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Synthesis of quarternary ammonium salts with dithiocarbamate moiety and their antifungal activities against *Helminthosporium oryzae*

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Abstract. Quaternary ammonium salts containing dithiocarbamate moiety were synthesized and evaluated for their antifungal activities against *Helminthosporium oryzae*. All the synthesized compounds showed moderate to promising fungitoxicity against the test. Some of the synthesized compounds inflicted antifungal activity greater than the standard fungicide.

Keywords. Dithiocarbamate; *Helminthosporium oryzae*; antifungal evaluation; QUATS.

1. Introduction

QUATS are emerging as new biopotential molecules. They have proven their efficacy in the fields of pharmaceuticals,[1] as anticancer, antiviral, antiparasitic, antifungal and antibacterial agents,[2] as agrochemicals[3] and as potential wood preservatives.[4] Correlation of QUATS with antifungal activity is related to fungal phospholipase inhibition.[5] Dithiocarbamates, on the other hand, are widely used as standard fungicides (Metam, Maneb, Mancozeb, Ferbam, methylene-*bis*(dithiocarbamate) against variety of diseases in agriculture. They act as multisite contact fungicides that work by protecting the plant surface to prevent infection.[6] They are converted to various salts to improve their solubility and biological potential. The present work is aimed to combine two potential antifungal moieties viz dithiocarbamate and quaternary ammonium salts in a single molecule and to evaluate the effectiveness of newly synthesized compounds as fungicides.

2. Experimental

2.1 *General*

All the melting points were determined in open capillary tubes and are uncorrected. PMR spectra were taken in $CDCl_3$ on BURKER AVANCE II 400 NMR spectrometer at SAIF, Punjab University, Chandigarh and IR spectra were recorded as neat liquid on Perkin Elmer-800 spectrometer. Purity of newly synthesized compounds was checked by TLC. Test fungi *Helminthosporium oryzae* is procured from Department of Plant Pathology, PAU, Ludhiana.

2.2 *Synthesis*

2.2a *Synthesis of sodium dialkyl or cycloamine-aminedithiocarbamates* (**1**): NaOH (0.1 mol, 4 g) in minimum quantity of water (2–3 ml) was taken in 500 ml, 3-necked, round bottom flask equipped with magnetic stirrer bar, a 100 ml pressure equalizing additional funnel and a double walled condenser. Diethyl amine (7.3 g, 0.1 mol) was added, followed by diethyl ether (125 ml) under continuous stirring. After 30 min, the temperature of the system was decreased to 0°C and the additional funnel charged with CS_2, added to the reaction mixture over a period of 10 min and stirring was continued for 1 h. Bluffy mass that appeared was filtered and dissolved in acetone. This separates out the red oily mass of polysulphide formed during the course of reaction. The two layers of oil and acetone were separated by separating funnel. The acetone layer was concentrated to 1/3rd of its original volume and sodium diethyldithiocarbamate was precipitated out by addition of diethyl ether. The precipitates were dissolved again in minimum quantity of acetone and re-precipitated by addition of diethyl ether. The sodium diethyldithiocarbamate (**1a**) was finally washed with benzene to remove any non-polar impurities.

Similar procedure was followed for the synthesis of sodium diisopropylaminedithiocarbamate (**1b**) and sodium piperidinedithiocarbamate (**Ic**) using diisopropyl amine and piperidine,[8] respectively.

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2.2b *Synthesis of oxiran-2-ylmethyl dialkylcarbamodithioates* (**2**): Sodium diethyldithiocarbamate (**1a**) (5.13 g, 0.03 mol) and epichlorohydrin (120 ml) were refluxed under stirring for 13 h. the reaction mixture was filtered. The filterate was concentrated and residue was extracted with benzene. The organic phase was washed with 10% NaOH (50 ml), water, saturated aqueous NaCl, dried and concentrated to get epoxy compound oxiran-2-ylmethyl diethylcarbamodithioate (**2a**).

Similar procedure was followed for the synthesis of oxiran-2-ylmethyl diisopropylcarbamodithioate (**2b**) and oxiran-2-ylmethyl piperidine-1-carbodithioate (**2c**) by using **1b** and **1c** respectively.[9]

2.2c *Synthesis of 3-(dialkylamino)-2-hydroxypropyl diethylcarbamodithioates* (**3–5**): A mixture of epoxide **2a** (3.38 g, 0.0165 mol), diethylamines (6.32 g, 0.0827 mol) and absolute alcohol (35 ml) was refluxed over water bath for 2 h with constant stirring. The excess of ethanol was distilled off. The residue was diluted with water and extracted with ether. The ether extract was dried over anhyd. Na_2SO_4 and ether was removed by distillation to get tertiary amine (**3**).

Similar procedure was followed for the synthesis of **4** and **5** with compounds **2b** and **2c** by treating them with diisopropylamine and piperidine, respectively.

2.2d *Synthesis of N-(3-(dialkylcarbamothioylthio)-2-hydroxypropyl)-N,N-diethylpentan-1-aminium bromides* (**3a–c**, **4a–c**, **5a–c**): The mixture of t-amine (**3**), (1.9 g, 0.007 mol) and *n*-bromopentane (5.28 g, 0.035 mol), dissolved in dry acetone (10 ml), was refluxed for 4 h on water bath. Excess of solvent was distilled off; the residue was scratched with anhydrous ether (to remove unreacted amine, if any) and ether was decanted off to get quaternary salt of ammonia N-(3-(diethylcarbamothioylthio)-2-hydroxypropyl)-N,N-diethylpentan-1-aminium bromide (**3a**). Following the same procedure synthesis of N-(3-(diethylcarbamothioylthio)-2-hydroxypropyl)-N,N-diethylhexan-1-aminium bromide (**3b**) and N-(3-(diethylcarbamothioylthio)-2-hydroxypropyl)-N,N-diethylhexadecan-1-aminium bromide (**3c**) were carried out by treating **3** with *n*-bromohexane and *n*-bromohexadecane, respectively.

N-(3-(diisopropylcarbamothioylthio)-2-hydroxypropyl)-N,N-diisopropylpentan-1-aminium bromide (**4a**), N-(3-(diisopropylcarbamothioylthio)-2-hydroxypropyl)-N,N-diisopropylhexan-1-aminium bromide (**4b**), N-(3-(diisopropylcarbamothioylthio)-2-hydroxypropyl)-N,N-diisopropylhexadecan-1-aminium bromide bromide (**4c**), 1-(2-hydroxy-3-(piperidine-1-carbonothioylthio) propyl)-1-pentylpiperidinium bromide (**5a**), 1-hexyl-1-(2-hydroxy-3-(piperidine-1-carbonothioylthio)propyl) piperidinium bromide (**5b**) and 1-hexadecyl-1-(2-hydroxy-3-(piperidine-1-carbonothioylthio) propyl) piperidinium bromide (**5c**) were synthesized following the similar procedure treating compounds **4** and **5** with *n*-bromopentane *n*-bromohexane and *n*-bromohexadecane, respectively. All of them gave positive copper wire test.

2.3 *In vitro screening for fungitoxicity*

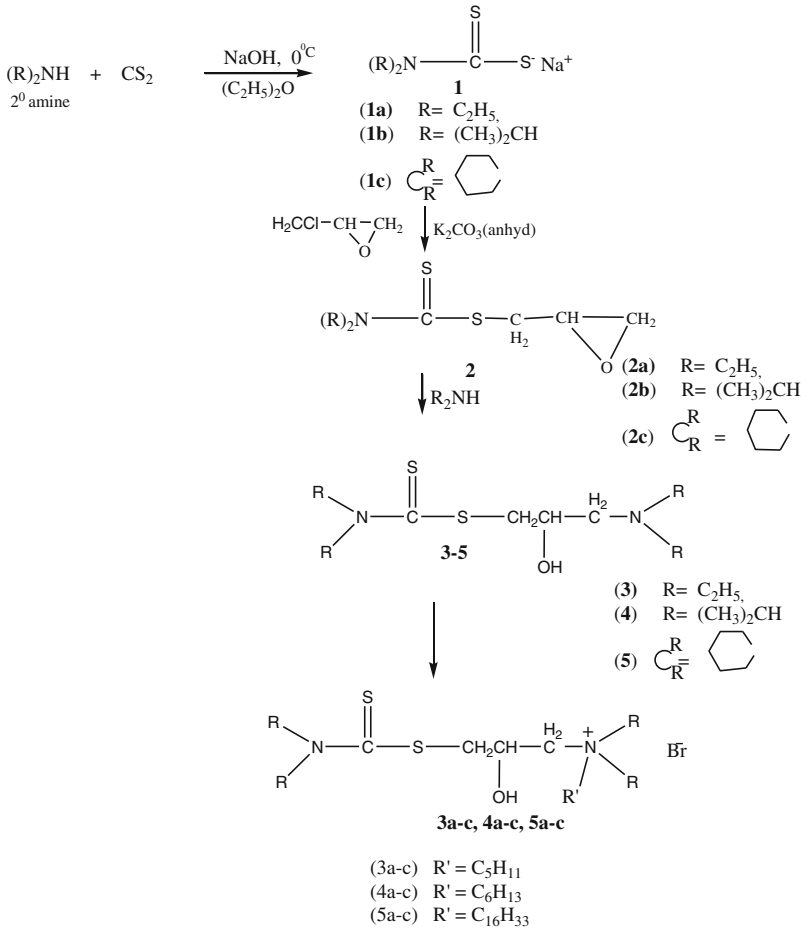
Stock solution of the test compounds and fungicide Indofil M-45 (methyl-2-benzimidazole carbamate) was prepared by dissolving each chemical in absolute alcohol (0.5) and making up the final volume to 10 ml with sterilized distilled water. Stock solution of 2000 µg/mL, thus, prepared on active ingredient basis were kept in refrigerator till further use to prepare the solution of required concentration.

Actively growing 10 days old culture of the test fungi were taken from PDA (Potato Dextrose Agar) slants and spore suspension was made by addition of sterilized distilled water. The suspension was filtered through three layers of sterilized cheese cloth under aseptic conditions in order to remove agar bits and mycelium. Haemocytometer was used to get spore suspension (1×10^6 spores/mL).

Small droplets (0.02 mL) of the test solution and spore suspension in equal amount were seeded in the cavity slides. These slides were kept in petriplates lined with moist filter paper and incubated for 24 h at 25 ± 1°C. the slides were checked for germination[10] and percent spore germination inhibition was determined from which ED_{50} values were calculated using Polo Software Program.

3. Result and discussion

Nine novel quaternary ammonia salts having dialkyldithiocarbamate moieties were synthesized by reacting different alkyl halides (*n*-bromopentane, *n*-bromohexane, *n*-bromohexadecane) with the synthesized tertiary amines (**3a–c**) under experimental conditions. **3a–c** were prepared through by the reaction of the epoxy compounds (**2a–c**) with appropriate secondary amines to yield corresponding tertiary amines with dialkyldithiocarbamate moiety (**3a–c**). Epoxy compounds (**2a–c**) were synthesized from appropriate sodium salt of dialiphatic or cycloalkyl dithiocarbamate (**1a–c**) with epichlorohydrin. General scheme for



Scheme 1. Diagrammatic representation of the reaction sequence.

preparation of QUATS with dialkyl or cyclic dithiocarbamate moiety is given in scheme 1. The physical characteristics and elemental analysis of quarternary ammonium salts are given in table 1.

3.1 *Spectral analysis*

The products were characterized on the basis of IR, spectral studies and mixed melting point determination.

3.1a *3-(Diethylamino)-2-hydroxypropyl diethylcarbamodithioate (***3***)*: ν max(cm^{-1}): 3435, 2873, 2970, 2812, 2934, 1381, 1071, 860, 665.

^{1}H NMR signals ($CDCl_3$, 400 MHz) of tertiary amine (**4**) δ at: **CH**-OH (δ 3.69–3.72, m, 1H), N-C**H**$_2$CH$_3$ (δ 2.52–2.55, m, 8H), NC**H**$_2$CH$_3$ (δ 1.18, t, 12H), CH(OH)-C**H**$_2$N (δ 2.43, d, 2H, J = 6.4 Hz), S-C**H**$_2$ (δ 3.22, d, 2H, J = 7.6 Hz), CH(O**H**) (δ 3.4, s, 1H).

3.1b *3-(Diisopropylamino)-2-hydroxypropyl diisopropylcarbamodithioate* (**4**): ν max(cm^{-1}): 3445, 2933, 2971, 2933, 2877, 2917, 1285, 1037, 913, 819, 668.

^{1}H NMR signals($CDCl_3$, 400 MHz) of tertiary amine (**2b**): C**H**(OH)(δ 3.61–3.67, m, 1H), CH(OH)-C**H**$_2$-N (δ 2.45, d, 2H, J = 6.2 Hz), CH$_3$-C**H**-CH$_3$ (δ 2.93–2.98, m, 1H), C**H**$_3$-CH-C**H**$_3$ (δ 1.03, d, 12H, J = 6.28 Hz), S-C**H**$_2$ (δ 3.24, d, 2H, J = 8.6 Hz), CH(O**H**) (δ 3.43, s, 1H).

3.1c *2-Hydroxy-3-(piperidin-1-yl)propyl piperidine-1-carbodithioate* (**5**): ν max(cm^{-1}): 3368, 2935, 2855, 1277, 1041, 997, 675.

^{1}H NMR signals ($CDCl_3$, 400 MHz): C**H**(OH) (δ 3.85–3.91, m), N-C**H**$_2$-C**H**$_2$-C**H**$_2$-CH$_2$ (δ 1.55–1.64, m, 12H), N-C**H**$_2$-CH$_2$ (δ 2.27, t, 8H), N-C**H**$_2$ (δ 2.46, d, 2H, J = 8.8 Hz), S-CH$_2$ (δ 3.69, d, 2H, J = 7.2 Hz), CH(O**H**) (δ 3.46, s, 1H).

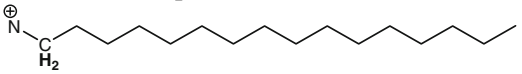
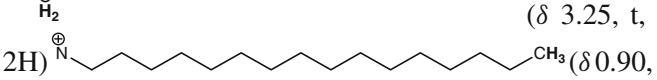
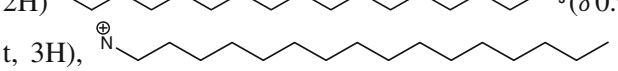
3.1d *N-(3-(diethylcarbamothioylthio)-2-hydroxypropyl)-N,N-diethylpentan-1-aminium bromide* (**3a**): ^{1}H NMR signals ($CDCl_3$, 400 MHz): δ at: C**H**-OH (δ 3.69–3.72,

Table 1. Physical characteristics of N-(3-(dialkylcarbamothioylthio)-2-hydroxypropyl)-N,N-diethylpentan-1-aminium bromides.

					Elemental analysis calculated % (found)			
Compd	R	R′	M.P (°C)	Yield (%)	C	H	N	S
3a	C_2H_5	C_5H_{11}	Liq	73	47.54 (47.55)	8.68 (8.65)	6.52 (6.55)	14.9 (14.7)
3b	C_2H_5	C_5H_{11}	Liq	80	48.52 (48.55)	9.27 (9.24)	6.29 (6.27)	14.39 (14.41)
3c	C_2H_5	C_5H_{11}	Liq	82	57.60 (57.58)	10.19 (10.21)	4.80 (4.81)	10.98 (10.97)
4a	$(CH_3)_2CH$-	C_6H_{13}	Liq	86	51.94 (51.93)	9.34 (9.35)	5.77 (5.78)	13.21 (13.20)
4b	$(CH_3)_2CH$	C_6H_{13}	Liq	84	52.88 (52.60)	9.42 (9.70)	5.61 (5.59)	12.83 (12.85)
4c	$(CH_3)_2CH$	C_6H_{13}	Liq	71	60.06 (60.04)	10.55 (10.56)	4.38 (4.39)	10.02 (10.01)
5a		$C_{16}H_{33}$	Liq	85	47.99 (48.00)	7.82 (7.80)	6.58 (6.60)	15.07 (15.08)
5b		$C_{16}H_{33}$	Liq	80	49.19 (49.20)	8.03 (8.00)	6.37 (6.40)	14.59 (14.60)
5c		$C_{16}H_{33}$	Liq	78	58.00 (58.00)	9.56 (9.59)	4.83 (4.80)	11.06 (11.03)

m, 1H), N-C**H**$_2$CH$_3$ (δ 2.58, q, 4H), N-CH$_2$C**H**$_3$ (δ 1.10, t, 6H), CH(OH)-C**H**$_2$-N$^+$ (δ 3.50, 3.27, dd, 2H, J = 6.4 Hz), S-C**H**$_2$ (δ 3.14, 2.88 dd, 2H, J = 7.6 Hz), CH(O**H**) (δ 4.8, s, 1H), CH$_3$-C**H**$_2$-N$^+$ (δ 3.30, q, 4H), C**H**$_3$-CH$_2$-N$^+$ (δ 1.25, t, 6H), C**H**$_3$- CH$_2$- CH$_2$- CH$_2$ - CH$_2$-N$^+$ (δ 0.95, t, 3H), CH$_3$- C**H**$_2$- CH$_2$- CH$_2$ - CH$_2$-N$^+$ (δ 1.33, m, 2H), CH$_3$- CH$_2$- CH$_2$- C**H**$_2$ - CH$_2$-N$^+$ (δ 1.29, m, 2H), CH$_3$- CH$_2$- CH$_2$- C**H**$_2$ - CH2-N$^+$ (δ 1.74, m, 2H), CH$_3$- CH$_2$- CH$_2$- CH$_2$ - C**H**$_2$-N$^+$ (δ 3.30, t, 2H).

3.1e *N-(3-(diethylcarbamothioylthio)-2-hydroxypropyl)-N,N-diethylhexan-1-aminium bromide* (**3b**): ^{1}H NMR signals (CDCl$_3$, 400 MHz): δ at: C**H**-OH (δ 3.69–3.72, m, 1H), N-C**H**$_2$CH$_3$ (δ 2.58, q, 4H), N-CH$_2$C**H**$_3$ (δ 1.10, t, 6H), CH(OH)-C**H**$_2$-N$^+$ (δ 3.50, 3.27, dd, 2H, J = 6.4 Hz), S-C**H**$_2$ (δ 3.14, 2.88 dd, 2H, J = 7.6 Hz), CH(O**H**) (δ 4.8, s, 1H), CH$_3$-C**H**$_2$-N$^+$ (δ 3.30, q, 4H), CH$_3$-CH$_2$-N$^+$ (δ 1.25, t, 6H), C**H**$_3$- CH$_2$- CH$_2$-CH$_2$ -CH$_2$ -CH$_2$-N$^+$ (δ 0.95, t, 3H), CH$_3$- C**H**$_2$- CH$_2$-CH$_2$ -CH$_2$ -CH$_2$-N$^+$ (δ 1.33, m, 2H), CH$_3$- CH$_2$- C**H**$_2$-CH$_2$ -CH$_2$ -CH$_2$-N$^+$ (δ 1.29, m, 2H), CH$_3$- CH$_2$- CH$_2$-CH$_2$ -C**H**$_2$ -CH2-N$^+$ (δ 1.29, m, 2H) CH$_3$- CH$_2$- CH$_2$-CH$_2$ -C**H**$_2$ -CH$_2$-N$^+$ (δ 1.74, m, 2H), CH$_3$- CH$_2$- CH$_2$-CH$_2$ -CH$_2$ -C**H**$_2$-N$^+$ (δ 3.30, t, 2H).

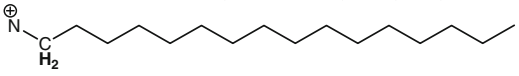
3.1f *N-(3-(diethylcarbamothioylthio)-2-hydroxypropyl)-N,N-diethylhexadecan-1-aminium bromide* (**3c**): ^{1}H NMR signals (CDCl$_3$, 400 MHz): δ at: C**H**-OH (δ 3.69–3.72, m, 1H), N-C**H**$_2$CH$_3$ (δ 2.58, q, 4H), N-CH$_2$C**H**$_3$ (δ 1.10, t, 6H), CH(OH)-C**H**$_2$-N$^+$ (δ 3.50, 3.27, dd, 2H, J = 6.4 Hz), S-C**H**$_2$ (δ 3.14, 2.88 dd, 2H, J = 7.6 Hz), CH(O**H**) (δ 4.8, s, 1H), CH$_3$-C**H**$_2$-N$^+$ (δ 3.30, q, 4H), C**H**$_3$-CH$_2$-N$^+$ (δ 1.25, t, 6H),  (δ 3.25, t, 2H)  (δ 0.90, t, 3H),  (δ 1.27–1.72, m, 26H).

3.1g *N-(3-(diisopropylcarbamothioylthio)-2-hydroxypropyl)-N,N-diisopropylpentan-1-aminium bromide* (**4a**): ^{1}H NMR signals (CDCl$_3$, 400 MHz): δ at: C**H**-OH (δ 3.69–3.72, m, 1H), N-C**H**(CH$_3$)$_2$ (δ 2.80–2.97, m, 2H), N- CH(C**H**$_3$)$_2$ (δ 1.06, d, 12H), CH(OH)-C**H**$_2$-N$^+$ (δ 3.50, 3.27, dd, 2H, J = 6.4 Hz), S-C**H**$_2$ (δ 3.14, 2.88 dd, 2H, J = 7.6 Hz), CH(O**H**) (δ 4.8, s, 1H), N$^+$C**H**(CH$_3$)$_2$ (δ 3.90–3.92, m, 2H), N$^+$CH(C**H**$_3$)$_2$ (δ 1.29, d t, 6H), C**H**$_3$- CH$_2$- CH$_2$- CH$_2$ - CH$_2$-N$^+$ (δ 0.95, t, 3H), CH$_3$- C**H**$_2$- CH$_2$- CH$_2$ - CH$_2$-N$^+$ (δ 1.33, m, 2H), CH$_3$- C**H**$_2$- CH$_2$- CH$_2$ - CH$_2$-N$^+$ (δ 1.29, m, 2H), CH$_3$- CH$_2$- CH$_2$- C**H**$_2$ - CH2-N$^+$ (δ 1.74, m, 2H), CH$_3$- CH$_2$- CH$_2$- CH$_2$ - C**H**$_2$-N$^+$ (δ 3.30, t, 2H).

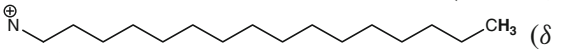
3.1h *N-(3-(diisopropylcarbamothioylthio)-2-hydroxypropyl)-N,N-diisopropylhexan-1-aminium bromide* (**4b**): ^{1}H NMR signals (CDCl$_3$, 400 MHz): δ at: C**H**-OH (δ 3.69–3.72, m, 1H), N-C**H**(CH$_3$)$_2$ (δ 2.80–2.97, m, 2H), N- CH(C**H**$_3$)$_2$ (δ 1.06, d, 12H), CH(OH)-C**H**$_2$-N$^+$ (δ 3.50, 3.27, dd, 2H, J = 6.4 Hz), S-C**H**$_2$ (δ 3.14, 2.88 dd, 2H, J = 7.6 Hz), CH(O**H**) (δ 4.8, s, 1H), N$^+$C**H**(CH$_3$)$_2$ (δ 3.90–3.92, m, 2H), N$^+$CH(C**H**$_3$)$_2$ (δ

1.29, d t, 6H), C**H**$_3$- CH_2- CH_2-CH_2 -CH_2 -CH_2-N^+ (δ 0.95, t, 3H), CH_3- C**H**$_2$- CH_2-CH_2 -CH_2 -CH_2-N^+ (δ 1.33, m, 2H), CH_3- CH_2- C**H**$_2$-CH_2 -CH_2 -CH_2-N^+ (δ 1.29, m, 2H), CH_3- CH_2- C**H**$_2$-CH_2 -CH_2 -CH_2-N^+ (δ 1.29, m, 2H) CH_3- CH_2- CH_2-CH_2 -C**H**$_2$ -CH_2-N^+ (δ 1.74, m, 2H), C**H**$_3$- CH_2- CH_2-CH_2 -CH_2 -C**H**$_2$-N^+ (δ 3.30, t, 2H).

3.1i *N-(3-(diisopropylcarbamothioylthio)-2-hydroxypropyl)-N,N-diisopropylhexadecan-1 aminium bromide bromide* (**4c**): ^{1}H NMR signals ($CDCl_3$, 400 MHz): δ at: C**H**-OH (δ 3.69–3.72, m, 1H), N-C**H**$(CH_3)_2$ (δ 2.80–2.97, m, 2H), N- CH(C**H**$_3)_2$ (δ 1.06, d, 12H), CH(OH)-C**H**$_2$-N^+ (δ 3.50, 3.27, dd, 2H, J = 6.4 Hz), S-C**H**$_2$ (δ 3.14, 2.88 dd, 2H, J = 7.6 Hz), CH(O**H**) (δ 4.8, s, 1H), N^+C**H**$(CH_3)_2$ (δ 3.90–3.92, m, 2H), $N^+CH(CH_3)_2$ (δ 1.29,d t, 6H),



(δ 3.25, t, 2H),



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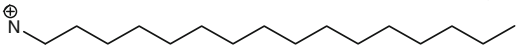
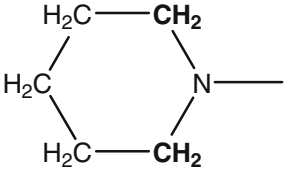
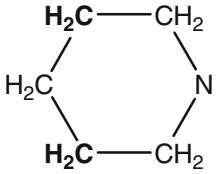


(δ 1.27–1.72, m, 26H).

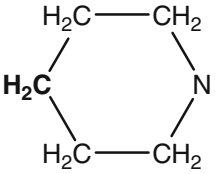
3.1j *1-(2-Hydroxy-3-(piperidine-1-carbonothioylthio)-propyl)-1-pentylpiperidinium bromide* (**5a**):: ^{1}H NMR signals ($CDCl_3$, 400 MHz): δ at: C**H**-OH (δ 3.69–3.72, m, 1H), CH(OH)-C**H**$_2$-N^+ (δ 3.50, 3.27, dd, 2H, J=6.4 Hz), S-C**H**$_2$ (δ 3.14, 2.88 dd, 2H, J = 7.6 Hz), CH(O**H**)



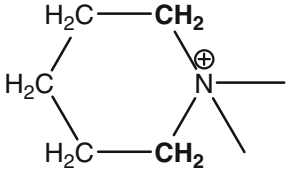
(δ 4.8, s, 1H),



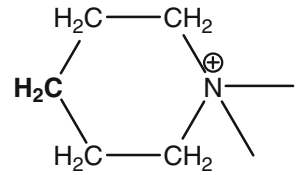
(δ 2.7, m, 4H),



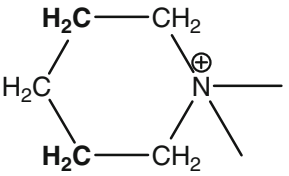
(δ 1.50, m, 4H),



(δ 1.45, m, 2H),

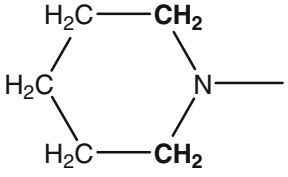


(δ 3.25, m, 4H), (δ 1.29, m, 2H),

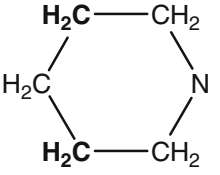


(δ 1.73, m, 4H), C**H**$_3$- CH_2-CH_2- CH_2 - CH_2-N^+ (δ 0.95, t, 3H), CH_3- C**H**$_2$- CH_2-CH_2 - CH_2-N^+ (δ 1.33, m, 2H), CH_3- CH_2- C**H**$_2$- CH_2 - CH_2-N^+ (δ 1.29, m, 2H), CH_3- CH_2- CH_2- C**H**$_2$ - CH2-N^+ (δ 1.74, m, 2H), CH_3- CH_2- CH_2- CH_2 - C**H**$_2$-N^+ (δ 3.30, t, 2H).

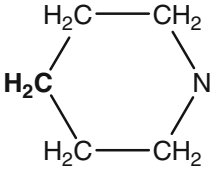
3.1k *1-Hexyl-1-(2-hydroxy-3-(piperidine-1-carbonothioylthio) propyl)piperidinium bromide* (**5b**):: ^{1}H NMR signals ($CDCl_3$, 400 MHz): δ at: C**H**-OH (δ 3.69–3.72, m, 1H), CH(OH)-C**H**$_2$-N^+ (δ 3.50, 3.27, dd, 2H, J = 6.4 Hz), S-C**H**$_2$ (δ 3.14, 2.88 dd, 2H, J = 7.6 Hz), CH(O**H**)



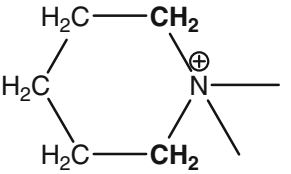
(δ 4.8, s, 1H),



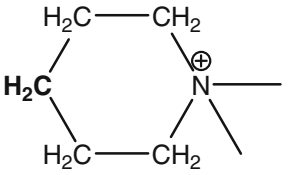
(δ 2.7, m, 4H),



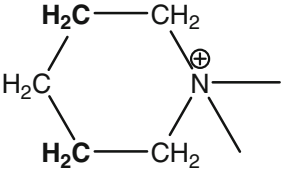
(δ 1.50, m, 4H),



(δ 1.45, m, 2H),



(δ 3.25, m, 4H),



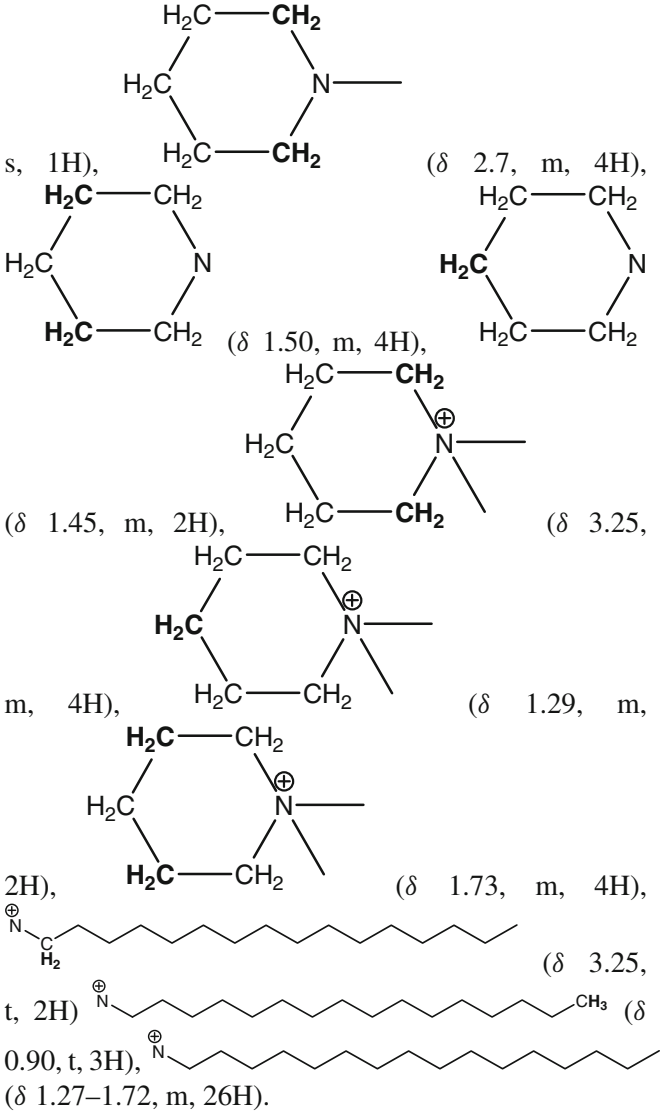
(δ 1.29, m, 2H), (δ 1.73, m, 4H), CH_2 -CH_2 -CH_2-N^+ (δ 1.33, m, 2H), CH_3- C**H**$_2$- CH_2-CH_2 -CH_2 -CH_2-N^+ (δ 1.29, m, 2H), CH_3- CH_2- C**H**$_2$-CH_2 -CH_2 -CH_2-N^+ (δ 1.29, m, 2H) CH_3- CH_2- CH_2-C**H**$_2$ -CH_2 -CH_2-N^+ (δ 1.74, m, 2H), C**H**$_3$- CH_2- CH_2-CH_2 -CH_2 -C**H**$_2$-N^+ (δ 3.30, t, 2H).

3.1l *1-Hexadecyl-1-(2-hydroxy-3-(piperidine-1-carbonothioylthio) propyl) piperidinium bromide* (**5c**):: ^{1}H NMR signals ($CDCl_3$, 400 MHz): δ at: C**H**-OH (δ 3.69–3.72, m, 1H), CH(OH)-C**H**$_2$-

Table 2. Antifungal potential of N-(3-(dialkylcarbamothioylthio)-2-hydroxypropyl)-N,N-diethylpentan-1-aminium bromides against *Helminthosporium oryzae*.

	Concentrations (μg/ml)					
Compound	1000	500	250	100	50	ED_{50} (μg/ml)
3a	98.5	95.4	94.8	60.8	47	60
3b	100	100	92.6	56	35	85
3c	89.7	60.4	1.9	–	–	460
4a	100	83	34	20	19.8	333
4b	88.8	77.7	59.1	48.7	12.7	120
4c	100	100	100	23.2	4.4	147
5a	100	100	90.4	87	30	68
5b	100	100	100	97.4	84.4	30
5c	100	100	84.4	77.2	59.9	40
Indofil M-45				35		
H_2O(control)				0.00		

N^+ (δ 3.50, 3.27, dd, 2H, J = 6.4 Hz), S-C**H**$_2$ (δ 3.14, 2.88 dd, 2H, J = 7.6 Hz), CH(O**H**) (δ 4.8, s, 1H), (δ 2.7, m, 4H), (δ 1.50, m, 4H), (δ 1.45, m, 2H), (δ 3.25, m, 4H), (δ 1.29, m, 2H), (δ 1.73, m, 4H), (δ 3.25, t, 2H) (δ 0.90, t, 3H), (δ 1.27–1.72, m, 26H).



3.2 *Fungitoxicity*

N-(3-(dialkyl or cyclic carbamothioylthio)-2-hydroxypropyl)-N,N-diethylpentan-1-aminium bromides were screened *in vitro* for their antifungal potential against test fungi *Helminthosporium oryzae* using spore germination inhibition technique at various concentrations. The results have been expressed in terms of ED_{50} value i.e. the effective dose at which 50 per cent spore germination inhibition has occurred. Table 2 shows the effect of different concentrations of various compounds on percent spore germination inhibition after 24 h. Spore germination in control was 100 per cent. All the compounds showed ED_{50} values of less than 500 μg/ml. The compounds with piperidine moiety have inflicted best fungitoxicity against the test fungi. Hexyl-1-(2-hydroxy-3-(piperidine-1-carbonothioylthio)propyl)piperidinium bromide (**5b**) was found to be most potent with the ED_{50} value of 30 μg/ml, which was comparable with the standard fungicide Indofil M45 (ED_{50} 35 μg/ml). Increasing the size of the molecule by isopropyl amine group did not favour the antifungal potential of the compounds.

4. Conclusion

The compounds containing multiple active moieties were successfully synthesized and characterized. The synthesized compounds showed promising antifungal potential against the phytopathogenic test fungi *Helminthosporium oryzae*. Hexyl-1-(2-hydroxy-3-(piperidine-1-carbonothioylthio)propyl)piperidinium bromide (**5b**) was found to inflict maximum

fungitoxicity with the ED_{50} value of 30 μg/ml, which was greater than the standard fungicide Indofil M45 (ED_{50} 35 μg/ml).

References

1. Badawi A M, EL-Marzibani M M, Haroun B and Soliman H 1983 *Curr. Sci.* **52** 1169
2. Zhishen Jia, Dongfeng Shen, Weiliang Xu 2001 *Carbohydr. Res.* **333(1)** 1
3. Fischer H, Giba G A G and Summer L A 1980 *J. Heterocycl. Chem.* **17** 333
4. Pernak J, Smiglak M, Griffin S T, Hough W L, Wilson T B, Pernak A, Matejuk J Z, Fojutowski A, Kita K and Rogers R D 2006 *Green Chem.* **8** 798
5. Clarissa K L Ng, Daniel Obando, Fred Widmer, Lesley C Wright, Tania C Sorrell, and Katrina A 2006 *J. Med. Chem.* **49(2)** 811
6. Jirina Z, Ferdinard D, Ivan L, Eva M, Libase S, Pavol N and Solvakia S K 1995 *Chem. Astr.* **126** 47
7. http://www.dpi.nsw.gov.au
8. Cavell K J, Hill J O and Magee R J 1979 *J. Inorg. Nucl. Chem.* **41(9)** 1277
9. Tonkyn R G and Wynstra J 1967 *J. Appl. Polymer Sci.* **11(1)** 145
10. Nene Y L and Thapliyal P N 1993 *Fugicides in plant disease control* (New Delhi: Oxford and IBH Publishing Co.) p. 525