Mono-substituted p-*tert*-butylthiacalix[4]arene: Regioselective Synthesis and Toxicological Activity Against Cowpea Aphid, *Aphis craccivora* (Koch)

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Abstract: Tetraethylamonium bromide (TEAB) in dry benzene has been utilized as the base enabling Phase Transfer Catalysis PTC for the synthesis of some novel mono-substituted thiacalix[4]arene **2** and **3** at the lower rim from 2-chloro(*p*-tolyl)acetamide and 2-chloro(*p*-acetylphenyl)acetamide, respectively. Bromine and mono-*p*-acetylphenylacetamide-*p*-*tert*-butylthiacalix[4]arene **3** were reacted in chloroform under solar radiation to give mono-*p*-phenacylbromideacetamide-*p*-*tert*-butylthiacalix[4]arene **4**. Derivatives of mono-substituted thiacalix[4]arenes **2-4** were reacted with Lawesson reagent (LR) affording mono-substituted thiacalix[4]arene derivatives **5-7**, respectively. The temple of the novel compounds was illustrated based on elemental analyses, ^{1}H-, ^{13}C-, and Dept-NMR spectroscopy. Synthesized derivatives have been tested against adult and nymph Cowpea Aphid (Aphis craccivora) in laboratory conditions as insecticidal agents. to calculate the LC_{50} values for each one of them. Bioassay experiments showed that synthesized compounds **4** and **7** possess the highest insecticidal bio-efficacy, with LC_{50} values of 1.16 and 2.08 ppm, respectively against nymphs, and 11.96 and 13.52 ppm, respectively, against adults of *Aphis craccivora*.

Keywords: *Thiacalix[4]arene, Tetraethylamonium bromide, Lawesson reagent, Aphis craccivora, Eco-friendly insecticides.*

1. Introduction

The original synthesis of *p*-*tert*-butylthiacalix[4]arene (TCA) substituted sulfur atom bridges for methylene groups that linked the phenolic moieties was reported by Miyano et al. in 1997. [**1**]. This class of macrocycles has become more popular due to its ease of preparation and wide range of applications [**2-7**]. TCA has the ability for selective alkylation due to containing four hydroxyl groups. Initial research on the chemistry of thiacalix[4]arenes primarily involved adjustments at the low rim[**6,7**]. The conventional Williamson method to synthesize ethers, which involves alkyl halides and a base, is used to derivatize thiacalixarenes and make similar alterations [**8**]. According to the circumstances and the proportion of thiacalixarenes, alkylation reagents, and base, their reactions gave 1,3-di or tetrasubstituted items [**9**]. Dialkylation of thiacalixarenes led ordinarily to distally (1,3-) di-substituted items [**8-12**]. On the other hand, the upper rim substituted thiacalix[4]arenes are active sites other than the lower rim [**11**]. In 2004, According to Kon et al., ethyl bromoacetate was alkylated under nitrogen gas conditions with TCA in a regulated manner selectively for the synthesis of monosubstituted *p*-*tert*-butylthiacalix[4]arene [**13**]. This approach opened several avenues for the manufacture of monosubstituted *p*-*tert*-butylthiocalix[4]arene derivatives. Recently, researchers have begun to develop new methods to produce these products. for example, Lamouchi et al in 2012 synthesized the monosubstituted *p*-*tert*-butylthiocalyx[4]arene in two steps, through which the substituted TCA was first precipitated *via* a phase transition catalyst, using tetrabutylammonium bromide and dimethylformamide [**14**]. Also, Omran in 2016 succeeded in synthesis of monosubstituted *p*-*tert*-butylthiacalix[4]arene under Phase Transfer Catalysis PTC, which is faster than the latter method [**15**]. On the other hand, calixarenes are known as safe materials and are used to get rid of pesticide residues [**16-18**]. Also, their derivatives have toxicity against bacteria and fungi [**19**].

Here in this work, we aim to synthesize some new derivatives of *p*-*tert*-butylthiacalix[4]arene at the lower rim and in addition to eco-friendly insecticides against aphids, which causes huge damage to many crops around the world.

2. Results and Discussion

Phase transfer catalysis was found to be the most suitable technique for the synthesis of monosubstituted *p*-*tert*-butylthiocalixl[4]arenes. Thus, the reaction of *p*-*tert*-butylthiocalixl[4]arene **1** with mole equivalent of 2-chloro-*N*-(*p*-tolyl)acetamide and/or 2-chloro(*p*-acetyl phenyl)acetamide using potassium iodide, potassium carbonate and tetraethylamonium bromide (TEAB) in dry benzene gave mono substituted *p*-*tert*-butylthiacalixl[4]arene **2** and **3,** respectively, in an excellent yield, (**Scheme 1**).

The reaction condition for the synthesis of mono-thiacalix[4]-arenes **3** was optimized using different solvent; base and reaction time to improve the yield of 5,11,17,23-tetra-*tert*-butyl-25-[*N*-(4-acetylphenyl)-acetamide]-26,27,28-trihydroxy-thiacalix[4]arene **3**, **Table 1.** From these data, we found that the yield was dependent on (i) Base strength; (ii) Solvent type; and (iii) Time of the reaction.

(i.) 2-chloro-*N*-(*p*-tolyl)acetamide, KI, TEAB, K₂CO₃, C₆H₆
(ii.) 2-chloro(p-acetyl phenyl)acetamide , KI, TEAB, K₂CO₃, C₆H₆
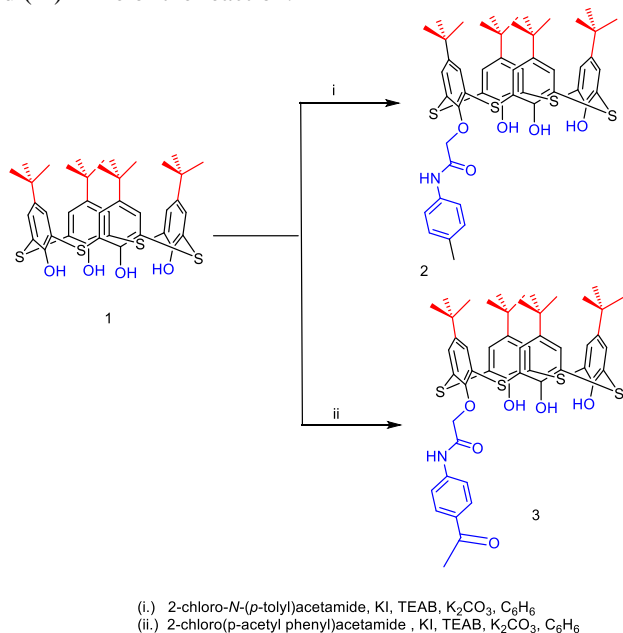
Scheme 1. Synthesis of monosubstituted butylthiacalixarene **2** and **3**

* Optimized method
Table 1: The optimal circumstances for the synthesis of TCA **3**.

| Base	Solvent	Time (h)	Yield (%)
Na₂CO₃	Benzene	30	62
Na₂CO₃	Acetone	48	43
Na₂CO₃	CCl₄	48	34
Na₂CO₃	Dioxane	36	23
K₂CO₃	**Benzene**	**3**	**89***
K₂CO₃	Acetone	36	54
K₂CO₃	CCl₄	24	60
K₂CO₃	Dioxane	24	36

It seems that the non polar chacter of benzene solvent and the reaction temperature (> or = 80 C) accelerate the alkylation of Calixarenes OH and lowering the self alkylation of acetamides (dimerization) through COCH₂Cl in one molecule and COCH₃ln another molcule: which is clear in other used solvents.

The spectral data (IR, ¹H NMR, ¹³C NMR, and Dept-NMR) of the newly synesized compounds confirmed their chemical structure. (*see* **Experimental Part** & **SI**). The infrared spectra of mono-*p*-tolylacetamide-*p*-tert- butylthiacalix[4]arene **2** showed new characteristic absorption bands for amino N-H at $\bar{\upsilon}$ 3337 cm⁻¹ and carbonyl C=O at $\bar{\upsilon}$ 1686 cm⁻¹. Its ¹H NMR spectrum showed the appearance of two singlet signals at δ 1.24 & 1.29 ppm for Buᵗ protons; two singlet signals at δ 2.38 & 4.87 ppm for methyl and methylene protons, respectively; multipet signals at δ 7.24-7.82 ppm for aromatic protons, three

OH protons appeared as two singlet signals at δ 9.24 and 9.52 ppm; and broad singlet signal at δ 10.63 ppm for NH proton. The ¹³C NMR spectrum revealed seventeen signals in the aromatic region for sp^2-carbons at δ 120.0, 120.6, 120.7, 128.2, 129.5, 133.9, 135.6, 136.0, 136.4, 137.0, 144.4, 144.6, 150.4, 155.8, 156.3, 157.4, and 165.8 ppm; and six signals in the aliphatic region for p-tert butyl and O-CH₂ group carbons at δ 20.9, 31.0, 31.3, 34.3, 34.6, and 76.4 ppm, respectively.

The infrared spectrum of mono-*p*-acetylphenylacetamide-*p*-*tert*-butylthiacalix[4]arene **3** showed new absorption bands for amino N-H and two carbonyl C=O groups at $\bar{\upsilon}$ 3061, 1789, and 1682, respectively. The ¹H NMR spectrum of compound **3** confirmed the appearance of Buᵗ protons as two singlet signals at δ 1.13 and 1.17 ppm; two singlet singles at δ 2.53 and 4.77 ppm for methyl and methylene protons, respectively; multiplet signals in the aromatic region at δ 7.18-7.95 ppm for aromatic protons; two singlet signals at δ 9.18 and 9.46 ppm due to three protons of hydroxyl group; and singlet signal at δ 10.87 ppm for NH proton. The¹³C NMR spectrum of compound **3** demonstrated twenty signals at δ 119.8, 120.0, 120.6, 124.2, 128.1, 128.3, 129.7, 133.2, 136.0, 136.4, 137.0, 142.4, 144.6, 144.7, 150.8, 155.7, 156.1, 157.2, 166.4, and 197.0 ppm due to carbons of aromatic and carbonyl groups; and seven signals in the aliphatic region at δ 26.4, 30.9, 31.3, 34.2, 34.3, 34.6, and 76.2 (exchangeable by Dept NMR) ppm assigned to carbons of *p*-*tert*butyl group, CH₃, and *O*-CH₂, respectively.

The reaction of mono-*p*-acetylphenylacetamide-*p*-*tert*-butylthiacalix[4]arene **3** with one equivalent mole of bromine in chloroform under solar radiation (sunlight) produced 5,11,17,23-tetra-tert-butyl-25-[*N*-(4-(2-bromoacetyl)phenyl)-acetamide]-26,27,28-trihydroxy-thiacalix[4]arene **4**, (**Scheme 2**).
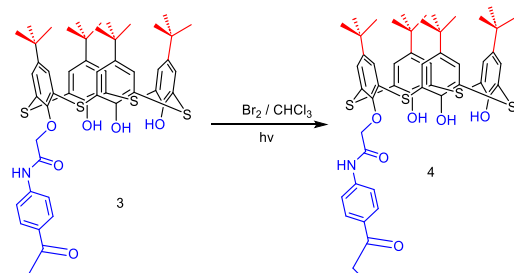

Scheme 2. Synthesis of 5,11,17,23-Tetra-tert-butyl-25-[*N*-(4-(2-bromoacetyl)phenyl)-acetamide]-26,27,28-trihydroxy-thiacalix[4]arene (**4**)

The infrared spectrum of compound **4** presented the emergence of distinctive absorption bands at $\bar{\upsilon}$ 3491, 3380, 3060, and 2906 cm⁻¹ for OH, NH, CH$_{arom.}$ and CH$_{aliph.}$. groups, respectively; 1785 cm⁻¹ for the carbonyl ketone group; and 1678 cm⁻¹ for the carbonyl group. Its ¹H NMR spectrum revealed that *tert*-butyl protons appeared as two singlet signals at δ 1.23 ppm for nine protons and at δ 1.28 ppm for twenty-seven protons; two singlet signals at δ 4.48 and 4.88 ppm due to protons of (*O*-CH₂) and (Br-CH₂), respectively; multiplet signals at δ 7.68 8.10 ppm for aromatic protons; while three protons of hydroxyl phenolic groups appeared as two singlet signals at δ 9.25 and 9.53 ppm; and protons of NH appeared as an individual signal at δ 10.98 ppm. Its ¹³C NMR spectrum presented seventeen signals at δ 120.0, 120.6, 128.1, 129.8,

130.0, 136.0, 136.4, 137.1, 143.3, 144.6, 144.8, 150.8, 155.7, 156.1, 157.2, 166.6, and 190.1 ppm for sp^2-carbons; seven signals in aliphatic region at δ 30.8, 31.0, 31.3, 34.2, 34.3, 34.6 and 76.2 ppm for aliphatic carbons. Its dept-135 showed the appearance of two signals for two methylene carbons of (O-CH$_2$) and (Br-CH$_2$), in the opposite direction at δ 30.8 and 76.2 ppm, respectively three signals for CH aliphatic carbon at δ 31.0, 31.3, and 31.3 ppm; and five signals in the aromatic region at δ 120.0, 136.0, 136.4, 136.5 and 137.1 ppm due to the CH aromatic carbons.

Reaction of the newly prepared *p-tert*-butylthiacalix[4]arenes **2**-**4** with Lawesson's reagent in dry benzene afforded the thiated *p-tert*-butylthiacalix[4]arenes **5**-**7**, respectively, **Scheme 3**.
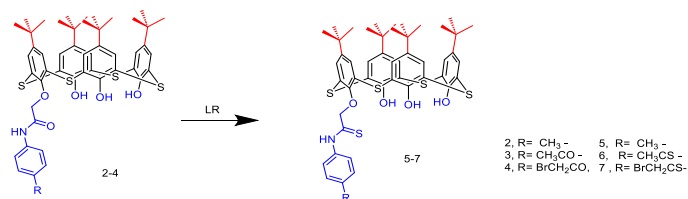
Scheme 3. Synthesis of compounds **5-7**

Infrared in the mono-*p*-tolylthioacetamide-*p-tert*-butylthiacalix[4]arene **5** spectrum, the distinctive carbonyl (C=O) group absorption band vanished. Its ^{1}H NMR spectrum showed the appearance of two singlet signals for four *tert*-butyl protons at δ 1.24 and 1.29 ppm; two singlet signals for methyl and methylene protons at δ 2.42 and 5.26 ppm, respectively; two singlet signals for sp^2-aromatic protons in the aromatic region at δ 7.32–7.98 ppm; two singlet signals for three OH protons at δ 9.18 and 9.51 ppm; and singlet signal for NH proton at δ 12.22 ppm.

3. 1. Insecticidal bio-efficacy screening:

Calixarene compounds have many uses and applications especially separation [16], purification [17], and pollution control [18]. Thus, calixarenes are classified as eco-friendly compounds, however, the last year's toxicity of calixarenes against bacteria and fungi was recorded [19], here a novel attempt to demonstrate the insecticidal efficacy of calixarene compounds against Cowpea aphids, with the hope to find out eco-friendly insecticides, avoiding the traditional chemical insecticides with their harmful impact to the environment.

To determine the LC50 values, each toxicological data about aphid mortality was examined using probity analysis using a statistical program (LDP-line). The results are shown in **Table 2 and Figure 1**. including slope, toxic ratio, and LC$_{50}$ values.

3.2. A) Toxicological activity against nymphs of *Aphis craccivora* after 24 h of treatment.

The results, which are displayed in Table 2, demonstrate that all six tested substances exhibit weak to moderate toxicological action against A. craccivora nymphs, with LC$_{50}$ values ranging from 1.16 to 6.54 ppm during a 24-hour treatment period. In particular, LC$_{50}$ values of compounds **2, 3, 4, 5, 6,** and **7** are

6.26, 6.54, 1.16, 3.91, 5.29, and 2.08 ppm respectively. Compounds 4 and 7 had the highest toxicological activity of all the investigated derivatives, with LC$_{50}$ values of 1.16 and 2.08 ppm, respectively; due to the presnce of Br atom in the molecules.

Table 2. Insecticidal activity of compounds **2, 3, 4, 5, 6,** and **7** after 24 h of treatment against nymphs and adults of *Aphis craccivora* insects

	Adults of *A. craccivora*			Nymphs of *A. craccivora*		
Comp.	LC$_{50}$ (ppm)	Slope	Toxic ratio	LC$_{50}$ (ppm)	Slope	Toxic ratio
2	15.03	1.0388 ± 0.4334	0.79	6.26	0.9772 ± 0.3876	0.18
3	13.62	0.8147 ± 0.3737	0.87	6.54	0.6066 ± 0.2349	0.17
4	11.96	0.6629 ± 0.3781	1	1.16	0.3424 ± 0.2189	1
5	18.71	0.8634 ± 0.3772	0.64	3.91	0.4715 ± 0.2271	0.29
6	22.00	0.9571 ± 0.3883	0.54	5.29	0.5620 ± 0.2320	0.22
7	13.52	0.6359 ± 0.3773	0.88	2.08	0.3944 ± 0.2221	0.55

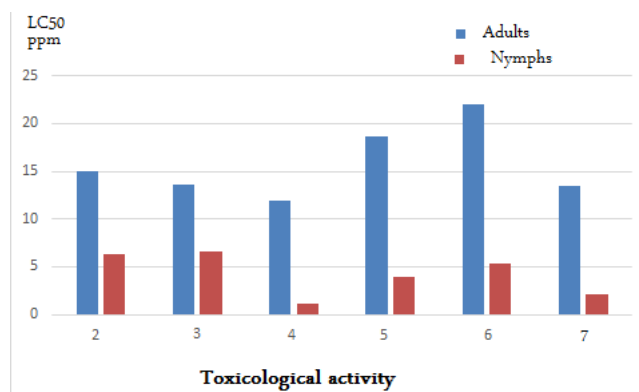**Fig. 1**: Insecticidal activity of compounds **2, 3, 4, 5, 6,** and **7** against nymphs and adults of *Aphis craccivora* insects after 24 hrs of treatment.

3.2. B) toxicological activity against Aphis craccivora adults over a 24-hour treatment period.

According to the insecticidal activities of derivatives **2, 3, 4, 5, 6,** and **7** against adults of *A. craccivora* insect, after 24 hrs of

treatment, All chemicals exhibited LC50 values ranging from 11.96 to 22.00 ppm, indicating moderate to mild toxicological action against adult A. cracivora. With LC50 values of 11.96 and 13.52, respectively, the analogs 4 and 7 exhibited the highest levels of toxicological activity. Compounds 2, 3, 4, 5, 6, and 7 have LC50 values of 15.03, 13.62, 11.96, 18.71, 22.00, and 13.52 ppm, respectively.

4. Experimental

4.1. Chemistry

General Information:

We used all commercially available reagents without further purification; they were acquired from Fluka, Aldrich, and Merck. For all reactions, thin-layer chromatography (TLC) was employed. Percolated silica gel G/UV-254 plates with a 0.25 mm thickness (Merck 60F254) were used, and UV light (254 nm/365 nm) was used for visualization. A Kofler melting points instrument was used to find the uncorrected melting points. An FT-IR-ALPHBROKER-Platinum-ATR spectrometer was used to gather infrared spectra using the attenuated total reflection (ATR) method. The spectra are displayed as cm^{-1}.

The ^{1}H and ^{13}C NMR spectra of each chemical were acquired with a Bruker Bio Spin AG spectrometer running at 400 MHz and 100 MHz, respectively, in DMSO-d$_6$ and CDCl3. The water TQD quadruple spectrometer, which is connected to the water UPLC, was used to record electrospray (ESI) low-resolution mass spectra. Chemical shifts (δ) for 1H NMR were reported in parts per million (ppm) with tetramethylsilane (TMS) serving as an internal standard (δ=0); coupling constants (J) were reported in hertz (Hz); the data were presented in the following formats: multiplicity (s = singlet, d = doublet, m = multiplet), integration, and chemical shift. The elemental analyses were obtained using a Perkin-Elmer CHN-analyzer model.

5,11,17,23-Tetra-tert-butyl-25-[N-(p-tolyl)acetamide]26,27,28 -trihydroxy-thiacalix [4]arene (2)

A mixture of TCA **1** (1gm, 1.38 mmole), 5 gm of anhydrous K$_2$CO$_3$, 0.5 gm TEAB, (2.7 mmole) potassium iodide, and 2-chloro (*p*-tolyl)acetamide (0.27 gm, 1.52 mmole) refluxed in 20 mL of benzene while stirring for 10 hrs. After filtering out the reaction mixture, the benzene layer was dried out by evaporating it under low pressure. The solid residue was washed with hydrochloric acid and then extracted with CH$_2$Cl$_2$. Next, methanol was added to the layer of saturated CH$_2$Cl$_2$. The resulting white solid was dried and filtered out. (**2**, C$_{49}$H$_{57}$NO$_5$S$_4$) Yield 87%; white solid, mp 180 ºC; MS: *m/z* 868.24 [MH]$^+$; IR (KBr): ν$_{max}$ 3386 (OH) 3337 (NH) 3061 (CH$_{arom}$), 2960 (CH$_{aliph}$) and 1686 (CO) cm^{-1}; ^{1}H NMR (CDCl$_3$)δ (ppm): 1.24 (9H, s, Bu^t), 1.29 (27H, s, Bu^t), 2.38 (3H, s, CH$_3$), 4.87 (2H, s, CH$_2$), 7.24 (2H, d, CH$_{arom}$), 7.70 (6H, d, CH$_{arom}$), 7.75 (2H, s, CH$_{arom}$), 7.82 (2H, d, CH$_{arom}$), 9.24 (2H, s, OH), 9.52 (1H, s, OH), 10.63 (1H, s, NH); ^{13}C NMR (CDCl$_3$) δ (ppm): 20.9, 31.0, 31.3, 34.3, 34.6, 76.4, 120.0,

120.6, 120.7, 128.2, 129.5, 133.9, 135.6, 136.0, 136.4, 137.0, 144.4, 144.6, 150.4, 155.8, 156.3, 157.4, 165.8.

5,11,17,23-Tetra-tert-butyl-25[N-(4-acetylphenyl)acetamide]-26,27,28-trihydroxy-thiacalix-[4]arene (3)

A mixture of TCA **1** (1gm, 1.38 mmole), 5 gm of anhydrous K$_2$CO$_3$, 0.5 gm TEAB, potassium iodide (2.7 mmole), and 2-chloro-*N*-(*p*-acetyl phenyl)acetamide (0.33g, 1.56 mmole)) refluxed in 20 mL of benzene while stirring for 3 hrs. After filtering out the reaction mixture, the benzene layer was dried out by evaporating it under low pressure. The solid residue was washed with hydrochloric acid and then extracted with CH$_2$Cl$_2$. Next, methanol was added to the layer of saturated CH$_2$Cl$_2$. The resulting white solid was dried and filtered out. Methanol was added after the concentration of the CH$_2$Cl$_2$ layer. Filtered off and allowed to dry, the white solid developed. (**3**, C$_{50}$H$_{57}$NO$_6$S$_4$) Yield 89 %; white solid, mp 160 ºC; MS: *m/z* 895.31 [MH]$^+$; IR (KBr): ν$_{max}$ 3386 (OH) 3337 (NH) 3061 (CH$_{arom}$), 2960 (CH$_{aliph}$), 1789 (CO$_{ketone}$), 1682 (CO$_{amide}$) cm^{-1}; ^{1}HNMR (CDCl$_3$) δ (ppm): 1.13 (9H, s, Bu^t), 1.17 (27H, s, Bu^t), 2.53 (3H, s, CH$_3$), 4.77 (2H, s, CH$_2$), 7.18 (1H, br. s, Ar-H), 7.57-7.65 (9H, m, Ar-H), 7.95 (4H,br. s, Ar-H), 9.18 (2H, s, OH), 9.46 (1H, s, OH), 10.87 (1H, s, NH); ^{13}C NMR (CDCl$_3$) δ (ppm): 26.4, 30.9, 31.3, 34.2, 34.3, 34.6, 76.2(exchangeable), 119.8, 120.0, 120.6, 124.2, 128.1, 128.3, 129.7, 133.2, 136.0, 136.4, 137.0, 142.4, 144.6, 144.7, 150.8, 155.7, 156.1, 157.2, 166.4, 197.0.

5,11,17,23-Tetra-tert-butyl-25-[*N*-(4-(2-bromoacetyl)-phenyl)acetamide]-26,27,28-trihydroxy-thiacalix[4]arene (4)

To a solution of *p*-(acetylphenyl)acetamide-TCA **3** (1gm, 1.11mmole) in 15 mL of dry chloroform, After adding the bromine (0.059 mL, 0.36 mmole) dropwise and stirring the reaction liquid for five minutes in the presence of sunlight, the reaction was allowed to continue. after that, the reaction mixture was then stirred for thirty minutes. Product **4** was separated after the addition of 5 mL of methanol into the reaction mixture and recrystallized from a mixture of methanol: chloroform (1:3). (**4**, C$_{50}$H$_{56}$BrNO$_6$S$_4$) Yield 91 %; white solid, mp 225 ºC; MS: *m/z* 973.22 [MH]$^+$; IR (KBr): ν$_{max}$ 3491 (OH), 3380 (NH), 3060 (CH$_{arom}$), 2906 (CH$_{aliph}$), 1785 (CO$_{ketone}$), 1678 (CO$_{amide}$) cm^{-1}; ^{1}H NMR (CDCl$_3$) δ (ppm): 1.23 (9H, s, Bu^t), 1.28 (27H, s, Bu^t), 4.48 (2H, s, CH$_2$), 4.88 (2H, s, CH$_2$), 7.68-7.75 (8H, m, CH$_{arom}$), 8.05-8.10 (4H, m, CH$_{arom}$), 9.25 (2H, s, OH), 9.53 (1H, s, OH), 10.98 (1H, s, NH); ^{13}C NMR (CDCl$_3$) δ (ppm): 30.8 (exchangeable), 31.0, 31.3, 34.2, 34.3, 34.6, 76.2 (exchangeable), 120.0, 120.6, 128.1, 129.8, 130.0, 136.0, 136.4, 137.1, 143.3, 144.6, 144.8, 150.8, 155.7, 156.1, 157.2, 166.6, 190.1.

5,11,17,23-Tetra-tert-butyl-25-[N-(p-tolyl)ethanethioamide]-26,27,28-trihydroxy-2,8,14,20-thiacalix-[4]arene (5)

A combination of Lawesson's reagent (0.23 g 0.57 mmole) and mono-*p*-tolylacetamide-TCA **2** (1g, 1.15 mmole) refluxed in 20 mL of benzene while stirring for 3 hrs. A whitish-yellow solid product was precipitated, filtered, and crystallized by a mixture of methylene chloride and methanol (2:1). (**5**, C$_{49}$H$_{57}$NO$_4$S$_5$) Yield 63 %; Whitish yellow crystals, mp 240 ºC; MS: *m/z* 883.29 [MH]$^+$; IR (KBr): ν$_{max}$ 3340 (OH), 3259 (NH), 3065 (CH$_{arom}$), 2960 cm^{-1} (CH$_{aliph}$); ^{1}HNMR (CDCl$_3$) δ (ppm): 1.24 (9H, s, Bu^t), 1.29 (27H, s, Bu^t), 2.42 (3H, s, CH$_3$),

5.26 (2H, s, CH$_2$), 7.32 (2H, d, CH$_{arom}$), 7.68 (6H, d, Ar-H), 7.75 (2H, s, CH$_{arom}$), 7.98 (2H, d, CH$_{arom}$), 9.18 (2H, s, OH), 9.51 (1H, s, OH), 12.22 (1H, s, NH); ^{13}C NMR (CDCl$_3$) δ (ppm): 21.2, 31.0, 31.2, 31.3, 34.2, 34.3, 34.6, 82.5 (exchangeable), 120.0, 120.6, 124.0, 128.3, 129.4, 136.0, 136.4,136.7, 137.1, 144.5, 144.6, 150.7, 155.8, 156.2, 157.0, 192.9.

5,11,17,23-Tetra-tert-butyl-25-[N-(4-ethanethioylphenyl)thio-acetamide]-26,27,28-trihydroxy-thiacalix-[4]arene (6)
A combination of Lawesson's reagent (0.44 gm, 1.11 mmole) and mono-*p*-(acetylphenyl)acetamide-TCA **3** (1gm, 1.15 mmole) refluxed in 10 mL of benzene while stirring for overnight. A whitish yellow solid product was precipitated, filtered, and recrystallized from methylene chloride and methanol (2:1). (**6**, C$_{50}$H$_{57}$NO$_4$S$_6$) Yield 68 %; Whitish yellow, mp. 255 ºC; MS: *m/z* 927.26 [MH]$^+$; IR (KBr): ν_{max} 3354 (OH) 3332 (NH) 3063 (CH$_{arom}$) cm^{-1}; ^{1}HNMR (CDCl$_3$) δ (ppm): 1.23 (9H, s, Bu^t), 1.28 (27H, s, Bu^t), 2.25 (3H, s, CH$_3$), 5.24 (2H, s, CH$_2$), 7.67-7.75 (9H, m, CH$_{arom}$), 8.10 (1H, d, CH$_{arom}$), 8.32 (1H, d, CH$_{arom}$), 9.19 (2H, s, OH), 9.52 (1H, s, OH), 12.37 (1H, s, NH); ^{13}C NMR (CDCl$_3$) δ (ppm): 26.7, 31.0, 31.3, 31.3, 34.2, 34.4, 34.7, 82.7, 119.9, 120.5, 120.6, 123.4, 128.1, 129.3, 135.1, 136.1, 136.6, 137.2, 142.6, 144.6, 144.7, 150.9, 155.7, 156.1, 156.8, 194.0, 197.1.

5,11,17,23-Tetra-tert-butyl-25-[N-(4-(2-bromoethanethioyl)-phenyl)ethanethioamide]-26,27,28-trihydroxythiacalix[4]-arene (7)
A mixture of mono-*p*-(phenacyl bromide)acetamide-TCA **4** (1gm, 1.02 mmole) and Lawesson's reagent (0.41 gm, 1.03 mmole) in 10 mL benzene was stirred under reflux overnight. A whitish-yellow solid product was precipitated, filtered, and recrystallized from methylene chloride and methanol (2:1). (**7**, C$_{50}$H$_{56}$BrNO$_4$S$_6$) Yield 58 %; Whitish yellow, mp 190 ºC; MS: *m/z* 1007.26 [MH]$^+$; IR (KBr): $_{max}$ 3473 (OH), 3360 (NH), 3062 (CH$_{arom}$), 2960 (CH$_{aliph}$) cm^{-1}; ^{1}HNMR (CDCl$_3$) δ (ppm): 1.12 (9H, s, Bu^t), 1.18 (27H, s, Bu^t), 3.78 (2H, s, CH$_2$), 5.13 (2H, s, CH$_2$), 7.56- 7.64 (10H, m, CH$_{arom}$), 8.09-8.11 (2H, m, CH$_{arom}$), 9.09 (2H, s, OH), 9.52 (1H, s, OH), 12.19 (1H, s, NH).

2.2. Insect Collection and Rearing

The cowpea aphid bug is a very dangerous and destructive pest that attacks a wide variety of Egypt's agricultural crops. The initial batches of Aphis craccivora insects were taken from the Agricultural Research Center, Plant Protection Research Institute, and Pest Laboratory. A. craccivora lab strain was used to test the newly generated compounds' insecticidal efficacy.

2.3. Laboratory Bioassay.

Under the same laboratory conditions, all six derivatives were examined using the leaf dipping method to demonstrate their insecticidal activities [20]. In the control experiment, only water, acetone, and 0.1% Tween-80 were used. Different concentrations of each derivative were utilized (in acetone and 0.1% Tween-80 as a surfactant was used). Twenty nymphs and

twenty adults of A. craccivora, three times, roughly the same size, were submerged for 10 seconds in each analogous concentration. The test aphids were left to dry at room temperature for about half an hour. These toxicological experiments were conducted at 25 °C with 5% relative humidity. The used pests were transferred to glass jars filled with water once they had dried. Using a modern binocular microscope, the aphid mortality was determined following a single day of therapy. Because it was immobile, the aphid was considered dead. Using Abbott's formula, all of the synthetic derivatives' mortality data were examined. [21]. Insecticidal activity evaluation is dependent on LC50 values, which are determined by probit analysis [22].

5. Conclusion
Synthesis of a novel compound of monosubstituted thiacaix-arene derivatives used as insecticidal chemicals against Cowpea Aphid adults and nymphs.

CRediT authorship contribution statement:

Conceptualization, Mohamed Sharaf, Amr H. Moustafa, Ali M. Drar, Mounir A. A. Mohamed, Omran A. Omran, Software, Mohamed Sharaf,, and Omran A. Omran, Validation, Mohamed Sharaf, Amr H. Moustafa, Ali M. Drar, Mounir A. A. Mohamed, and Omran A. Omran Formal analysis, Mohamed Sharaf, Investigation, Amr H. Moustafa, Ali M. Drar, Mounir A. A. Mohamed, Omran A. Omran. Resources: Mohamed Sharaf, Mounir A. A. Mohamed, and Omran A. Omran Data curation, Mohamed Sharaf. Writing-original draft preparation, , Mohamed Sharaf. Writing- review and editingAmr H. Moustafa, Ali M. Drar, Mounir A. A. Mohamed, and Omran A. Omran. Visualization, R. A. Mahmoud, Supervision, Mohamed Sharaf, Amr H. Moustafa, Ali M. Drar, Mounir A. A. Mohamed, and Omran A. Omran. All authors have read and agreed to the published version of the manuscript.

Data availability statement

Declaration of competing interest

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