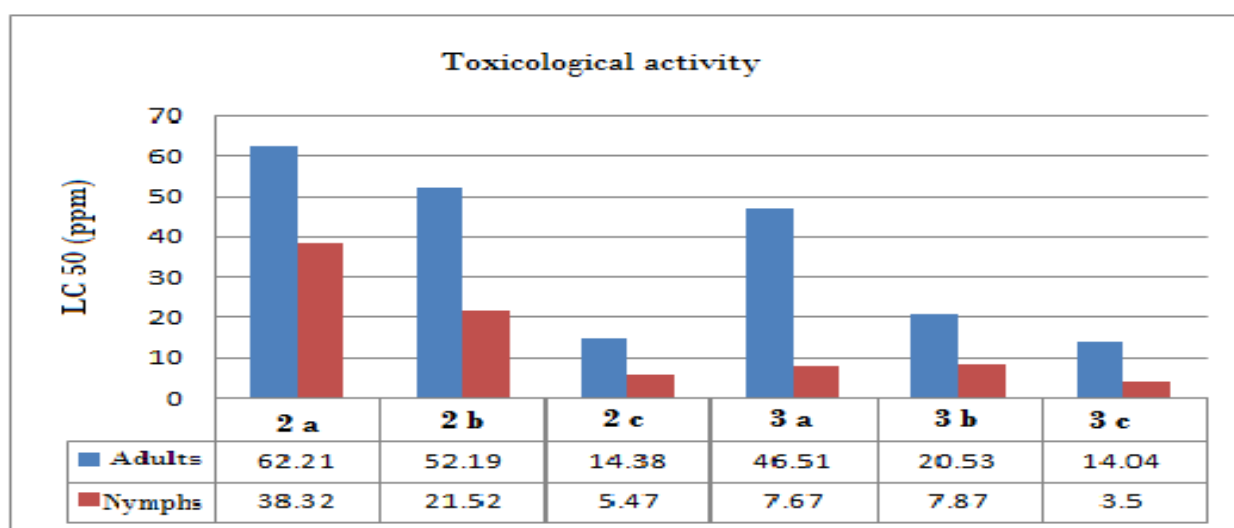
### Toxicological activity against adults of *Aphis craccivora*.

Similarly, the insecticidal activities of as-prepared derivatives **3a-c** and **2a-c**, against insect of *A. craccivora* after 24 h of treatment are shown in Table 1 and Figure 1. Results indicate that all compounds have moderate to weak toxicological activity against the adults of *A. craccivora* with LC<sub>50</sub> values varied

from 14.04 to 62.21 ppm and the congeners **3c** and **2c** gave rise to the highest toxicological activity with LC<sub>50</sub> values 14.04 and 14.38, respectively.

**Table 1.** Insecticidal activity of compounds **2a-c** and **3a-c** against both nymphs and adults of *Aphis craccivora* insects upon 24 h of treatment

Adults of <i>A. craccivora</i>				Nymphs of <i>A. craccivora</i>		
Comp	LC <sub>50</sub> (ppm)	Slope	Toxic ratio	LC <sub>50</sub> (ppm)	Slope	Toxic ratio
<b>2a</b>	62.21	0.4685 ± 0.5156	0.22	38.32	0.5491 ± 0.2619	0.09
<b>2b</b>	52.19	0.4033 ± 0.4988	0.27	21.52	1.2492 ± 0.5118	0.16
<b>2c</b>	14.38	0.3860 ± 0.5435	0.97	5.47	0.8599 ± 0.5118	0.64
<b>3a</b>	46.51	1.5135 ± 0.6124	0.30	7.67	1.0673 ± 0.3643	0.45
<b>3b</b>	20.53	0.5967 ± 0.5992	0.68	7.87	0.8116 ± 0.3957	0.44
<b>3c</b>	<b>14.04</b>	<b>0.3950 ± 0.4582</b>	<b>1</b>	<b>3.50</b>	<b>0.1571 ± 0.7046</b>	<b>1</b>



**Figure 1.** Insecticidal activity of compounds **2a-c** and **3a-c** against both nymphs and adults of *Aphis craccivora* insects after 24 h of treatment

### Structure-activity relationship

In view of the data presented in Table 1 and Figures 1, it is clearly established that the as-prepared thiacalixarenes derivatives all possess reasonable insecticidal activity due to stereochemistry of the aliphatic chains attached to *p-tert*-butylthiacalixarene. The changes in the number of sulfur atoms and direction of aliphatic chains are most likely to be responsible for differences in reactivity and toxicity among all conformers. Additionally, all of the six derivatives, **2a-c** and **3a-c** showed higher activity against nymphs of *Aphis craccivora* than the adults' counterpart after 24 h of treatment. We also found that the prepared thiacalixarenes (**3a-c**) have much higher potency compared to their congeners **2a-c**. This behavior could be attributed to the presence of the thiocarbonyl groups in the former compounds, which exhibit remarkable efficacy than the carbonyl groups in the latter. Surprisingly, among all-prepared derivatives, compounds **3c** and **2c** displayed the highest toxicological activity against both nymphs and adults of *Aphis craccivora*. This behavior is probably associated with the presence of four aliphatic chains in different conformers, which is expected to enhance the toxicological activity of these compounds more than the other congeners, which have the same number of aliphatic chains but with different conformers. On comparing the structure-activity of the two most efficient compounds (i.e. **3c** vs **2c**) in terms of LC<sub>50</sub> for nymphs of *Aphis craccivora*, we found that compound **3c** has a dramatically lower LC<sub>50</sub> (3.5 ppm) value than **2c** (5.47 ppm). However, the only difference between the two compounds is that compound **3c** has four aliphatic chains of ethanthioyl-N,N-dimethylhydrazonoformamide (thiocarbonyl groups), whereas in **2c** the four aliphatic chains are of acetyl-N,N-dimethylhydrazonoformamide (carbonyl groups). This slight difference in the chemical structure made **3c** to have a much higher insecticidal activity than **2c**. By analogy, the same trend was also noted for the other congeners (e.g. **3b** vs **2b**) and (**3a** vs **2a**). Taken together, the combined finding of this work clearly emphasizes that the potency (toxicity) of the synthesized thiacalixarene derivatives is highly correlated to the increased number of sulfur atoms along with the type of the conformers, with overall order of the toxicological activity as **3c** > **3b** > **3a**.

### CONCLUSION

In this work, six *p-tert*-butylthiacalixarene derivatives **2a-c** and **3a-c** were prepared and fully characterized via wide range of spectroscopic techniques and then screened for their potential insecticidal activity against Cowpea aphid in an attempt to provide promising, efficient and eco-friendly insecticides. The obtained data attested that all the prepared thiacalixarenes derivatives have moderate/reasonable insecticidal activity owing to the stereochemistry of the aliphatic chains in the conformers as well as the number of sulfur atoms related to the thiocarbonyl groups. For the newly prepared compounds **3a-c**, the overall order of the toxicological activity followed the trend: **3c** > **3b** > **3a**. Despite the modest toxicological activity exhibited by some members of the prepared compounds, the obtained results are

promising enough to strongly encourage pursuing various investigations and functionalization of thiacalixarenes to manipulate their efficiency and hence offering new candidates for biological and insecticidal fields.

## EXPERIMENTAL

$^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopic analyses were carried out using JEOL ECP-400 MHz spectrometers in deuterated chloroform ( $\text{CDCl}_3$ ) and dimethyl sulfoxide ( $\text{DMSO-}d_6$ ) at room temperature. The starting materials and reagents were of analytical grade. The starting material, *p-tert*-butylthiacalix[4]arene derivatives were prepared from their raw material in our laboratory. Melting points ( $^\circ\text{C}$ , uncorrected) were measured using an open glass capillary *via* a Melting Point Apparatus (Stuart, model SMP10). The Fourier transform infrared (FT-IR) analysis of the prepared compounds was conducted via PerkinElmer Spectrum 1000 FT-IR Spectrometer. The chemical shifts were expressed in  $\delta$  7.29 downfield from  $\text{CDCl}_3$ , which was used as a reference.

Synthesis of 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis{2-oxo-2-[2-(dimethylaminomethylidene)-hydrazino]ethoxy}-2,8,14,20-tetrathiacalix[4]arenes.<sup>36</sup> **2a-c** (general methods).

A mixture of *p-tert*-butylthiacalix[4]arene tetrahydrazides **1a**, **1b** or **1c** and dimethylformamide dimethyl acetal (DMF-DMA) in 30 mL dioxane as a solvent was prepared. The reaction mixture was refluxed for 4 h, then concentrated to 15 mL and left to cool for 1 h. The white precipitate was filtered off, dried then to afford 85-95% yield for all derivatives.

Synthesis of 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis{2-oxo-2-[2-(dimethylaminomethylidene)-hydrazino]ethoxy}-2,8,14,20-tetrathiacalix[4]arene **3a**.

A mixture of 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis{2-oxo-2-[2-(dimethylaminomethylidene)-hydrazino]ethoxy}-2,8,14,20-tetrathiacalix[4]arenes **2a** (0.5 g, 0.41 mmol) with Lawesson's reagent (0.58 g, 4.95 mmol) in 40 mL  $\text{CHCl}_3$  has been refluxed for 24 h. Then, the mixture was concentrated almost to dryness, 50 mL of water was added and stirred for 2 h. The white solid product was separated and filtered. The product was purified by chromatography using  $\text{CH}_2\text{Cl}_2$  / EtOH mixture (100:1) (v/v), to yield ~ 90% of the desired products.

**3a**, *cone*, yield 80%; white powder; Mp 240  $^\circ\text{C}$ , IR (KBr,  $\text{v}/\text{cm}^{-1}$ ): 3420 (NH), 3090.5, 2962 (C-H aliph.).

$^1\text{H}$  NMR (400 MHz,  $\text{DMSO}$ )  $\delta$ : 1.33 (s, 36H,  $\text{Bu}^t$ ), 3.81 (s, 24H,  $\text{N}(\text{CH}_3)$ ), 5.75 (s, 8H,  $\text{OCH}_2\text{CS}$ ), 7.01 (s, 8H, ArH), 7.74 (s, 4H,  $\text{N}=\text{CH}$ ), 9.65 (s, 4H, CSNH).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 30.75, 31.32, 34.13, 55.37, 113.49, 113.65, 132.72, 133.21, 162.26, 163.11.

Synthesis of 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis{2-oxo-2-[2-(dimethylaminomethylidene)-hydrazino]ethoxy}-2,8,14,20-tetrathiacalix[4]arene **3b** and **c** (general methods).



A mixture of 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis{2-oxo-2-[2-(dimethylaminomethylidene)-hydrazino]ethoxy}-2,8,14,20-tetrathiocalix[4]arenes **2b** or **2c** (0.5 g, 0.41 mmol) with Lawesson's reagent (0.58 g, 4.95 mmol) in 40 mL CHCl<sub>3</sub>, has been refluxed for 24 h. The mixture was concentrated approximately to dryness then 50 mL of MeOH was added. The white solid product was separated, filtrated and washed with MeOH. The product was left to dry overnight then weighted and the yield calculated ranged from 80-90%.

**3b**, *partial cone*, white powder; Mp 300 °C. IR (KBr, v/cm<sup>-1</sup>): 3426 (NH), 3067.47, 2962 (CO), 1262 (COC). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 0.97 (s, 18H, Bu<sup>t</sup>), 1.15 (s, 9H, Bu<sup>t</sup>), 1.37 (s, 9H, Bu<sup>t</sup>), 2.75-2.89 (m, 18, 3N(CH<sub>3</sub>)<sub>2</sub>), 3.73-3.85 (m, 6H, N(CH<sub>3</sub>)<sub>2</sub>), 5.43 (s, 4H, 2OCH<sub>2</sub>CS), 5.56-5.60 (d, 2H, OCH<sub>2</sub>CS), 5.63-5.67 (d, 2H, OCH<sub>2</sub>CS), 6.92-7.97 (m, 8H, ArH + 4H, N=CH), 8.59 (s, 1H, CSNH), 9.00 (s, 1H, CSNH), 9.24 (s, 1H, CSNH). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 30.94, 31.16, 31.49, 34.17, 34.45, 34.57, 55.32, 64.31, 68.96, 113.62, 127.15, 128.43, 129.14, 129.29, 130.12, 131.03, 132.72, 135.33, 135.69, 148.31, 148.47, 152.02, 153.83, 154.16, 154.93, 157.27, 157.85, 164.63, 165.96, 167.00.

**3c**, *1,3-alternate*, white powder; Mp 310 °C. IR (KBr, v/cm<sup>-1</sup>): 3421 (NH), 3090.5, 1233 (COC). <sup>1</sup>H NMR (400 MHz, DMSO) δ: 0.94 (s, 36H, Bu<sup>t</sup>), 2.09 (s, 24H, 4N(CH<sub>3</sub>)<sub>2</sub>), 5.42 (s, 8H, OCH<sub>2</sub>CS), 7.17 (s, 8H, ArH), 8.30 (s, 4H, N=CH), 9.46 (s, 4H, CSNH). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 29.65, 30.97, 34.25, 65.06, 127.98, 128.53, 148.33, 153.70, 155.55, 166.00.

### Insect Collection and Rearing

Cowpea aphid insects are notoriously harmful and extremely destructive pests, attacking large number of agricultural crops in Egypt. The original batches of *Aphis craccivora* insects were collected from pests' laboratory (PPRI), at Agricultural Research Center, Sohag, Egypt. The new derivatives were tested for their insecticidal activity against laboratory strain of adults and nymphs of *A. craccivora*.

**Laboratory Bioassay.** In this study, all six prepared thiacalixarene derivatives were tested to illustrate their insecticidal activities by using leaf dipping method under the same laboratory conditions,<sup>32-35</sup> with various concentrations of each compound in acetone and 0.1% Tween-80 as a surfactant, whereas only water, acetone and 0.1% Tween-80 are used in the control experiment. Nearly the same size of 20 nymphs and 20 adults of the *A. craccivora* were dipped for 10 sec in every concentration of each compound, and the procedures were repeated at least three times. The tested insects were dried at room temperature for about 1/2 h. Additionally, all the toxicological tests were undertaken at 5% relative humidity at a temperature of 25 °C. After the used pests had dried, they were transferred to glass jars containing water. The aphid mortality was taken after 24 h of treatment by a new binocular microscope. The unmoved aphid was considered dead. All toxicity data of all synthesized derivatives were analyzed

by using Abbott's formula.<sup>37</sup> The evaluation of insecticidal activity depend on LC<sub>50</sub> values which were estimated by probit analysis.<sup>38</sup>

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