*Pure Appl. Chem.*, Vol. 79, No. 11, pp. 2031–2038, 2007.
doi:10.1351/pac200779112031


# Arjunolic acid: A renewable template in supramolecular chemistry and nanoscience*

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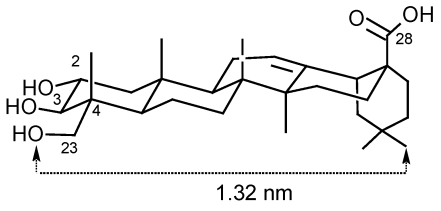
*Abstract*: Arjunolic acid, a triterpenoid, renewably resourced from *Terminalia arjuna* sawdust, has the potential of being used as a structural molecular framework in supramolecular chemistry and nanoscience. The nanosized chiral triterpenoid on derivatization could immobilize varieties of organic solvents at low concentrations. The low-molecular-mass organic compounds self-assembled in organic media to form fibrous network structures having fibers of nano- to micrometer diameters. A dual-component supramolecular gelation has been demonstrated, exhibiting interesting thermochromic property. An arjunolic acid-derived crown ether showed efficient binding to monovalent cations, including a primary ammonium ion paving the way for chiral recognition of amino acids.

*Keywords*: arjunolic acid; renewable; template; nanoscience; thermochromes; terpenes; self-assembly; soft-materials; organogel; *Terminalia*.

## INTRODUCTION

Primary plant metabolites such as sugars, amino acids, and nucleotides are essential to the life of the plant. Secondary metabolites stored in plants may not be essential to the life of the plant, but may play an important role in self-defenses against harmful organisms, coloring petals, and fruits, etc. [1]. Many of these plant secondary metabolites are used as medicines for the treatment of various physiological disorders [2]. The triterpenoids are an important class of plant secondary metabolites derived from $C_{30}$ precursors [3]. In spite of the abundance of many naturally occurring chiral *triterpenes* having well-defined three-dimensional structures, there is little activity in the use of those in the general area of supramolecular chemistry and nanoscience.




*Arjunolic acid* **1**

**Pure Appl. Chem.* **79**, 1831–2100. An issue of reviews and research papers based on lectures presented at the 1st International IUPAC Conference on Green–Sustainable Chemistry, held in Dresden, Germany, 10–15 September 2006.

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Arjunolic acid **1**, a *triterpenoid*, is the major component of the extracts of the heavy wood of *Terminalia arjuna* [4]. The chiral triterpenic acid has a rigid pentacyclic backbone with two equatorial hydroxyl and one equatorial hydroxymethyl groups attached at the "A" ring. The carboxyl group is attached at the ring junction of the *cis*-fused "D" and "E" rings [5–7]. Herein, we report the use of this nanometer-long naturally occurring chiral triterpenoid having uniquely positioned functional groups in supramolecular chemistry and nanoscience.

## ARJUNOLIC ACID-DERIVED ORGANOGELATORS

Supramolecular organogelation has become an active area of research in recent years for an improved understanding of the self-assembly process in a medium [8]. In addition, the supramolecular structures obtained by self-assembly of the molecules have many potential technological applications [9]. Excellent gelation abilities of some arjunolic acid derivatives are discussed here, with their electron microscopic images of the xero-gels revealing fibrous network structures, along with an interesting dual-component *thermochromic* supramolecular gel.

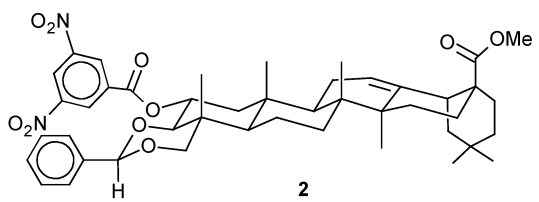
### First triterpene-based organogelator

The arjunolic acid derivative **2** showed excellent gelation of varieties of alcohols and mixed solvents at a low concentration (Table 1) [10]. The thermoreversible transparent gels obtained from 2-propanol and compound **2** at various concentrations are shown in Fig. 1a. Gelation of methanol could be done at 0.5 wt % of the gelator **2**, indicating that one gelator molecule is capable of immobilizing more than 3500 solvent molecules. To determine the thermal stability of the gels, the gel-to-sol transition temperature $T_{gel}$ was plotted against the concentration of **2** [11]. The increase of $T_{gel}$ with increase in gelator concentration (Fig. 1b) indicates stronger intermolecular interactions [12].

**Table 1** Results of gelation test of **2**.[a]

| Sl. no. | Solvent | Concn. (g/100 mL) | State | $T_{gel}$ (°C) |
|---|---|---|---|---|
| 1 | Methanol | 0.50 | G | 38 |
| 2 | Ethanol | 0.66 | G | 46 |
| 3 | *n*-Propanol | 0.66 | G | 46 |
| 4 | 2-Propanol | 0.66 | G | 51 |
| 5 | Methanol-$CH_2Cl_2$ (3:1 v/v) | 0.66 | G | 43 |
| 6 | Ethanol-$CH_2Cl_2$ (6:1 v/v) | 0.66 | G | 40 |
| 7 | Ethanol-$CHCl_3$ (5:1 v/v) | 0.66 | G | 37 |
| 8 | 2-Propanol-$CH_2Cl_2$ (8:1 v/v) | 0.66 | G | 43 |
| 9 | 2-Propanol-$CHCl_3$ (6:1 v/v) | 0.66 | G | 33 |

[a]Compound **2** was dissolved in a solvent by warming and then left at room temperature for several hours to allow gel formation. In the case of mixed solvents, compound **2** was initially solubilized in the chlorinated solvents and then mixed with the alcohols. G = gel, S = solution, $T_{gel}$ values were measured by using the "ball drop method" [11].




**2**

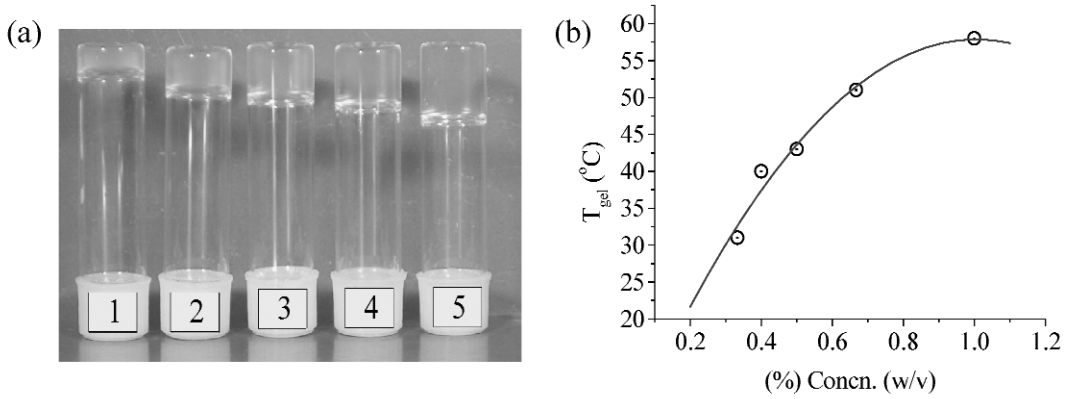



**Fig. 1** (a) Inverted vials containing the gels obtained from **2** and 2-propanol (w/v: 1: 1 %, 2: 0.66 %, 3: 0.5 %, 4: 0.4 %, 5: 0.33 %), (b) plot of $T_{gel}$ vs. % concn. for the gel in 2-propanol.

Morphology of the xero-gels studied by scanning electron microscopy (SEM) revealed a fibrous network structure having fibers of 24–30 nm diameter (Fig. 2).

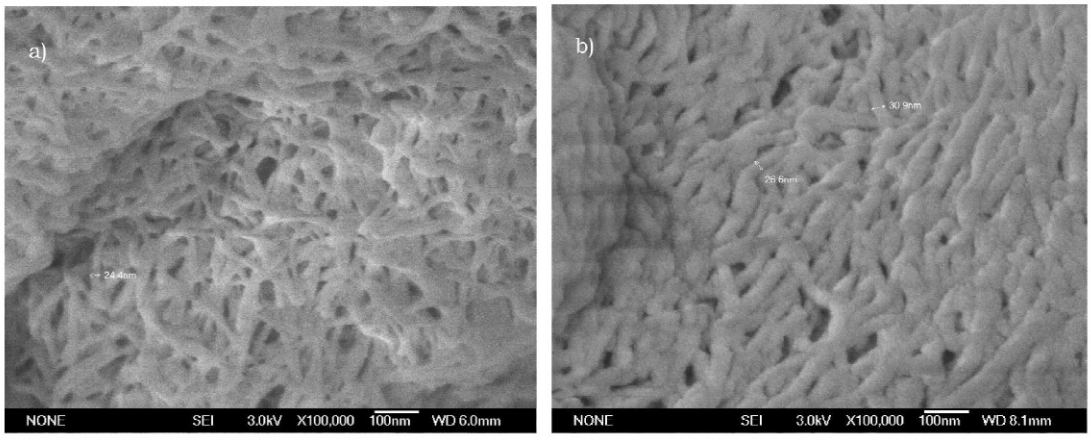
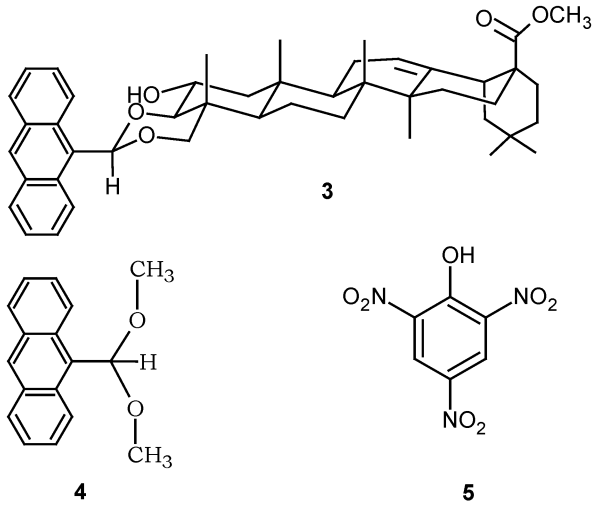



**Fig. 2** SEMs of the xero-gels obtained from the organogelator **2** in (a) ethanol/chloroform (5:1 v/v), fiber diameter shown is 24.4 nm, (b) 2-propanol/chloroform (6:1, v/v), diameters of the fibers as shown are 26.6 and 30.9 nm.

## A THERMOCHROMIC SUPRAMOLECULAR ORGANOGEL

The anthrylidene derivative **3** formed a weak gel only in methanol. Interestingly, in the presence of stoichiometric amounts of electron-deficient guests, compound **3** formed gels efficiently with varieties of organic solvents such as ethanol, *n*-propanol, 2-propanol, cyclohexanol, carbon tetrachloride, etc. [13]. Thermoreversible organogelation could be observed visually in the presence of stoichiometric amount of picric acid as a guest (Fig. 3). The deep red-colored gel transformed reversibly into a light yellow-colored solution during melting.




**Scheme 1** Anthrylidene derivative of arjunolic acid **3**, dimethoxymethyl anthracene **4**, and picric acid **5**.

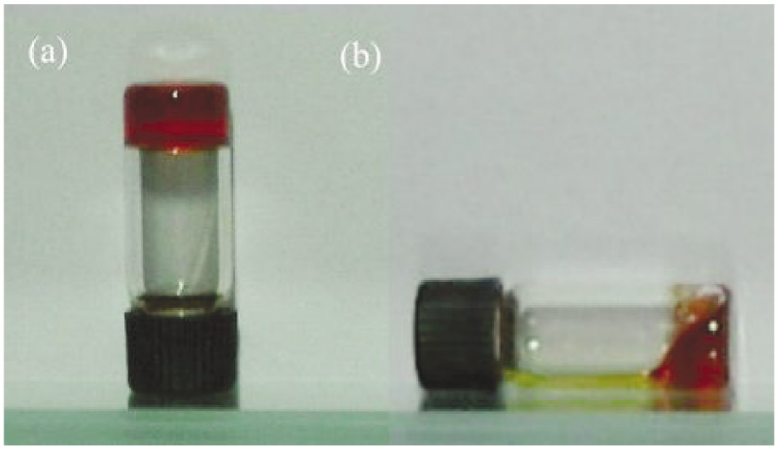



**Fig. 3** (a): Inverted vial containing a gel from a stoichiometric mixture of compound **3** and picric acid in carbon tetrachloride at 8 mM concentrations, (b) melting of the gel at 49 ºC. A change of color from dark red to light yellow is observed during melting.

UV–vis absorption spectra of the compounds in carbon tetrachloride are shown in Fig. 4. Both at lower (8 μM, Fig. 4a) as well as at higher concentrations (8 mM, Fig. 4b), there are no absorptions around 490 nm for the compound **3** and picric acid **5**. Interestingly, for a gel from a 1:1 mixture of **3** and **5** (at 8 mM concentration), a broad charge transfer (CT) band was observed around 490 nm. But, at a concentration (8 μM) below the critical gel concentration, no CT band was observed even with the 1:1 mixture of **3** and **5**. This observation that a new CT band was formed in the gel along with the observation that the $T_{gel}$ was maximum at a 1:1 molar ratio of **3** and **5** [13] support the fact that the self-assembly was driven by donor/acceptor interaction (with concomitant CT band around 490 nm).

To find out the role of the rigid triterpene backbone in the self-assembly process, gelation tests and UV–vis absorption spectroscopy were carried out with the model compound **4** and with a 1:1 mixture of **4** and **5**. The finding that compound **4** alone as well as a 1:1 mixture of **4** and **5** did not form gel in any of the solvents and the absence of any CT band both at lower (8 μM, Fig. 4c) as well as at higher

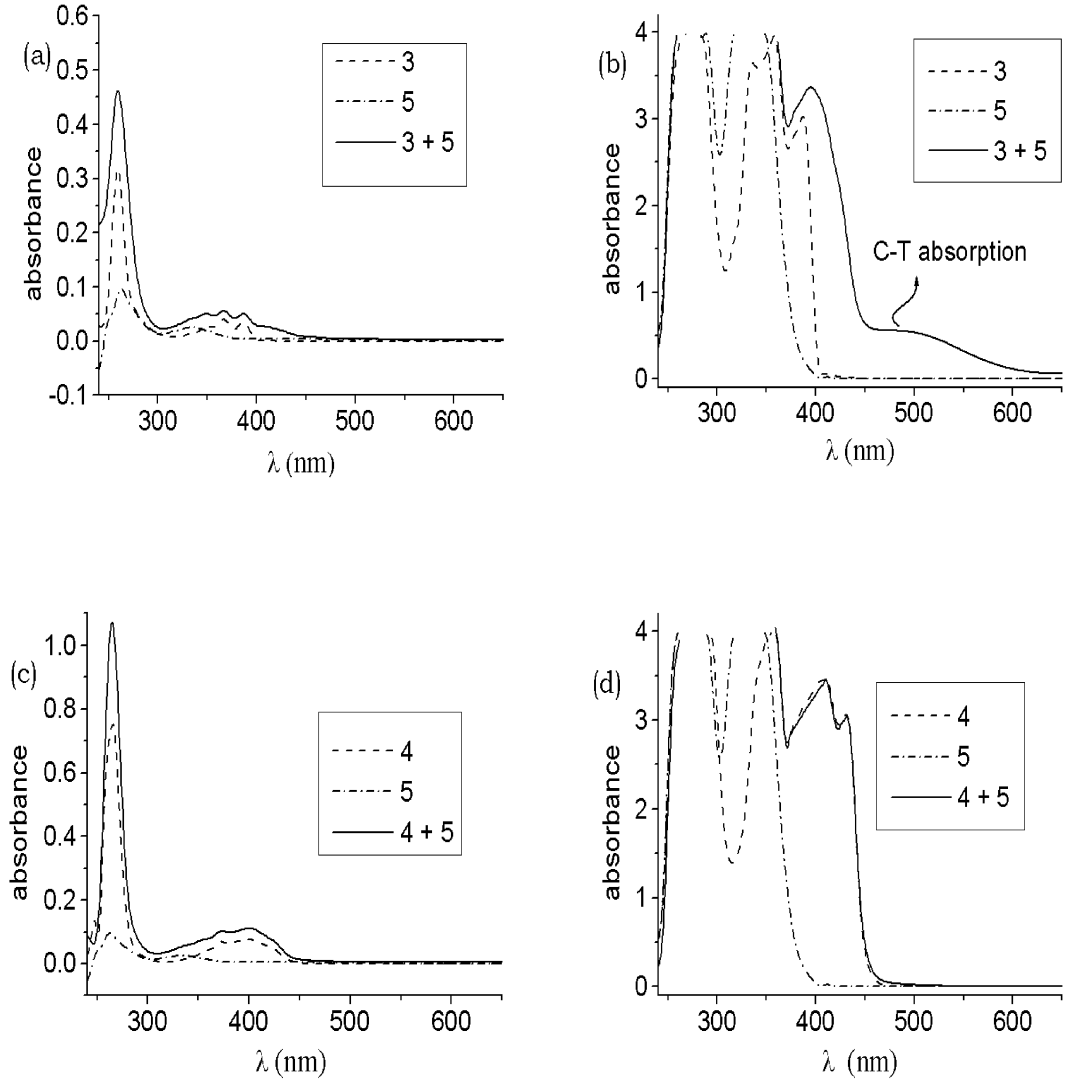



**Fig. 4** UV–vis absorption spectra of (a) **3** and **5** and their 1:1 mixture in carbon tetrachloride at 8 μM concentration, (b) **3** and **5** and a gel from their 1:1 mixture in carbon tetrachloride at 8 mM concentration, (c) **4** and **5** and their 1:1 mixture in carbon tetrachloride at 8 μM concentration, (d) **4** and **5** and their 1:1 mixture in carbon tetrachloride at 8 mM concentration. A new CT band was observed around 490 nm only in the gel state which was absent in all the other absorption spectra. The absorptions at higher concentration (8 mM) were measured using a 2-mm quartz cell and at lower concentration (8 μm) using a 10-mm quartz cell.

concentrations (8 mM, Fig. 4d) indicated that the long lypophilic triterpene backbone helped the molecules to assemble in one dimension.

Morphology of the xero-gels was studied under SEM. Entangled fibrous networks having submicron diameter fibers formed by self-assembly of the molecules were observed (Fig. 5).

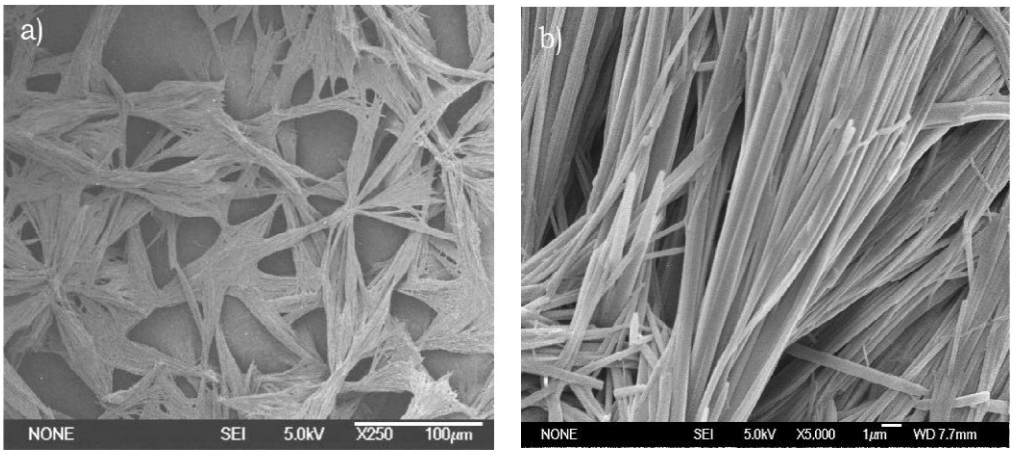



**Fig. 5** SEMs of the dried gel from a 1:1 mixture of **3** and **5** in *n*-octanol at different magnifications. The fibers are micrometer long and of submicron diameter.

## ARJUNA CROWN ETHER

Arjunolic acid-derived crown ether **6** was designed utilizing the gauche disposed "O-C-C-O" unit of the 2 and 3 hydroxyl groups by molecular mechanics calculation [14]. Interestingly, the arjuna crown ether showed excellent binding to monovalent cations with a peak selectivity to $K^+$ ion (Fig. 6). Efficient binding of the crown ether **6** to a primary ammonium ion opens up the possibility of designing arjunolic acid-based hosts for the selective binding of α, ω-diammonium ions. A carboxylate binding group at the 23 position would convert the crown ether to a chiral receptor for diastereoselective complexation of amino acids [15].

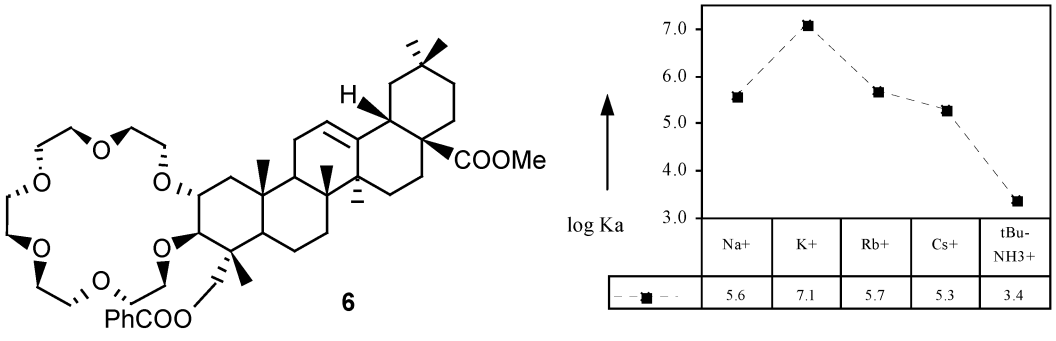



**Fig. 6** Plot of log $K_a$ vs. cations.

## CONCLUSIONS AND OUTLOOK

A variety of molecular frameworks have been utilized during the past two decades in the design of molecular receptors and self-assembling, self-replicating, and supramolecular systems capable of performing specific tasks or mimicking certain biological phenomenon [16]. A sustainable chemical strategy necessitates switching from depleting finite resources to renewable feedstocks [17]. The triterpenoids are an important class of secondary plant metabolites, many of which contain rigid structural framework with well-separated functional groups [3]. We have demonstrated that arjunolic acid, one such secondary plant metabolite, extractable from *T. arjuna* sawdust, can be used as a rigid molec-

ular framework in the general areas of supramolecular chemistry and nanoscience. In one approach, we have demonstrated that arjunolic acid on simple structural modification can act as an efficient gelator of varieties of organic solvents [10]. The dual-component gelator consisting of an anthrylidene derivative of arjunolic acid and picric acid can act as a thermochrome where the gel-to-sol transition temperature can be varied by changing the concentration of the solutes [13]. Such thermochromic property can be utilized in designing thermochromic switches, sensor devices, etc.

In another approach, we have synthesized the arjuna crown ether **6** and studied its complexation with cations [10]. The crown ether can bind monovalent cations efficiently including a primary ammonium ion. We plan to convert the 23-OH group to a carboxylate-binding group so that the crown derivative can act as a chiral receptor for the diastereoselective complexation of amino acids [15].

The geometry of the hydroxyl and the hydroxymethyl groups attached to $C_2$–$C_4$ of arjunolic acid has a mirror image resemblance to the $C_3$–$C_5$ carbons of D-glucopyranose (Fig. 7). This opens up the possibility of using arjunolic acid as an analog of D-glucopyranose. The rigid triterpene backbone and the carboxyl group in it will give additional advantage. The chirality of the triterpene can also be exploited in asymmetric transformations [18].

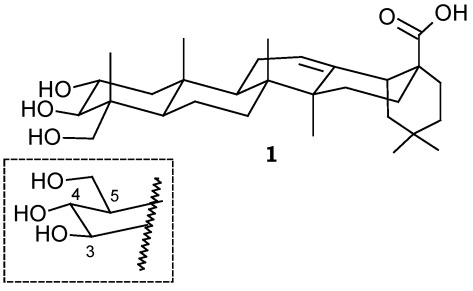



**Fig. 7** Arjunolic acid **1** (inset: corresponding enantiomorphic array of hydroxy groups in the D-glucopyranose scaffold).

Self-assembly of the molecules in organic media during gelation is reflective of molecular organizations and order. Such properties open up the possibility of designing terpene-based newer liquid crystals [19].

## ACKNOWLEDGMENTS

Financial assistance from CSIR and DST, New Delhi and the Alexander von Humboldt Foundation, Germany, is gratefully acknowledged. BGB thanks Profs. Guenter von Kiedrowski and G. S. R. Subba Rao for helpful discussions. The SEM unit of IACS, Kolkata is thanked for helping us in electron microscopy. SKD thanks CSIR, New Delhi for a research fellowship.

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6. Very often in nature, arjunolic acid is mixed with another triterpenic acid, *asiatic acid*, having a close structural resemblance. Conversion of the carboxyl group to an ester group enables the two to be separated by high-performance liquid chromatography. An efficient practical method for the separation of the two triterpenic acids in grams scale has been developed in our laboratory and will be reported elsewhere.
7. For an example of ursane to olenane biotransformation, see Z.-H. Cheng, B.-Y. Yu, G. A. Cordell, S.-X. Qui. *Org. Lett.* **6**, 3163 (2004).
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