Synthesis and Gelation Study of (4-Nitrophenyl)methyl arjunolate: A Triterpene Based Novel Organogelator

Dr. Shaishab Kumar Dinda
Assistant Professor in Chemistry
Government General Degree College Dantan-II, Paschim Medinipur, West Bengal, India

Abstract : Triterpenes, the C30 subset of the major plant secondary metabolite terpenes, are promising in this respect because of their abundant skeletal types and included functional groups.[1] Moreover, the extended lengths of triterpenoids, whether acyclic, monocyclic, or rigid pentacyclic structures, are in the nanometer range. As such, they may be useful building blocks for nano-science and nano-technology applications.[2] Arjunolic acid a 6-6-6-6-6 pentacyclic triterpenoid, arjunolic acid (1), from *Terminalia Arjuna*[22] and discovered that an arjunolic acid-derived molecule forms thermochromic organogels.[3]

Benzyl and (4-nitrophenyl) methyl arjunolate were synthesized and their gelation abilities were tested. (4-nitropheyl)methyl arjunolate formed thermo reversible transparent gels efficiently mostly with aromatic solvents while benzyl arjunolate did not form gel with any of the solvents. Electron micrographs of the xero-gels revealed a fibrous network consisting of fibers of micrometer lengths and nanometer diameters.

Key words **- arjunolic acid, triterpenes, organogel, self-assembly.**

1. INTRODUCTION

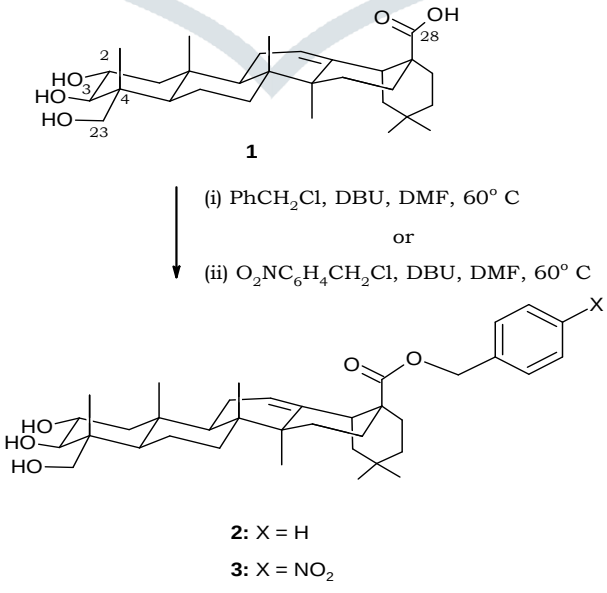
Supramolecular gels formed by the self-assembly of *low molecular mass* organic compounds in a medium have attracted considerable attention in recent years and efficient gelation has been reported with compounds of wide structural diversities[3,4]. The studies in this area have been motivated not only to gain a better undrestanding of the self-assembly process in a medium but also because of their numerous technological applications[5-22]. The long range molecular order, obtained by self-assembly of the low molecular mass organic compounds, have recently been utilized to create self-assembled nanowires[3].

The low molecular mass gelators include long chain hydrocarbons, steroids[3-8], carbohydrates[3,4], peptides[3,4], alkoxy polycyclic aromatic hydrocarbons[3], etc[3-7]. Arjunolic acid, a naturally occurring chiral trihydroxy triterpenic acid offers a great opportunity for the design of molecular receptors, supramolecular architectures and nano-materials[3,4]. We have recently reported the first arjunolic acid derived efficient organogelator[3,4]. Herein we report the synthesis and gelation test results of benzyl and (4-nitrophenyl)methyl arjunolate.

2.Results and Discussions:

2.1 Synthesis

Benzyl arjunolate was synthesized from arjunolic acid **1** by heating with benzyl chloride in DMF in the presence of DBU in 90% yield (scheme 1) [i,ii]. Similarly, (4-nitrophenyl)methyl arjunolate was synthesized from arjunolic acid and p-nitrobenzyl bromide in 84% isolated yield.



Scheme 1: Synthesis of compounds 2 and 3

2.2 Gelation Studies:

5 mg of compound **3** taken in a vial was dissolved in a solvent by heating and the solution was kept at room temperature. When no significant flow of the material was observed visually on turning the vial upside down, we called it a gel. Compound **3** formed colorless and transparent gels mostly with aromatic solvents (Table 1). But, compound **2** did not form gel with any of the solvents.

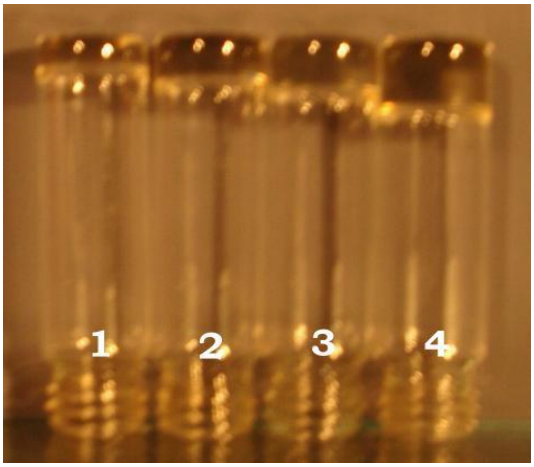


Figure 1: Inverted vials containing the gels obtained from 3 and toluene at various concentrations (w/v:: 1: 2.14%, 2: 1.66%, 3: 1.36%, 4: 1.15%).

Table 1. Results of Gelation Test of **3**[a]

Entry	Solvent	Concn. (g/100 mL)	State	T_{gel} (°C)
1.	Benzene	1.0	G	37
2.	Toluene	1.0	G	29
3.	o-Xylene	1.0	G	46
4.	m-Xylene	1.0	G	42
5.	p-Xylene	1.0	G	46
6.	Mesitylene	1.0	G	49
7.	Bromobenzene	1.6	G	27
8.	Chlorobenzene	3.3	G	45
9.	o-dichlorobenzene	2.0	G	39
10	Nitrobenzene	2.5	S	…
11.	Pyridine	5	S	…
12.	Chloroform	2.5	S	…
13.	Carbon tetrachloride	0.20	G	38
14.	Petroleum ether	1.0	I	…
15.	Methanol	3.33	S	…
16.	Ethanol	3.33	S	…
17.	n-Propanol	2.50	S	…
18.	2-Propanol	2.50	S	…
19.	n-Butanol	3.33	S	…
20.	tert-Butanol	2.50	S	…

[a]Compound 3 was warmed with a solvent and the solution was kept at room temperature for several hours to allow gel formation. G = gel, S = solution, I = almost insoluble. T_{gel} values were measured by using the 'ball drop method'[23].

2.2.1 Sol-Gel Transition Studies:

The gel to sol melting temperature T_{gel} was plotted against the % gelator concentration to determine the thermal stability of the gels[6]. The increase in T_{gel} with increasing gelator concentration indicates that self-assembly is driven by strong intermolecular interactions.

In most of the cases, the gels obtained in o-, m- and p-xylenes have higher T_{gel} values than the gel in benzene (Figure 2). At 0.83 wt %, the T_{gel} in benzene and m-xylene are same. But the value increases steeply with the gel in m-xylene than the gel in benzene. The steeper increase in the T_{gel} values indicates that with increase in concentration of the compound **3** the intermolecular association increases in m-xylene to a greater extent than in benzene.

The steeper increase of T_{gel} is also observed in tolulene compared to benzene and mesitylene (Figure 3). In the case of halobenzenes, a regular increase of T_{gel} were observed (Figure 4).

Increase of T_{gel} with increasing gelator concentration allowed us to calculate the thermodynamic parameters and the free energy changes (Table 2) [17]. The free energy change during sol-gel transition in various solvents were 15 – 20 kJ/mol. The contribution of both enthalpic and entropic contributions for the overall free energy changes were evident.

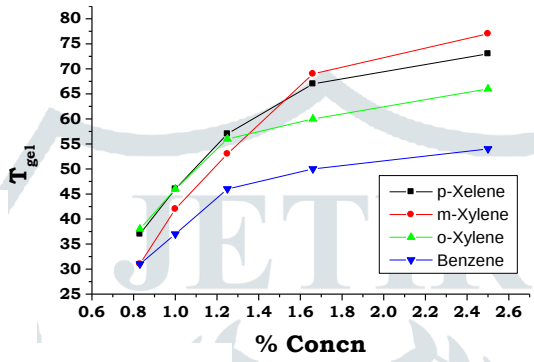


Figure 2: Plot of T_{gel} vs wt % concentration of compound 3 in p-xylene (-■-), m-xylene (-●-), o-*xylene (-▲-) and benzene (-▼-)*

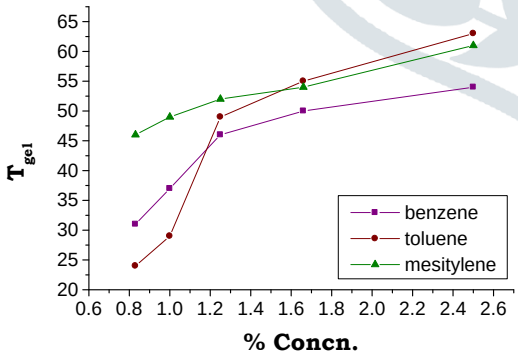


Figure 3: Plot of T_{gel} vs wt % concentration of compound 3 in benzene (-■-), toluene (-●-), mesitylene (-▲-)

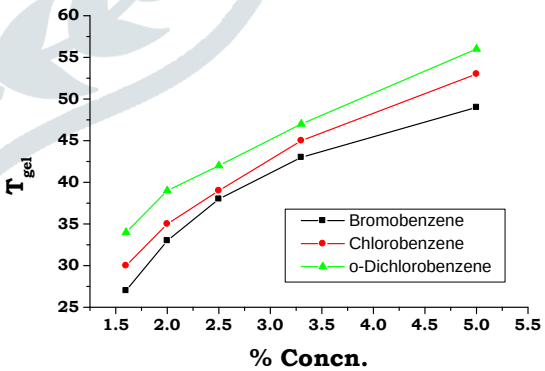


Figure 4: Plot of T_{gel} vs wt % concentration of compound 3 in bromobenzene (-■-), chlorobenzene (-●-), dichlorobenzene (-▲-)

Table 2: Thermodynamic parameters (ΔH^o, ΔS^o) and free energy (ΔG^o) at 298º K) of gel melting in various solvents

solvent	ΔH^o kJ/mol	ΔS^o J/mol/ºK	ΔG^o kJ/mol
Benzene	35.9	61.5	17.6
Toluene	54.5	117.3	19.6
o-Xylene	33.6	50.2	18.6
m-Xylene	24.0	18.8	18.4
p-Xylene	25.3	27.7	17.0
Mesitylene	67.1	157.9	20.0
Bromobenzene	48.8	112.3	15.3
Chlorobenzene	40.0	82.8	15.4
o-dichlorobenzene	43.1	91.9	15.7

2.3 Scanning electron microscopic (SEM) studies

Morphological studies of the reported compound were investigated using scanning electron microscope (SEM). The scanning electron microscopic studies of the gel was done using a thin slice of gel on microscopic slides and drying at room temperature, finally under reduced pressure for several hours. The dried sample was platinum coated and observed under the SEM instrument. The SEM pictures were taken in a SEM instrument (Jeol Scanning Microscope-JSM-5200 and Jeol Scanning Microscope-JSM-6700F). The SEM images show the fibrillar network structures having intertwined fibers of 50 - 70 nm diameter and micrometer lengths were obtained from xero-gels of (4-Nitrophenyl) methyl arjunolate (3) in *figure 5(a) chlorobenzene* (3.3 % w/v), *figure 5(b) bromobenzeme* (1.6 % w/v) *and figure 5(c) toluene* (1 % w/v). The dimensions of the fibers indicate that there are several molecules present both in lengths and breadths of the fibers.

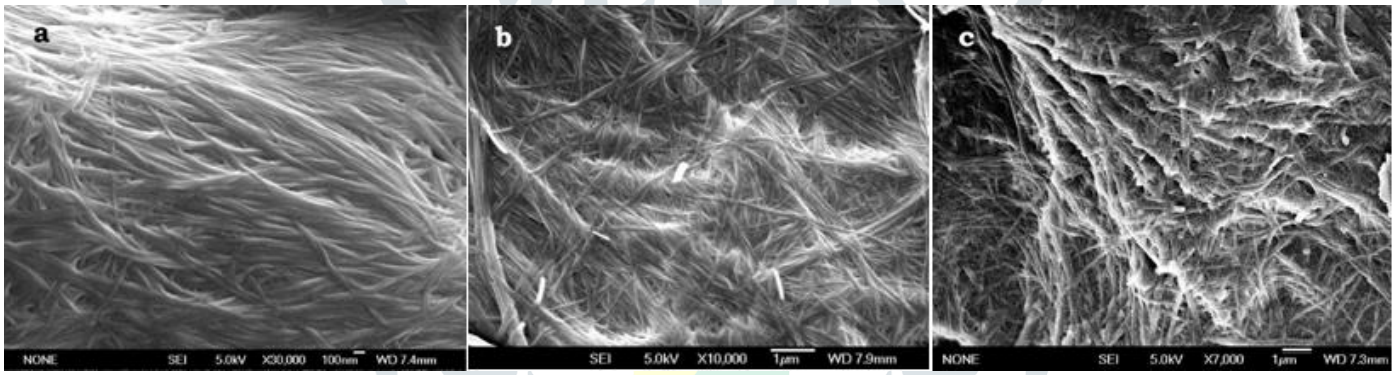


Figure 5: SEM micrographs of xero-gels of compound 3 in: (a) chlorobenzene, (b) bromobenzeme, (c) toluene.

2.4 Experimental:

(4-Nitrophenyl) methyl arjunolate 3: A mixture of crystalline arjunolic acid (0.101 g, 0.208 mmol) and 4-nitrobenzyl bromide (0.055 g, 0.258 mmol) contained in a dry 5 mL RB flask was suspended in dry DMF (0.10 mL) and treated with DBU (0.040 mL, 0.267 mmol). The mixture was heated over oil bath at 60 ˚C for 24 hours with continuous magnetic stirring. The reaction mixture was treated with an additional amount of 4-nitrobenzyl bromide (0.056 g, 0.258 mmol) and the reaction mixture was heated for another 7 hours. The volatiles were removed under reduced pressure and the crude product was purified by column chromatography (Si-gel, 100 -200 mesh, 1.0 X 12.5 cm) using 50% ethyl acetate/chloroform as eluant. The product was obtained as a white solid (0.109 g) in 84% yield.

mp = 226 ºC, **^{1}H-NMR (600 MHz, $CDCl_3$) δ:** 8.22 (d, J = 9.0 Hz, 2H), 7.51 (d, J = 9.0 Hz, 2H), 5.30 (t, 3.6 Hz, 1H, 12-H), 5.19 (d, J = 13.8 Hz, 1H, Ar-CH_a-), 5.11 (d, J = 13.8 Hz, 1H, Ar-CH_b-), 3.81 – 3.69 (m, 1H, 2-H), 3.60 (d, J = 10.8 Hz, 1H), 3.39 (d, J = 10.2 Hz, 1H), 3.38 (d, J = 10.8 Hz, 1H), 2.89 (dd, J_1 = 13.8 Hz, J_2 = 4.2 Hz, 1H, 18-H), 2.07 – 0.85 (m, terpenoid H's, 20H), 1.13 (s, 3H), 0.96 (s, 3H), 0.93 (S, 3H), 0.91 (s, 3H), 0.81 (s, 3H), 0.54 (s, 3H). **^{13}C-NMR (150 MHz, $CDCl_3$) δ:** 177.18, 147.55, 143.64, 128.41, 123.70, 122.35, 79.63, 69.31, 68.63, 64.53, 48.52, 47.37, 46.80, 46.00, 45.70, 42.54, 41.72, 41.34, 39.25, 38.06, 33.72, 33.02, 32.37, 32.21, 30.66, 27.49, 25.95, 23.57, 23.41, 23.02, 18.17, 16.94, 16.86, 12.85. FTIR: ν_{max} (neat, cm^{-1}) 3387 (s), 2946 (s), 2880 (s), 1726 (s), 1666 (w), 1606 (w), 1524 (s), 1460 (m), 1454 (m), 1388 (m), 1364 (m), 1347 (s). UV (MeOH, lg ε) λ_{max} = 266.4 nm (4.02). $[\alpha]_D^{298}$ = + 33.89 (c 0.226, MeOH). HRMS (ESI): m/z calcd ($C_{37}H_{53}NO_7Na$) 646.37197, found 646.3750 $[M + Na]^+$.

Figure 6: 600 MHz ^{1}H-NMR of compound 3

Selected Data for Benzyl Arjunolate 2

^{1}HNMR (500 MHz, $CDCl_3$) *δ*: 7.37 - 7.28 (m, 5H, Phe-H's), 5.28 (br. app. t, J = 3.5 Hz, 1H), 5.09 (d, J = 12.5 Hz, 1H, -O-C H_a-Ph), 5.04 (d, J = 12.5 Hz, 1H, -O-C H_b-Ph), 3.78 - 3.70 (br, m, 1H, 2-H), 3.64 (d, J = 10.5 Hz, 1H, 3-H), 3.60-3.44 (br. s, 1H), 3.41 (s, 1H, 23-H_a), 3.39 (s, 1H, 23-H_b), 2.90 (dd, J_1 = 13.7 Hz, J_2 = 3.5 Hz, 1H, 18-H), 2.80 - 2.50 (br. s, 2H), 2.02 - 0.84 (m, terpenoid H's, 20H), 1.12 (s, 3H), 0.98 (s, 3H), 0.92 (s, 3H), 0.90 (s, 3H), 0.86 (s, 3H), 0.60 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 177.85, 144.15, 136.81, 128.82, 128.38, 128.32, 122.64, 80.75, 70.73, 69.13, 66.35, 49.44, 47.94, 47.12, 46.46, 46.25, 42.87, 42.16, 41.75, 39.71, 38.59, 34.27, 33.50, 32.77, 32.75, 31.10, 27.98, 26.36, 24.04, 23.85, 23.43, 18.73, 17.41, 17.33, 17.31. $[\alpha]_D^{300.5}$ = + 45.88 (c 0.632 g /100 mL, $CHCl_3$). FTIR (neat): 3382, 3090, 2944, 1724, 1661, 1587, 1495, 1456, 1386, 1367, 1319, 1301, 1259, 1237 cm^{-1}. UV (2% $CHCl_3$ / MeOH, log ε) λ = 257.2 nm (3.22), 249.2 nm (3.24). HRMS (ESI): m/z calcd ($C_{37}H_{55}O_5$) 579.4049, found 579.4048 $[M + H]^+$.

3.Conclusions:

We have reported the facile syntheses and gelation test results of benzyl and (4-nitrophenyl)methyl arjunolate. Whereas (4-nitrophenyl)methyl arjunolate **3** is an excellent gelator of varieties of organic and especially aromatic solvents, benzyl arjunolate is not. The role of the 4-nitro group in **3** on gelation is not yet clear. The increase in T_{gel} values with increase in concentration of the gelator indicates stronger inermolecular interactions. Thermodynamic parameters ΔH^o, ΔS^o and ΔG^o were calculated from these data. The positive free energy change during sol-gel transition indicates the stability of the gels. Scanning electron micrographs of the xero-gels revealed a fibrous network structure. The fibers formed by self-assembly of **3** are of micrometer lengths and nanometer diameters.

4. ACKNOWLEDGMENT

I am thankful to the Department of Chemistry, Government General Degree College, Dantan-II, Government of West Bengal, India and my research supervisor Professor B. G. Bag, Department of Chemistry, Vidyasagar University, West Bengal, India for helpful discussion and encouragement.

REFERENCES

[1] Shibuya, M.; Xiang T.; Katsube, Y.; Otsuka, M.; Zhang, H.; Ebizuka, Y. *J. Am. Chem. Soc.* **2007**, *129*, 1450.
[2] Bag, B.G.; Garai, C.; Majumdar, R.; Laguerre, M. *Struct. Chem.* **2011**, DOI 10. 1007/s11224-011-9881-1.
[3] (a) Bag, B. G.; Maity, G. C.; Dinda, S. K. *Org. Lett.* **2006**, *8*, 5457; (b) Bag, B. G.; Maity, G. C.; Pramanik, S. R. *Supramol. Chem.* **2005**, *17*, 383; (c) Bag, B. G.; Maity, G. C.; Pramanik, S. R. *Pramana* **2005**, 925; (d) Bag, B. G.; Dinda, S. K.; Dey, P. Mallia, P. V. A.; Weiss, R. G. *Langmuir* **2009**, 25, 8663-8671; (e) Bag, B.G. Dash, S.S. *Nanoscale* **2011**, *3*, 4564 – 4566.
[4] Terech, $^{P.}$; Weiss, R.G. *Chem. Rev.*, **1997**, *97*, 3133
[5] Estroff, L.A.; Hamilton, A.D. *Chem. Rev.* **2004**, *104*, 1201
[6] ^{Sangeetha}, N.M.; ^{Maitra}, U., *Chem. Soc. Rev.* **2005**, *34*, 821.
[7] Messmore, B.W.; Hulvat, J.F.; Sone, E.D.; Stupp, S.I. *Am. Chem. Soc.* **2004**, 126, 14452.
[8] Mukkamala, R.; Weiss, R.G. *Chem Commun.* **1995**, 375.
[9] Lin, Y.C.; Kachar, B.; Weiss, R.G. *J. Am. Chem. Soc.* **2003**, 125, 8270.
[10] Lin, Y.C.; Weiss, R.G. *Macromolecules*, **1987**, *20*, 414.

[11] Maitra, U.; Mukhopadhyay, S.; Sarkar, A.; Rao, P.; S.S. Indi, *Angew Chem. Int. Ed. Engl.* **2001**, 40, 2341.
[12] Dastidar, P.; Okabe, S.; Nakano, K.; Iida, K.; Miyata, M.; Tohnai, N.; Shibayama, M. *Chem. Mater.* **2005**, *17*, 741.
[13] Vassil, P.; Simanek, E. E.; Wood, M. R.; Wong, C.-H.; *Chem.Commun.* **1998**, 1865.
[14] Hafkamp, R. J. H.; Fieters, M. C.; Nolte, R. J. M.; *J. Org. Chem*. **1999**, *64*, 412.
[15] Maji, S.K.; Malik, S.; Drew, M.G.B.; Nandi, A.K.; Banerjee, A. *Tetrahedron Lett.* **2003**, *44*, 4103.
[16] Suzuki, M.; Owa, S.; Yumoto, M.; Kimura, M.; Shirai, H.; Hanabusa, K. *Tetrahedron Lett.* **2004**, *45*, 5399.
[17] Reichwagen, J.; Hopf, H.; Guerzo, A.D.; Belin, C.; Bouas-Laurent, H.; Desvergne, J.-P. *Org. Lett.* **2005**, *7*, 971.
[18] Kato, T. *Science*, **2002**, *295*, 2414.
[19] Murata, K.; Aoki, M.; Nishi, T.; Ikeda, A.; Shinkai, S. *Chem. Commun.*, **1991**, 1715.
[20] Srivastava, A.; Ghorai, S.; Bhattacharya, A.; Bhattacharya, S. *J. Org. Chem.* **2005**, *70*, 6574.
[21] Ajayaghosh, A.; Vijayakumar, C.; Varghese, R. *Angew. Chem. Int. Ed.* **2006**, *45*, 456.
[22] King, F.E.; King; T.J.; Ross, J.M. *J. Chem. Soc.* **1954**, 3995.
[23] Takahashi, A.; Sakai, M.; Kaio, T. *Polymer J.**1980,**12335-341.*