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Synthesis, Characterization, DFT Studies of Novel Phase Transfer Catalyst and Application in O-Propargylation Reaction

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The present work reports the synthesis and characterization of 1-benzyl-1,4-diazoniabicyclo[2.2.1]hepta-2,4(7)-diene dibromide for phase transfer catalyst (PTC) applications. The derived quaternary salt was characterized by UV, FTIR and NMR spectral techniques. The structure has been optimized by density functional theory (DFT) in water and diethyl ether solvation conditions. The DFT outcomes showed the good chemical potential of the compound between 2.15 eV and 6.8 eV in both media. Extended research examined the nature of phase transfer by adjusting dosage, temperature and solvents in the O-propargylation reaction under normal conditions for useful precursor synthesis. The kinetic data revealed that the novel bisite quaternary amine bromide salt was effective in a variety of conditions. The chlorobenzene and water biphasic system yielded 88% of bioactive molecule precursor when compare to other immiscible systems.

Keywords: Phase transfer catalyst, DFT, O-Propargylation, Kinetics.

INTRODUCTION

Insoluble reactants in one solvent prevent many beneficial reactions and affect the yield and purity of the product. Traditional solvents can dissolve all reactants, but they are expensive and not necessarily cost-effective [1]. Due to high nucleophile solvation, the reaction rate is too low and hard to separate useful product from the chemical reaction mixture [2].

To tackle these kinds of issues, reactants are permitted to dissolve in both aqueous and immiscible organic solvents and then phase transfer catalyst (PTC) is introduced to transport the reactant from the aqueous or solid phase into the organic phase, where reaction happens [3-5]. The reaction is producing a high yield after the chemicals have been mixed. Also, PTC is now employed in numerous synthesis applications, including medicines, fragrances, agrochemicals, flavours, dyes, polymers, pollution management, *etc*. [6,7]. Phase transfer catalyst (PTC) outperforms the conventional synthesis due to its moderate operating conditions, cheaper reagents, high product selectivity in less time and suppression of unwanted side reactions [8]. It also features faster reaction rates, cheaper raw materials and less waste. Phase transfer catalysts enable water-based green chemistry. Many publications have been published on phase transfer catalyst technology [8-10]. Likely, the metal-catalyzed cyclization of homopropargylic and α-allenyl alcohols and amines yields bioactive chemicals, especially heterocyclic compounds [11]. Recently, allenyl and propargyl boronates have become versatile reagents for regioselective propargylation or allenylation reactions involving aldehydes, ketones or imines [12].

This work reports the synthesis and characterization of 1-benzyl-1,4-diazoniabicyclo[2.2.1]-hepta-2,4(7)-diene dibromide using phase transfer catalytic applications in the O-propargylation of biological active heterocyclic molecules. The HOMO-LUMO energy calculation were carried out in different solvation such as vacuum, water and diethyl ether. From the outcomes, the solvent suitability of derived PTC was optimized using HOMO-LUMO energy [13,14]. Then, the PTC efficiency and its kinetics of O-propargylation reaction has been investigated by varying the parameters such as quantity of catalyst and organic solvents [15].

EXPERIMENTAL

The chemicals *viz.* imidazole (Sigma-Aldrich, India), benzyl bromide (Sigma-Aldrich, India), 1,2-dibromo ethane (SRL, Chemicals, India), *n*-butyl bromide pure, 98% (SRL Chemicals, India), 3-bromoprop-1-ynemethyl 3,5-dihydroxybenzoate (Sigma-Aldrich, India), acetonitrile, ethanol, ethyl acetate, hexane, Na_2SO_4 and NaOH (SRL Chemicals, India) were procured and used as such. Readymade TLC plate was purchased from Merck, India and used to monitor the reaction using 60:40 ethyl acetate and hexane. The UV absorption spectra were analyzed using Shimadzu UV-2600 in ethanol and water mixture. The vibrational spectra recorded in JASCO 6300 by KBr pellet method. ^1H & ^{13}C NMR analysis were performed in Bruker NMR-400 spectrometer in $CDCl_3$. Density functional theory (DFT) calculation conducted in 32 bit windows 8 desktop using Spartan-14 application-Hartree Fock methods at different solvation conditions.

Synthesis of 1-benzyl-1,4-diazoniabicyclo[2.2.1]hepta-2,4(7)-dienedibromide (QA^+Br^-): Imidazole (2 g) dissolved in 50 mL acetonitrile solvent was agitated for 5 min. Then, 2.0 equiv. (8.12 g) of K_2CO_3 and 1.0 equiv. (5.02 g) of benzyl bromide were added one by one dropwise at room temperature. After adding, the reaction mixture was agitated at 50 ºC for 6 h and monitored by TLC. After workup with 60 mL ethyl acetate, 50 mL water quenched the reaction **(Scheme-I: Step-1**). The organic layer was dried using anhydride Na_2SO_4 and vacuumed the solvent. Ethyl acetate/hexane (9:1) solvent mixture was used in column chromatography to purify the crude mixture. Isolated 1-benzyl-1-imidazole (1 g) was treated with 3 mL of 1,2-dibromo ethane in 75 mL ethanol. The reaction was gently refluxed at 40 ºC for 12 h in nitrogen. Under vacuum, 1-benzyl-1,4-diazoniabicyclo[2.2.1]hepta-2,4(7)-dienedibromide (DSPTC, **Scheme-I: Step-2**) was rinsed with *n*-hexane (3 × 20 mL). A white solid DSPTC was stored in $CaCl_2$ desiccator.

Characterization: Absorption spectrum of light yellow dried DSPTC was recorded in ethanol and water mixture between 200 and 400 nm. The vibrational spectrum of catalyst DSPTC (in KBr) was recorded between 4000 and 500 cm^{-1} for asymmetric and symmetric stretching vibrations.

For NMR analysis, synthesized PTC 'b' and its precursor 'a' were dissolved in $CDCl_3$ and its significant protons and carbons were analyzed. From the outcomes of the precursor's NMR spectrum, five membered diazo ring, six-membered aromatic ring and two aliphatic protons were identified. Similarly, the respective carbon peaks were observed.

1-Benzyl-1*H*-imidazole (a-$C_{10}H_{10}N_2$): Yield: 94%; ^1H NMR (500 MHz, $CDCl_3$) δ ppm: 5.07 (s, 2H-Ar- C**H₂**), 6.88 (s, 1H, N=N-**H**), 7.07 (s, 2H-N-C**H**=C**H**), 7.13, 7.31, 7.51 (Ar-**H**), ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 50.46 (Ar-**C**H_2), 114.74, 119.05, 127.01, 127.96, 128.70, 129.47, 135.98, 137.15 (Ar-**C**). Elemental analysis of $C_{10}H_{10}N_2$ calcd. (found) %: C, 75.92 (75.82); H, 6.37 (6.29); N, 17.71 (17.68).

4-Benzyl-1,4-diazoniabicyclo[2.2.1]hepta-1(7),2-diene dibromide (b-DSPTC-$C_{12}H_{14}N_2Br_2$): Yield: 91%; ^1H NMR (500 MHz, $CDCl_3$) δ ppm: 1.25-1.22 (t, 2H, C**H₂**), 3.69-3.72 (t, 2H-C**H₂**), 5.12 (s, 2H- C**H₂**), 6.90 (s, 1H, N=N-**H**) 7.08 (s, 2H-N-C**H**=C**H**), 7.5, 7.27, 7.35, 7.55 (Ar-**H**), ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm: 18.38, 50.75 (aliphatic-**C**H_2),58.15 (Ar-**C**H_2), 119.25, 127.22, 128.22, 128.93, 129.65, 136.07, 137.35 (Ar-**C**). Elemental analysis of $C_{12}H_{14}N_2Br_2$ calcd. (found) %: C, 41.65 (41.60); H, 4.08 (3.98); N, 8.09 (8.01).

DFT calculation: The derived PTC structure was optimized by DFT using SPARTAN'14 quantum mechanics driver in Windows 32bit desktop. The geometry (Fig. 1) was optimized at restricted Hartree–Fock simulations with the basis set of 3-21G* and the different solvation systems such as vacuum, aqueous and diethyl ether [16]. After the successful calculation, the energy orbitals such as highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) are calculated and the DFT based parameters are calculated as per the following formulas.

Chemical potential:

$$\mu = -\frac{\text{IPO} + \text{EAF}}{2}$$

Hardness:

$$\eta = \frac{\text{IPO} - \text{EAF}}{2}$$

Softness:

$$S = \frac{1}{2\eta}$$

Electronegativity:

$$\chi = \frac{\text{IPO} + \text{EAF}}{2}$$

Global electrophilicty index:

$$\omega = \frac{\mu^2}{2\eta}$$

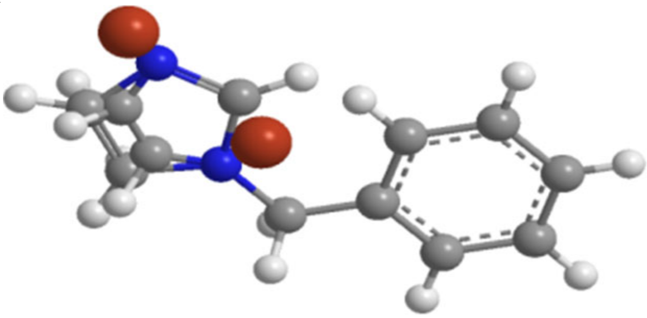
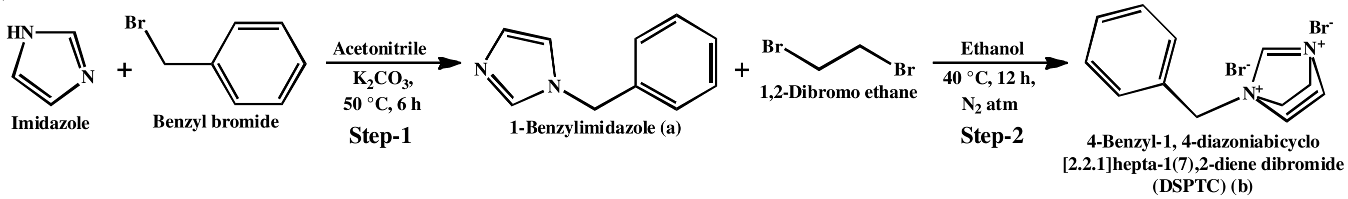
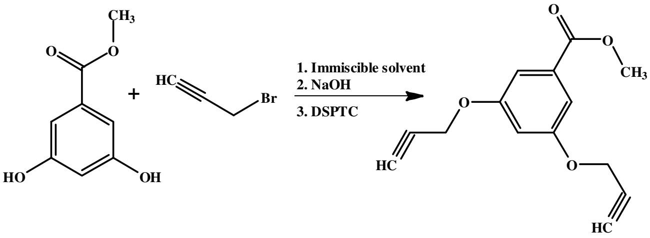


Fig. 1. 3D structure of compound DSPTC



Scheme-I: Synthesis of 1-benzyl-1,4-diazoniabicyclo[2.2.1]hepta-2,4(7)-dienedibromide (DSPTC)

Application of DSPTC in synthesis of methyl-3,5-*bis*(prop-2-yn-1-yloxy)benzoate: The synthesized compound was used as phase transfer catalyst in O-propargylation reaction (**Scheme-II**) and its kinetics was studied by changing the parameters. To a mixture of NaOH (21.4 g) in water (40 mL) and DSPTC, 1-benzyl-1,4-diazoniabicyclo[2.2.1]hepta-2,4(7)-diene dibromide (0.5 g), methyl-3,5-dihydroxybenzoate (1.75 g) was added under overhead stirring to generate the phenoxide anion. Then, propargyl bromide (1.5 mL) in suitable immiscible solvents such as cyclohexane, benzene, toluene, anisole and chlorobenzene (40 mL) was added slowly and heated at 45 ºC for 6 h with vigorous stirring. The title compound was separated by simple extraction with diethyl ether (3 × 25 mL), then the organic layer was collected and the solvent was evaporated under low pressure. The obtained pure mono-derivative of the title compound was allowed to pass through SiO_2 stationary phase using hexane:ethyl acetate (9:1) as eluting system [17].



Scheme-II: O-Propargylation reaction route of DSPTC

DSPTC in various solvents and its effect in O-propargylation: The influence of various organic solvents on the rate of propargylation of methyl-3,5-dihydroxybenzoate was followed under standard reaction conditions. Five organic solvents such as toluene, anisole, cyclohexane, chlorobenzene and benzene were employed for the kinetic study. From the pseudo first-order plot of –ln (1-X) *vs.* time and the rate constants were calculated. The relation between the dielectric constant and the rate constant was examined using synthesized DSPTC compound.

Effect of DSPTC weight in O-propargylation reaction: Experiments were conducted by varying the amounts of the synthesized DSPTC and keeping the other experimental parameters constant. The influence of the amount of DSPTC on the propargylation of methyl-3,5-dihydroxybenzoate was studied by varying the amount of DSPTC from 0.1 g to 0.9 g under normal conditions. Apparent rate constants were determined from the plot of –ln (1-X) *versus* time, which follow the pseudo first-order kinetics.

RESULTS AND DISCUSSION

A novel aromatic diazoniabicyclo quaternary ammonium bromide salt with two active sides for phase transfer catalytic activity was successfully synthesized and characterized. Initially, derived compound '**a**' was characterized by both ^1H and ^{13}C NMR. Precursor of DSPTC, 1-benzyl-1*H*-imidazole 'a' exhibits the aromatic chemical shifts between δ 7 ppm and 7.6 ppm. Aliphatic group and imidazole protons have shown significant peaks at 5.07 and 6.88 ppm, respectively. Likewise, the aromatic carbons of six and five-membered rings are observed between 120 ppm and 137 ppm in ^{13}C NMR spectrum. The joining $–CH_2–$ carbon exhibits near 77 ppm. After the chemical shifts coincidence with the expected structure, second step was carried using dibromoethane. Both spectra are presented in Fig. 2a-b.

After the successful formation of compound a, the DSPTC was synthesized and characterized by UV, FTIR and NMR. From the absorption spectrum (Fig. 3), quaternary salt nature was observed from the absence of amine nitrogen lone pair excitation**.** Also, the broad absorption exposed the salt of quartanry amine.

In FTIR spectra (Fig. 4), alkyl group of *tert*-amine attached bicyclodiene exposed the vibrational frequency between 3550 and 3450 cm^{-1} for asymmetric and symmetric stretching vibrations. Likely, aliphatic $–CH_2–$ exhibited the vibrational frequency between 3186 and 3085 cm^{-1}. Significant vibrational band for –CN is observed at 1225 cm^{-1}. Also, the –CH– stretching

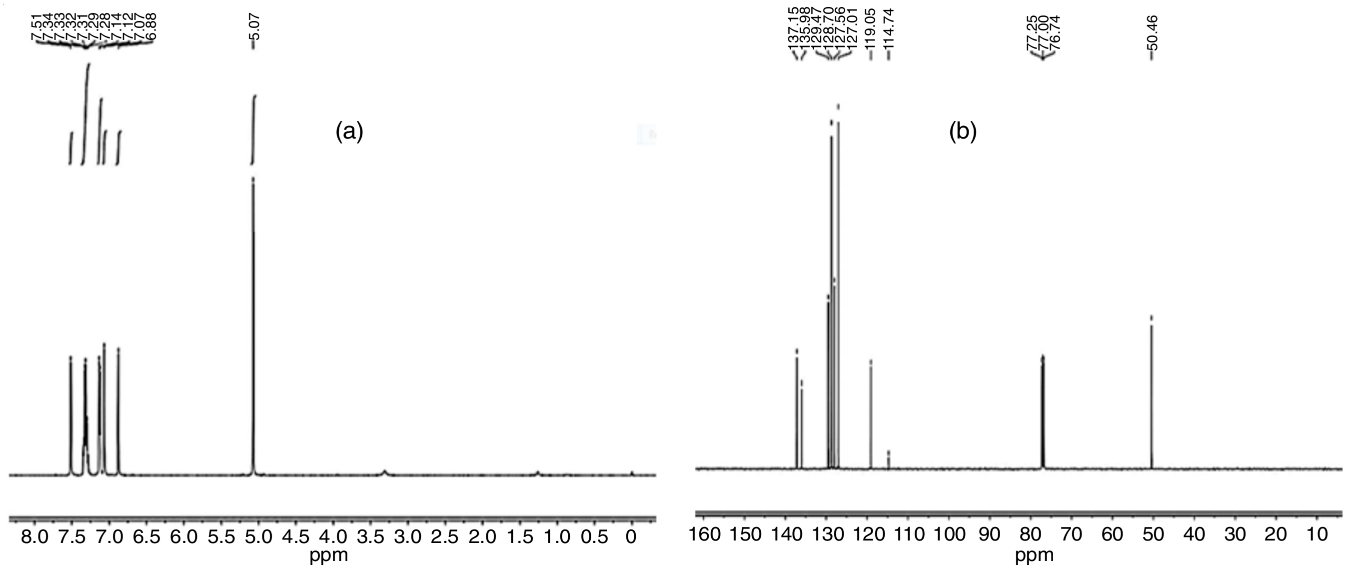


Fig. 2. (a) ^1H NMR and (b) ^{13}C NMR of the compound '**a**'

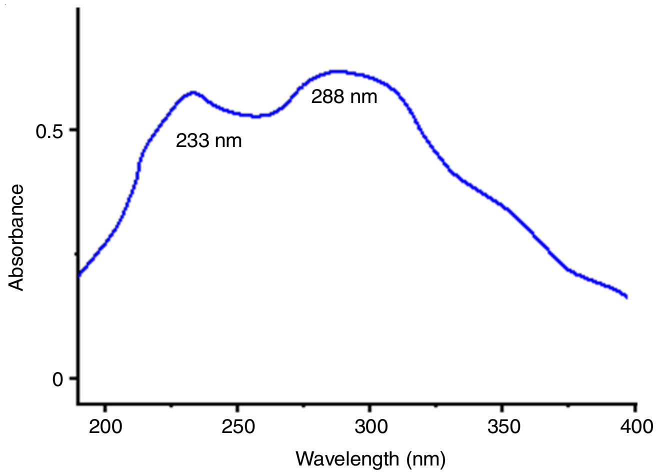


Fig. 3. Absorption spectra of DSPTC

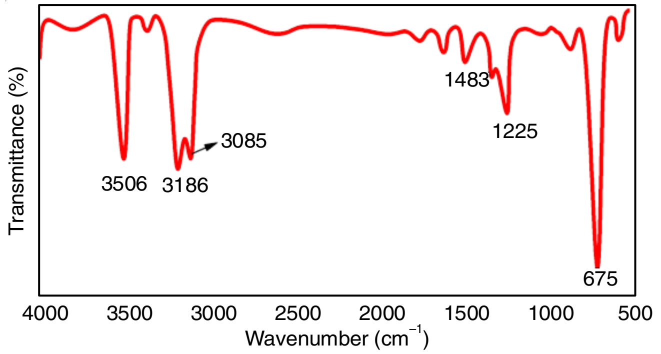


Fig. 4. Vibrational spectra of DSPTC

vibrations are observed between 1500 cm^{-1} and 1450 cm^{-1}. The stretching vibrations of five membered rings are observed between 720 cm^{-1} and 600 cm^{-1}. The peaks are nearly coincidence with the reported vibrational data [18,19].

The isolated light yellow di-site DSPTC crystals was carried for the further structural analysis instead of preliminary step. ^1H NMR of DSPTC exposed the similar peaks like 'a' and additional aliphatic protons are observed between δ 1.25 and 3.72 ppm. The prepared QA^+Br^- structure was confirmed by UV, FTIR and NMR characterization (Fig. 5a-b). The NMR chemical shifts were almost coincidenced with the reported compounds [19].

Then, the derived compound DSPTC structure was optimized using density functional theory (DFT). The structure optimized at three conditions such as vacuum, water and diethyl ether. The calculated energy levels have presented with the orbital picture in Fig. 6. From the energy orbitals, DFT parameters were calculated and the values are shown in Table-1. DSPTC exhibited the similar softness in all conditions. Also, the compound exposed higher chemical potential (μ) in diethyl ether (6.8 eV) and lower potential in toluene (2.15 eV). Similarly, global electrophilic index (ω) is higher in toluene (6.91 eV) and lower in water medium (0.4 eV). DSPTC has higher global softness and significant global electrophilic index. The result revealed that DSPTC has significant potential in both aqueous and immiscible solvent medium especially in toluene. Also, it reveals the biphasic reaction suitability in organic synthesis. DSPTC electrostatic potential map (Fig. 7) showed two corners such as most negative and most positive potentials based on the functional groups. Intermediary potentials colour spectrum

TABLE-1
DFT OUTCOMES OF THE DSPTC IN DIFFERENT SOLVATION

DFT parameters	Vacuum	Water	Diethyl ether	Toluene
HOMO (eV)	-7.3	-8.2	-10.9	-7.6
LUMO (eV)	3	3.6	-2.7	-3.3
HOMO + LUMO (eV)	-4.3	-4.6	-13.6	-10.9
Chemical potential (μ)	2.15	2.3	6.8	2.15
LUMO-HOMO	10.3	11.8	8.2	4.3
Hardness (η)	5.15	5.9	4.1	2.15
Global electrophilicty index (ω)	0.45	0.4	5.64	6.91
Softness (S)	0.05	0.04	0.06	0.12
Electronegativity (σ)	0.19	0.17	0.24	0.47

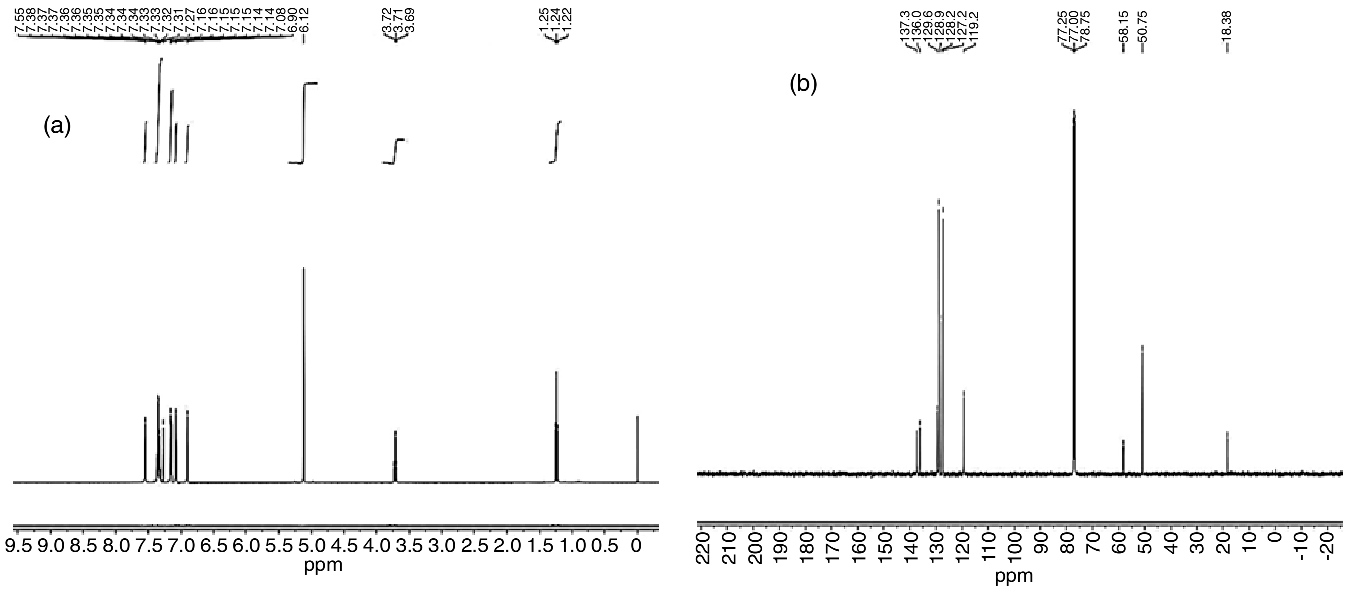


Fig. 5. (a) ^1H NMR and (b) ^{13}C NMR of the compound DSPTC

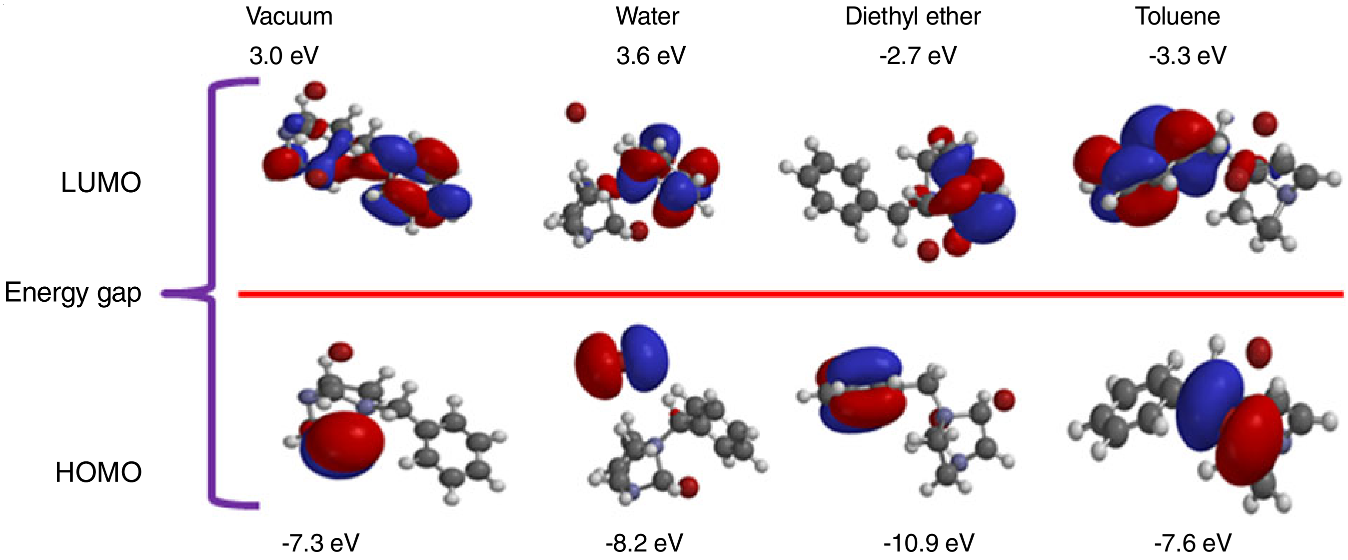


Fig. 6. DFT outcomes of DSPTC in different solvation

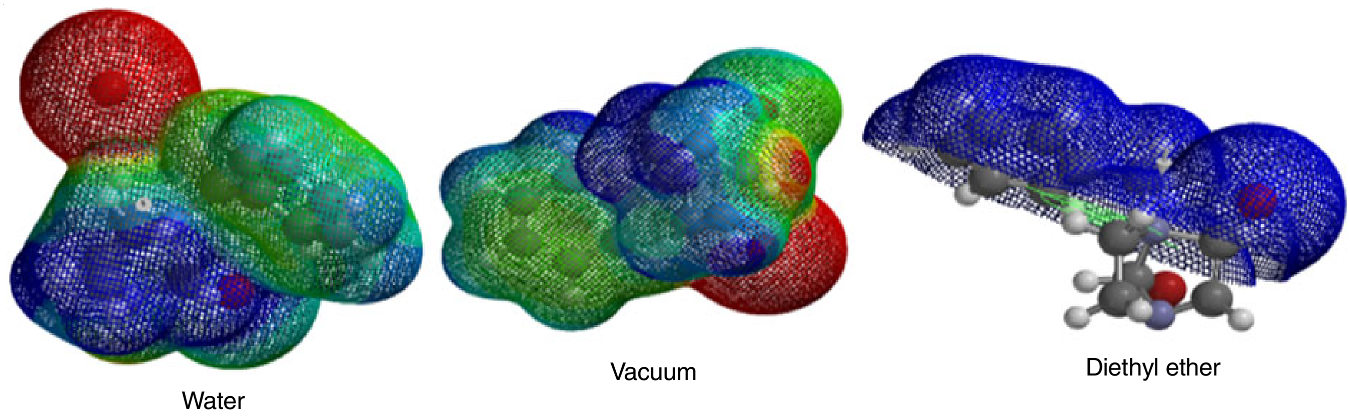


Fig. 7. Electrostatic potential map of DSPTC

exhibited like red (most negative) < yellow < green < light blue < dark blue (most positive). Most positive areas are more in water and diethyl ether, which confirmed the phase transformation ability.

After the theoretical chemical potential, softness and electrostatic potential confirmation, the compound was carried for the O-propargylation reaction in biphasic condition using DSPTC. At first, the solvent effect was investigated in various solvents using 0.1 g of DSPTC. Each reaction completion was confirmed by TLC using 60:40 ethyl acetate:hexane mixture. From the outcomes, this work observed that the solvents having high dielectric constant played a major role in phase transfer reaction. Also, it was observed that chlorobenzene possess a higher k_{app} value among the five organic solvents, due to its higher dielectric constant. Bar graph (Fig. 8) demonstrates the comparison results of all selected solvents with water.

After the solvent effect, reaction was conducted using chlorobenzeneas a solvent with different quantities of DSPTC. Rate constants by varying the amount of DSPTC from 0.1 to 0.9 g and the results are shown in Table-2. It was found that k_{app} values are linearly dependent on the amount of phase-transfer catalyst. An increase in the k_{app} value is attributed to the positive effect [20].

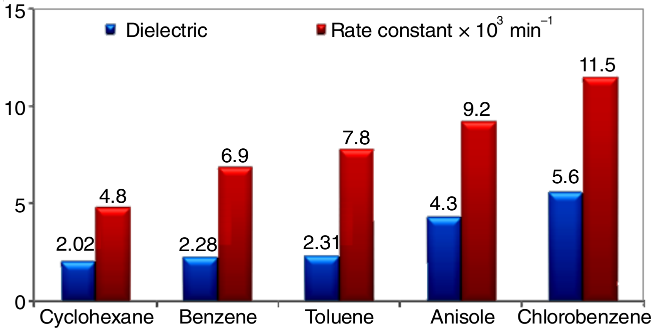


Fig. 8. Comparison graph of rate Constants, dielectric constants of different organic solvents with DSPTC

TABLE-2
AMOUNT OF DSPTC EFFECT ON
O-PROPARGYLATION REACTION

Weight of DSPTC (g)	0.1	0.3	0.5	0.7	0.9
$k_{app} \times 10^3$ (min^{-1})	17.03	24.33	28.54	36.68	42.03

Final compound of O-propargylation reaction in chlorobenzene with 0.9 g of DSPTC was recrystallized in diethyl ether and characterized by NMR and mass spectral technique. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.59-2.58 (t, 2H, C**H**), 3.90 (s, 3H, OC**H$_3$**), 4.72-4.71 (d, 2H, OC**H$_2$**), 6.81-6.80 (t, 1H, Ar-**CH**), 7.29-7.28 (d, 2H, Ar-**CH**). ^{13}C NMR (75 MHz, CDCl$_3$): δ 52.28 (OCH$_3$), 56.07 (OCH$_2$), 77.01 (H**C**), 77.02 (Alli-q-**C**) 107.41, 108.85, 132.09, 162.49, (Ar-**C**H), 166.37 (ester **C**OO), MS (EI, 70 eV %): *m/z*: 244.07.

Conclusion

From the overall investigations, 4-benzyl-1,4-diazonia-bicyclo[2.2.1]hepta-1(7),2-diene dibromide (DSPTC) has acted as a good phase transfer catalyst in biphasic system such as chlorobenzene and aqueous system. Using HOMO-LUMO gap-related DFT parameters, DFT theoretical findings showed favourable outcomes and supported the compound for phase transfer catalyst nature. The electrostatic potential map revealed the positive sites and negative sites of catalyst which is required for the biphasic reactions. Also, the experimental investigations revealed that the weight and solvents play an important role in DSPTC based reaction. Moreover, this work observed the relation between the theoretical and experimental outcomes of DSPTC based reaction. Finally, this work concluded that the solvent having high dielectric constant with higher amount of DSPTC results in the good yield due to the transformation of the reactants from aqueous to solvent phase and good purity.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

REFERENCES

1. O.V. Kharissova, B.I. Kharisov, C.M. Oliva-González, Y. Peña-Méndez and I. López, *R. Soc. Open Sci*., **6**, 191378 (2019); https://doi.org/10.1098/rsos.191378
2. T.A. Hamlin, M. Swart and F.M. Bickelhaupt, *ChemPhysChem*, **19**, 1315 (2018); https://doi.org/10.1002/cphc.201701363
3. G. Pupo, F. Ibba, D.M.H. Ascough, A.C. Vicini, K.E. Christensen, P. Ricci, L. Pfeifer, J.R. Morphy, J.M. Brown, R.S. Paton and V. Gouverneur, *Science*, **360**, 638 (2018); https://doi.org/10.1126/science.aar7941
4. M. M¹kosza and M. Fedoryñski, *Catal. Rev., Sci. Eng.*, **45**, 321 (2003); https://doi.org/10.1081/CR-120025537
5. S. Shirakawa and K. Maruoka, *Angew. Chem. Int. Ed. Engl.*, **52**, 4312 (2013); https://doi.org/10.1002/anie.201206835
6. C.M. Starks, *J. Am. Chem. Soc.*, **93**, 195 (1971); https://doi.org/10.1021/ja00730a033
7. K. Urata and N. Takaishi, *J. Am. Oil Chem. Soc.*, **73**, 831 (1996); https://doi.org/10.1007/BF02517983
8. S.D. Naik and L.K. Doraiswamy, *AIChE J.*, **44**, 612 (1998); https://doi.org/10.1002/aic.690440312
9. S. Liu and W. Zhu, *Biomed. J. Sci. Technol. Res.*, **45**, 36691 (2022); https://doi.org/10.26717/BJSTR.2022.45.007237
10. S.P. Neofotistos, A. Tzani and A. Detsi, *Catalysts*, **13**, 474 (2023); https://doi.org/10.3390/catal13030474
11. D.R. Fandrick, J. Saha, K.R. Fandrick, S. Sanyal, H. Lee, F. Roschangar, J. Ogikubo, J.J. Song and C.H. Senanayake, *Org. Lett.*, **13**, 5616 (2011); https://doi.org/10.1021/ol202343c
12. G. Zweifel, S.J. Backlund and T. Leung, *J. Am. Chem. Soc.*, **100**, 5561 (1978); https://doi.org/10.1021/ja00485a049
13. J. Xiao, M. Khan, A. Singh, E. Suljoti, L. Spiccia and E.F. Aziz, *ChemSusChem*, **8**, 872 (2015); https://doi.org/10.1002/cssc.201403219
14. T.T. Adejumo, N.V. Tzouras, L.P. Zorba, D. Radanovic, S. Grubisic, A. Pevec, D. Mitic, K.K. Andelkovic, G.C. Vougioukalakis, B. Cobeljic and I. Turel, *Molecules*, **25**, 4043 (2020); https://doi.org/10.3390/molecules25184043
15. M. Boz and S.S. Basturk, *J. Surfactants Deterg.*, **19**, 663 (2016); https://doi.org/10.1007/s11743-016-1821-z
16. R. Jayaprakash, S.K. Sha, S. Hemalatha and D. Easwaramoorthy, *Int. J. Chemtech Res.*, **9**, 48 (2016).
17. V. Selvaraj and V. Rajendran, *Ultrason. Sonochem.*, **21**, 612 (2014); https://doi.org/10.1016/j.ultsonch.2013.09.013
18. N. Ayashi, M. Fallah-Mehrjardi and A.R. Kiasat, *Russ. J. Org. Chem.*, **53**, 846 (2017); https://doi.org/10.1134/S1070428017060069
19. P.A. Vivekanand and T. Balakrishnan, *Appl. Catal. A Gen.*, **364**, 27 (2009); https://doi.org/10.1016/j.apcata.2009.05.014
20. C. Li and J. Wang, *J. Org. Chem.*, **72**, 7431 (2007); https://doi.org/10.1021/jo0709192