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Green dual-action potential of newly synthesized sulfonamide-based ionic liquids: larvicidal activity against *Culex pipiens* and purification of oil-polluted water

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The discovery of novel ionic liquids incorporating a sulfonamide moiety has attracted significant attention owing to their unique bioactive properties and versatile applications. The present study focuses on the design, spectroscopic characterization, and evaluation of the petroleum-dispersing and insecticidal activities of seven newly synthesized compounds (**4a–e**, **5c**, and **5e**). The synthesized ionic liquid compounds were successfully characterized by spectroscopic methods. Their efficiency in dispersing or collecting thin films of petroleum was evaluated in various water systems. Notably, most of the compounds, especially **4d**, demonstrated strong capabilities in removing petroleum films from water. Additionally, the larvicidal activity of the compounds was evaluated against *Culex pipiens*, one of the most hazardous mosquito vectors. Among them, compounds **4d**, **4b**, and **5e** exhibited significant potency, with LC₅₀ values of 161.03, 207.82, and 229.72 ppm, respectively. These compounds were found to be more effective than **5c**, showing 3.07-, 2.38-, and 2.15-fold higher activity. In conclusion, the synthesized compounds demonstrated a dual functionality: efficiently dispersing or collecting oil films from water while also exhibiting larvicidal activity against aquatic *Culex pipiens* larvae, with compound **4d** showing the highest efficacy. Hence, these compounds hold promise for application in both water purification and mosquito control.

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1. Introduction

Ionic liquids (ILs) are salts that have a melting point below 100 °C¹ and are formed from anions and cations, such as pyridine, imidazole, and other organic or inorganic cations. Because of their enhanced properties over conventional solvents, ILs have been described as new “green solvents” that will eventually replace organic solvents, such as outstanding solubility in inorganic, organic, low melting point, easy recovery, high

stability, and polymer materials, almost no vapor pressure, etc.^{2–4} Because of their unique physical and chemical characteristics, ILs are utilized extensively in various industries, including organic synthesis,^{6,7} food processing,⁵ electrochemistry,^{8,9} and biocatalysis.^{10–14} In the past decade, the scientific community has focused a lot of attention on the potential uses of ILs in the development of creative, effective antiseptics, disinfectants, insecticides, and antiviral medication.^{15–19}

Mosquitoes are the most dangerous vector, transmitting various infectious diseases. *Culex pipiens* causes a variety of infections, such as lymphatic filariasis, Japanese encephalitis, West Nile fever, and Sindbis fever.²⁰ Females of *C. pipiens* are blood feeders on humans and birds and hence transmit infectious diseases to them.²¹ Most of these infectious diseases aren't vaccine-preventable in humans.²² Therefore, mosquito control remains an indispensable tool in the prevention of mosquito-borne infections.

Vector management strategies have traditionally relied on killing mosquito aquatic stages, larvae, using many insecticides, including chemical larvicides.²³ Larvicides are applied in the breeding habitat to target larvae before maturation into adult mosquitoes. Therefore, the larvicidal application in

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breeding aquatic habitats reduces the emergence of adult mosquitoes in nearby areas.²⁴ Temephos, *O,O,O',O'*-tetramethyl *O,O'*-thiodi-*p*-phenylene bis(phosphorothioate), is an organophosphate recommended larvicide by WHO used for the control of various vectors of diseases.²⁵ Aggressive application of chemical insecticides in mosquito control programs which have negative effects on the environment and human health.²⁶ In addition, the buildup of insecticide resistance among mosquito vectors became widespread.²⁷ Consequently, novel compounds with new characteristics are needed to reduce disease transmission. The water solubility of insecticides appears to impact their efficacy. Although it might not have enough residual activity (persistence) over a long period, they don't harm non-target organisms and the environment, and don't develop insecticide resistance.

Sulfonamides are a broad class of bioactive substances that include antiviral, anticancer, insecticidal, and antibacterial activities.^{28,29} Temephos as a class of sulfonamides (A, Fig. 1) has long been employed as a larvicide in many countries worldwide. It disrupts the mosquito life cycle by targeting the larval stage and acts through a cholinergic pathway common to both insects and mammals, resulting in neurotoxic effects.³⁰ A

sulfonamide-incorporating quaternary ammonium iodide derivative (B, Fig. 1) gave good larvicidal activity against *C. pipiens* with potent activity ($LC_{50} = 26.71$ ppm).³¹ Also, a cationic surfactant-sulfonamide conjugate (C, Fig. 1) showed high activity toward *B. subtilis* and *E. coli*, with values comparable to the evaluated reference drugs.³² Against *Mythimna separata* Walker, a derivative of propargyloxy-substituted benzenesulfonamide (D, Fig. 1) has shown great insecticidal action. The isothermal titration calorimetry results show a substantial interaction between subunit H of compound D with the ATPase enzyme and show highly significant activity with a lower LD_{50} value ($28.0 \mu\text{g g}^{-1}$) than celangulin ($344.0 \mu\text{g g}^{-1}$).³³ Various *p*-twerelsulfonamide (E) derivatives containing alkyl *N*-substituents were found to have a favorable inhibitory effect against the CA IX enzyme with an IC_{50} of 94 nM.³⁴ Aliphatic sulfonamido-quaternary ammonium salts (F, G) caused apoptosis by up-regulating RhoB.^{35,36}

One of the major issues facing the world is the pollution of water surfaces with petroleum. A significant amount of petroleum oil enters the hydrosphere for various reasons, such as accidents involving oil tankers and pipelines. While the thin petroleum layer remains environmentally dangerous, the

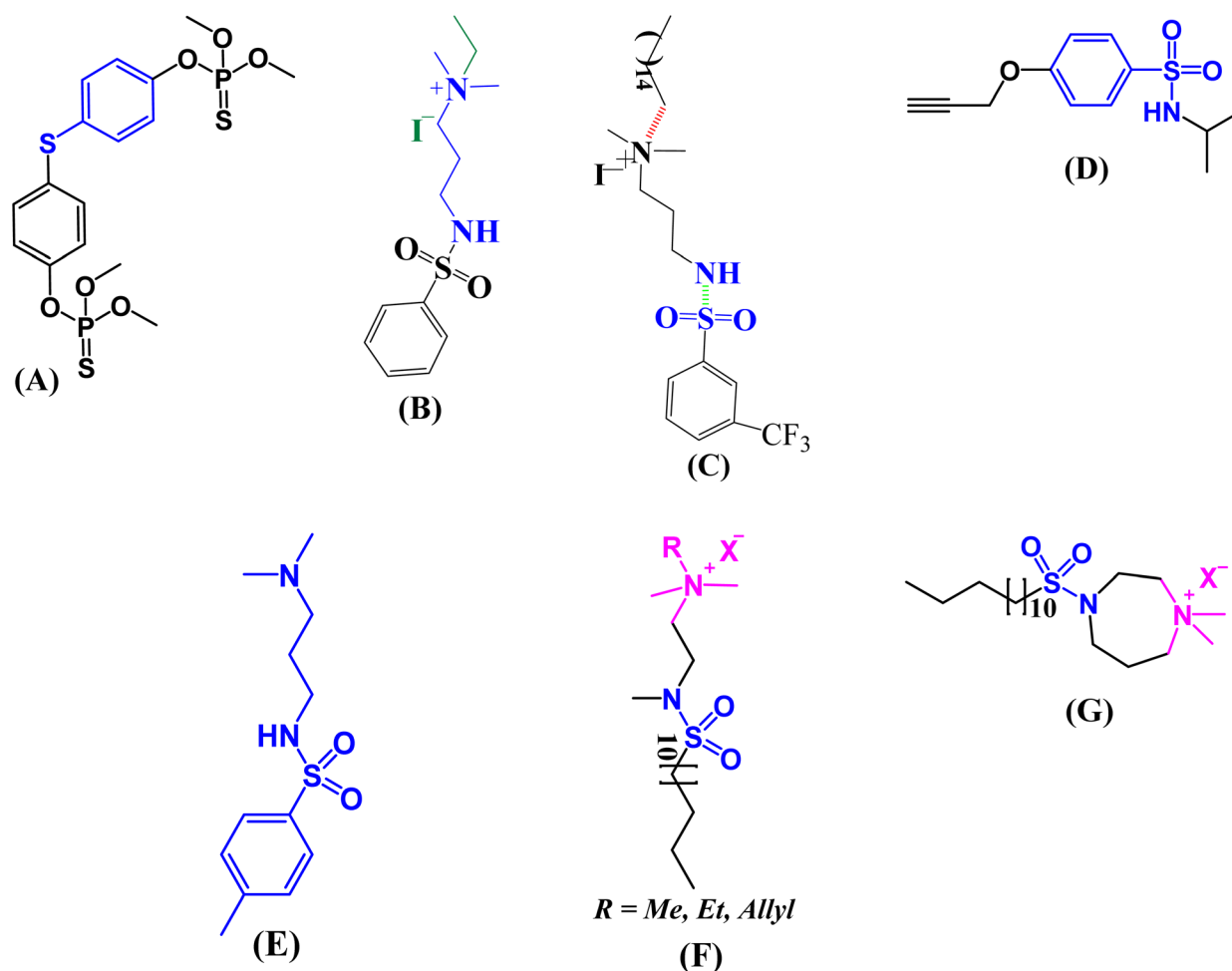


Fig. 1 Some bioactive sulfonamides, sulfonamido-quaternary ammonium salts and temephos.



mechanical procedures can separate the thick petroleum film. To address this particular problem, various techniques were used, such as colloid-chemical techniques, which involved applying petro-collecting and dispersing agents to remove such thin oil layers.^{37–39}

Ionic Liquids and ionic liquid-based surfactants, particularly gemini and conventional cationic surfactants, are the most effective methods to clean the water surface by dispersing and/or collecting compounds that form thin petroleum films during oil processing stages.^{40–44}

The rationale of this study is that the design compounds of four moieties: aromatic sulfonamide moieties, quaternary ammonium groups, long polymethylene ether chain and chloride/tetrafluoroborate. The aromatic sulfonamide moieties (Ar-SO₂-NH-) have strong enzyme inhibition, targeting insect physiological pathways. Quaternary ammonium groups are a permanent positive charge, enhancing interaction with nucleophilic enzymes or receptors for better binding and inhibition. The long polymethylene ether chain enhances membrane permeability and solubility, aiding compound translocation into insect cells. These designed compounds contain an amphiphilic structure with a long polymethylene ether chain, which is a flexible hydrophobic tail that combines with oil. Moreover, these amphiphilic molecules reduce surface tension, helping break oil into smaller droplets (dispersing) or gather droplets together (collecting). The positively charged quaternary ammonium head is hydrophilic, allowing good interaction with water, which interacts electrostatically with negatively charged particles in oil, enhancing aggregation or dispersion. Replacing chloride with tetrafluoroborate (BF₄⁻) in the compounds enhances chemical stability and may reduce toxicity to non-target organisms.

The current work aims to prepare several sulfonamido-quaternary diammonium iodides with dual function, purifying water from thin films of oil and reducing the aquatic stage of the dreadful disease vector (larvae of *C. pipiens*). Hence, their petro-collecting/dispersing indices in the diluted and undiluted form on the water surface with various degrees of mineralization were investigated. Furthermore, their larvicidal effectiveness against *C. pipiens* larvae was assessed.

2. Experimental

2.1. Materials and reagents

2.1.1. Reagents. All utilized solvents and chemicals were used without further purification. Sinopharm Chemical Reagent Co., Ltd. was the supplier of 4-methylbenzenesulfonyl chloride (99.0%) and 4-cyanobenzenesulfonyl chloride (≥98.0%). Naphthalene-2-sulfonyl chloride (99.0%) and thiophene-2-sulfonyl chloride (96.0%) were from Shanghai Macklin Biochemical Co., Ltd., and 2,4,6-triisopropylbenzenesulfonyl chloride (97.0%) and 4-(*tert*-butyl)benzenesulfonyl chloride (98.0%) were from Alfa Aesar China Co. Ltd. (Shanghai, China). Sinopharm Chemical Reagent Co. Ltd. was also the supplier of *p*-toluenesulphonic acid (PTSA), tetrahydrofuran (THF, ≥99.0%), ethyl acetate (≥99.6%), sodium tetrafluoroborate (NaBF₄), dichloromethane (DCM,

99.5%), ethanol (≥99.5%), methanol, petroleum ether (60–90 °C, >99.7%), and diethyl ether.

2.1.2. Synthesis of ILs (4a–e, 5c and 5e)

General preparation of hexane-1,6-diyl bis(2-chloroacetate) (3). In the presence of PTSA (1 mol%), in dry toluene, the appropriate 1,6-hexanediol (**2a–c**, 1 equiv.) was mixed with chloroacetic acid (1.3 equiv.). After that, Dean–Stark equipped the mixed solutions and refluxed them at 135 °C while stirring until an equivalent amount of water formed. The alkanes bis(2-chloroacetate) (**3a–c**) were created and removed by extraction using *n*-hexane, followed by drying over anhydrous Na₂SO₄, evaporating the solvent, and then vacuum-drying to produce the desired product with a 94% yield.

Hexane-1,6-diyl bis(2-chloroacetate) (3). Colorless viscous with yield = 94%. FT-IR (ATR) ν/cm^{-1} ; bands at 2956 for νCH aliphatic chain, 1753 for C=O ester, 1476 for CH₂ bending, 1170 for C–O ester (Fig. S1).

Procedure for producing sulfonamide derivatives, 2a–e. 3-(*N,N*-Dimethylamino)-1-propylamine (1.14 g, 11.30 mmol) and Et₃N (43.02 g, 14.15 mmol) in 60 mL of CH₂Cl₂ were mixed with sulfonyl chloride derivatives (**1a–e**, 5.65 mmol) across several portions. After the addition was finished, the resulting solution mixture was stirred for ten hours. Following treatment with a 50 mL half-saturated sodium chloride solution, the mixture was extracted three times using 50 mL of CH₂Cl₂. After drying the organic layer over anhydrous Na₂SO₄, the solvent was filtered, evaporated, and extracted using a high vacuum. Flash chromatography (SiO₂, CHCl₃:MeOH, 5:1) was used to purify the crude product, yielding **2a–i** with a range of 91–95% as white to yellow solids. All spectroscopic analysis and method of preparation were reported *via* our previous work.⁴⁹

Quaternization process of sulfonamide derivatives (2a–e) with hexane-1,6-diyl bis(2-chloroacetate) (3). In five round-bottom flasks, solutions of sulfonamide derivatives (**2a–e**, 5 mmol) in 20 mL acetonitrile were prepared separately. Next, the previously generated solutions were mixed with 20 mL of acetonitrile to dissolve 10 mmol of hexane-1,6-diyl bis(2-chloroacetate). For around twenty-four hours, the mixtures are refluxed at 70 °C. Following the completion of the reaction and evaporation of the solvent, the residual materials were cleaned three times using diethyl ether in order to eliminate the unreacted components and purify the final compounds. The products' yields range from 88 to 90% with various colors and shapes.

***N,N'*-((Hexane-1,6-diylbis(oxy))bis(2-oxoethane-2,1-diyl))bis(3-(4-cyanophenylsulfonamido)-*N,N*-dimethylpropan-1-aminium) chloride (4a).** Yellowish white, mp = 72–75 °C yield = 88%. FT-IR (ATR) ν/cm^{-1} ; 3321–3273 (νNH stretching), 3091 (νCH aromatic), 2851–2975 (νCH aliphatic fatty chain), 2231 ($\nu\text{C}\equiv\text{N}$, cyano group), 1741 ($\nu\text{C}=\text{O}$ ester), 1632 ($\nu\text{C}=\text{N}$), 1451 (νCH_2 bending), 1154 ($\nu\text{C}-\text{O}$ ester). ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.46 (t, *J* = 5.7 Hz, 2H), 8.11 (d, *J* = 8.2 Hz, 4H), 8.01 (d, *J* = 8.3 Hz, 4H), 4.52 (s, 4H), 3.77 (s, 6H), 3.62–3.52 (m, 6H), 3.21 (s, 12H), 2.83 (d, *J* = 5.8 Hz, 4H), 1.95–1.82 (m, 4H), 1.46–1.34 (m, 4H), 1.34–1.23 (m, 4H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 165.71, 144.58, 133.98, 127.85, 118.10, 115.58, 62.61, 61.33, 53.49, 51.58, 33.01, 25.87, 23.15.



N,N'-((Hexane-1,6-diylbis(oxy))bis(2-oxoethane-2,1-diyl))bis(*N,N*-dimethyl-3-(thiophene-2-sulfonamido)propan-1-aminium)chloride (**4b**). Viscous yellow, yield = 90%. FT-IR (ATR) ν/cm^{-1} ; 3369–3275 (νNH stretching), 3091 (νCH aromatic), 2845–2971 (νCH aliphatic chain), 1745 ($\nu\text{C}=\text{O}$ ester), 1641 ($\nu\text{C}=\text{N}$), 1451 (νCH_2 bending), 1152 ($\nu\text{C}-\text{O}$ ester). ^1H NMR (400 MHz, DMSO- d_6) δ 8.22 (t, $J = 5.5$ Hz, 2H), 7.96 (d, $J = 4.9$ Hz, 2H), 7.64 (d, $J = 3.2$ Hz, 2H), 7.27–7.17 (m, 2H), 4.54 (s, 4H), 3.76 (s, 4H), 3.58 (dd, $J = 7.6, 4.4$ Hz, 4H), 3.23 (s, 12H), 2.88 (d, $J = 6.0$ Hz, 4H), 1.95–1.85 (m, 4H), 1.47–1.35 (m, 4H), 1.29 (ddd, $J = 18.3, 6.8, 3.6$ Hz, 4H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 165.34, 140.78, 132.82, 131.91, 128.03, 62.34, 60.85, 53.00, 51.28, 32.67, 32.41, 27.94, 25.54, 25.25, 25.21, 22.49.

N,N'-((Hexane-1,6-diylbis(oxy))bis(2-oxoethane-2,1-diyl))bis(*N,N*-dimethyl-3-(naphthalene-1-sulfonamido)propan-1-aminium)chloride (**4c**). Yellowish white viscous, yield = 88%. ^1H NMR (400 MHz, DMSO- d_6) δ 8.47 (s, 2H), 8.23–8.12 (m, 6H), 8.06 (d, $J = 7.7$ Hz, 2H), 7.92–7.84 (m, 2H), 7.69 (t, $J = 7.9$ Hz, 4H), 4.55 (d, $J = 15.5$ Hz, 4H), 4.16 (t, $J = 6.4$ Hz, 4H), 3.66–3.52 (m, 4H), 3.22 (d, $J = 3.9$ Hz, 12H), 2.90–2.74 (m, 4H), 1.91 (s, 4H), 1.61 (s, 4H), 1.38–1.24 (m, 4H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 164.92, 136.89, 134.68, 132.16, 129.35, 129.17, 128.58, 128.28, 127.89, 127.46, 122.43, 72.52, 64.85, 58.85, 45.88, 43.29, 37.02, 29.83, 23.84.

N,N'-((Hexane-1,6-diylbis(oxy))bis(2-oxoethane-2,1-diyl))bis(*N,N*-dimethyl-3-(2,4,6-triisopropylphenylsulfonamido)propan-1-aminium)chloride (**4d**). White solid, mp = 80–82 °C, yield = 87%. ^1H NMR (400 MHz, DMSO- d_6) δ 7.71 (dd, $J = 15.7, 5.9$ Hz, 2H), 7.24 (d, $J = 2.8$ Hz, 4H), 4.67–4.34 (m, 4H), 4.15–4.07 (m, 4H), 3.75 (s, 4H), 3.57–3.45 (m, 4H), 3.23 (s, 12H), 2.98–2.83 (m, 6H), 1.88 (dd, $J = 33.3, 6.9$ Hz, 4H), 1.45–1.30 (m, 4H), 1.26 (dd, $J = 13.2, 9.6$ Hz, 4H), 1.20 (d, $J = 5.1$ Hz, 36H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 166.44, 151.97, 148.92, 130.92, 122.02, 69.76, 66.08, 62.40, 58.02, 44.91, 41.88, 33.92, 29.03, 24.54, 24.05, 22.03.

N,N'-((Hexane-1,6-diylbis(oxy))bis(2-oxoethane-2,1-diyl))bis(*N,N*-dimethyl-3-(4-methylphenylsulfonamido)propan-1-aminium)chloride (**4e**). White semisolid, yield = 89%. ^1H NMR (400 MHz, DMSO- d_6) δ 8.48 (d, $J = 5.5$ Hz, 2H), 8.11 (d, $J = 8.2$ Hz, 4H), 8.01 (d, $J = 8.3$ Hz, 4H), 4.52 (s, 4H), 3.77 (s, 6H), 3.61–3.49 (m, 6H), 3.22 (s, 12H), 2.84 (d, $J = 11.6$ Hz, 4H), 2.68 (s, 6H), 1.87 (t, $J = 18.4$ Hz, 4H), 1.48–1.34 (m, 4H), 1.27 (t, $J = 10.8$ Hz, 4H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 165.25, 143.90, 133.53, 128.25, 124.34, 62.61, 61.07, 53.92, 50.70, 32.32, 28.64, 26.10, 22.68.

Preparation of *N,N'*-((hexane-1,6-diylbis(oxy))bis(2-oxoethane-2,1-diyl))bis(*N,N*-dimethyl-3-(naphthalene-1-sulfonamido)propan-1-aminium)tetrafluoroborate (5c**) and *N,N'*-((hexane-1,6-diylbis(oxy))bis(2-oxoethane-2,1-diyl))bis(*N,N*-dimethyl-3-(4-methylphenylsulfonamido)propan-1-aminium)tetrafluoroborate (**5e**).** Using a specific amount of acetone as a solvent, 1 g (0.001 mol) of compounds **4c** and **4e** were added individually to a single-mouth flask together with 0.23 g (0.0021 mol) of NaBF_4 for 10 hours at 40 °C while being vigorously stirred. Filtration and vacuum distillation (at 60 °C and 450 mm Hg) were performed on the reaction mixture. After adding dichloromethane

to the **[4e]**Cl and NaBF_4 residual, white particles precipitated. Thereafter, filtering was used to separate the solid precipitate. Lastly, the product was vacuum-dried for two hours at 80 °C in an oven to eliminate any remaining dichloromethane.⁴⁸ The typical synthesis route of **[5e]** BF_4 is shown in Scheme 1.

N,N'-((Hexane-1,6-diylbis(oxy))bis(2-oxoethane-2,1-diyl))bis(*N,N*-dimethyl-3-(naphthalene-1-sulfonamido)propan-1-aminium)tetrafluoroborate (**5c**). Yellowish white viscous, yield = 91%. FT-IR (ATR) ν/cm^{-1} ; 3374 (νNH stretching), 3091 (νCH aromatic), 2845–2971 (νCH aliphatic chain), 1743 ($\nu\text{C}=\text{O}$ ester), 1635 ($\nu\text{C}=\text{N}$), 1475 (νCH_2 bending), 1372 (S=O (sulfonyl) symmetric component), 1204 (S=O asymmetric stretch (sulfonyl)), 1194 (C–O stretch, $\nu\text{C}-\text{O}$ ester). ^{19}F NMR (565 MHz, DMSO- d_6) δ –74.52.

N,N'-((Hexane-1,6-diylbis(oxy))bis(2-oxoethane-2,1-diyl))bis(*N,N*-dimethyl-3-(4-methylphenylsulfonamido)propan-1-aminium)tetrafluoroborate (**5e**). White viscous, yield 93%. FT-IR (ATR) ν/cm^{-1} ; 3373 (νNH stretching), 3067 (νCH aromatic), 2932 (νCH aliphatic chain), 1745 ($\nu\text{C}=\text{O}$ ester), 1629 ($\nu\text{C}=\text{N}$), 1468 (νCH_2 bending), 1319 (S=O (sulfonyl) symmetric component), 1217 (S=O asymmetric stretch (sulfonyl)), 1135 (C–O stretch, $\nu\text{C}-\text{O}$ ester). ^{19}F NMR (565 MHz, DMSO- d_6) δ –61.21.

2.2. Methods of ILs characterization

2.2.1. Instrumentals. Thermo Scientific Nicolet iS10 FT-IR spectrometers were utilized to get the FT-IR spectra of every synthetic compound. *Via* tetramethylsilane (TMS) as the internal standard, Bruker Avance 400 MHz was used to collect NMR spectra, including ^1H and ^{13}C NMR, in DMSO- d_6 solutions.

2.3. Collecting and dispersing of petroleum capacities

The new series of **4a–e**, **5c**, and **5e** were found to be water soluble. We investigated their ability to disperse and collect petroleum films in two forms (2.5% aqueous solution and solid) on the water surface with various degrees of salinity. The crude petroleum oil, which had a density of 0.85 g cm^{-3} and a viscosity of $0.17 \text{ cm}^2 \text{ s}^{-1}$ at 293 K, was extracted from the Red Sea of South Sinai, Egypt. The thin layer of crude oil (about 0.14 mm thick) on the water's surface with varying salinities was covered with 0.01 g of each produced compound or a 2.5% aqueous solution of the synthesized compound. Petro-collecting behavior (K) was calculated using the formula $K = S_0/S$, where S_0 is the surface area of the petroleum film at the start of the experiment and S is the surface area of the petroleum spot produced by the action of the synthesized compounds. The surface area of the film was routinely measured during the monitoring procedure, and K values were computed at predetermined intervals (τ). The ratio of the surface area of clean water to the initial area of petroleum film is known as K_D (petroleum-dispersing ability).

2.4. Larvicidal activity against *Culex pipiens* larvae

2.4.1. Mosquito rearing. The larvae of *C. pipiens* were obtained from a stock colony that was reared in our insectary for several generations without exposure to any chemicals. The larval stage was maintained in a glass jar containing 500 mL of





Scheme 1 A schematic pathway for the synthesis of sulfonamide-tethering cationic ionic liquids.

distilled water at a controlled photoperiod of 14 : 10 (L : D) and a temperature of 25–28 °C.⁴⁵ The larvae were fed on a mixture of dried yeast and biscuit (25 : 75 by weight). The emerged pupae are transferred in screened cages (25 × 25 × 25 cm³) for adult emergence. Adults were supplied with a glucose solution (10%), and females only fed on a periodic time. The laid egg rafts were transferred daily for stock-rearing plates.

2.4.2. Larvicidal bioassay. The synthesized compounds were tested at various concentrations on third-instar larvae of *C. pipiens* to evaluate their toxic effects on mosquito larvae, as referenced in 46. Five concentrations of tested compounds were prepared by dissolving them in distilled water to produce 80 mL of the final solution (100, 200, 400, 600, and 800 ppm) in a 100 mL jar. In the same manner, temephos, larvicide recommended by WHO (50% EC, LARVIGUARD®, Shri Ram Agro

Chemicals, India) was dissolved in water to obtain the concentrations (50, 100, 200, 300 and 400 ppm). The test was performed using three replicates, each containing 20 newly educated third instar larvae. In the control series, only 80 mL of distilled water was used. After 48 h of exposure, the mortality was estimated.²⁴

2.4.3. Statistical analysis. The mortality percentage of various concentrations was recorded, and toxicity data were estimated by probit analysis.⁴⁷ The LDP line software calculated LC₅₀ and LC₉₀ with 95% confidence limits, along with the slope of the different concentrations and their mortality lines.

3. Results and discussion

3.1. Synthesis

Creating compounds containing a unique activity against a variety of targets is simple with a hybrid method. Depending on the application, a single-functionalized molecule can only effectively target one destination. In certain situations, or issues, these molecules won't be the best options. The development of compounds with two or more functionalities (conjugates or hybrids) will increase the range of applications for which they can be used, ultimately influencing several targets.

Ionic liquids incorporating sulphonamide groups have been used as antifungal and antibacterial agents. In the present work, we designed a novel ionic liquid bearing two ammonium salt moieties conjugated with different heteroaryl/aryl sulphonamides through a hexane spacer to synthesize ionic liquid-sulphonamide conjugates (**4a–d**, **5c**, **5e**) for multiple applications. In the synthetic strategy, *N*-substituted sulphonamides (**2a–e**) are first created by dehydrochlorinating sulphonyl chloride moieties (**2a–e**) with *N,N*-dimethylpropyl-1,3-diamine in dichloromethane under the effect of a base. Their chemical structures were confirmed previously *via* our work.⁴⁹ In parallel, hexane-1,6-diyl bis(2-chloroacetate) (**3**) was formed as a colorless viscous liquid with a yield of roughly 95% by reacting 1,6-hexanediol with chloroacetic acid and catalyzed by the acid catalyst PTSA in dry toluene as an essential solvent. Whereas the IR spectrum of compound **3** was utilized to elucidate the chemical structure through the ester group band's appearance at 1735 cm⁻¹, besides peaks for C–O and C–Cl at 1170 and 680 cm⁻¹, respectively. Secondly, a variety of two equivalent *N*-substituted sulphonamides (**2a–e**) were quaternized with hexane-1,6-diyl bis(2-chloroacetate) (**3**), individually in the presence of ethyl acetate as a solvent at 70 °C to produce the targeted ionic liquids incorporating sulphonamide groups (**4a–e**).

The FT-IR spectra of compounds **4a–e** exhibited characteristic absorption peaks for NH of the amido group at about 3274–3369 cm⁻¹, and peaks at about 3091 cm⁻¹ for aromatic CH, peaks at about 2845–2975 cm⁻¹ for aliphatic CH. Furthermore, the IR spectrum showed a peak at about 1741–1745 cm⁻¹ for carbonyl of ester group and at about 1622–1632 cm⁻¹ for the C=N group, then peaks at about 1152–1154 cm⁻¹ for C–O–C bond (ether group). Furthermore, their ¹H NMR spectrum showed a signal for NH protons between 8.12 and 8.47 ppm,

aromatic protons in the range 8.12–8.47 ppm, and protons adjacent to the quaternized nitrogen and oxygen of the ether group at 2.8–4.6 ppm. Also, the ¹³C NMR spectrum exhibited a peak between 164 and 166 ppm, which confirmed the presence of the carbonyl carbon atom of the ester group, aromatic carbon atoms at *d* = 120–145 ppm, and long-chain aliphatic carbon atoms (the deshielding aliphatic carbons) at *d* = 50–70 ppm and shielded aliphatic carbon atoms at *d* = 20–40 ppm. Finally, the ion exchange reaction was carried out by treating selected two synthesized compounds **4c** and **4e** with sodium tetrafluoroborate in a definite amount of acetone as solvent, for 10 h at 40 °C to obtain the targeted ionic liquid compounds bearing tetrafluoroborate anion (**5c** and **5e**). The structures of synthesized compounds were elucidated *via* ¹⁵F NMR spectrum by the appearance of bands at 61.21 and 74.5 ppm, which related to the presence of fluorine atoms in the synthesized compounds.

As a model, the infrared spectra of **4a** displayed, in addition to the bands already indicated, an extra band at 2233 cm⁻¹ that was attributed to the C–N group and an N–H band at 3374 cm⁻¹. Its ¹³C NMR spectra elucidated the presence of a signal at δ = 127 ppm for cyano-carbon, and aromatic carbon atoms at δ = 115–144 ppm (Fig. S2). Interestingly, the IR exhibited a special peak at 2231 for the cyano group (CN) that appeared only in compound **4a** (Fig. S2–S8).

3.2. Collecting and dispersing of petroleum studies

Water surface pollution is mostly caused by oil leaks from storage tanks, pipelines, and transportation systems.⁵⁰ Thick oil stains are removed using technical techniques, but fine oil films are left on the water surface and can't be successfully removed using these techniques. Because they prevent sunlight from penetrating and interfere with oxygen exchange, these thin layers are a major hazard to marine life.⁵¹ Therefore, it is thought that the most effective way to remove these remaining thin oil films is to use agents that disperse and/or collect oil films.

Results showing the dispersion and collection capabilities of **4a–e**, **5c**, and **5e** in 2.5% weight aqueous solution and solid states are summarized in Table 1 and Fig. 2. The effectiveness of **4a–e**, **5c**, and **5e** as cleaning agents that disperse and/or collect oil films was affected by the aryl/heteroaryl sulfonamide moiety with a rigid spacer enhancing performance. Notably, in all used waters, compounds **4a**, **4b**, **4e**, and **5e** had a moderate effect on the dispersing or collecting of thin films from water surfaces in the diluted and undiluted forms, whereas *K_D* ranges from 56.44 to 66.11% and *K* ranges from 3.45 to 11.38. Unlikely, the undiluted form of **4c** exhibited the greatest petro-dispersing action, whereas *K_D* = 82.42 in seawater and *K_D* = 83.32 in freshwater and a solid form. In contrast, the solid and solution forms of **4c** demonstrated significant collecting stability for thin petroleum, whereas *K* ranged from 14.57 to 16.45 in the distilled water and maintained petro-collecting stability for four days. Interestingly, compound **4d** showed the strongest effect as petro-dispersing and/or collecting action on the water surface. Whereas both forms of **4d** demonstrated the accumulation of fine oil film in



Table 1 Petro-collecting/dispersing properties of the synthesized ionic liquids compounds (4a–e and 5c, 5e)

Compd no.	Undiluted product						2.5% wt water solution					
	Distilled water		Fresh water		Sea water		Distilled water		Fresh water		Sea water	
	τ (h)	$K(k_D)$	τ (h)	$K(k_D)$	τ (h)	$K(k_D)$	τ (h)	$K(k_D)$	τ (h)	$K(k_D)$	τ (h)	$K(k_D)$
4a	0–2	NE ^a	0–2	5.33 ± 0.7	0–2	NE ^a	0–2	NE ^a	0–2	5.33 ± 0.9	0–2	NE ^a
	30–96	5.28 ± 1.4	30–96	11.38 ± 1.5	30–96	4.66 ± 1.3	30–96	6.86 ± 1.6	30–96	10.86 ± 1.6	30–96	8.44 ± 1.6
4b	0–2	4.66 ± 0.8	0–2	3.45 ± 0.7	0–2	4.43 ± 0.8	0–2	4.34 ± 0.7	0–2	5.28 ± 0.7	0–2	5.67 ± 0.9
	30–96	9.87 ± 1.6	30–96	10.34 ± 1.3	30–96	7.98 ± 1.2	30–96	9.55 ± 1.5	30–96	10.55 ± 1.5	30–96	7.77 ± 1.5
4c	0–2	NE ^a	0–2	NE ^a	0–2	NE ^a	0–2	NE ^a	0–2	NE ^a	0–2	NE ^a
	30–96	16.45 ± 1.2	30–96	83.32 ± 1.3%	30–96	80.11 ± 2.1%	30–96	14.57 ± 1.5	30–96	81.21 ± 2.3%	30–96	82.42 ± 1.8%
4d	0–2	NE ^a	0–2	NE ^a	0–2	NE ^a	0–2	NE ^a	0–2	NE ^a	0–2	NE ^a
	30–96	17.78 ± 1.2	30–96	95.22 ± 1.6%	30–96	96.16 ± 2.6%	30–96	18.44 ± 1.5	30–96	96.16 ± 2.6%	30–96	98.15 ± 1.5%
4e	0–2	NE ^a	0–2	5.31 ± 0.7	0–2	NE ^a	0–2	NE ^a	0–2	4.13 ± 0.9	0–2	NE ^a
	30–96	6.11 ± 1.4	30–96	9.55 ± 1.8	30–96	66.11 ± 1.6%	30–96	6.13 ± 1.8	30–96	10.86 ± 1.7	30–96	56.44 ± 1.6%
5c	0–2	NE ^a	0–2	NE ^a	0–2	NE ^a	0–2	NE ^a	0–2	NE ^a	0–2	NE ^a
	30–96	15.66 ± 1.8	30–96	81.44 ± 1.9%	30–96	83.22 ± 2.2%	30–96	11.66 ± 1.7	30–96	83.33 ± 1.8%	30–96	78.33 ± 1.6%
5e	0–2	NE ^a	0–2	5.31 ± 0.7	0–2	NE ^a	0–2	NE ^a	0–2	4.13 ± 0.9	0–2	NE ^a
	30–96	6.77 ± 1.7	30–96	10.66 ± 1.9	30–96	63.11 ± 1.2%	30–96	7.01 ± 1.6	30–96	9.22 ± 1.3	30–96	59.44 ± 1.1%

^a NE = no effect.

distilled water, as their K value equals 17.78 and 18.44, respectively, for 96 hours, with a high stability effect. Moreover, in diluted form, **4d** also caused a highly dispersing effect of fine films after 96 hours, whereas the K_D values are 96.16 and 98.15% in sea and fresh waters, respectively. The solid form of **4d** showed a good dispersing character of fine oil from the water surface, especially in the fresh and sea waters, whereas the K_D values were equal to 95.22 and 96.16%, respectively.

After modification of the structure of synthesized compounds **4c** and **4e**, a suitable model was formed to form a new structure as **5c** and **5e**. Table 1 shows that the petroleum properties of synthesized compounds **5c** and **5e** exhibited slightly different effects compared to those of compounds **4c** and **4e**; this difference is attributed to the structural change, specifically the alteration of the negative ion from Cl^- to BF_4^- . The hydrophobic part plays an important role in determining

Fig. 2 Effect of the synthesized ionic liquid (**4d**) on petroleum. (A) Untreated thin film, (B) petro-collecting, and (C) petro-dispersing.

the petroleum effects and the strength of the effect, and this feature appears clearly in compound **4d**, which gave the greatest effects due to the presence of six isopropyl groups (high hydrophobic part).

Building on our previous work, the synthesized compound **4d** proved to be a more effective petro-dispersing agent for removing petroleum films than the earlier reported compounds **3a–g**.⁵² In addition, the present study revealed that **4d** surpassed the dispersing capabilities of **PS2** and **PS3**.⁵³ Remarkably, compound **4d** also showed greater efficiency than the comparable **AISM** and **AISE** compounds in cleaning petroleum-contaminated water surfaces.⁵⁴ (All abbreviations are reported in the SI, Table S1).

3.3. Larvicidal activity against *Culex pipiens* larvae

The synthesized compounds had moderate toxicity against the third instar of *C. pipiens* larvae. The mortality percentages of *C. pipiens* larvae varied with the different concentrations of the investigated compounds. The high concentration of 800 ppm showed mortality percentages of 73.33, 90, 81.66, 98.33, 78.33, 70, and 86.66% for **4a**, **4b**, **4c**, **4d**, **4e**, **5c**, and **5e**, respectively, as shown in Fig. 3. On the other hand, the lowest concentration, 100 ppm, exhibited 18.33, 35, 26.66, 38.33, 20, 13.33, and 33.33% for **4a**, **4b**, **4c**, **4d**, **4e**, **5c**, and **5e**, respectively, as represented in Fig. 3. Temephos achieved high mortality of 93.33% at 400 ppm (Fig. S9).

The probit regression analysis between concentration and mortality was used to calculate the LC_{50} and LC_{90} values for all tested compounds (Table 2). According to the LC_{50} values, **4d**

was the most effective compound with LC_{50} values of 161.03 ppm, followed by **4b** and **5e** with 207.82 and 229.72 ppm, respectively (Table 2). The least active compounds, **4a** and **5c**, had LC_{50} values of 424.47 and 495.78 ppm, respectively. The relative potency was estimated for tested compounds relative to the least active; **5c**, **4d**, **4b**, and **5e** were 3.07, 2.38, and 2.15 times more potent than **5c**. The tested population showed a homogeneous response to all tested compounds except **4d**, with an χ^2 value of 8.17.

The absence of hydrophobic alkyl substituents in the ionic liquid (ILs) molecules increased their solubility in water. The synthesized ionic liquids are soluble in water, which facilitates application as larvicides. A cation salt was proven to be an effective antifeedant against stored product insects. Didecyltrimethylammonium cations exhibited excellent activity and are commercially available in the chloride form; therefore, ILs become a promising alternative to the currently used insect antifeedants. To design new active ILs, the biological roles of cations, arylsulphonamide derivatives, and halogens were studied. The synthesized salts by Pernak⁵⁵ showed insect antifeedant activities towards larvae and/or adults of *Tribolium confusum*, *Sitophilus granaries*, and *Trogoderma granarium* by estimating the amount of consumed food. ILs showed antifeedant activity against the rice weevil, the granary weevil, khapra beetle, and the confused flour beetle; especially those with long alkyls (hexadecyl and tetradecyl) had the highest efficacy. The results indicated that the alkyl substituent length was an essential parameter that substantially improved the antifeedant activity of ILs.⁵⁶

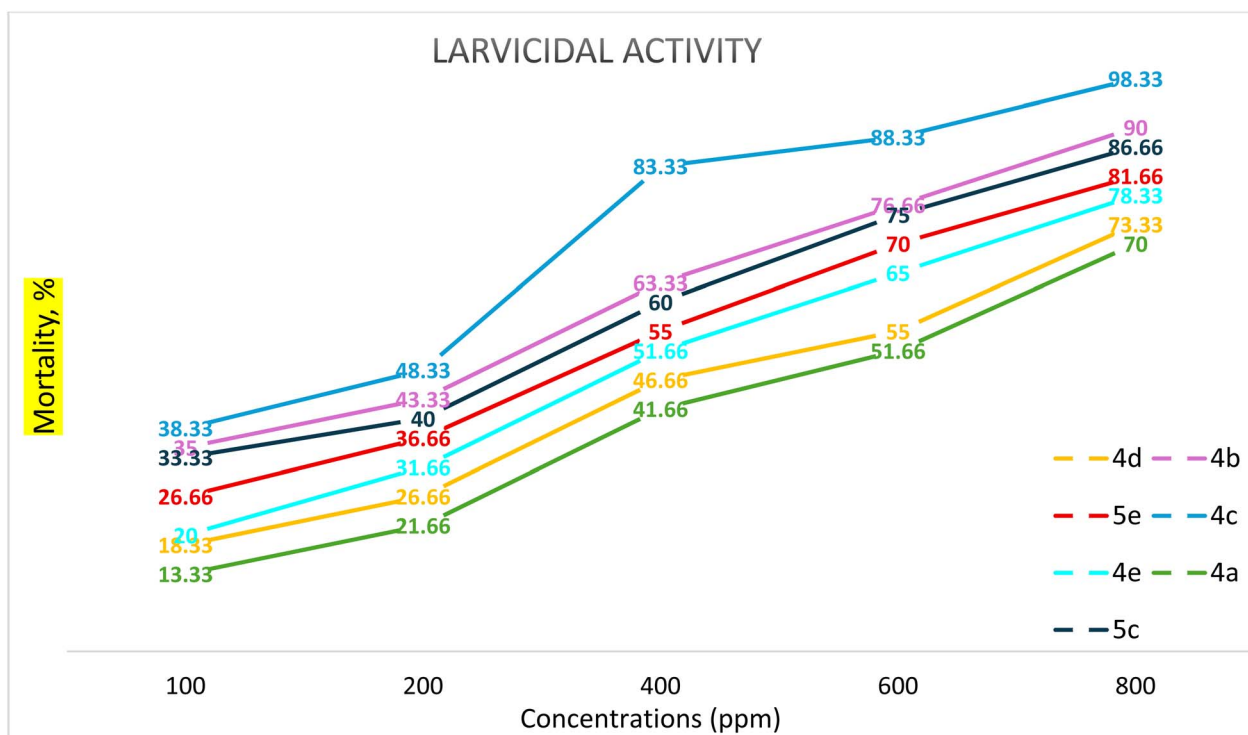


Fig. 3 Mortality percentages of early third larval instar of *Culex pipiens* after exposure to ionic liquids incorporating sulfonamide moiety derivatives (**4a–e**, **5c**, **5e**), 48 h post-treatment.



Table 2 Larvicidal toxicity parameters of ionic liquids incorporating sulfonamide moiety derivatives (**4a–e**, **5c**, **5e**) against early third instar larvae of *Culex pipiens* at 48 h post-treatment

Compd (ppm)	LC ₅₀ (F.I. at 95%) ^a	LC ₉₀ (F.I. at 95%) ^a	Slope ± SE ^b	χ ^{2c}	P	Relative potency
4a	424.47 (360.06–510.43)	2615.07 (1748.71–4893.04)	1.62 ± 0.19	3.81	0.28	1.16
4b	207.82 (169.01–245.86)	1187.41 (895.46–1799.11)	1.69 ± 0.18	6.80	0.07	2.38
4c	282.70 (236.58–332.57)	1700.92 (1219.24–2812.74)	1.64 ± 0.18	3.47	0.32	1.75
4d	161.03 (90.53–213.68)	593.33 (455.04–1155.72)	2.26 ± 0.20	8.17	0.04	3.07
4e	341.87 (292.37–399.58)	1832.59 (1324.51–2969.70)	1.75 ± 0.19	2.15	0.54	1.45
5c	495.78 (424.23–596.52)	2618.16 (1792.26–4671.05)	1.77 ± 0.20	3.20	0.36	1.00
5e	229.72 (188.00–271.64)	1390.10 (1021.14–2207.25)	1.63 ± 0.18	6.24	0.10	2.15
Temephos	119.44 (63.88–175.16)	529.98 (439.68–1911.71)	1.98 ± 0.19	9.67	0.02	4.15

^a F.I.: fiducial limits. ^b Slope ± SE: slope of concentration-mortality regression line ± standard error. ^c χ²: chi-square at significance value (<0.05); relative potency calculated relative to compound **5c**.

From the previous studies, it was noted that most of the ILs were used as deterrents or antifeedant agents, while few studies showed insecticidal properties, leading to mortality. The contact activity is influenced by the length of the alkyl chains in the cation and the functional groups. The ionic liquids exhibited deterrent activity against storage insects, and the alkyl length of the linker and the ester bond in the cation are the main determinants of their biological activity.⁵⁷ Also, the ionic liquid 3-(2-((3,7-dimethyloct-6-en-1-yl)oxy)-2-oxoethyl)-1-methyl-1*H*-imidazol-3-ium chloride showed remarkable mortalities of 68–88% and 63–76% towards *Callosobruchus analis* F. and *Sitophilus oryzae* L. at 5 and 10 μL, respectively, after 24 h of treatment. In addition, it exerted oviposition deterrence on females of *C. analis*, therefore, there was a reduction in egg hatchability and progeny production even at low concentrations.⁵⁸ A monoterpene-based ionic liquid exhibited adulticidal, larvicidal, repellent, and antifeedant activity against *Tribolium castaneum* Herbst and *Stegobium paniceum* L.⁵⁹ Adults of *C. pipiens* were treated with aminopyridinium-based IL derivatives by two methods: spraying and orally. Accumulated mortality rates were higher in sprayed mosquitoes than in those orally treated.⁶⁰

3.4. Structure–activity relationship study

The synthesized compounds have a common scaffold, a bis-ether linker [(hexane-1,6-diylbis(oxy))bis(2-oxoethane-2,1-diyl)], two quaternary ammonium groups with *N,N*-dimethylpropan-1-aminium and counter ions (Cl[−] or BF₄[−]). This scaffold has amphiphilic behavior, causing disruption of the cell membrane.⁶¹ Also, it exerts electrostatic interaction with negatively charged components in insect cuticles or membranes.⁶² Compound **4d** was the most active compound, since it had a pair of triisopropylphenylsulfonamide. The presence of these polycyclic aromatics enhanced the interaction with the hydrophobic cuticle of larvae, boosting penetration through the cuticle. Additionally, this aromatic group can form π–π stacking interactions with chitin or active protein targets in the insect body, thereby enhancing the larvicidal activity. **4b** contained thiophene-2-sulfonamide, which enhances the activity. Thiophene-containing derivatives showed beneficial activity against *C. pipiens* larvae.⁶³ Additionally, the presence of

electron-withdrawing Cl increases lipophilicity that may lead to oxidative disruption in insect tissues.

In **5c** and **5e**, the counterion Cl[−] was replaced by BF₄[−], which modified the ionic strength and solubility and could improve environmental persistence. Moreover, BF₄[−] is a less reactive counterion that may reduce cytotoxicity and enhance stability in aqueous environments. **5e**, 4-methylphenylsulfonamide with BF₄[−], showed good activity; hence, the insertion of a methyl group at the *meta* position leads to resonance in the phenyl group and boosts contact toxicity. On the other hand, **5c** showed the least toxicity as a result of the linkage of a large bulking naphthalene moiety to sulfonamide.

The sulfonamide quaternary ammonium compounds look promising as larvicides and as petro-collecting/dispersing agents. The surfactant action and the significant larvicidal activity of quaternary ammonium groups suggest that they can be developed into mosquito control agents, helping reduce disease spread and collect or disperse oil spills to aid environmental cleanup. These multifunctional compounds offer great potential for eco-friendly larvicides and environmental clean-up agents. According to the SAR study, the long hydrophobic chain halogenated aromatic groups and presence of methoxy groups greatly enhanced the activity. Further work can optimize their structure to balance bioactivity and environmental safety. Also, more studies on formulations were needed for efficient delivery in water environments will be key for practical use in pest control and oil spill remediation.

4. Conclusion

In this work, a series of novel ionic liquid-based sulphonamides (**4a–d**, **5c**, **5e**) was effectively synthesized tethering a bis-ether linker, two quaternary ammonium groups, and numerous aryl/heteroaryl sulphonamide moieties. These ionic liquids were tested to disperse or collect thin petroleum films from water surface, as well as kill larvae.

The results approved their effectiveness as pesticides in controlling mosquitoes and as collecting/dispersing agents for removing oil films. Compounds **4c**, **4d**, and **4e** exhibited better activity in dispersing and collecting small layers of petroleum from water. The best result was achieved by compound **4d**, with good dispersion (*K_D* up to 98.15%) and collection stability (*K_U* up to 98.15%) and collection stability (*K_U* up to 98.15%).



to 18.44) in both solid and liquid forms. The presence of large hydrophobic groups, especially isopropyl groups in **4d**, made it much better at interacting with oil. In compounds **5c** and **5e**, displacement of the chloride counterion to the borofluoride ion had a slight effect on their response to petroleum layer. In addition, compound **4d** with its triisopropylphenylsulfonamide moiety possessed the best activity at killing larvae ($LC_{50} = 161.03$ ppm). This moiety facilitates the penetration of the compound molecules to the larval cuticle and breaking down the membrane of cells. Furthermore, the presence of BF_4^- anion in compounds **5c** and **5e** instead of Cl^- , made them less reactive and more stable, and hence safer to the environment.

Generally, these conjugates represent compounds with dual functionality that can be used to clean up the water surfaces from oil spills and control mosquitoes that carry disease.

Conflicts of interest

All authors declare that they have no conflict of interest.

Data availability

All data are available upon request from the authors.

Supplementary information is available. See DOI: <https://doi.org/10.1039/d5ra07077e>.

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References

- 1 Y. Zhao, B. Han and Z. Liu, Ionic-liquid-catalyzed approaches under metal-free conditions, *Acc. Chem. Res.*, 2021, **54**(16), 3172–3190, DOI: [10.1021/acs.accounts.1c00251](https://doi.org/10.1021/acs.accounts.1c00251).
- 2 K. Dong, X. Liu, H. Dong, X. Zhang and S. Zhang, Multiscale studies on ionic liquids, *Chem. Rev.*, 2017, **117**(10), 6636–6695, DOI: [10.1021/acs.chemrev.6b00776](https://doi.org/10.1021/acs.chemrev.6b00776).
- 3 B. Panchal, K. Bian, T. Chang, Z. Zhu, J. Wang, S. Qin, C. Zhao and Y. Sun, Synthesis of generation-2 polyamidoamine based ionic liquid: efficient dendrimer based catalytic green fuel production from yellow grease, *Energy*, 2021, **219**, 119637, DOI: [10.1016/j.energy.2020.119637](https://doi.org/10.1016/j.energy.2020.119637).
- 4 Y. L. Wang, B. Li, S. Sarman, F. Mocci, Z. Y. Lu, J. Yuan, A. Laaksonen and M. D. Fayer, Microstructural and dynamical heterogeneities in ionic liquids, *Chem. Rev.*, 2020, **120**(13), 5798–5877.
- 5 A. A. R. Setiawan, A. Sulaswatty, Y. Meliana and A. Haryono, Innovation readiness assessment toward research commercialization: case of surfactants for food processing, *Int. J. Innov.*, 2018, **6**(2), 180–193.
- 6 N. R. Lee, M. Cortes-Clerget, A. B. Wood, D. J. Lippincott, H. Pang, F. A. Moghadam, F. Gallou and B. H. Lipshutz, Coolade. A low-foaming surfactant for organic synthesis in water, *ChemSusChem*, 2019, **12**(13), 3159–3165, DOI: [10.1002/cssc.201900369](https://doi.org/10.1002/cssc.201900369).
- 7 P. Wasserscheid and T. Welton, *Ionic Liquids in Synthesis*, Wiley Online Library, 2008, vol. 1, p. 145.
- 8 M. C. Buzzeo, R. G. Evans and R. G. Compton, Non-haloaluminate room-temperature ionic liquids in electrochemistry—a review, *ChemPhysChem*, 2004, **5**(8), 1106–1120, DOI: [10.1002/cphc.200301017](https://doi.org/10.1002/cphc.200301017).
- 9 F. Endres and S. Z. El Abedin, Air and water stable ionic liquids in physical chemistry, *Phys. Chem. Chem. Phys.*, 2006, **8**(18), 2101–2116.
- 10 Y. Zhang, B. Zhen, H. Li and Y. Feng, Basic ionic liquid as catalyst and surfactant: green synthesis of quinazolinone in aqueous media, *RSC Adv.*, 2018, **8**(64), 36769–36774, DOI: [10.1039/C8RA06378H](https://doi.org/10.1039/C8RA06378H).
- 11 C. Qian, C. Yao, L. Yang, B. Yang, S. Liu and Z. Liu, Preparation and application of silica films supported imidazolium-based ionic liquid as efficient and recyclable catalysts for benzoin condensations, *Catal. Lett.*, 2020, **150**(5), 1389–1396, DOI: [10.1007/s10562-019-03030-z](https://doi.org/10.1007/s10562-019-03030-z).
- 12 F. Van Rantwijk, R. M. Lau and R. A. Sheldon, Biocatalytic transformations in ionic liquids, *Trends Biotechnol.*, 2003, **21**(3), 131–138, DOI: [10.1016/S0167-7799\(03\)00008-8](https://doi.org/10.1016/S0167-7799(03)00008-8).
- 13 C. Deraedt and D. Astruc, Supramolecular nanoreactors for catalysis, *Coord. Chem. Rev.*, 2016, **324**, 106–122, DOI: [10.1016/j.ccr.2016.07.007](https://doi.org/10.1016/j.ccr.2016.07.007).
- 14 Y. Pei, J. Ru, K. Yao, L. Hao, Z. Li, H. Wang, X. Zhu and J. Wang, Nanoreactors stable up to 200 °C: a class of high temperature microemulsions composed solely of ionic liquids, *Chem. Commun.*, 2018, **54**(49), 6260–6263, DOI: [10.1039/C8CC02901F](https://doi.org/10.1039/C8CC02901F).
- 15 D. M. Correia, L. C. Fernandes, M. M. Fernandes, B. Hermenegildo, R. M. Meira, C. Ribeiro, S. Ribeiro, J. Reguera and S. Lanceros-Méndez, Ionic Liquid-Based Materials for Biomedical Applications, *Nanomaterials*, 2021, **11**, 2401, DOI: [10.3390/nano11092401](https://doi.org/10.3390/nano11092401).
- 16 R. M. Moshikur, M. K. Ali, R. Wakabayashi, M. Moniruzzaman and M. Goto, Favipiravir-Based Ionic Liquids as Potent Antiviral Drugs for Oral Delivery: Synthesis, Solubility, and Pharmacokinetic Evaluation, *Mol. Pharmaceutics*, 2021, **18**, 3108–3115, DOI: [10.1021/acs.molpharmaceut.1c00324](https://doi.org/10.1021/acs.molpharmaceut.1c00324).
- 17 N. Nikfarjam, M. Ghomi, T. Agarwal, M. Hassanpour, E. Sharifi, D. Khorsandi, M. Ali Khan, F. Rossi, A. Rossetti, E. N. Zare, N. Rabiee, D. Afshar, M. Vosough, T. K. Maiti, V. Mattoli, E. Lichtfouse, F. R. Tay and P. Makvandi, Antimicrobial Ionic Liquid-Based Materials for Biomedical Applications, *Adv. Funct. Mater.*, 2021, **31**, 2104148, DOI: [10.1002/adfm.202104148](https://doi.org/10.1002/adfm.202104148).
- 18 T. A. Shmool, L. K. Martin, L. Bui-Le, I. Moya-Ramirez, P. Kotidis, R. P. Matthews, G. A. Venter, C. Kontoravdi, K. M. Polizzi and J. P. Hallett, *Chem. Sci.*, 2021, **12**, 9528–9545.
- 19 A. N. Vereshchagin, N. A. Frolov, K. S. Egorova, M. M. Seitkalieva and V. P. Ananikov, Quaternary Ammonium Compounds (QACs) and Ionic Liquids (ILs) as



- Biocides: From Simple Antiseptics to Tunable Antimicrobials, *Int. J. Mol. Sci.*, 2021, **22**(13), 6793.
- 20 V. A. Brugman, L. M. Hernández-Triana, J. M. Medlock, A. R. Fooks, S. Carpenter and N. Johnson, The Role of *Culex pipiens* L. (Diptera: Culicidae) in Virus Transmission in Europe, *Int. J. Environ. Res. Publ. Health*, 2018, **15**, 389–394, DOI: [10.3390/ijerph15020389](https://doi.org/10.3390/ijerph15020389).
- 21 E. K. Jang, B. K. Jung, G. S. Park, A. R. Khan, S. J. Hong, Y. J. Park, W. C. Kim, J. H. Shin, K. M. S. Al-Ghamdi, B. O. Al-Johny, Y. Anwar, M. F. Siddiqui and I. Ullah, Cloning and expression of the insecticidal toxin gene “tccB” from *Photobacterium temperata* M1021 in *Escherichia coli* expression system, *J. Asia-Pac. Entomol.*, 2020, **23**(1), 172–176.
- 22 M. U. Rehman, S. Rashid, A. Arafah, W. Qamar, R. M. Alsaffar, A. Ahmad, N. M. Almatroudi, S. M. A. Alqahtani, S. M. Rashid and S. B. Ahmad, RETRACTED: Piperine Regulates Nrf-2/Keap-1 Signalling and Exhibits Anticancer Effect in Experimental Colon Carcinogenesis in Wistar Rats, *Biology*, 2020, **9**, 302, DOI: [10.3390/biology9090302](https://doi.org/10.3390/biology9090302).
- 23 N. Becker, D. Petric, M. Zgomba, C. Boase, C. Dahl, M. Madon and A. Kaiser, *Mosquitoes and Their Control*, Springer, Berlin/Heidelberg, 2010, p. 577.
- 24 M. H. Hekal, Y. M. Ali, D. R. Abdel-Haleem and F. S. M. Abu El-Azm, Diversity oriented synthesis and SAR studies of new quinazolinones and related compounds as insecticidal agents against *Culex pipiens* L. larvae and associated predator, *Bioorg. Chem.*, 2023, **133**, 106436.
- 25 J. P. Martínez-Mercado, A. Sierra-Santoyo, F. A. Verdín-Betancourt, A. E. Rojas-García and B. Quintanilla-Vega, Temephos, an organophosphate larvicide for residential use: a review of its toxicity, *Crit. Rev. Toxicol.*, 2022, **52**(2), 113–124, DOI: [10.1080/10408444.2022.2065967](https://doi.org/10.1080/10408444.2022.2065967).
- 26 S. C. Weaver, C. Charlier, N. Vasilakis and M. Lecuit, Zika, Chikungunya, and other emerging vector-borne viral diseases, *Annu. Rev. Med.*, 2018, **69**, 395–408.
- 27 G. Benelli, C. L. Jeffries and T. Walker, Biological Control of Mosquito Vectors: Past, Present, and Future, *Insects*, 2016, **7**(4), 52, DOI: [10.3390/insects7040052](https://doi.org/10.3390/insects7040052).
- 28 H. E. D. M. Zahran, H. K. Abou-Taleb and S. A. M. Abdelgaleil, Adulticidal, larvicidal and biochemical properties of essential oils against *Culex pipiens* L., *J. Asia-Pac. Entomol.*, 2017, **20**(1), 133–139.
- 29 Y. J. Zhu, X. F. Guo, Z. J. Fan, L. Chen, L. Y. Ma, H. X. Wang, Y. Wei, X. M. Xu, J. P. Lin and V. A. Bakulev, Approach to thiazole-containing tetrahydropyridines via Aza-Rauhut–Currier reaction and their potent fungicidal and insecticidal activity, *RSC Adv.*, 2016, **6**(113), 112704–112711.
- 30 A. A. Garza-Robledo, J. F. Martínez-Perales, V. A. Rodríguez-Castro and H. Quiroz-Martínez, Effectiveness of spinosad and temephos for the control of mosquito larvae at a tire dump in Allende, Nuevo Leon, Mexico, *J. Am. Mosq. Control Assoc.*, 2011, **27**(4), 404–407.
- 31 A. H. Tantawy, S. M. Farag, L. Hegazy, H. Jiang and M. Q. Wang, The larvicidal activity of natural inspired piperine-based dienehydrazides against *Culex pipiens*, *Bioorg. Chem.*, 2020, **94**, 103464, DOI: [10.1016/j.bioorg.2019.103464](https://doi.org/10.1016/j.bioorg.2019.103464).
- 32 A. H. Tantawy, M. M. Shaban, H. Jiang, M. Q. Wang and H. I. Mohamed, Construction, petroleum-collecting/dispersing capacities, antimicrobial activity, and molecular docking study of new cationic surfactant-sulfonamide conjugates, *J. Mol. Liq.*, 2021, **334**, 116068, DOI: [10.1016/j.molliq.2021.116068](https://doi.org/10.1016/j.molliq.2021.116068).
- 33 C. Yang, X. Li, J. Wei, F. Zhu, F. Gang, S. Wei, Y. Zhao, J. Zhang and W. Wu, Synthesis and insecticidal activity in vitro and vivo of novel benzenesulfonyl derivatives based on potent target subunit H of V-ATPase, *Bioorg. Med. Chem. Lett.*, 2018, **28**(19), 3164–3167.
- 34 E. Rosatelli, A. Carotti, M. Ceruso, C. T. Supuran and A. Gioiello, Flow synthesis and biological activity of aryl sulfonamides as selective carbonic anhydrase IX and XII inhibitors, *Bioorg. Med. Chem. Lett.*, 2014, **24**(15), 3422–3425.
- 35 D. Song, J. S. Yang, S. J. Kim, B. K. Kim, S. K. Park, M. Won, K. Lee, H. M. Kim, K. Y. Choi, K. Lee and G. Han, Design, synthesis and biological evaluation of novel aliphatic amido/sulfonamido-quaternary ammonium salts as antitumor agents, *Bioorg. Med. Chem.*, 2013, **21**(3), 788–794.
- 36 D. Song, J. S. Yang, C. Oh, S. Cui, B. K. Kim, M. Won, J. I. Lee, H. M. Kim and G. Han, New synthetic aliphatic sulfonamido-quaternary ammonium salts as anticancer chemotherapeutic agents, *Eur. J. Med. Chem.*, 2013, **69**, 670–677.
- 37 S. M. El-Saeed, R. K. Farag, M. E. Abdul-Raouf and A. A. A. Abdel-Azim, Synthesis and Characterization of Novel Crude Oil Dispersants Based on Ethoxylated Schiff Base, *Int. J. Polym. Mater. Polym. Biomater.*, 2008, **57**, 860–877.
- 38 C. Cojocar, M. Macoveanu and I. Cretescu, Peat-based sorbents for the removal of oil spills from water surface: application of artificial neural network modeling, *Colloids Surf., A*, 2011, **384**, 675–684.
- 39 F. Peeters, R. Kipfer, D. Achermann, M. Hofer, W. Aeschbach-Hertig, U. Beyerle, D. M. Imboden, K. Rozanski and K. Fröhlich, Analysis of deep-water exchange in the Caspian Sea based on environmental tracers, *Deep Sea Res., Part I*, 2000, **47**, 621–654.
- 40 S. W. Jung, O. Y. Kwon, C. K. Joo, J. H. Kang, M. Kim, W. J. Shim and Y. O. Kim, Stronger impact of dispersant plus crude oil on natural plankton assemblages in short-term marine mesocosms, *J. Hazard. Mater.*, 2012, **217–218**, 338–349, DOI: [10.1016/j.jhazmat.2012.03.034](https://doi.org/10.1016/j.jhazmat.2012.03.034).
- 41 M. Abo-Riya, A. H. Tantawy and W. El-Dougdoug, Synthesis and evaluation of novel cationic gemini surfactants based on Guava crude fat as petroleum-collecting and dispersing agents, *J. Mol. Liq.*, 2016, **221**, 642–650, DOI: [10.1016/j.molliq.2016.05.083](https://doi.org/10.1016/j.molliq.2016.05.083).
- 42 Z. H. Asadov, A. H. Tantawy, I. A. Zarbaliyeva and R. A. Rahimov, Petroleum-Collecting and Dispersing Complexes Based on Oleic Acid and Nitrogenous Compounds as Surface-Active Agents for Removing Thin Petroleum Films from Water Surface, *J. Oleo Sci.*, 2012, **61**, 621–630, DOI: [10.5650/jos.61.621](https://doi.org/10.5650/jos.61.621).



- 43 H. I. Mohamed, M. Z. Basyouni, A. A. Khalil, K. A. Hebash and A. H. Tantawy, Petroleum-dispersing and antimicrobial activity of newly synthesized polymeric surfactants tethering tetrachlorophthalimide moiety, *J. Iran. Chem. Soc.*, 2021, **18**, 265–274.
- 44 A. H. Tantawy, H. I. Mohamed, A. A. Khalil, K. A. Hebash and M. Z. Basyouni, Novel bioactive imidazole-containing polymeric surfactants as petroleum-collecting and dispersing agents: synthesis and surface-active properties, *J. Mol. Liq.*, 2017, **236**, 376–384, DOI: [10.1016/j.molliq.2017.04.040](https://doi.org/10.1016/j.molliq.2017.04.040).
- 45 S. M. Farag, O. M. H. M. Kamel, A. A. El-Sayed, A. E. Abdelhamid and D. R. Abdel-Haleem, Green synthesis of ZnO and Se nanoparticles based on *Achillea fragrantissima* (Forssk.) extract and their larvicidal, biological and ultrastructural impacts on *Culex pipiens* Linnaeus, Egypt, *J. Aquat. Biol. Fish.*, 2023, **27**(2), 773–794, DOI: [10.21608/ejabf.2023.297695](https://doi.org/10.21608/ejabf.2023.297695).
- 46 World Health Organization (WHO), Guidelines for laboratory and field testing of mosquito larvicides, *Bull. World Health Organ.*, 2005, 1–4.
- 47 D. J. Finney, Quantal responses to mixtures, in *Probit Analysis*, Cambridge University Press, 3rd edn, 1971, pp. 230–268.
- 48 S. A. Dharaskar, K. L. Wasewar, M. N. Varma, D. Z. Shende and C. Yoo, Synthesis, characterization and application of 1-butyl-3-methylimidazolium tetrafluoroborate for extractive desulfurization of liquid fuel, *Arab. J. Chem.*, 2016, **9**(4), 578–587, DOI: [10.1016/j.arabjc.2013.09.034](https://doi.org/10.1016/j.arabjc.2013.09.034).
- 49 A. H. Tantawy, S. M. Farag, D. R. Abdel-Haleem and H. I. Mohamed, Facile synthesis, larvicidal activity, biological effects, and molecular docking of sulfonamide-incorporating quaternary ammonium iodides as acetylcholinesterase inhibitors against *Culex pipiens* L, *Bioorg. Chem.*, 2022, **128**, 106098, DOI: [10.1016/j.bioorg.2022.106098](https://doi.org/10.1016/j.bioorg.2022.106098).
- 50 M. Fingas and C. E. Brown, A Review of Oil Spill Remote Sensing, *Sensors*, 2018, **18**, 91, DOI: [10.1016/j.marpolbul.2014.03.059](https://doi.org/10.1016/j.marpolbul.2014.03.059).
- 51 J. L. Gray, L. K. Kanagy, E. T. Furlong, C. J. Kanagy, J. W. McCoy, A. Mason and G. Lauenstein, Presence of the Corexit component dioctyl sodium sulfosuccinate in Gulf of Mexico waters after the 2010 Deepwater Horizon oil spill, *Chemosphere*, 2014, **95**, 124–130, DOI: [10.1016/j.chemosphere.2013.08.049](https://doi.org/10.1016/j.chemosphere.2013.08.049).
- 52 A. H. Tantawy, M. M. Shaban, H. Jiang, M. Q. Wang and H. I. Mohamed, Construction, petro-collecting/dispersing capacities, antimicrobial activity, and molecular docking study of new cationic surfactant-sulfonamide conjugates, *J. Mol. Liq.*, 2021, **334**, 116068, DOI: [10.1016/j.molliq.2021.116068](https://doi.org/10.1016/j.molliq.2021.116068).
- 53 A. H. Tantawy, H. I. Mohamed, A. A. Khalil, K. A. Hebash and M. Z. Basyouni, Novel bioactive imidazole-containing polymeric surfactants as petroleum-collecting and dispersing agents: synthesis and surface-active properties, *J. Mol. Liq.*, 2017, **236**, 376–384, DOI: [10.1016/j.molliq.2017.04.040](https://doi.org/10.1016/j.molliq.2017.04.040).
- 54 M. A. Abo-Riya, L. M. Reda, A. H. Tantawy and A. M. Metwally, Novel cationic copolymeric surfactants bearing imidazole moiety as petro-dispersing/petro-collecting agents: synthesis, surface activity and characterization, *J. Mol. Liq.*, 2022, **364**, 120057, DOI: [10.1016/j.molliq.2022.120057](https://doi.org/10.1016/j.molliq.2022.120057).
- 55 J. Pernak, J. Nawrot, M. Kot, B. Markiewicz and M. Niemczak, Ionic liquids based stored product insect antifeedants, *RSC Adv.*, 2013, **3**(47), 25019–25029, DOI: [10.1039/C3RA41716F](https://doi.org/10.1039/C3RA41716F).
- 56 W. Stachowiak, T. Rzemieniecki, T. Klejdysz, J. Pernak and M. Niemczak, “Sweet” ionic liquids comprising the acesulfame anion–synthesis, physicochemical properties and antifeedant activity towards stored product insects, *New J. Chem.*, 2020, **44**(17), 7017–7028, DOI: [10.1039/C9NJ06005G](https://doi.org/10.1039/C9NJ06005G).
- 57 D. K. Kaczmarek, D. Gwiazdowska, K. Marchwińska, T. Klejdysz, M. Wojcieszak, K. Materna and J. Pernak, Amino acid-based dicationic ionic liquids as complex crop protection agents, *J. Mol. Liq.*, 2022, **360**, 119357, DOI: [10.1016/j.molliq.2022.119357](https://doi.org/10.1016/j.molliq.2022.119357).
- 58 J. Brari and S. Thakur, Bioactivity of an Ionic Liquid against Two Major Coleopteran Stored Grain Insect Pests, *Int. J. Pharm. Biol. Sci. Arch.*, 2021, **12**(4), 163–169.
- 59 J. Brari and D. R. Thakur, Insecticidal potential properties of citronellol derived ionic liquid against two major stored grain insect pests, *J. Entomol. Zool. Stud.*, 2016, **4**(3), 365–370.
- 60 R. Ibrahim, S. Alahmadi, A. Almarwani, D. Shower and M. Ali, Do aminopyridinium-based ionic liquids promising to control *Culex pipiens* mosquitoes in the future?, *J. Asia-Pac. Entomol.*, 2020, **23**(4), 1130–1137, DOI: [10.1016/j.aspen.2020.09.007](https://doi.org/10.1016/j.aspen.2020.09.007).
- 61 R. Cavanagh, S. Shubber, D. Vllasaliu and S. Stolnik, Enhanced permeation by amphiphilic surfactant is spatially heterogenous at membrane and cell level, *J. Contr. Release*, 2022, **23**(4), 734–743, DOI: [10.1016/j.jconrel.2022.03.053](https://doi.org/10.1016/j.jconrel.2022.03.053).
- 62 S. I. Kusakari, Y. Matsuda and H. Toyoda, Electrostatic Insect Repulsion, Capture, and Arc-Discharge Techniques for Physical Pest Management in Greenhouses, *Agronomy*, 2022, **13**(1), 23, DOI: [10.3390/agronomy13010023](https://doi.org/10.3390/agronomy13010023).
- 63 S. I. Elewa, D. R. Abdel-Haleem, A. H. Tantawy, H. I. Mohamed and W. H. Lashin, Exploring the larvicidal and pupicidal activities of new functionalized pyridines against *Culex pipiens* L. Referring to molecular docking and SAR studies, *Bioorg. Chem.*, 2025, **157**, 108283, DOI: [10.1016/j.bioorg.2025.108283](https://doi.org/10.1016/j.bioorg.2025.108283).

