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ORIGINAL ARTICLE

Experimental and theoretical study of bifunctionalized PEO–PPO–PEO triblock copolymers with applications as dehydrating agents for heavy crude oil

César A. Flores-Sandoval [a,*], Laura V. Castro [a,b], Eugenio A. Flores [a], Fernando Alvarez [a], Antonieta Garcia-Murillo [c], Alfonso López [a], José G. Hernández-Cortez [a], Flavio S. Vázquez [a]

[a] *Instituto Mexicano del Petróleo, Programa de Ingeniería Molecular, Eje Central Lázaro Cárdenas No. 152, San Bartolo Atepehuacan, C.P. 07730 Distrito Federal, Mexico*
[b] *Escuela Superior de Ingeniería Química e Industrias Extractivas, Instituto Politécnico Nacional, Unidad Profesional Adolfo López Mateos, C.P. 07738 Distrito Federal, Mexico*
[c] *Centro de Investigación e Innovación Tecnológica, Instituto Politécnico Nacional, Cerrada de Cecati S/N, C.P. 02250 Distrito Federal, Mexico*

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Abstract A series of α,ω-diamines of polyoxyethylene–polyoxypropylene–polyoxyethylene (POE–POP–POE) triblock copolymer was synthesized and experimentally evaluated as dewatering agents for heavy crude oil. A quantitative structure–activity relationship (QSAR) study of the effect of the secondary amine structure over the yield of nucleophilic substitution reactions with α,ω-ditosylate ester of PEO–PPO–PEO triblock copolymer was performed exclusively at the DFT level. Multiple linear regression (MLR) analysis including softness or hardness parameters gave $R^2 = 0.9062$, producing an equation with an acceptable $r^2_{m(test)}$ value. Furthermore, in order to understand the physicochemical interaction between the functionalizing copolymers and water, QSAR models

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Abbreviations: A, electron affinity; AM1, Austin model 1; DFT, density functional theory; HOMO, highest occupied molecular orbital; *I*, ionization potential; I_p, polydispersity index; LUMO, lowest unoccupied molecular orbital; MLR, multiple linear regression; Mn, number average molecular weight; η, absolute hardness; *S*, absolute softness; ω, philicity

[*] Corresponding author. Tel.: +52 55 9175 8269.
E-mail address: caflores@imp.mx (C.A. Flores-Sandoval).

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based on AM1 semiempirical and DFT (B3LYP functional) descriptors were carried out for comparative purposes. For the MLR analysis at the AM1 level, $R^2 = 0.9058$, whereas at the DFT level, $R^2 = 0.9879$. 2-(Methylamino)ethanol was employed to evaluate the equations obtained. The residual of the $\log \mathrm{ER}_{\mathrm{calc}}$ S_N2 reaction was −0.0043, showing a good correlation with experimental efficiency. Regarding water removal efficiency, the residuals of $\log \mathrm{WR}_{\mathrm{calc}}$ at the AM1 and DFT levels were of 0.0220 and 0.0041, respectively. Even though, DFT produced a better correlation, a QSAR study at the AM1 level could be employed to study the behavior of α,ω-diamines of PEO–PPO–PEO triblock copolymer and to destabilize water/oil emulsions, with a computational cost relatively low compared to DFT calculations.

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1. Introduction

Petroleum contains different amounts of water and salts; namely, it is a heterogeneous mixture of hundreds of hydrocarbon compounds and comprises several endogenous emulsifiers, as well as clays, naphthenic acids, heterocyclic nitrogenated and sulfured compounds, oxidized hydrocarbons, and resins and asphaltenes.

Water can cause corrosion and scale damage in pipelines, refinery equipment and, of course, this increases costs. As a result, it is very important to break up emulsions of all types: water in oil (W/O), oil in water (O/W), even ternary emulsions (O/W/O and W/O/W).

The breaking up of crude oil emulsions has been accomplished for a long time by adding surface active components (demulsifiers) that exhibit both hydrophilic and hydrophobic properties (Papirer et al., 1982; McLean and Kilpatrick, 1997; dos Santos et al., 2011) or by using nonionic polymers (Roodbari et al., 2011).

Demulsifier blends for application include epoxy resin-based alkoxylates; polyoxyethylene–polyoxypropylene–polyoxyethylene (POE–POP–POE); alkylphenol–formaldehyde resin alkoxylates; orthoesters alkoxylates; and fatty acid alkoxylated and polyoxyalkylenated amines (Hellberg and Uneback, 2007; Al-Sabagh et al., 2008; Atta and Elsaeed, 2011).

Recently, some triblock copolymers, PEO–PPO–PEO with α,ω-diamine bifunctionalization, were synthesized and tested for their capability to break up water-in-oil emulsions, and these novel agents achieved greater removals of water from heavy petroleum than commercial demulsifiers (Cendejas et al., 2013).

On the other hand, quantitative structure–activity relationship (QSAR) searches predict the relationship of chemical structure to both biological and other activities through the use of predictive models (Larif et al., 2013; Sharma et al., 2013). Several molecular descriptors are employed to quantify the structural features of the lead molecule. The purpose of using QSAR-descriptors is to determine properties of molecules that can serve as numerical descriptors of characterizing molecules in other calculations. QSAR analysis can play an important role in molecular electronics, solid physics, materials chemistry, and the ability of chemists to predict a specific property. Dguigui et al. (2010) carried out a QSAR study of conductor polymers based on monothiophene derivatives. QSAR has been applied to studies of the activity of corrosion inhibitors for mild steel (Ashassi-Sorkhabi et al., 2005; Eddy and Ita, 2011; Danaee et al., 2013), and to free-radical polymerization chain-transfer constants for styrene (Xu et al., 2012).

In order to understand the mode of action of amine-functionalized block copolymers as demulsifying agents in water-in-oil emulsion, theoretical studies were performed in this work, which consisted of carrying out QSAR studies to analyze the effect of the functionalizing amine structure on the substitution reaction performed to obtain a bifunctionalized triblock copolymer. Furthermore, the structure–activity relation of α,ω-diamine positioned at the ends of a PEO–PPO–PEO triblock copolymer employed as a dehydrating agent for heavy crude oils, was determined. It is also worth mentioning that no similar QSAR study of dewatering agents for heavy crude oils has been previously reported in the literature.

2. Experimental

2.1. Materials

The following reagents were purchased from Aldrich: propylene oxide (PO, 99%), ethylene oxide (EO, 99%), phosphoric acid 85%, ethanol 99.5%, methanol 99.8%, hexane 95%, benzene 99.8%, toluene 99.8, xylenes 98.5%, Tosyl chloride (TsCl, 99.0%), triethylamine (TEA, 99%), 4-(dimethylamino)pyridine (DMAP, 99%), methylene chloride 99%, sodium sulfate anhydrous, KOH (pellets, Fermont, 99%), ethylene glycol (JT Baker, 99%), and tetrahydrofuran (THF, Mallinckrodt, 99.8%). These were used with no further purification.

2.2. Synthesis

The synthesis of bifunctionalized block copolymers (Cendejas et al., 2013) is shown in Fig. 1. It comprises four stages: (1) initiator preparation, (2) polymerization of a central block of propylene oxide (Cendejas et al., 2008), (3) polymerization of ethylene oxide side sequences, and (4) functionalization of the triblock copolymer.

2.2.1. Preparation of di-potassium ethyleneglycolate (DKEG)

In a balloon flask equipped with a condenser, thermometer, magnetic stirrer and Dean Stark trap, were placed ethylene glycol (0.01 mol) and potassium hydroxide (0.01 mol), dissolved in 50 mL of methanol, heated at 80 °C for 1 hour, and then 1 mL of benzene was added. The solvent was removed by distillation until ethylenglycolate was obtained as a viscous liquid.

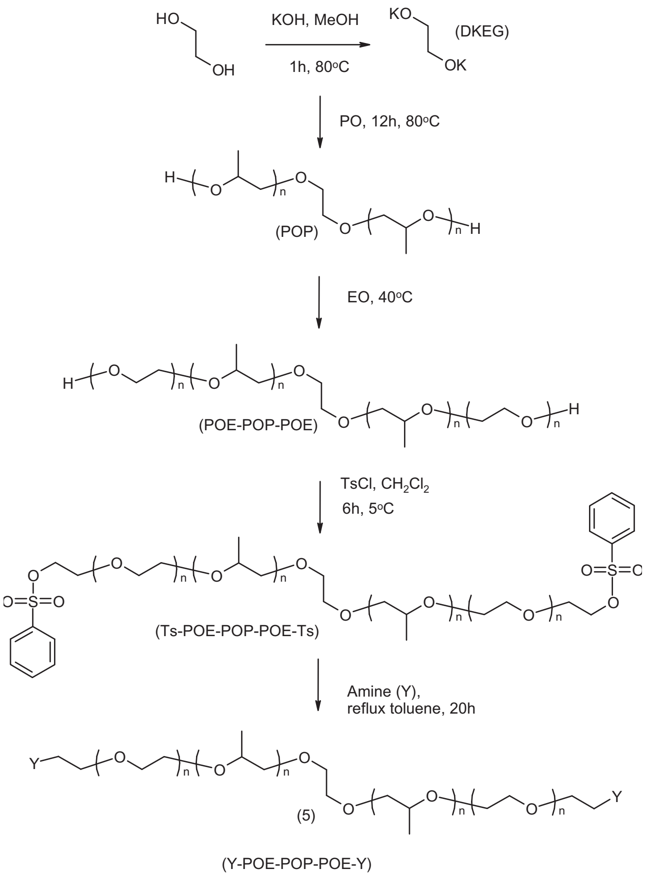

Figure 1 Scheme of the synthesis of copolymer bifunctionalized with secondary amines.

2.2.2. *Preparation of polyoxypropylene homopolymer (POP)*

The reactions were carried out in a Parr® reactor with digital controls for stirring, pressure and temperature. The reactor was charged with an appropriate quantity of DKEG and PO. Subsequently, the reactor was drained and pressurized with nitrogen to ensure an inert atmosphere. The temperature was fixed at 80 °C. After 12 hours of reaction, the conversions reached were between 70 and 85 wt.% (Cendejas et al., 2012).

2.2.3. *Preparation of POE–POP–POE block copolymer*

Once the first stage of polymerization was complete, EO was slowly added in the reactor at 40 °C, in amounts ranging from 0.05 to 0.3 moles. The reactor was drained and pressurized with nitrogen to ensure an inert atmosphere. The ratio of the monomers EO and PO was fixed at 17:45. Once the addition was completed, the reaction was stopped by adding a solution containing phosphoric acid at 85 vol.% concentration, followed by two volumes of methylene chloride to separate copolymer to the organic phase. The copolymer was washed with water and the phases separated; the organic phase was evaporated, reaching a conversion between 90% and 95%.

2.2.4. *Functionalization of the triblock copolymer*

2.2.4.1. Preparation of the di-α,ω-tosylate ester (TsO–POE–POP–POE–OTs) block copolymer. In a balloon flask equipped with a magnetic stirrer and thermometer was placed 7.0 mmol of POE–POP–POE copolymer, to which was added 50 mL of a 1:1 ratio mixture of dichloromethane:toluene, and the resulting mixture was kept in agitation for 30 minutes; subsequently, the reaction flask was placed in an ice bath, and when the temperature reached a range of 0–5 °C, 21.0 mmol of triethylamine, 21.0 mmol of TsCl and 0.9 mmol of DMAP were slowly added. The reaction was stirred for 6 hours, and the reaction mixture was successively washed with water (3 × 50 mL) and 0.1 N HCl (2 × 25 mL). Finally, the organic phase was separated and concentrated under reduced pressure (Cendejas et al., 2013).

2.2.4.2. Preparation of the di-α,ω-amine (Y-POE-POP-POE-Y) block copolymer. In a balloon flask fitted with a magnetic stirrer and condenser was placed 3.0 mmol of TsO–POE–POP–POE–OTs, ($Mn = 2939\ \mathrm{g\ mol^{-1}}$, $I_p = 1.12$), which was dissolved in 50 mL of toluene. Afterwards, 7.8 mmol of the amine (Y) was added and heated to reflux for 20 hours; after that time, the solvent was removed under reduced pressure. The product reaction was dissolved in methylene chloride (50 mL), and the mixture was washed with distilled water (4 × 50 mL). The organic phase was dried with sodium sulfate anhydrous, and finally the solvent was removed under reduced pressure, to obtain (Y–POE–POP–POE–Y).

2.3. *Polymer characterization*

Homopolymers and copolymers were characterized using the following instrumental methods.

Fourier transform infrared spectroscopy (FTIR). The synthesized copolymers were characterized by FTIR with a Brucker® Tensor model 27.

Nuclear magnetic resonance (NMR) spectrometry. A Varian® BB model was employed at 200 MHz and 50 MHz for ^{1}H and ^{13}C nuclei, respectively, using deuterated chloroform as a solvent; chemical shifts (δ) are in ppm from the tetramethylsilane signal (TMS).

The molecular weight distributions of the polymer samples were determined by size exclusion chromatography (SEC), using an Agilent 1100 Chromatograph consisting of a 5 μm column of Plegl and using THF as an eluent. The number of average molecular weights (Mn) and polidispersity (I_p) was calculated from the SEC data. Calibration was made with a polystyrene standard kit and verified using internal polypropylene oxide standards.

2.4. *Demulsifier evaluation*

The crude oil samples from the Gulf of Mexico were characterized as described elsewhere (Castro and Vazquez, 2009); Table 1 lists the characteristics physicochemical properties of the heavy Mexican crude oil employed in this work (Castro and Vazquez, 2009; Diaz-Ponce et al., 2010). Evaluation by bottle testing was roughly performed as follows: to graduated bottles (15 mL volume), crude oil was added in quantities up to 100 mL. The bottles were placed in a temperature-controlled water bath at 80 °C for a period of 30 minutes, after which they were removed. Subsequently, one aliquot of the dissolution of Y–POE–POP–POE–Y blocks copolymers in xylenes was added; in the case of untreated oil, an aliquot of xylene was added; all the bottles were shaken for 2 minutes at a rate of 2 shakes per second. After mixing, the bottles were

Table 1 Physicochemical properties of Mexican crude oil.

Parameter	Heavy crude oil
API density	19.9
Sal/lb by 1000 bls of crude oil	100
Wax content (wt.%)	4.7
Water by distillation (vol.%)	7.0
Saturates (wt.%)	13.7
Aromatics (wt.%)	10.5
Resins (wt.%)	64.5
Asphaltenes from *n*-C_7 (wt.%)	11.3

placed in the controlled temperature bath, and the water removal from petroleum was monitored for 240 minutes (Cendejas et al., 2010).

2.5. Computational procedure

The structure of the amines was geometry-optimized at the DFT level using the hydrid functional B3LYP and basis 6-31G(*d*) (Curtiss et al., 1990; Ditchfield et al., 1971; Hehre et al., 1972; Hariharan and Pople, 1973, 1974; Gordon, 1980), followed by a single-point calculation at the B3LYP/6-311+G(*d*) level (Binning and Curtiss, 1990; Clark et al., 1983), implemented in Gaussian 03 software (Gaussian 03, 2000). The energy values were corrected by zero-point energy (ZPE) correction. The calculated vibrational frequencies demonstrated that the structure was stable (no imaginary frequencies). Natural bond orbital (NBO) analyses were carried out using NBO 5.0. Finally, the structure of the α,ω-diamine of PEO–PPO–PEO copolymer was optimized at the AM1 level, followed by a single-point calculation at B3LYP/6-31G(*d*). The QSAR parameters of the amines and functionalized copolymers were obtained using Hyperchem (version 6.0, 1993).

On the other hand, reactivity descriptors such as absolute electronegativity, χ; absolute hardness, η; and absolute softness, *S*, have been widely used to understand the global nature of molecules in terms of their stability (Parr et al., 1978; Parr and Pearson, 1983; Koopmans, 1934). Moreover, electrophilicity is a descriptor of reactivity, providing a quantitative classification of the global electrophilic nature of a molecule, within a relative scale; it is effectively the power of a system to "soak up" electrons (Parr et al., 1999).

Statistical analyses were performed using stepwise subroutine multiple linear regression (MLR) (Xu and Zhang, 2001), implemented in SPSS 12.0 for Windows (SPSS for Windows, 1999). The optimal of the linear models was determined by considering the *t*-statistical models (with all absolute values > 2.0 accepted), as well as the overall *F*-statistical test. We also performed Akaike's Information Criterion (AIC) (Akaike, 1974) and took into consideration a suggestion made by Guha and Jurs (2005), who showed that compounds that are very similar in the training set generally exhibit smaller residuals and standard errors of prediction.

The root mean squared error (*RMSE*) is defined as:

$$RMSE = \sqrt{\frac{\sum_{i=1}^{n}(y_i^{pre} - y_i^{obs})^2}{n}} \tag{1}$$

where y_i^{pre} and y_i^{obs} express the predicted and observed log ER or log WR values, respectively, and *n* stands for the number of compounds in the training set (Xu and Zhang, 2001). One of the most commonly applied internal validation techniques is the leave-one-out cross-validation (LOO-CV). The measure connected to internal validation by LOO-CV, q^2_{cv}, is defined as follows:

$$q^2_{loo} = 1 - \frac{\sum_{i=1}^{n}\left(y_i^{obs} - y_i^{predcv}\right)^2}{\sum_{i=1}^{n}(y_i^{obs} - \bar{y}_i^{obs})^2} \tag{2}$$

where y_i^{obs} is the experimental (observed) value of the property for the *i*th compound; y_i^{predcv} is the predicted value for the temporarily excluded (cross-validated) *i*th compound; $\bar{y}_i^{obs}$ is the mean experimental value of the property in the training set; and *n* is the number of compounds in the training set (Chirico and Gramatica, 2011). Excluding more than one element in each iteration is the leave-many-out (LMO) technique; in this case, $G = 3$ (Chirico and Gramatica, 2011; Huang and Fan, 2011). LOO and LMO are widely used to evaluate whether overfitting occurs, and whether the model is robust and stable.

3. Results and discussion

3.1. Spectroscopic characterization of functionalized copolymers

POE–POP–POE triblock copolymers bifunctionalized with secondary amines were obtained and characterized by FTIR and NMR spectra, according to a method described earlier by our work group (Cendejas et al., 2013). Fig. 2 shows the

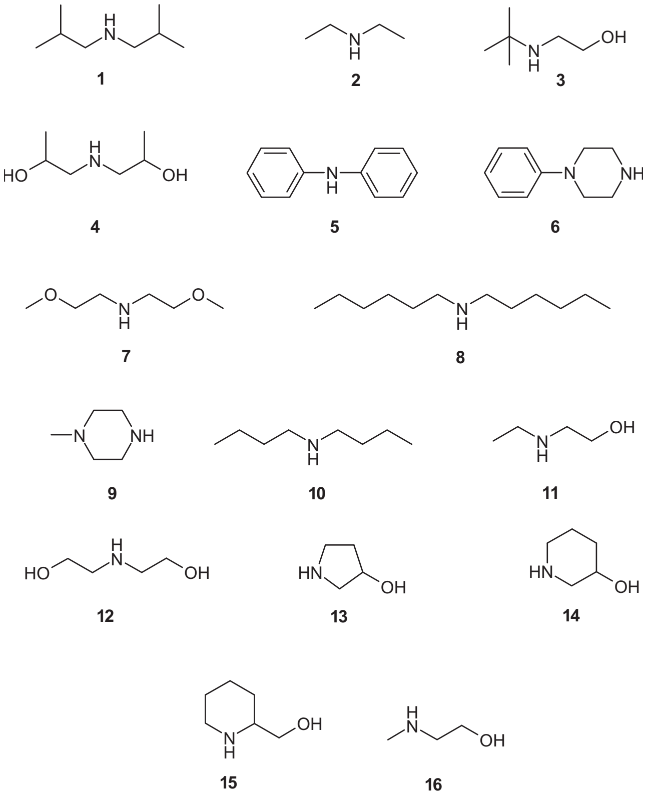

Figure 2 Structure of all amines.

amines (Y) employed for this purpose: acyclic amines included di-isobutylamine (**1**), diethylamine (**2**), 2-(*ter*-butylamino) ethanol (**3**), di-isopropanolamine (**4**), diphenylamine (**5**), bis-(2-methoxyethyl)amine (**7**), dihexylamine (**8**), dibutylamine (**10**), 2-(ethylamino)ethanol (**11**), and diethanolamine (**12**), and cyclic amines included 1-phenylpiperazine (**6**), 1-methylpiperazine (**9**), 3-pyrrolidinol (**13**), 3-hydroxipiperidine (**14**), and 2-piperidinemethanol (**15**). To validate established equations, 2-(methylamino)ethanol (**16**) was selected as an independent dataset for this purpose.

Copolymers (**1′**–**16′**) displayed common spectroscopic characteristics in FTIR spectra; for example, bands observed around 2750–2990 cm^{-1} were assigned to methyl and methylene groups, as confirmed by the signals in 1455 and 1380 cm^{-1}, and bands located in the interval of 1090–1105 cm^{-1} assigned to the alkyl-substituted ether stretching bond C—O; copolymers **3′**, **4′**, **11′**–**16′** showed a band corresponding to the hydroxyl group at about 3400–3500 cm^{-1}. Signals observed in the 1590–1610 cm^{-1} interval in the spectrum of copolymers **5′**and **6′**, confirmed the presence of an aromatic ring.

Moreover, the ^{13}C NMR spectra showed signals located at 17–18 ppm, which were attributed to the methyl carbon of the PPO chain. The set of signals appearing in the range of 73–77 ppm were related to oxygenated carbons corresponding to either methine or methylene groups. Some signals located at 45–60 ppm were related to nitrogenous carbons. The chemical shifts noted above are common to copolymers **1′**–**15′**. In the case of copolymers **3′**, **4′**, **11′**–**16′**, signals were observed around 65–70 ppm; these were attributed to hydroxyl groups. Copolymers **5′** and **6′** showed a set of signals at around 110–160 ppm, indicating aromatic ring carbons (Cendejas et al., 2013).

3.2. Bimolecular nucleophilic substitution (S_N2) reaction

Table 2 shows the experimental yield values obtained for the bimolecular nucleophilic substitution (S_N2) reaction. Regarding amines **6** and **9**, which are piperidine derivatives with an aromatic ring and a methyl group as substituents, it was evidenced that a secondary nitrogen atom is chemoselectively preferred to act as a nucleophile, giving an exclusive substitution product of this nitrogen atom. The highest conversion value corresponds to diethylamine (**2**), which has the lowest molecular volume, being the less bulky amine, which is an important condition in a S_N2 reaction. Amine **5** has the lowest yield value because of the resonance effect between the lone pair electrons of the nitrogen atom and the aromatic rings; according to the second-order perturbation theory analysis of the Fock matrix in the NBO basis, $n_N \rightarrow \pi^*_{C—C}$ was 32.0 kcal mol^{-1}. In amine **6**, the tertiary nitrogen bonded an aromatic ring and showed a $n_N \rightarrow \pi^*_{C—C}$ interaction of 22.8 kcal mol^{-1}. In sum, in order to have a good yield for this reaction, it is preferable to employ amines with low volume molecular, not bonded to a group, so that the lone pair of electrons in the nitrogen atom can be in resonance. Evidently, secondary amines react better as nucleophiles than tertiary ones.

Table 2 Yield of the functionalization reaction with amines (S_N2 reaction) and the water removal efficiency of the heavy crude oil emulsion with diamine α,ω-functionalized copolymers after 240 min (T = 80 °C).

Amine	S_N2 reaction (%)	Diamine α,ω-copolymer	Water removal efficiency on heavy crude oil (%)
1	73	1′	63
2	78	2′	64
3	74	3′	58
4	77	4′	60
5	64	5′	50
6	71	6′	55
7	76	7′	62
8	73	8′	25
9	76	9′	49
10	75	10′	59
11	77	11′	60
12	76	12′	75
13	77	13′	70
14	73	14′	68
15	75	15′	67

3.3. Evaluation of the di-α,ω-amine (Y–POE–POP–POE–Y) triblock copolymer as a demulsifier of Mexican crude oil

It must be remarked that the crude oil employed in this study had a great amount of asphaltenes (11.3 wt.%), which act as natural surfactants of oil and help to stabilize the water drops dispersed in crude oil (Cendejas et al., 2013). A low amount of water in oil makes dehydrating very difficult, because a poor separation gradient is presented by the system; therefore, it is very complicated to break up this emulsion. Table 2 shows the results of the evaluation of water removal for the α,ω-diamine of POE–POP–POE triblock copolymer as a dewatering agent for heavy crude oil from the Gulf of Mexico. Fig. 3 shows the graphical results of the evaluation at 300 ppm and 80 °C. These water removal values were employed in the QSAR analysis.

Dewatering efficiency is low when triblock copolymers with *n*-alkylamines are employed as demulsifiers, and it diminishes as the number of carbon atoms increases (copolymer **2′** > **10′** > **8′**) (Fig. 3a). Branched alkyl amines showed dehydrating efficiencies 4% higher than those of linear *n*-alkylamines with the same carbon atoms (copolymer **1′** versus **10′**) (Fig. 3b). The presence of oxygen atoms in the amine structure increases water removal; thus, copolymer **13′**, which is diethanolamine-grafted, has two hydroxyl groups bonding to a primary carbon atom; this functionalized copolymer showed the highest dewatering efficiency, whereas the absence of one of the oxygen atoms produces a 15% reduction in efficiency. However, in the case of copolymers grafted with branched alkyl amines (copolymer **4′**), the demulsification performance is low if the OH groups bond to a secondary carbon atom. In contrast, copolymers grafted with cyclic-amines (copolymers **13′**, **14′**, and **15′**) (Fig. 3c) always perform better as demulsifiers, regardless of the primary or secondary nature of the carbon atom in the functional group, and all of them have a lower polarizability value (Table S8 of Supplementary Information) than the amines in copolymer **4′**. The substitution of a hydrogen atom by a methyl group caused an efficiency decrease of approximately 1% (copolymer **16′** versus **11′**). Thus, the hydroxyl group plays an important role in the efficiency of the α,ω-diamine of POE–POP–POE triblock copolymer as a dewatering agent.

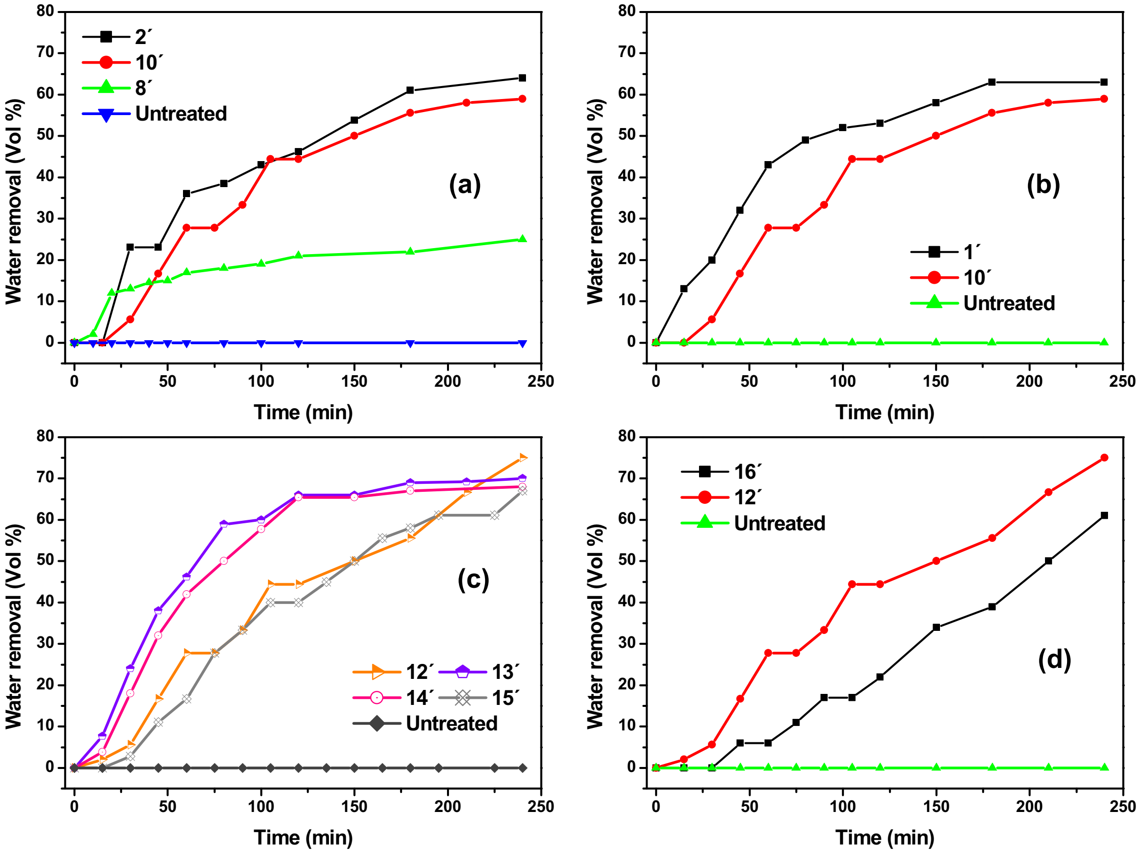

Figure 3 Demulsifying activity of Y-POE-POP-POE-Y, evaluated at 300 ppm and 80 °C. (a) Compounds 2′, 10′, and 8′; (b) compounds 1′ and 10′; (c) compounds 12′, 13′, 14′, and 15′; (d) compounds 16′ and 12′.

3.4. QSAR analysis

Synthesized mono- or di-functionalized polyethylene glycol (PEG), polypropylene glycol (POP) or POE/POP block copolymers with NH_2 or alkylamines group are widely employed in the industry. However, no one QSAR study has reported upon the effect of the amine structure in the reaction yield values to obtain a functionalized triblock copolymer. Hence, we decided to carry out this QSAR study at the DFT level. Furthermore, a second QSAR analysis was done in order to correlate the α,ω-diamine in the PEO–PPO–PEO triblock copolymer structure with its activity as dehydrating agent of crude oil. This analysis was done at the AM1 semiempirical level and the relatively costly DFT level, both based upon the following quantum descriptors: frontier orbital energy (E_{HOMO} and E_{LUMO}), molecular volume (V_{M}), dipolar moment (μ), absolute softness (S), absolute hardness (η), electronegativity (χ), electrophilicity (ω) and electrostatic potential (EP), and obtained as well at the DFT level. Vijayaraj et al. (2009) carried out a QSAR analysis of chlorobenzenes (n = 13) employing global reactivity descriptors such as chemical hardness, chemical potential, and electrophilicity, which were obtained from various density functionals. In this case, given the inverse relationship between softness and hardness, the MLR analysis was carried out considering each one individually. Finally, physico-chemistry parameters, such as the partition coefficient (log P) and molecular refractivity (MR), were obtained from a QSAR analysis implemented in Hyperchem.

3.4.1. QSAR for copolymer functionalization with amines by bimolecular nucleophilic substitution (S_N2)

Although DFT calculations are relatively costly, the optimization of small molecules is relatively rapid; for this reason, quantum descriptors were obtained at this level; these are listed in Tables S1–S4 (Supplementary Information). In regard to the sample number used in the QSAR study, several publications in the literature report samples where $n > 15$, demonstrating that QSAR studies are feasible on this scale (Zhu et al., 2010; Khaled, 2011; Hemalatha et al., 2012). The QSAR study was performed using MLR analysis with stepwise selection and the elimination of variables, considering the t-test value. Thus, the MLR regression model for absolute softness and absolute hardness yielded the same equation:

$$\mathrm{LogER_{calc}} = -15.4701 - 0.9433\ EP - 0.0017\ MR \tag{3}$$

$$n = 15,\ R^2 = 0.9062,\ R^2_{\mathrm{adj}} = 0.8905,\ SD = 0.007,\ F = 57.93,$$
$$q^2_{\mathrm{loo}} = 0.8964,\ q^2_{\mathrm{lmo}} = 0.4332,\ AIC = 0.80,\ RMSE = 0.0063$$

In this equation, EP and MR gave a t-Student of 7.90 and 4.52, respectively.

Cross-validation provides a reasonable approximation of the capability of QSAR analysis to predict the activity values of new compounds. However, external validation gives the ultimate proof of the true predictability of a model. In this sense, for better external predictive potential of the model, a modified $r^2_{m(rest)}$ was introduced by the following equation (Roy and Roy, 2008; Roy et al., 2009):

$$r^2_{m(test)} = r^2 * \left(1 - \sqrt{r^2 - r_0^2}\right) \tag{4}$$

where r^2 is squared correlation coefficient between the observed and predicted values, and r_0^2 is the squared correlation coefficient between the observed and predicted values with intercept set to zero. The value of $r^2_{m(rest)}$ should be higher than 0.5 for an acceptable model; moreover, it may be used for the selection of the best predictive models among comparable models. The $r^2_{m(rest)}$ value for Eq. (3) was higher than 0.5; therefore, it is an acceptable model. Fig. 4 shows a graphic of the MLR regression model for Eq. (3). The amine selection process is an important step in getting a good yield from the S_N2 reaction, but mainly, in synthesizing a suitable demulsifier agent. Hence, a QSAR study is an important step in designing new bifunctionalized copolymers.

3.4.2. QSAR of the α,ω-diamine of PEO–PPO–PEO copolymer with a PEO:PPO ratio of 30:70

A PEO–PPO–PEO triblock copolymer structure with two OH terminal groups was built, taking into account 28 molecules of PO, forming a central block, and two side segments, consisting of 6 molecules of EO, with a ratio of 30:70; this copolymer had a number average molecular weight (*Mn*) of 2172.9 g mol^{-1}, obtained from QSAR parameters implemented in Hyperchem. In contrast, SEC characterization (based on polystyrene standards) revealed a copolymer average molecular weight where Mn = 2630 g mol^{-1} and a polydispersity index where I_p = 1.09, meaning that the built copolymer is approximately 458 g mol^{-1} lower than the experimental value, so this structure is a representative model. Subsequently, OH terminal groups were substituted for each amine and reoptimized at AM1. Finally, a single-point calculation at the B3LYP/6-31G(*d*) level was done. Puzyn et al. (2008) has described the use of semiempirical methods instead of relatively expensive calculations at the DFT level for persistent organic pollutants like polychlorinated dibenzo-*p*-dioxins, dibenzofurans and diphenyls. Considering that the α,ω-diamine of PEO–PPO–PEO copolymer consists of 389–441 atoms, the computational cost was a very important consideration when planning the QSAR study. In order to make a comparison, quantum descriptors at the semiempirical and DFT levels and physico-chemistry parameters from Hyperchem software were obtained for the α,ω-diamine of PEO–PPO–PEO copolymer (Tables S5–S8 in Supplementary Information). It is important to mention that copolymer **12′** (water removal = 75%) was the dewatering agent with the lowest log *P* value (3.50), a descriptor that measures the hydrophobicity of compounds. Hence, a low value is preferable, because the bifunctionalized copolymer could interact with the hydrophobic part of the emulsion to break it up and remove the water. The bifunctionalized copolymer could act as if it were a crown-ether, due to its structure attracting dissolved ions and water molecules. Copolymer **8′** (water removal = 25%) showed the highest log *P* value (13.28), being a compound tending more to the hydrophobic phase, and not efficient enough to break up the emulsion, which is reflected in the water removal efficiency value.

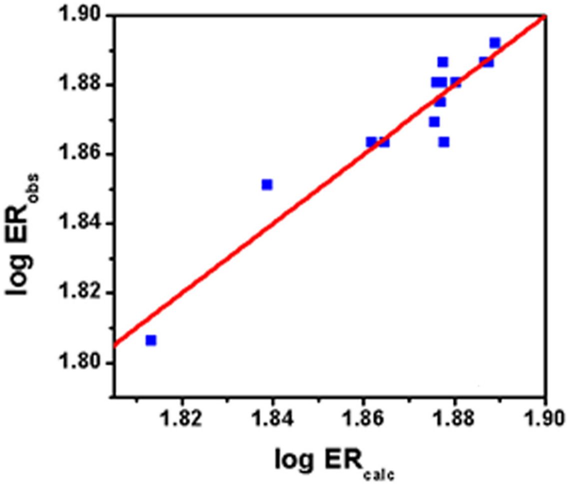

Figure 4 Graphic of log ER$_{calc}$ vs log ER$_{obs}$ for the (S_N2) reaction for Eq. (3).

Using the same quantum and physico-chemistry parameters as in the QSAR analysis of the S_N2 reaction, a MLR regression model for the α,ω-diamine of PEO–PPO–PEO copolymer for both theoretical levels gave R^2 values lower than 0.5. Zhu et al. (2010) carried out a QSAR study where n = 11 and 29 physico-chemistry and quantum chemistry. Therefore, other quantum and physico-chemistry parameters were included in this QSAR analysis, such as: energy total (E_T), molecular surface area (S_M), hydration energy ($E_{Hydration}$), and molecular weight (*MW*). The MLR analysis was done considering 13 parameters. The Pearson correlation coefficients for the AM1 and DFT levels are summarized in Tables S9 and S10. The matrix obtained provides information on the negative and positive correlations among variables, with indications of several strong correlations where $r \geqslant 0.8$. For both theoretical levels, μ shows a low correlation: $r \leqslant 0.55$. An MLR analysis of parameters at the AM1 level considered absolute hardness and absolute softness separately, yielding Eqs. (5) and (6), respectively;

AM1 level

$$\begin{aligned}\log \mathrm{WR_{calc}} = {} & -6.5438 + 2.1638\ E_{\mathrm{T}} + 13476.9674\ E_{\mathrm{HOMO}} \\ & + 13582.9337\ E_{\mathrm{LUMO}} + 0.00258\ V_{\mathrm{M}} \\ & + 26844.4364\ \chi + 317.86598\omega - 0.0554\ MR \\ & + 0.0123\ MW\end{aligned} \tag{5}$$

$n = 15,\ R^2 = 0.8066,\ R^2_{\mathrm{adj}} = 0.5487,\ SD = 0.0753,\ F = 3.13,$
$q^2_{\mathrm{loo}} = 0.7602,\ q^2_{\mathrm{lmo}} = 0.7112,\ AIC = 0.99,\ r^2_{m(rest)} = 0.4529,$
$RMSE = 0.0476$

$$\begin{aligned}\log \mathrm{WR_{calc}} = {} & -101.1207 + 2.4588\ E_{\mathrm{T}} + 21393.3770\ E_{\mathrm{HOMO}} \\ & + 21674.6650\ E_{\mathrm{LUMO}} + 0.0032\ V_{\mathrm{M}} \\ & + 18.5539\ S - 43043.9908\ \chi + 0.0204\ E_{\mathrm{Hydration}} \\ & - 0.0774\ MR + 0.0179\ MW\end{aligned} \tag{6}$$

$n = 15,\ R^2 = 0.9058,\ R^2_{\mathrm{adj}} = 0.7362,\ SD = 0.0575,$
$F = 5.347,\ q^2_{\mathrm{loo}} = 0.8960,\ q^2_{\mathrm{lmo}} = 0.9511,\ AIC = 0.99,$
$r^2_{m(rest)} = 0.6305,\ RMSE = 0.0332$

In Eq. (5), absolute hardness was eliminated during the MLR analysis due to the restriction of the *t*-Student value, giving a $r^2_{m(rest)}$ value of less than 0.5; while Eq. (6) gave an acceptable $r^2_{m(rest)}$ value. In Eq. (6), in contrast with Eq. (5), beside absolute softness, $E_{\mathrm{Hydration}}$ was considered, showing a correlation with MR where $r = 0.553$, whereas for the correlation of ω with MR $r = 0.432$ (Table S9).

On the other hand, the MLR analysis considering DFT parameters yielded Eqs. (7) and (8), taking into account hardness and softness, respectively.

DFT level

$$\begin{aligned}\log \mathrm{WR}_{\mathrm{calc}} = {} & -9.2249 + 0.0262\ E_{\mathrm{T}} - 36451.4147\ E_{\mathrm{HOMO}} \\ & - 21300.2681\ E_{\mathrm{LUMO}} - 0.0146\ S_{\mathrm{M}} + 0.0044\ V_{\mathrm{M}} \\ & - 0.1615\ \mu - 14780.3463\ \eta - 58704.6835\ \chi \\ & + 1300.8218\ \omega + 0.07145\ E_{\mathrm{Hydration}} - 0.2828\ MR \\ & + 0.1687\ MW \qquad (7)\end{aligned}$$

$$n = 15,\ R^2 = 0.9879,\ R^2_{\mathrm{adj}} = 0.9151,\ SD = 0.0326,\ F = 13.58,$$
$$q^2_{\mathrm{loo}} = 0.9877,\ q^2_{\mathrm{lmo}} = 0.9718,\ AIC = 0.99,\ r^2_{m(rest)} = 0.8823,$$
$$RMSE = 0.0119$$

$$\begin{aligned}\log \mathrm{WR}_{\mathrm{calc}} = {} & -7.7295 + 0.0207\ E_{\mathrm{T}} - 26386.7574\ E_{\mathrm{HOMO}} \\ & - 26057.3202\ E_{\mathrm{LUMO}} - 0.0126\ S_{\mathrm{M}} \\ & + 0.0041\ V_{\mathrm{M}} - 0.1582\ \mu - 53286.4179\ \chi \\ & + 1147.3108\ \omega + 0.0678\ E_{\mathrm{Hydration}} \\ & - 0.2329\ MR + 0.1358\ MW \qquad (8)\end{aligned}$$

$$n = 15,\ R^2 = 0.9569,\ R^2_{\mathrm{adj}} = 0.7987,\ SD = 0.0503,$$
$$F = 6.05,\ q^2_{\mathrm{loo}} = 0.9549,\ q^2_{\mathrm{lmo}} = 0.9584,\ AIC = 0.99,$$
$$r^2_{m(rest)} = 0.7598,\ RMSE = 0.0225$$

Contrary to what was observed in Eq. (5), hardness was preferred instead of considering absolute softness. According to $r^2_{m(rest)}$ restriction, Eqs. (7) and (8) are acceptable models; however, absolute hardness was included in Eq. (7), which obtained better statistical values than Eq. (8), from which the parameter of absolute softness was omitted. Furthermore, Eqs. (7) and (8) involve more parameters than the AM1 parameters, such as S_{M} and μ, which evidently contributed to a model with a better fit.

It is important to point out that in Eqs. (5)–(8), molecular refractivity shows the highest *t*-Student values: 3.28, 4.91, 8.19, and 5.67, respectively, highlighting the importance of this parameter in the QSAR analysis. Although the R^2 of Eq. (6) is lower than in Eqs. (7) and (8), it is possible to carry out a feasible QSAR study for the α,ω-diamine of $\mathrm{PEO_x}$–$\mathrm{PPO_y}$–$\mathrm{PEO_x}$ copolymer using a low computational-time method like AM1. Fig. 5 shows the graphics from the MLR analysis using the AM1 and DFT levels.

On the other hand, 2-(methylamino)ethanol (**16**) was employed to evaluate the equations obtained. Experimentally, for the S_N2 reaction, the efficiency obtained was 75% (log $\mathrm{ER_{obs}}$ = 1.8751), whereas for the copolymer functionalized as a demulsifier with this amine, the water removal efficiency was 61% (log $\mathrm{WR_{obs}}$ = 1.7853). Table 3 presents the quantum and physico-chemistry data for amine and the copolymer-diamine, respectively. Table 4 shows the log $\mathrm{ER_{calc}}$ for the

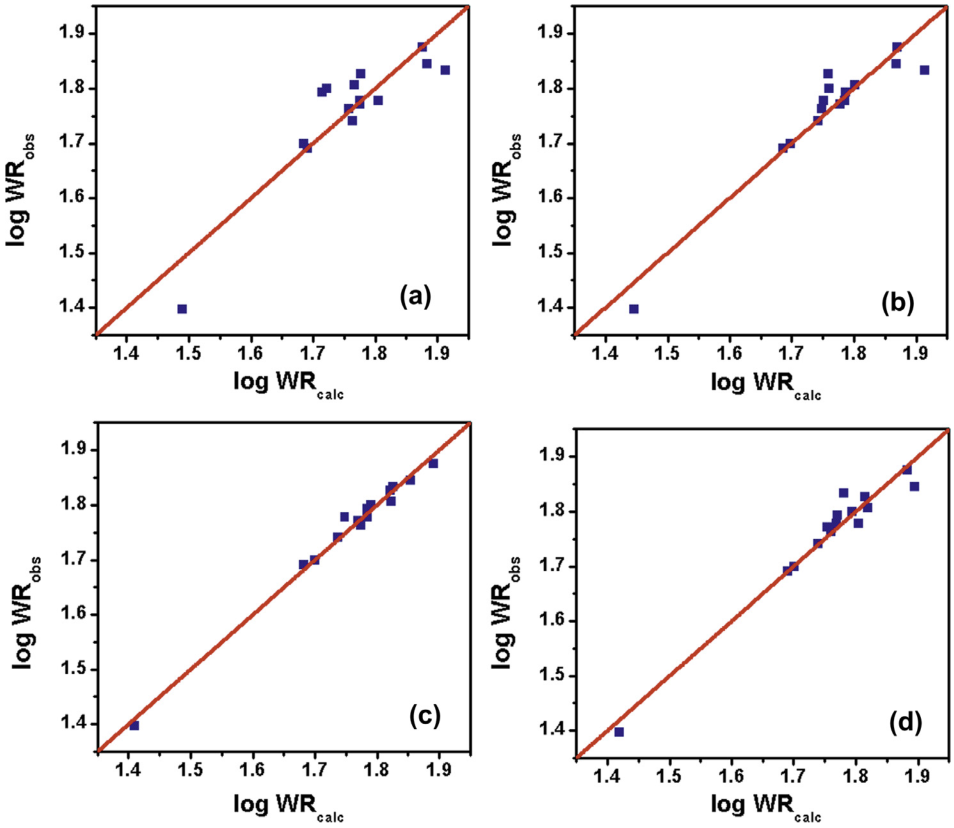

Figure 5 Graphic of log $\mathrm{WR_{calc}}$ vs log $\mathrm{WR_{obs}}$ for POE-PPO-POE triblock copolymer with a 30:70 relationship: (a) the AM1 level using Eq. (5); (b) the AM1 level using Eq. (6); (c) the DFT level using Eq. (7); and (d) the DFT level using Eq. (8).

Table 3 Quantum and physico-chemical parameters for 2-(methylamino)ethanol and copolymer difunctionalized with this amine.

Parameter	Compound 16	Copolymer 16′	
		AM1	DFT
$E_T{}^*$	–	-3.23615[a]	-7674.4706[b]
E_{HOMO} (eV)	-0.0025	-0.3197	-0.1893
E_{LUMO} (eV)	0.0031	0.0821	0.0423
S_M ($Å^2$)	–	1932.67	
V_M ($cm^3\ mol^{-1}$)	79.69	5307.94	
μ (Deybe)	1.6595	0.8099	0.8450
EP (a.u.)	-18.4076	–	
S (eV)	356.5062	2.4886	4.3189
η (eV)	0.0028	0.2009	0.1158
χ (eV)	-0.0003	0.1188	0.0735
ω (eV)	1.45E-05	0.0351	0.0233
log P	-0.65	4.39	
$E_{Hydration}$ ($kcal\ mol^{-1}$)	–	-5.96	
MR ($Å^3$)	8.27	605	
MW (amu)	–	2287.09	

[a] $kcal\ mol^{-1}$.

[b] Hartrees.

Table 4 Log ER_{calc} calculated for the S_N2 reaction and the water removal efficiency of 2-(methylamino)ethanol (**16**).

Equation	Log ER_{calc}	Residual	Efficiency calculated (%)
Bimolecular nucleophilic substitution (S_N2)			
3	1.8794	-0.0043	75.8
Water removal efficiency			
6	1.8073	0.0220	64.2
7	1.7894	0.0041	61.6
8	1.9065	0.1212	80.6

S_N2 reaction and water removal efficiency compared to the experimental values. In regard to the S_N2 reaction, Eq. (3) showed a good correlation with the experimental value, giving a low residual value. Thus, what is relevant in this QSAR analysis is that both equations can be employed to obtain the log ER_{calc} for this system.

In regard to water removal efficiency, Eq. (6) gave an acceptable log WR_{calc} and residual values at the AM1 level. For the DFT level, Eq. (7) gave the lowest residual value and depicted the log WR_{obs} value well. Eq. (8) gave an overestimation of log WR_{obs}, being even greater than that obtained in Eq. (5). Hence, only Eqs. (6) and (7), depending upon the theoretical level employed, should be considered as having the right correlations for obtaining water removal efficiency for the newly synthesized α,ω-diamine of PEO–PPO–PEO copolymer.

In sum, every crude oil has specific characteristics; hence the design of a suitable α,ω-diamine of PEO–PPO–PEO copolymer is key to developing an efficient dewatering agent for a specific heavy crude oil. This QSAR study establishes the relationship between a bifunctionalized copolymer structure and its effectiveness as a dewatering agent for a form of crude oil with characteristics similar to those described in Table 1.

4. Conclusions

Bimolecular nucleophilic substitution (S_N2) of α,ω-ditosylate ester of POE–POP–POE triblock copolymer with secondary amines enabled synthesis of a series of α,ω-diamine PEO–PPO–PEO triblock copolymers, which were evaluated as demulsifing agents for heavy crude oil. The hydroxyl group in the amine structure proved to have an important role in dewatering capabilities, the copolymer functionalized with diethanolamine being the best dewatering agent.

Copolymers bifunctionalized with dialkylamines showed low efficiency values for water removal. They were low even when the carbon atoms increased; hence, the amine structure plays an important role in the efficiency of functionalized copolymer.

Furthermore, two QSAR analyses were carried out in this work: the first one examined the correlation between the amine structure, with the efficiency value in the substitution reaction, and the α,ω-ditosyl ester of PEO–PPO–PEO triblock copolymer, to obtain a α,ω-diamine PEO–PPO–PEO triblock copolymer giving the MLR regression an excellent fit.

A second QSAR analysis was established between the structure of the α,ω-diamine PEO–PPO–PEO triblock copolymer and its effectiveness as a dewatering agent for heavy crude oil, using parameters obtained at the AM1 and DFT levels. In this case, Eq. (7), which addressed the hardness parameter, gave the model with the best fit. Eq. (6), obtained using parameters at the AM1 level, yielded a lower R^2 value than the DFT level; however, $r^2_{m(rest)}$ was 0.6305; therefore, it could be considered an acceptable correlation. The molecular refractivity parameter showed the highest *t*-Student value, highlighting the importance of this parameter in the QSAR analysis.

Finally, equations obtained for the MLR analysis in this QSAR study will make possible the design of new diamine PEO–PPO–PEO triblock copolymers as dewatering agents for a wide variety of heavy crude oils.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.arabjc.2014.01.021.

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