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Dear Reviewer #3:

Thank you very much for taking the time to review our manuscript [gels-1665237](#). Our responses to your feedback is provided below in red.

Sincerely,

Darren

Darren Makeiff, PhD
Research Officer
National Research Council of Canada
Nanotechnology Research Center
Edmonton, AB, Canada

Canada 

Comments and Suggestions for Authors

In this work titled: "Self-Assembly of Alkylamido Isophthalic Acids Toward the Design of a supergelator: Phase Selective Gelation and Dye Absorption", Makeiff et al. report on a series of 5 new supramolecular gelators derived from 5-amido isophthalic acid with linear and branched alkyl chains. Even though many other isophthalic acid derived gelators were already reported in the literature the structures of the present work are new and the organogels, their properties and potential applications and characterization were performed exhaustively so I consider the work will be of interest to the supramolecular gel community of the journal. But there are some minor points that need to be revised before this manuscript is accepted to be published.

In a structure based search I found that the authors have patented the use of these gelators as phase selective gelators and organogel formulations, it would be interesting to cite those patents and refer to them in the text, since they reflect the potential applications of the materials:

Phase selective gelation with alkylated aromatic acid compounds

Application number: CN201210548127 20121217

Priority number(s): US201113327664 20111215

Organogel Compositions Comprising Alkylated Aromatic Acids

Application number: US201113327655 20111215

Priority number(s): US20100820497 20100622 ; US201113327655 20111215

National Center for Biotechnology Information (2022). PubChem Patent Summary for US-2011311813-A1, Self-assembled nanostructures. Retrieved April 18, 2022 from <https://pubchem.ncbi.nlm.nih.gov/patent/US-2011311813-A1>.

Yes this work was initially done in partnership with the Xerox Research Centre of Canada, which resulted in several patents filed in Canada, the USA, Europe and Asia. The US patents have been added to the references as suggested.

62. Makeiff, D.A.; Carlini, R. Nanosized particles of benzimidazolone pigments. US Patent US7905954B2, 15 March 2011.

63. Makeiff, D.A.; Carlini, R. Sterically bulky stabilizers. US Patent US9067878B2, 23 April 2013.

64. Makeiff, D.A.; Carlini, R. Self-assembled nanostructures. US Patent US8703988B2, 22 April 2014.

65. Makeiff, D.A.; Carlini, R. Organogel compositions comprising alkylated aromatic acids. US Patent US9067878B2, 30 June 2015.

66. Makeiff, D.A.; Carlini, R. Phase selective gelation with alkylated aromatic acid compounds. U.S Patent US9623435B2, 18 April 2017.

At the abstract, line 16 "...gelators for low, polarity solvents" should say "...gelators for low polarity solvents..."

Thank you for pointing this out. The comma has been removed.

Since the chemical structures of the 5-alkylamido ISA compounds in Figure 2 are different (but closely related) than the alkylated ISA gelators previously reported by Hamilton et al [37] or Lv et al [38]. I consider that Figure 1 should be completed with the identity of R at position 5 present on the isoftalic acid derived gelators previously reported by Hamilton and Lv (as they are related structures it would make it easy to the reader to relate to the gelators of the present work).

Done

Gelator ISA16 L is similar to CP14IP from reference 38. The main difference being the inverted amide group (and one carbon on the alkyl chain). Both gelators should be compared and their properties discussed in base of the structural difference, and if possible, a conclusion about the effect of the amide inversion.

We thank the reviewer for this suggestion. ISA16 is also similar to CP18IP (both CP14IP and CP18IP 2 C atoms less and more, respectively). Only the gelation behavior with ethanol-water mixtures can be compared since there is no data for CP14IP and CP18IP with other solvents. The following text has been added to the end of the gelation behavior section:

“Note that the chemical structure of the gelator ISA16L is similar to the previously reported gelators CP14IP and CP18IP (Figure 2) [38]. The only differences are the reversed direction of the amide linker group and minus or plus two methylene groups, respectively (Figure 2). Although no data was reported on the gelation behavior of CP14IP and CP18IP with low polarity solvents, both compounds were good gelators for highly polarity ethanol:water (97:3 to 92.5:7.5) solvent mixtures at 10 mM [38]. For this work, ISA16L only formed crystallites/precipitates and not gels with similar ethanol:water solvent compositions at 10 mM. Clearly, the subtle structural change of reversing the direction of the amide group has a significant impact on the ability of alkylamido ISA compounds to form gels with polar solvents.”

Gel of ISA12 in xlenes has a MCG of <0.5 according to table S1, but in figure 4a, blue line, it can be seen that it can form gels even at concentrations as low as 0.01. I wonder if this difference has a reason, if not in table S1 it should say MCG <0.01. check the other MCGs.

We thank this reviewer very much for pointing out this mistake. The data for the gels with xylenes and decalin were plotted on the wrong panels. The graphs in Figure 4a and 4b have been switched to correct this. Also all the data has been checked and corrected in Table S1. The MGC for ISA16 of 2 has been corrected to <0.1. Also, a missing data point for ISA12 at 2 wt % was added to Figure 4a. Three data points were also removed for ISA24 in Figure 4a (0.2, 2.5 and 3 wt %). These experiments could not be found amongst the pages of 10 lab notebooks and thus were deleted as they do not change any of the results.

The authors used a cryo-SEM microscope to take images of what they call in situ aerogels, (freeze- dried), I do not understand why it is necessary to use the expensive cryo-SEM microscope if the sample is an

aerogel, so it is already dried and there is no liquid to freeze, I understand you can use regular SEM to analyze the aerogels or xerogels (formed in situ or ex situ). If my analysis is wrong, the text should be revised to clarify this.

We apologize for this confusion. The in and ex situ aerogels were prepared at different scales. The in situ was small scale by drying a small piece of “wet” organogel (<0.1 mL) directly on the microscopy substrate. The sample was freeze-dried *in vacuo* in the chamber of a cryo-coater and subsequently coated with a metal film. In contrast, “ex situ” aerogel was prepared in a vial on larger scale (1-20 mL), by freezing and then freeze drying using a conventional freeze drier. Then a small piece of aerogel was transferred onto the microscopy substrate, sputter-coated with a metal film, and then analysed using regular SEM at room temp. Clearly, different results were obtained. Features are seen in Figure 7c that are not present in Figures 7e and f. Also, the cryo-SEM work was added only recently just before submission of this manuscript as it is a new capability at our research center.

Although the details of the preparation of the in situ and ex situ aerogel samples are clearly explained in the experimental section (Lines 674-689, 704-711 and 721-724), to alleviate confusion, the main text has been changed to

“In the context of this report, in situ indicates that the aerogel or xerogel was formed at small scale (i.e., <0.1 mL) directly on the substrate for cryo-SEM analysis, while ex situ refers to aerogel samples that were prepared separately on a larger scale (i.e., 1-20 mL), and deposited onto a substrate for room temperature SEM analysis (see experimental section).”

Also the caption for Figure 7 has been changed to:

“Microscopy images of SAFINs of ISA24. POM images of organogels of ISA24 with (a) cyclohexane and (b) toluene (2 wt %). Freeze-fractured Cryo-SEM images of in situ aerogels of ISA24 from (c) cyclohexane and (d) toluene organogels (2 wt %). SEM images of an ex situ, freeze-dried aerogel of ISA24 from a cyclohexane organogel (2 wt %) at 23°C (e) and (f). SEM images of dense, in situ xerogels of ISA24 from (g) toluene and (h) cyclohexane (2 wt %) at 23°C. AFM amplitude images of a thick in situ xerogel of ISA24 from cyclohexane (2 wt %) (i).”

NMR experiments does not give any highly relevant information, but that the gelator forms aggregates in chloroform. I think figure 8 can be placed at the supporting information file. Also, Figure S31 is not discussed, what is the information that it gives? Why there is a THF signal on the spectra, is not pure chloroform? If this experiment does not give any info should be removed, or if it does, the discussion should be added.

Done. Figure 8 has been moved to the supporting information and Figure 31 has been removed. Figure 31 was included to show that the aggregates formed are stable and do not disassemble quickly, otherwise signals for mobile **ISA24** would be restored. The NMR tubes were probably washed with THF previously

and an insignificant amount was still present even after drying (as indicated by their size relative to the ^{13}C satellite signals).

In figure 9, XR patterns of aerogels of ISA24 from freeze-dried cyclohexane organogels (2 wt %) are shown. What is the difference between a and b? I mean, they are the same aerogel? They were prepared with different methodology? With the info given, they seem to belong to the same sample, but that is not possible. Please indicate the difference between a and b samples on the text and figure.

Line 477, it refers to Figure 11a, but there is no figure 11, I think it should refer to figure 9a.

Indeed Figure 11a should be Figure 9a. Thank you for picking this up. With the NMR Figure moved to the supporting information Figure 9a is now Figure 8a.

As clearly mentioned into the main text, both D_L or Colr phases from cyclohexane gels were produced randomly in the xerogels or aerogels (line 505). Fig. 8a and Fig 8b show the patterns obtained for each type of organization (D_L vs. Colr). To lift the confusion pointed out by the reviewer, Fig.8 has been shifted to the end of the paragraph, so that the reader is well informed before seeing the patterns. Furthermore, the caption of Fig.9 has been modified with the following information:

Figure 8. PXRD patterns of representative (a) lamello-columnar (DL) and (b) rectangular columnar (Colr) phases in aerogels of ISA24 randomly observed from freeze-dried cyclohexane organogels (2 wt %). Schematic representation of the proposed columnar phases of ISA24. (c) Side and (d) top views of the Lamello columnar phase (DL). (e) Side and (f) top view of the Rectangular columnar phase (Colr). d_L = repeating interlayer distance. h_0 = distance between discoids. a_r , b_r = Colr phase unit cell parameters.

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Date of this review

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