Sugar-based surfactants via click chemistry

Salih Mahdi Salman* & Waseela Abdul Redah Abdul Razak**

*Department of Chemistry-College of Medicine-University of Diyala (waamrs@yahoo.com)

**Department of Chemistry-College of Education for Pure Sciences, University of Diyala

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Abstract

Two new surfactants were synthesized from renewable materials via click chemistry. The starting materials are carbohydrates (e.g. methyl glycoside) and fatty acid derivatives based on both saturated and unsaturated fatty acids with a total chain length of C_{12} and C_{18}. Target applications of these surfactants focus on the stabilization or emulsions, in particular water-in-oil emulsions. The synthetic scheme applied a multi-step methodology, including activation, functionalization and finally coupling with fatty acids derivatives by using click chemistry technique. Surfactants were identified and their purity confirmed by NMR type ^{1}H and ^{13}C in addition to high resolution mass spectroscopy. Physical properties were studied by optical polarizing microscopy (OPM), differential scanning calorimetry (DSC) and surface tension measurements. Lyotropic phases were investigated by contact penetration with water under the OPM, while surface tension measurements used the DuNouy ring approach. The latter enables the determination of critical micelle concentrations

Keywords : Click chemistry, oil-water surfactants, sugar-based surfactants

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Salih Mahdi Salman* & Waseela Abdul Redah Abdul Razak**

مستحلبات سكرية جديدة بطريقة كيمياء الضغطة

صالح مهدي سلمان & وسيلة عبد الرضا عبد الرزاق

الخلاصة

تم تخليق نوعين جديدة من المستحلبات من المواد القابلة للتجديد بطريقة كيمياء الضغطة . المواد الاولية المستخدمة في التخليق هي عبارة عن كاربوهيدرات كالمثيل كلايكوسايد ومشتقات الاحماض الدهنية بنوعيها المشبع وغير المشبع بطول سلسلة لمجموعة الالكيل C_{12} و C_{18}. الهدف المتوخى من هذه التخليق هو المستحلبات وتحديدا مستحلبات المياه في الزيت . المخطط التخليقي اشتمل على منهجية الخطوات المتعددة في التخليق والمتضمنة تفعيل وتوظيف ذرة الكاربون C-(6) المراد استبدالها ومن ثم اجراء تفاعل الربط النهائي مع مشتق الحامض الدهني عن طريق تفاعل كيمياء الضغطة (click chemistry) . تم تشخيص المستحلبات المحضرة , والتأكد من نقاوتها باستخدام طيف الرنين المغناطيسي بنوعية (H^1), (C^{13}) بالاضافة طيف الكتلة. اما الخواص الفيزيوكيمياوية للمستحلبات المحضرة فقد تمت دراستها باستخدام المجهر الضوئي المستقطب و مسعر المسح التبايني بالاضافة جهاز قياس الشد السطحي .

مفاتيح البحث: كيمياء الضغطة مستحلبات الزيت- مياه , المستحلبات السكرية

Introduction

The availability of chemical processes and raw material open the sky to develop a wide range of surface–active compounds. Today, ecologic demands increasing amounts due to population growth and raw material resources are the driving forces for surfactants technology. Most of processes depend on petrochemical raw material [1]. Environmental issues and the shortage of the latter, which is expected to increase, cause continuous shift of chemical developments towards the utilization of renewable biological recourses in order to ensure sustainable raw materials.

The development of surfactants from carbohydrates and fatty acids is a strategy for the exclusive utilization of natural renewable resources. Three classes of sugar surfactant can be differentiated based on the chemical linkage of the two starting materials, i.e. glycoside, e.g. polyglucoside (APGs), alkyl glucamides and sugar esters. Each of these surfactants exhibit surface active properties, biodegradable and expected to show low human toxicity based on

the natural components and linkages. The glycosides are the most chemical resistant but expensive compared to sugar esters, which are significantly less stable. Sugar amide surfactants are reasonable chemically stable and economic but unfortunately exhibit high krafft temperature. There is another accessible technique to connect the sugar moiety with the alkyl chain by 1,2,3 triazole ring which expects to keep the stability of the surfactants with reduce the krafft temperature. This work is aim to synthesis of new sugar surfactant based on click chemistry and study of the physicochemical properties of the synthesized surfactants.

Methyl glucoside was chosen as starting material for this surfactants for two reasons: first because of economy and accessibility and second based on its chemical stability as glycoside with reduce hydrophilicity compare to glucose because of the lower number of the hydroxyl groups, which potentially increase the surfactant's solubility in an oil-based medium.

Results and discussion

2.1. Synthesis

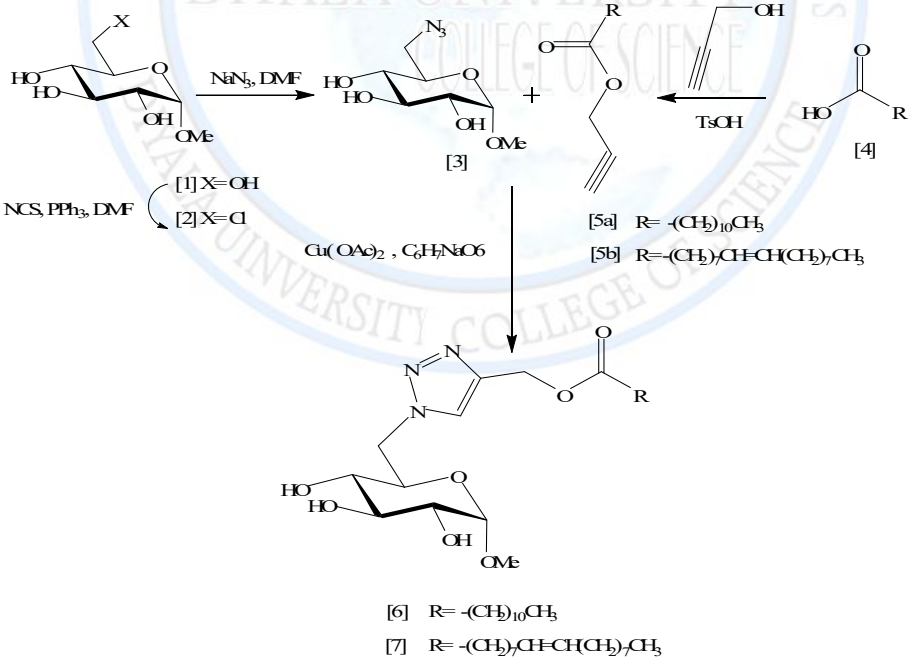

Figure1: Synthetic scheme of methyl glycoside surfactants

The synthesis of surfactants is based on methyl 6-azido-6-deoxy–α-D-glucopyranoside [3], which had been previously prepared by Hanssian et al in a one flask reaction[2]. Methyl glucoside **[1]** has only one primary hydroxyl group suitable for direct chlorination with *N*-chlorosccuinimde in the presence of triphenylphosphine in DMF. The reaction requires anhydrous conditions and furnishes methyl-6-deoxy-6-chloro-α-D-glucopyranoside [**2]** in good yield [3-5] The chloride was substituted with sodium azide after the excess of chlorination reagent was destroyed by addition of methanol. Since the reaction medium remains the same no solvent exchange is required to obtain **[3]**[6,7].Click chemistry based coupling of azide **[3]** with fatty acid propargyl ester ranging C_{12} and C_{18} was performed[8,9]. Saturated propargyl laurate **[5a]** and Unsaturated propargyl oleate **[5b**] was applied. The latter is easily accessible by simple treatment of lauric acid and oleic acid with propagyl alcohol under acidic conditions respectively. The click chemistry coupling used copper acetate $Cu(OAc)_2$ and Sodium ascorbate $C_6H_7NaO_6$ in methanol to offer compounds **[6]** and **[7]**[10]**.** The final surfactants were spectroscopically analyzed and the structural identities are based on NMR spectra (H^1 & C^{13}) and high resolution mass spectrometry.

^{1}H NMR for compound **[6]** (figure.2) show the proton signal of the triazol ring at δ 8.04, singlet of (CH_2-O) at δ 5.20, the anomeric signal (H-1) appears around δ 4.64, while the sugar protons (H-2 to H-5) are located between δ 3.85 and δ 3.14. The primary CH_2 (H-6a/b) appears between δ 4.53 and δ 3.34 and the methyl group at about δ 3.24. The protons of the alkyl chain appear between δ 2.31 (α-CH_2) and δ 0.91 (terminal CH_3). The ^{13}C NMR (figure.3) for compound [6] show the signal of the carbon of (C=O) at δ 173.62, (C-N) at about δ 142.64, (C=C) of the triazol ring at about δ125.88, the carbon of (C-O) at δ51.15, the anomeric carbon at around δ 100. Other sugar carbons appear between δ 72 and δ 70.50. The position of the primary carbon (C-6) is around δ40, while the methyl group is found at δ 54. The alkyl chain carbons appear in between δ 35 (α-CH_2) and δ 14 (CH_3). For detailed analysis see experimental data.

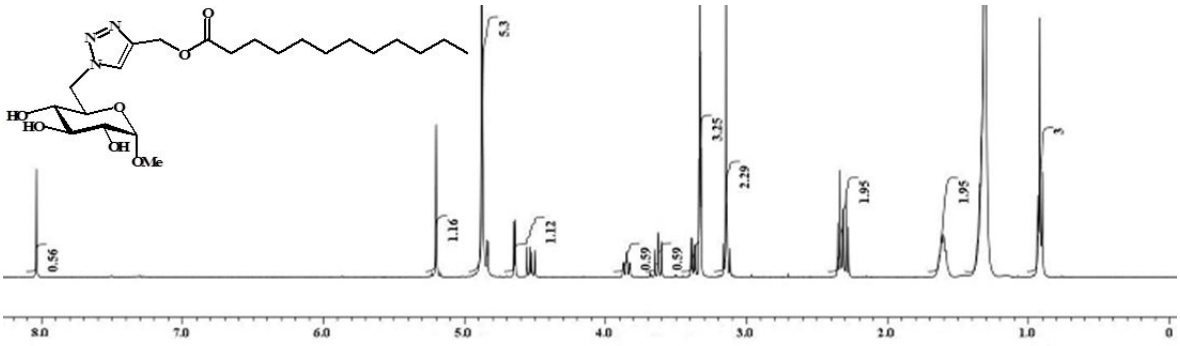

Figure 2: H^1 NMR spectra for surfactant [6]

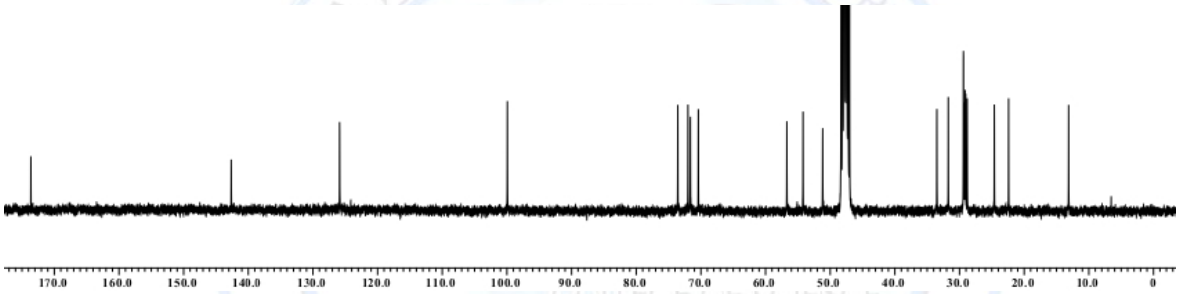

Figure 3: C^{13} NMR spectra for surfactant [6]

Both H^1 NMR and C^{13} NMR for surfactants **[7]** show approximately the same chemical shift in addition to the signal of (CH=CH) at δ 5.35 and the signal of (CH_2-CH) at δ 2.0. The structures of the synthesized surfactants were confirmed by the high resolution mass spectrum, which show $[M+H]^+$ fractions and their isotopes for details see the experimental data.

2. Physiochemical properties

Both triazol surfactants show low solubility in water at room temperature and reasonable kraffit temperature for surfactant **[6]** about (45 °C) and high Krafft temperature more than (100 °C) for surfactant **[7].** Non surfactant shows a liquid crystals phase in OPM

investigations, but both surfactants exhibit a crystalline phase (figure 4a) and isotropic liquid. In contact with water myelin figure were found (figure 4b)

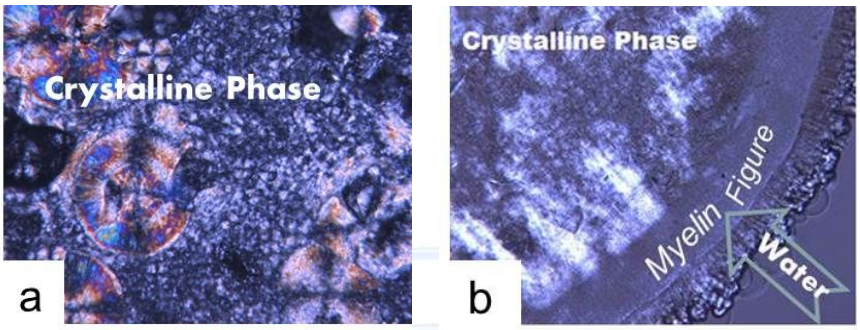

Figure 4: OPM investigations of surfactant [8]

The absence of thermotropic liquid crystalline of methyl glycoside triazol surfactants were confirmed by differential scanning calorimetry (DSC). Which show only single phase with an enthalpy that is outside the range of liquid crystalline phase termination (28 kg/mol for C_{12} and 38 kg/mol for C_{18}). The DSC spectrum of **[7] (**figure 5) show only one phase transition at 110 ºC for both heating and cooling cycle, which is refers to the melting and recrystallization of a crystalline phase.

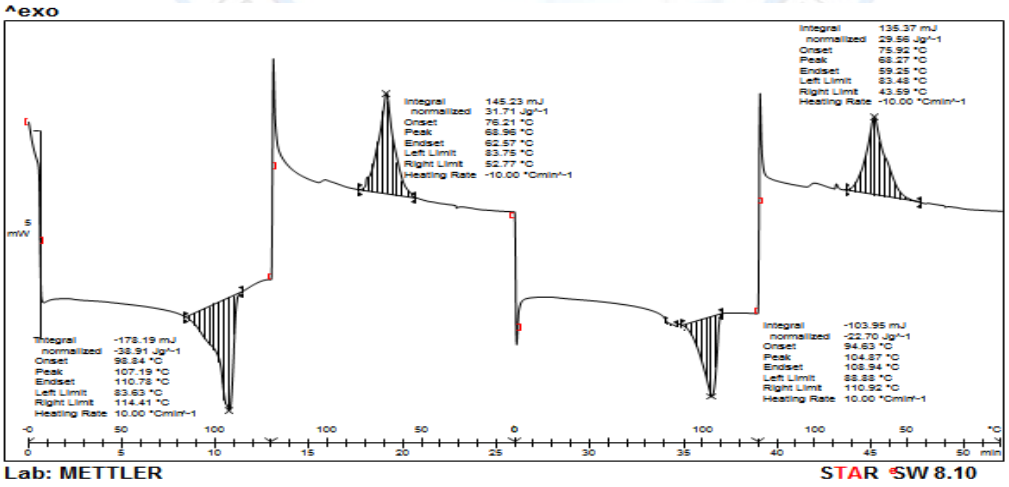

Figure 5: DCS spectrum of surfactant [7]

The critical micelle concentrations (CMC) were determined based on surface tension measurements carried out for the series of surfactant solutions with different concentrations[11]. The CMC investigation was limited to the C_{12} surfactants longer chained homologues, on the other hand, are extremely difficult to measure, due to the high Krafft temperature. The surface tensions and CMC for C_{12} surfactants are 30 mN/m at CMC 0.5 mmol/L (figure 6), which is in good agreement with previously reported mono saccharides linked to the same number of carbon atoms chain[12].

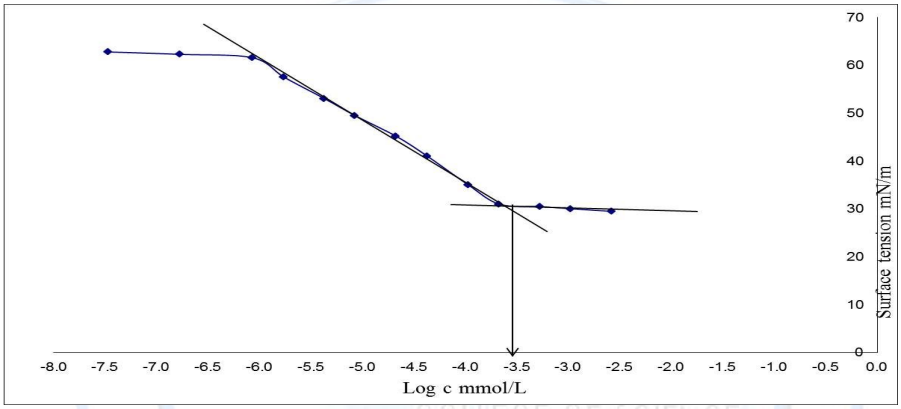

Figure 6: CMC investigation of surfactant [6]

Experimental

3.1. General procedures

Melting temperatures were determined using a manual melting point apparatus. Optical rotations were measured at 589 nm in 10 cm cells at room temperature. NMR spectra were recorded on Jeol and Bruker spectrometers at 400 MHz for ^{1}H and 100 MHz for ^{13}C, respectively. Assignments of ^{13}C-signals are based on HMQC spectra. High-resolution mass spectra were recorded on an LC–MS system, applying MeOH/water eluents. Phase-transition temperatures were determined by DSC in replicated heating–cooling cycles at a heating/cooling rate of 10 °C min^{-1}. Lyotropic phases were investigated using the contact penetration technique under OPM observation[13,14] . The determination of Krafft points applied heating 20 mL samples of the surfactant in water at a concentration of about 10% above the

CMC in an oil bath under moderate stirring until the mixture re cleared. Critical micelle concentrations were determined by surface tension measurements. Surface tension measurements were measured at rt in 5 replicates with a standard deviation below 0.1 mN m^{-1}. The intersection of the concentration dependent and the high concentration independent region in the plot of the surface tension versus the logarithmic concentration determines the CMC.

3.2. Chlorination.

A solution of methyl α-D-glucopyranoside (1.0 eq.), triphenylphosphine (2.0 eq) and N-chlorosuccinimide (2.0 eq.) in dry *N,N*-dimethylformamide (20 mL per gram) was heated to 60 ºC with stirring for about 2 hours. When the TLC (ethyl acetate:hexane 4:1) showed the consumption of the starting material the solution was cooled and 10 ml of methanol was added in order to decompose unreacted chlorinating agent (NCS). *N,N*-dimethylformamide was evaporated and triphenylphosphine oxide was removed by added water and extraction with dichloromethane. The filtrate was evaporated to yield methyl 6-chloro-6-deoxy-α-D-glucopyranoside, which subjected to azidation without further purification[15,16] .

3.3. Azidation

A suspension of chloro deoxy sugar (1.0 eq.) and sodium azide NaN_3 (6.0 eq) in *N,N*-dimethylformamide DMF (20 ml per gram) was heated to 80 ºC for 24 hours. The solution was cooled to room temperature, diluted with water and extracted with dichloromethane. The organic layer was washed with water, saturated $NaHCO_3$ solution and water, dried over $MgSO_4$ and concentrated under reduced pressure. After acetylation with acetic anhydride (2.0 eq.) in pyridine (20 mL per gram) and recrystallization with ethanol NMR pure white azide was obtained in very good yield [17,18] .

3.4. Esterification

Fatty acid (1.0 eq.) was refluxed with (1.2 eq.) of Propargyl alcohol and catalytic amount of p-toluene sulfonic acid in toluene at about 100 °C for about 6h. The mixture was cooled down

to room temperature and extracted two times with saturated $NaHCO_3$ solution and water to get NMR pure fatty acid ester in very good yield[19,20] .

3.5. Click chemistry

A solution of the sugar azide (1 equiv) was stirred with propargyl alcohol (1.1 equiv), (0.01 equiv) and 1 copper chloride and sodium ascorbate (0.1 equiv) in methanol until TLC showed no traces of the starting sugar azide. Filtrate the reaction mixture through ciliate and concentrated under reduced pressure, the residue was purified through silica gel with 9:1 chloroform: methanol as eluent to result the final surfactant[21, 22,23].

3.5.1. Synthesis of [1-(Methyl 6-deoxy- α -D-glucopyranosid-6-yl)-1H-1,2,3- triazol-4-yl]-methyl dodecanoate [6]

Methyl glycoside 6-azide (2 g, 0.01 mmol) was reacted with propargyl dodecanoate according the general procedures (3.5) to furnished (2g, 78%) of surfactant **[6]** as NMR pure white crystals. mp 107 ^{o}C. $[\alpha]_D^{25}$= + 65 (c 0.2, CH_3OH). ^{1}H NMR (400 MHz,CD_3OD) , 8.0 (s. 1H, CH=C triazol), 5.20 (s, 1H, CH_2-O) , 4.64 (d,1H, H-1), 4.55 (ddd,1H, H-6A), 3.85 (ddd, H-5), 3.62 (dd~t, H-3), 3.32 (s, 3H, Me), 3.32-3.33 (ddd~dt, H-6B), 3.11-3.16 (m,2H, H-4 and H-2), 2.31 (t, 2H, α-CH_2), 1.60 (m_c, 2H, β-CH_2), 1.30 (m_c, 16H, bulk-CH_2), 0.91 (t, 3H, CH_3; $^3J_{1,2}$=3.5, $^3J_{2,3}$=10.0, $^3J_{3,4}$=9.5, $^3J_{4,5}$=9.0, $^3J_{5,6A}$=2.0, $^3J_{5,6B}$=7.0, $^2J_6$= 14.0, . ^{13}C NMR (100 MHz , CD_3OD) 173.62 (C=O) , 142.6 (*C*-quat triazol), 125.88 (N-*C*=C triazol), 100 (C-1), 73.56 (C-2), 72.02 (C-3), 71.62 (C-5), 70.40 (C-4), 56.70 (CH_3), 54.20 (C-6),51.15 (C-O), 33.50 (α-CH_2), 31.74 (ω -2), 29.93-28.80 (bulk-CH_2), 24.62 (β-CH_2), 22.40 (ω -1), 13.12 (ω). HRMS: [M+H]+ calcd for $C_{22}H_{40}N_3O_7$: 458,2860,459.2893 (26%), found: 458.2857 (100%), 459.2890 (30%).

3.5.2. Synthesis of [1-(Methyl 6-deoxy- α -D-glucopyranosid-6-yl)-1H-1,2,3-triazol-4-yl]-methyl oleate [7]

Methyl glycoside 6-azide (2 g, 0.01 mmol) was reacted with propargyl oleate according the general procedures (3.4.4.1) to furnished (4g, 74%) of surfactant [7] as NMR pure white crystals. mp 111 ^{o}C. $[\alpha]_D^{25}$= + 90 (c 0.2,CH_3OH). ^{1}H NMR (400 MHz,CD_3OD), 8.0 (s. 1H,

CH=C triazol), 5.20 (s, 1H, CH_2-O) ,4.85 (mc, 2H, C*H*=C*H*),4.62 (d,1H, H-1),4.50 (ddd,1H, H-6A), 3.82 (ddd, H-5), 3.61 (dd~t, H-3), 3.37 (ddd~dt, H-6B), 3.30 (m,2H, H-4 ,3.15 (ddd, 1H, H-2), 3.11 (s, 3H, Me), 2.30 (t, 2H, α-CH_2), 1.89 (mc , 4H, CH_2-CH=CHCH_2), 1.60 (m_c, 2H, β-CH_2), 1.26 (m_c, 16H, bulk-CH_2), 0.88 (t, 3H, CH_3; $^3J_{1,2}$=3.5, $^3J_{2,3}$=10.5, $^3J_{3,4}$=9.0, $^3J_{4,5}$=9.0, $^3J_{5,6A}$=3.0, $^3J_{5,6B}$=6.5, $^2J_6$= 14.5, . ^{13}C NMR (100 MHz , CD_3OD) 173.71 (C=O) , 143.13 (*C*-quat triazol),129.10 ,129.78 (C=C), 125.73 (N-*C*=C triazol), 100 (C-1), 74.26 (C-2), 72.10 (C-3), 70.68 (C-5), 69.90 (C-4), 57.43 (CH_3), 55.60 (C-6),50.89 (C-O), 34.19 (α-CH_2), 31.98 (ω -2), 29.84-27.30 (bulk-CH_2), 24.90 (β-CH_2), 22.76 (ω -1), 14.19 (ω). HRMS: [M+H]+ calcd for $C_{28}H_{50}N_3O_7$: 540,3643,541.3676 (33%), found: 540.3646 (100%), 541.3679 (29%).

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