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Friedelane triterpenoids: transformations toward A-ring modifications including 2-*homo*derivatives†

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Abstract: Friedelin and its derivatives, commonly known as friedelane triterpenoids exhibit potential biological effects ranging from antimicrobial to anticancer to anti-HIV. In urge to modify the A-ring of the pentacyclic triterpenoid, various transformative scopes had been utilized. Herein, some simple unprecedented transformative protocols have been accomplished towards furnishing altogether 42 (25 new) A-ring modified pentacyclic friedelane triterpenoids. Of note, the modifications include the all-new 2-*homo*derivatives. One-pot $BF_3.OEt_2$-mediated oxidative transformation of friedelin to yield friedel-3-enol acetate as the major product was one of the key reactions. A group of isomeric A-ring modifications were then resulted on the basis of simple transformations on suitable friedelane-based molecules. The syntheses of the novel 2-*homo*friedelanes were envisioned on the basis of the transformative reactions of the designed triterpenoid 3-chlorofriedel-2-ene-2-carbaldehyde which was isolated as the major product from the reaction of friedelin with the novel Vilsmeyer-Haack reagent. A-ring modified new derivatives are also due to further interesting transformations of 3-chlorofriedel-3-ene, isolated as a side product from the same reaction. Again, considering the scope of 3-chloro-2-enal moiety, associated with the A-ring of the triterpenoid, some heterocycle-linked- (bonded to C3) 2-*homo*friedelane triterpenoids were synthesized. Thus, various common reaction strategies were employed on suitable substrates to achieve finally a series of C2,C3-; C3,C4-; and C2,C3,C4-functionalized as well as 2-*homo*friedelane triterpenoids just within one to four efficient steps.

Keywords:*Friedelin, pentacyclic triterpenoid, 2-homofriedelane triterpenoids,Vilsmeyer-Haack reaction*

†Electronic Supplementary Information (ESI) available: copies of ^{1}H and ^{13}C NMR spectra of the isolated products.

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1. Introduction:

Friedelane (**1**) is a natural 6-6-6-6-6 pentacyclic triterpenoid (PT) alkane and, the PTs having the same general skeleton are known as friedelane triterpenoids. The major fundamental compounds of the triterpenoid group include friedelin (**2**), 2α-hydroxyfriedelan-3-one (cerin, **3**) and friedel-2-oxo-3-enol (not shown) which are, in fact the main constituents of the cork smoker wash solids (**Figure 1**).[1] More than 400 natural friedelane triterpenoids have been isolated till date. In their review, Zhan et al. have summarized the natural sources of friedelane triterpenoids.[2] *Celastraceae*, *Hippocrateaceae*, *Euphorbiaceae*, *Flacourtiaceae*, and *Guttiferae* are the families of the plants where friedelanes were found most abundantly.[2] Friedelin itself is bioactive[3] and the friedelane triterpenoids possess a wide spectrum of bioactivities ranging from anti-microbial to anti-HIV to anti-cancer potential.[4] To be specific, there are some naturally occurring highly bioactive friedelane triterpenoids *viz.*, friedelane-3,15-dioxo-19α-ol,[5,6] celastrol,[7] netzahualcoyone,[8] demethylzeylasteral,[9] etc. which makes this class of PTs truly more promising.

Total synthesis as well as biosynthetic routes of friedelin was aimed successfully.[10] Majority of the structural modifications of friedelin occurred in A-ring due to the ease of transformative scopes, for '3-keto' is the only chemically active functional group in the molecule. A large number of transformative attempts on various friedelane PTs were achieved which include rearrangement-based transformations,[11] oxidation reactions (mediated by various oxidizing agents *viz.*, SeO_2, NBS, *m*CPBA, OsO_4, $KOBu^t$, LTA etc.),[4l,4m,12] reduction reactions,[13] photochemical transformations[14] and others.[15] Syntheses, transformations and rearrangements of bromo-friedelane triterpenoids were also noteworthy.[11f,12d,13c,16] Moiteiro et al. have reported a number of A-ring modified friedelane triterpenoids with their biological screening.[1a,15e] Our laboratory has also attempted to furnish bioactive A-ring modified friedelane PTs.[17] Again, Kang et al. has achieved a novel process of direct amidation of sp^3 C-H bonds, also applied to friedelin.[18]

However, in spite of easy availability along with in-built structural potentiality towards bioactivity of the friedelane triterpenoids, friedelin has remained a bit striped towards the transformative scopes, in comparison to other PTs. Thus in search of new facile transformative

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protocols as well as to produce more number of useful A-ring modifications, herein, we have accomplished various unprecedented transformations toward furnishing altogether 42 numbers of A-ring modified pentacyclic friedelane triterpenoids. These also include all-new 2-*homo*derivatives (31-carbon-based) which were envisioned to explore a useful new series of structural modifications contrary to all the earlier attempts with 30-carbon-based A-ring modifications. Vilsmeyer-Haack reaction, a well-known transformative protocol for 2-formylation of carbonyl compounds, was thus employed to utilize the carbonyl functionality of friedelin to result the primary *homo*derivative 3-chlorofriedel-2-ene-2-carbaldehyde (**28**). Compound **28** was further transformed to furnish altogether 16 such new series of 2-*homo*derivatives.

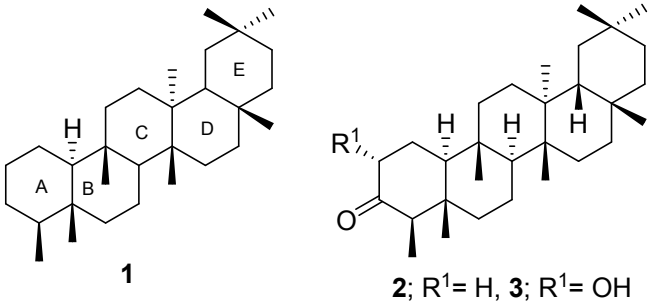

Figure 1. Friedelane (**1**), friedelin (**2**) and cerin (**3**).

2. Results and discussion

The starting materials, friedelin (**2**) and cerin (**3**), were isolated from the petroleum ether extract of the well known source *Quercus suber* bark. These were purified, and were characterized by routine spectroscopic experiments along with the comparison of the known data (please follow section 4.12). With the help of various known methodologies, transformations with friedelin resulted some unprecedented reactions, whereas cerin resulted some useful isomeric known derivatives. Hence incorporation of different functionalities directly into the friedelin skeleton along with further simple transformations were found interesting to produce overall a number of C2,C3-; C3,C4-; and C2,C3,C4- functionalized as well as 2-*homo*friedelane triterpenoids, the details of which is discussed as follows.

2.1 Action of $BF_3.OEt_2/Ac_2O$ on friedelin: an unprecedented transformation

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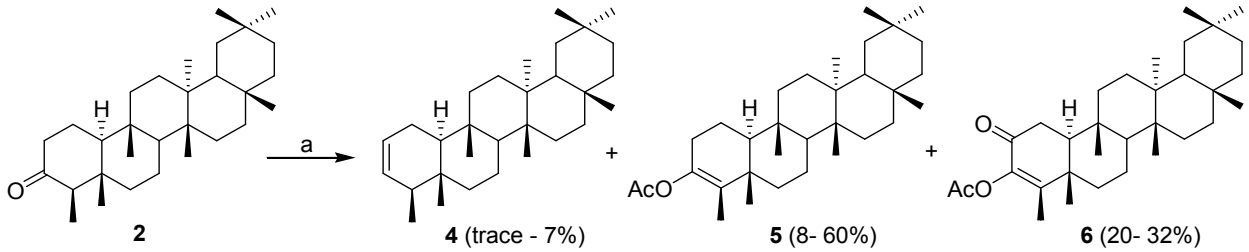
Anticipating the accelerating and versatile effect of $BF_3.OEt_2$ in organic synthesis,[19] friedelin was attempted with the reagent along with acetic anhydride as the oxidant. A successful unprecedented transformation was thus resulted in chloroform and at room temperature to isolate three products analyzed as friedel-2-ene (**4**, 7%), friedel-3-enol acetate (**5**, 42%; a new compound) and friedel-2-oxo-3-enol acetate (**6**, 22%)(**Scheme 1**).



Scheme 1. Treatment of $BF_3.OEt_2/OAc_2$ on friedelin (a: $BF_3.OEt_2$, OAc_2, $CHCl_3$, r.t.,24h).

While evaluating the major product friedel-3-enol acetate (**5**) from the above reaction, we found that the enol acetates, in general, are excellent reactive synthons for the functionalization of the corresponding precursor carbonyl compounds and it is, indeed, remarkably evident from a number of transformative reactions.[20] As a consequence, people have tried to find out more facile routes for the syntheses of enol acetates, and herein we have accomplished the isolation of friedel-3-enol acetate as the major reaction product by an unprecedented $BF_3.OEt_2$-mediated oxidation of friedelin.

The reaction was conducted also with other potential Lewis acids *viz.*, anhydrous aluminium chloride, ferric chloride, titanium trichloride, magnesium chloride, zinc chloride and nickel chloride at 100 mol% as well as in excess (5-10 eqv.) along with acetic anhydride; but no transformation was achieved at all. The reaction was then tested by varying time and temperature. Allowing the reaction for longer period of time yielded the enol acetate **5** better (r.t., 48h, yield: 60%; and the yield of keto-enol acetate **6** was not altered much) though change in the condition from room temperature to reflux reduced the percentage yield of product **5** (reflux, 8h, yield: 8%) and increase that of **6** (reflux, 8h, yield: 32%). The reaction was also attempted with different other oxidants *viz.*, acetyl chloride, chloroacetyl chloride, benzoyl chloride and benzyl bromide, instead of acetic anhydride. But none of them, in the same reaction condition, were able to furnish the expected products.

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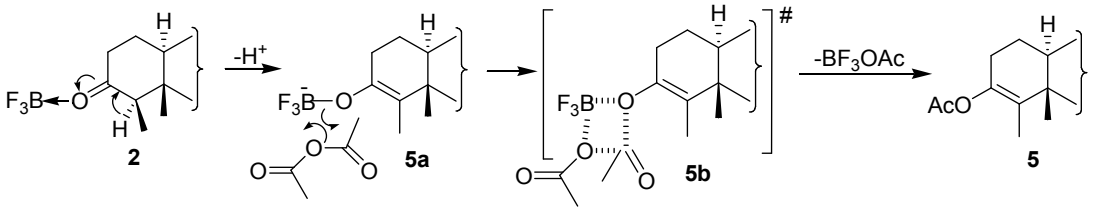
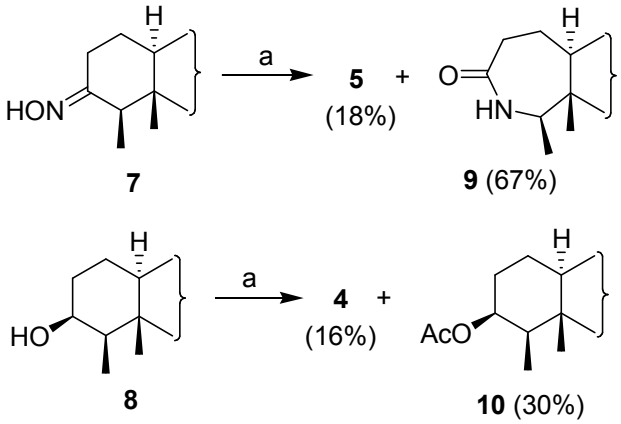
A probable mechanism was thus postulated for the formation of the major product enol acetate **5.** Utilizing the Lewis acidity of $BF_3.OEt_2$ and 4α-H (acidic, α- to 3-keto) of friedelin, 3-enol trifluoroborate moiety **5a** is proposed to be formed, which can then follow a transition state **5b** involving an acetic anhydride molecule to result ultimately enol acetate **5** (**Scheme 2**).



Scheme 2. Probable mechanism for the formation of enol acetate **5**.

2.2 Action of $BF_3.OEt_2/Ac_2O$ on friedelane-3-hydroxyimino (7) and friedelan-3β-ol (8)

Friedelane-3-hydroxyimino (**7**, 88%, m.p. 289-291°C) and friedelane-3β-ol (**8**, 72%, m.p. 290°C) were prepared separately from friedelin following the usual method (both **7** and **8** were obtained from friedelin (**2**) with the reaction of hydroxylamine hydrochloride and sodium borohydride respectively; please follow experimental section). The effect of $BF_3.OEt_2/Ac_2O$ was then tested on the oxime **7** and 3β-hydroxy compound **8** separately. Friedelane-3-hydroxyimino (**7**) resulted friedel-3-enol acetate (**5**, 18%) and friedelin lactam **9** (67%), whereas compound **8** furnished the hydrocarbon friedel-2-ene (**4**, 16%) and the acetate derivative of the starting material, friedelan-3β-acetate (**10**, 30%) (**Scheme 3**). The formation of the enol acetate from the oxime can be figured as the deoxymination (to generate friedelin, **2**) followed by fresh reaction with friedelin; and the lactam **9** can be assumed easily to be formed following the Beckmann rearrangement on the oxime.



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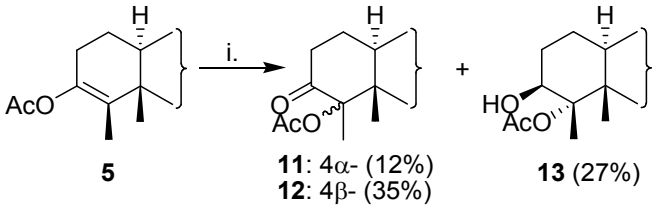
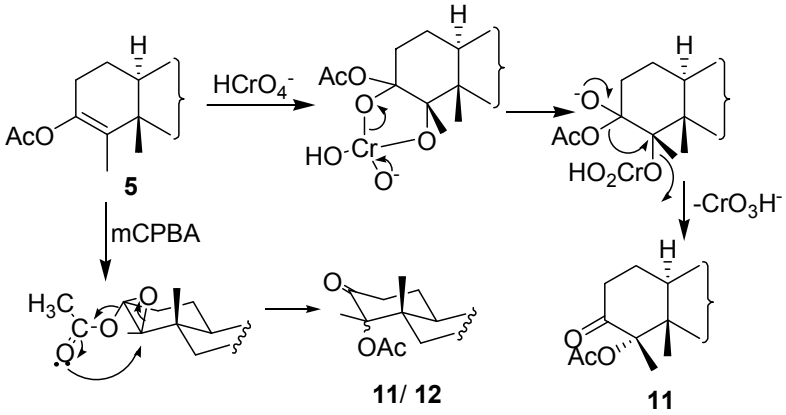
Scheme 3. Action of $BF_3.OEt_2/OAc_2$ on friedelane-3-hydroxyimino (**7**) and friedelan-3β−ol (**8**). a) $BF_3.OEt_2$, Ac_2O, $CHCl_3$, RT, 24h.

2.3 Oxidation of friedel-3-enol acetate (5): acetoxy migration from C3 to C4

When friedel-3-enol acetate (**5**) was treated with CrO_3/CH_3COOH, it was interesting to note that migration of the acetoxy group (-$OCOCH_3$) from C3 to C4 occurred to result a new compound friedel-3-oxo-4α-acetate (**11**, 41%, **Scheme 4**). To aim C3,C4-epoxidation and/or probable oxidative rearrangements, the enol acetate was treated with *m*-chloroperbenzoic acid (*m*CPBA). On oxidation in this milder reaction condition the enol acetate was found to result three products all having the acetoxy group migrated from C3 to C4. The products isolated were analyzed as friedel-3-oxo-4α-acetate and friedel-3-oxo-4β-acetate (both new; **11**, 12%; and **12**, 35% respectively), and friedel-3β-ol-4α-acetate (**13**, 27%; another new compound) (**Scheme 4**). Compound **11** is identical with the product obtained by chromic acid oxidation of enol acetate **5** and, compound **12** is the C4-epimer of it (**Scheme 4**). Probable mechanisms for the 1,2-acetoxy migration towards the formation of compounds **11** and **12** are shown in **Scheme 5**.



Scheme 4. *m*CPBA-Oxidation of enol acetate: acetoxy migration from C3 to C4. (i. *m*CPBA/CH_2Cl_2, aq. $NaHCO_3$, r.t., 2h). Chromic acid oxidation (CrO_3/CH_3COOH, r.t., 2h) of enol acetate **5** furnished only **11** (41%).



Scheme 5. Probable mechanism for the formation of **11** and **12**.

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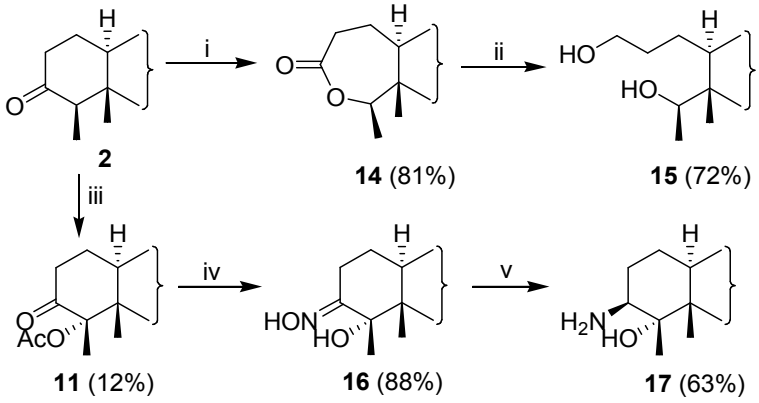
2.4 Access to 3,4-*seco*friedelane-3,4-diol (15), friedelan-3β-amin-4α-ol (17), Pachysandiol A (18) and its 3α-epimer (19), and others

Friedelin was oxidized into the lactone **14** (81%) with *m*CPBA. The lactone was then treated with $NaBH_4$ to produce the 3,4-*seco*friedelane-3,4-diol (**15**, 72%) at a good yield. Thus the sequence may be treated as an easy access to produce 3,4-*seco*derivatives selectively. Friedelin was transformed into the enol acetate **5** followed by oxidation with *m*CPBA to result friedel-3-oxo-4α-acetate, **11** (discussed previously). Then oximination of **11** with hydroxylamine hydrochloride in pyridine resulted a new derivative friedelane-3-oximino-4α–ol (**16**, 88%) which on reduction with $LiAlH_4$ finally yielded another new derivative friedelan-3β-amin-4α-ol (**17**, 63%; **Scheme 6**).



Scheme 6. i. *m*CPBA, $CHCl_3$, reflux, 2h; ii. $NaBH_4$, THF, reflux, 4h; iii) a. $BF_3.OEt_2$/ OAc_2, $CHCl_3$, r.t., 24h; b. *m*CPBA, CH_2Cl_2, aq. $NaHCO_3$, r.t., 2h; iv. $NH_2OH.HCl$, py, 100°C, 4h; v. $LiAlH_4$, dry THF, reflux, 4h.

Pachysandiol A (**18**), structurally friedelane-2α,3β-diol, is a natural compound available in many plants,[21] can also be achieved by the $NaBH_4$ reduction of cerin (**3**, **Figure 2**). However, the reduction of cerin with sodium in alcohol furnished a *cis*-diol as the major product, the 3α-epimer of pachysandiol A, structurally friedelane-2α,3α-diol (**19**, **Figure 2**). Acetylation of friedel-3β-ol-4α-acetate (**13**) with acetic anhydride in pyridine produced friedelane-3β,4α-diacetate (**20**, 95%). Friedel-3-oxo-4α-acetate (**11**) was treated with KOH in aqueous MeOH to produce friedelan-3-oxo-4α-ol (**21**, 84%). Compound **21** was reduced with $NaBH_4$ to produce

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friedelane-3β,4α-diol (**22**, 62%). Friedelin lactam **9** was reduced with lithium aluminium hydride to yield a new compound seven-membered cyclic amine **23** (63%;). (**Figure 2)**

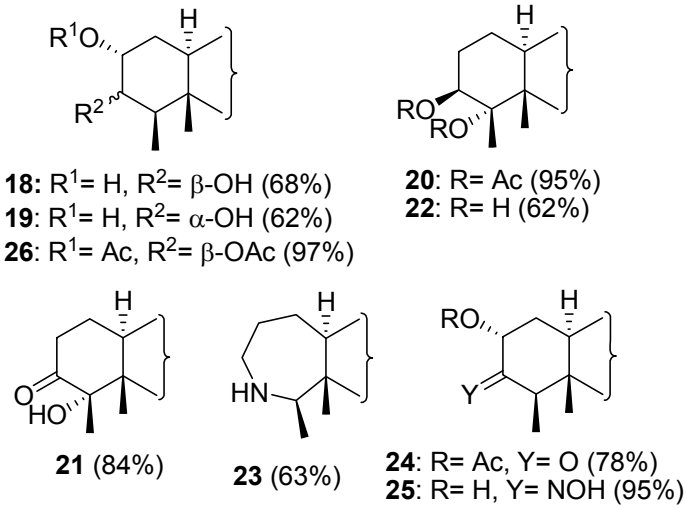

Figure 2. Few more A-ring modified friedelane PTs (many of them are isomeric within the series). *Preparation:* **18**: from **3**, $NaBH_4$, CH_2Cl_2/MeOH, r.t., 4h; **19**: from **3**, Na/isopropanol, reflux, 2h. **20**: from **13**, Ac_2O/ py, 100°C, 6h; **21**: from **11**, KOH, aq. MeOH, reflux, 30 min.; **22:** from **21**, $NaBH_4$, CH_2Cl_2/MeOH, r.t., 4h; **23**: from **9**, $LiAlH_4$, dry THF, reflux, 6h; **24**: from **3**, Ac_2O/py, 100°C, 6h**; 25**: from **3**, $NH_2OH.HCl$/py, 100°C, 4h; **26**: from **18**, Ac_2O/py, 100°C, 6h**.**

Considering the future evaluation scope of probable structure-activity relationships (SAR) of the different isomeric friedelane triterpenoids (modifications based on A-ring only), cerin (**3**, itself isomeric to friedelan-3-oxo-4α-ol, **21**) was allowed to have some simple transformations to result few derivatives which are indeed isomeric to at least one of the prepared friedelane triterpenoids based on the $BF_3.OEt_2/Ac_2O$-mediated transformative reaction. Thus, acetyl **24** (isomeric to **11** and **12**), oxime **25** (isomeric to **16**), diol **18** (isomeric to **22** and **19**) and diacetate **26** (isomeric to **20**) were prepared easily (please follow the experimental section). (**Figure 2**)

2.5 Action of Vilsmeyer-Haack reagent on friedelin: access to 2-*homo*friedelanes

Considering the useful scope of application of the Vilsmeyer-Haack reagent[22] (which uses phosphorus oxychloride along with *N,N*-dimethylformamide (DMF), we targeted friedelin as the substrate, to prepare the 2- (and/or 4)-formylated and associated derivatives. The derivatives were indeed envisioned to be used to achieve a number of all-new *homo*friedelane triterpenoids by employing further simple transformative reactions.

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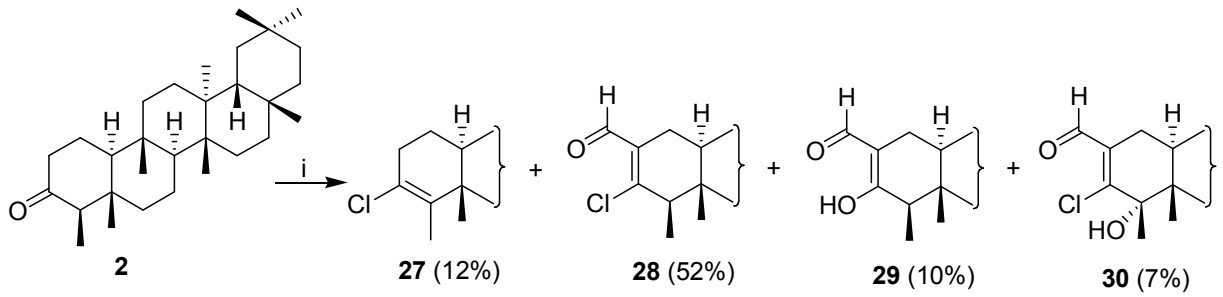
Thus first, when friedelin was treated with phosphorus oxychloride and DMF (please follow experimental section), four new products isolated were characterized as 3-chlorofriedel-3-ene (**27**, 12%), 3-chlorofriedel-2-ene-2-carbaldehyde (**28**, 52%), friedel-2-en-3-ol-2-carbaldehyde (**29**, 10%) and 3-chlorofriedel-2-en-4α-ol-2-carbaldehyde (**30**, 7%). (**Scheme 7**)



Scheme 7. Action of Vilsmeyer-Haack reagent on friedelin (i. DMF/$POCl_3$, $CHCl_3$, reflux, 6h).

According to the previous reports of the action of Vilsmeyer-Haack reagent on the ketosteroids, besides the α-formylated major product, a chloro-ene derivative was also isolated.[23] Likewise, for friedelin as the substrate, it could furnish two isomeric chloro-enes *viz.,* 3-chlorofriedel-2-ene and 3-chlorofriedel-3-ene (**27**); whereas in practice only the latter was isolated that can be attributed due to the greater stability of the more substituted alkene. However, on further simple transformative protocols, **27** resulted new A-ring modified friedelane triterpenoids and, **28** furnished new 2-*homo*friedelanes having different functional/ active group distributions as follows.

2.6 Further unprecedented A-ring modifications

Selenium dioxide, besides other transformative scopes, is a well known reagent for allylic hydroxylation. When the reagent was employed on 3-chlorofriedel-3-ene (**27**), the 23-methyl of the friedelane skeleton, an allylic one, was found to get oxidized into an aldehyde along with simultaneous dechlorination to furnish a new compound friedel-3-ene-23-al (**31**, 56%).

Oxidation of 3-chlorofriedel-3-ene (**27**) with *m*CPBA was found to result the α–epoxidation of the 3-ene functionality along with simultaneous dechlorination. Thus, the isolated product was structurally a new derivative friedelane-3α,4α-epoxide (**32**, 56%). NBS is a reagent occasionally used for allylic bromination although we were able to result selective A-ring aromatization of steroids by using the same.[24] Herein, while we aimed to achieve the corresponding 2 (and/or 4)-bromo derivatives by employing NBS on 3-chlorofriedel-3-ene (**27)** it was our surprise to isolate

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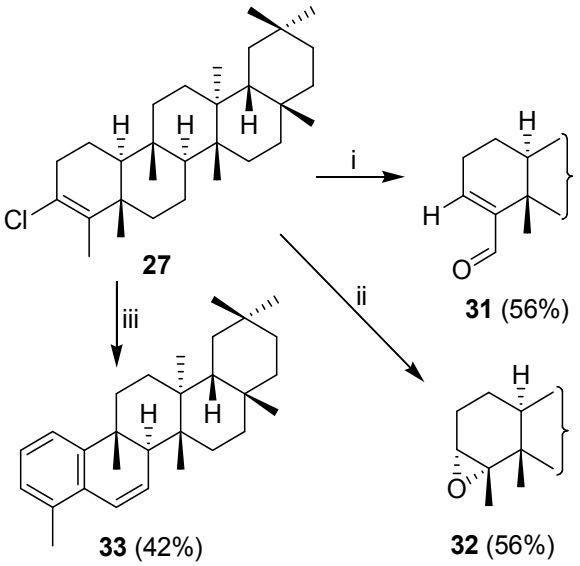
an interesting new derivative A-ring aromatized 24-*Nor*friedel-1,3,5(10),6-tetraene (**33**, 42%) as the only product (**Scheme 8**). To note, there are actually a number of important biologically active aromatized (or having their quinonoid structure)-friedelanes available in nature.[25]



Scheme 8.i: SeO_2/dioxane, 100°C, 36h; ii: *m*CPBA/$CHCl_3$, reflux, 4h; iii: NBS/$CHCl_3$, r.t., 24h.

2.7 *2-Homo*friedelanes including heterocycle-linked *homo*friedelanes

A series of 'all new' 2-*homo*friedelane triterpenoids were synthesized following two or more sequential steps starting from friedelin. The key reaction, as is mentioned earlier, was the 2-formylation of the triterpene by applying the novel Vilsmeyer-Haack reagent. Then *homo* derivative **28**, the major product isolated was transformed into some more new derivatives to enrich the friedelane triterpenoid series.

The 2-formyl group of the 2-*homo*derivative **28** was transformed, by usual common procedure, with hydroxylamine hydrochloride into the corresponding oxime, structurally 3-chlorofriedel-2-ene-2-carboxaldoxime **(34**, 98% after recrystallization, **Scheme 9**). Compound **28** was reduced with $NaBH_4$ to result a new allylic alcohol, 3-chlorofriedel-2-ene-2-methanol (**35**, 92%). The 2-methanol friedelane derivative **35** was acetylated (with acetic anhydride) to yield 3-chlorofriedel-2-ene-2-methanol acetate (**36**; new derivative) quantitatively (**Scheme 9**). Oxime **34** was allowed to reflux with anhydrous $FeCl_3$ in dry DMF to isolate 3-chlorofriedel-2-ene-2-carboxamide (**37**, 58%), the Beckmann rearranged product probably *via* the 2-nitrile

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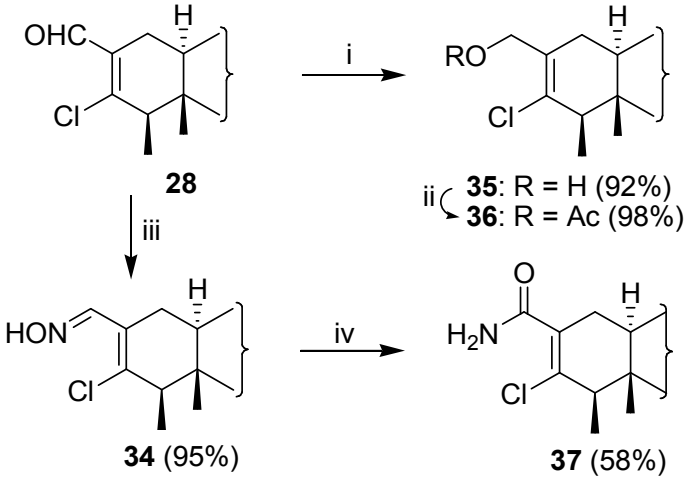
derivative (**Scheme 9**). Thus, from friedelin, the interesting new derivative **37** was synthesized in three steps only.



Scheme 9.i. $NaBH_4$, $CHCl_3$/MeOH, r.t., 24h; ii. Ac_2O/py, reflux, 1h; iii. $NH_2OH.HCl$, pyridine, 100^oC, 2h; iv. anh. $FeCl_3$, dry DMF, reflux, 5h.

Compound **28** possesses two allylic positions available for further functionalization (at C1 and C4), in what context selenium dioxide was employed to it for allylic hydroxylation. Among the two allylic positions available, only the C4 was found to be hydroxylated, leaving behind C1 completely. Thus the reaction of SeO_2 with compound **28** furnished 3-chlorofriedel-2-ene-4α-ol-2-carbaldehyde (**30**, 65%; **Scheme 10**), which was a minor reaction product obtained from the key reaction of friedelin with Vilsmeyer-Haack reagent. In this context, it may be concluded that the allylic C1 is much more reluctant towards hydroxylation, in comparison to the allylic C4. Like compound **28**, 3-chlorofriedel-2-ene-2-methanol (**35**) also possesses two allylic positions for further functionalization (at C1 and C4). The effort to transform **35** into the allylic hydroxylated products by using selenium dioxide resulted only the C4α-hydroxylated **30** (62%) where the primary allylic alcohol functionality of the reactant also got simultaneously oxidized into the aldehyde group (**Scheme 10**). The 2-formyl group of compound **30** was transformed into the corresponding new oxime, structurally 3-chlorofriedel-2-en-4α-ol-2-carboxaldoxime (**38**, 97%; **Scheme 10**). Aldehyde **30** was reduced by using sodium borohydride into the corresponding primary alcohol **39 (**78%; a new compound), structurally 3-chlorofriedel-2-en-4α-ol-2-methanol (**Scheme 10).**

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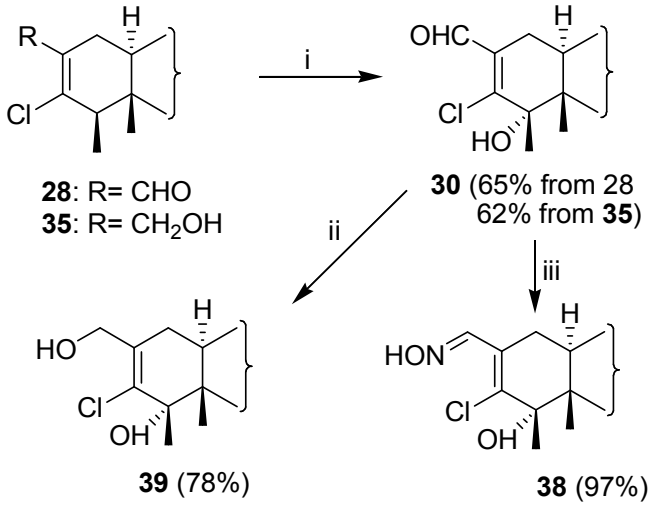
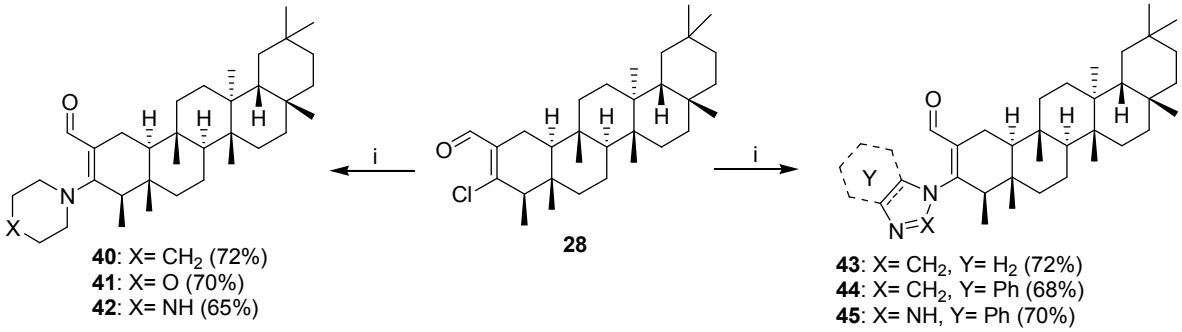


Scheme 10.i. SeO_2, 1,4-dioxane, 100°C, 24h; ii. $NaBH_4$, $CHCl_3$/MeOH, r.t., 24h; iii.$NH_2OH.HCl$, py, 100°C, 2h.

The C3(sp^2)-Cl of the *homo*friedelane **28** is susceptible to nucleophilic substitution reactions thanks to the associative conjugated ene-formyl functionality. Thus, some suitable nitrogen heterocycles of biological relevance were used as the nucleophiles to achieve the resultants which are, indeed, the new group of heterocycle-linked 2-*homo*friedelane derivatives (**40-45**). The heterocycles used for the preparation of such interesting molecules are rather simple and common, where we have used imidazole, benzimidazole and 1,2,3-benzotriazole as the aromatic *N*-heterocycles, and morpholine, piperidine and piperazine as the aliphatic *N*-heterocycles. Of note, the attempted reactions under air produced poor yields (<10%) of the desired products allowing compound **29** as the major yields (>75%) whereas under dinitrogen atmosphere the yield of the heterocycle-linked *homo*friedelane derivatives were found to be satisfactory (**Scheme 11**).



Scheme 11. Syntheses of aliphatic/ aromatic *N*-heterocycle-linked 2-*homo*friedelane derivatives (i. *N*-Heterocycle, K_2CO_3, dry DMF, N_2, 80°C, 3h).

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3. Conclusion

Syntheses of a number of A-ring modified friedelane triterpenoids including the all-new 2-*homo* derivatives have been accomplished following some unprecedented reaction protocols. Various key routes for the modifications include a one-pot $BF_3.OEt_2/Ac_2O$-mediated oxidative transformation of friedelin into friedel-2-ene (**4**), friedel-3-enol acetate (**5**, the major product) and friedel-2-oxo-3-enol acetate (**6**); *m*CPBA oxidation of enol acetate (**5**) to achieve the migration of C3 acetoxy group to C4; transformation of friedelin with Vilsmeyer-Haack reagent to isolate 3-chlorofriedel-2-ene-2-carbaldehyde (**28**) as the major product. Besides, some other new useful methodologies were established during various transformative attempts towards the A-ring modifications. These include a two-step aromatization of friedelin by *N*-bromosuccinimide, a one-pot dechlorination with simultaneous C-23 oxidation, and selective 4α-hydroxylation with simultaneous oxidation of allylic alcohol by selenium dioxide. Thus overall, synthetically useful derivatives such as friedel-3-enol acetate (**5**); friedel-2-oxo-3-enol acetate (**6**); friedel-3-oxo-4(α/β)-acetate (**11/12**, and their diol derivatives); friedelan-3β-ol-4α-acetate (**13**); 3,4-*seco*diol **15**; 3β-amino-4α-ol **17**; 3-chlorofriedel-2-en-4α-ol-2-carbaldehyde (**30**); 2-carboxamide **37**; 3-chlorofriedel-2-en-4α-ol-2-methanol (**39**); etc., were found very much effective to enrich the A-ring modifications of friedelane triterpenoids in a few steps starting from friedelin. On the other hand, as C3(sp^2)-Cl of the *homo*friedelane **28** is susceptible to nucleophilic substitution reactions thanks to the associative conjugated ene-formyl functionality, some suitable nitrogen heterocycles of biological relevance were used as the nucleophiles to achieve the resultants which are, indeed, the new group of heterocycle-linked (to C3 of friedelanes) 2-*homo*friedelane derivatives. We believe to use these friedelane triterpenoids for future biological applications as well as to explore more interesting and useful multifunctionalized derivatives of the particular class of pentacyclic triterpenoids. Thus, following few simple steps starting from friedelin, it rendered possible easily to produce a number of C2,C3-; C3,C4-; and C2,C3,C4- functionalized as well as 2-*homo*friedelane triterpenoids.

4. Experimental

4.1 General:

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Melting points were measured in open capillary methods and were uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on Brucker Avance 300MHz FT-NMR spectrometer using 5 mm BBO probe. $CDCl_3$ or DMSO-$d_6$were used as solvent and TMS as reference material. Data are presented as follows: chemical shift -in ppm on the scale relative to $\delta_{TMS} = 0$; coupling constant-*J*/Hz. Infrared spectra were recorded either in Shimudzu FT-IR 8300 Spectrometer or in Perkin Elmer FT-IR Spectrum *RX 1* Spectrometer as neat or thin films (KBr or Nujol) as indicated in the experimental procedures, and at room temperature. Frequencies are given in wave numbers (cm^{-1}). Mass spectra were recorded on a Qtof Micro YA263 high-resolution mass spectrometer. For column chromatography, silica gel G, 60-120 mesh was used with petroleum ether-ethyl acetate mixture as the eluent. For thin layer chromatography (TLC), freshly made silica gel plates (using silica gel for TLC and petroleum ether) were used and visualization was achieved by staining with iodine.

4.2 Extraction and isolation of friedelin (2) and cerin (3) from *Quercus suber*bark

2 Kg of finely powdered cork (*Quercus suber*) was extracted with petroleum ether in a soxhlet apparatus for 72h. The crude yellowish solid obtained (120 g approx.), after removal of the solvent by distillation, was dissolved in minimum volume of chloroform and chromatographed over silica gel column (250g). Eluting the column with 2% ethyl acetate in petroleum ether yielded pure white solid characterized as friedelin (**2**, 1.7g approx.) whereas ethyl acetate produced pure white crystalline solid characterized as cerin (**3**, 1.1g approx., m.p. 252-256^{o}C, after repeated recrystallization from $CHCl_3$).

4.3 General procedure for the $BF_3.OEt_2$ mediated reactions (towards the synthesis of the compounds **4**, **5**, **6**, **9** and **10**):

Compound (either **2** or **7** or **8**; 1mmol) was dissolved in $CHCl_3$ (10 mL). Acetic anhydride (5 mmol)followed by $BF_3.OEt_2$(5 mmol) was added to the solution and was allowed to stir for 24h at room temperature. 10 mL chloroform and 10 mL aqueous sodium acetate solution were added to the reaction mixture and was allowed to reflux for 30 minutes. The reaction mixture was cooled, extracted with chloroform (3x 25 mL), washed with saturated brine solution (2x 25 mL) followed by water (1x 25 mL), and dried (Na_2SO_4). The solvent was removed by distillation to obtain the reddish solid which after coloum chromatography furnished the products. In each case the separated compounds were further purified by recrystallization (chloroform-methanol).

4.4 Oxidation of friedel-3-enol acetate with CrO_3/ CH_3OOH

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Friedel-3-enol acetate (**10**, 100 mg, 0.21 mmol) was dissolved in glacial acetic acid (1 mL). CrO_3 (1.5eqv.) was added to it and stirred for 2 h at room temperature. The reaction mixture was poured into ice cold water (50 mL), filtered and washed with water repeatedly and dried (vacuum). The residue after column chromatography produced friedel-3-oxo-4α-acetate (**11**, 42 mg, 41%) which was further recrystallized from chloroform-methanol.

4.5 Oxidation of friedel-3-enol acetate (5) and 3-chlorofriedel-3-ene (27) with *m*CPBA:

Friedel-3-enol acetate (100 mg, 0.21 mmol) was dissolved in CH_2Cl_2 (10 mL), and then *m*-CPBA (84 mg, 0.37 mmol) and $NaHCO_3$ (aqueous, 0.5 M, 5 mL) were added (for the oxidation of 3-chlorofriedel-3-ene: substrate **27** (40.0 mg, 0.09 mmol) + *m*CPBA (20 mg, 0.12 mmol) in 10 mL chloroform). The mixture was stirred for 2h at room temperature. $CHCl_3$ (10 mL) was poured and the organic layer was separated, washed with saturated solution of $NaHCO_3$ (2x 15 mL), and with water (2x 15 mL), and then concentrated (vacuum) and dried (Na_2SO_4). Column chromatography followed by recrystallization yielded the desired products.

4.6 General procedure for the acetylation reactions (to synthesize compounds **10**, **20**, **24** and **26**)**:**

10 mg of the substrate was dissolved in dry pyridine (1 mL) and acetic anhydride (1.5eqv.) was added to it and allowed to heat at100^{o}C for specific time (please follow the respective schemes for the reaction times). The reaction mixture was cooled, poured into ice cold water (10 mL), filtered and washed with cold water repeatedly and the solid was vacuum dried. The residue was column chromatographed and further recrystallized from chloroform-methanol to obtain the corresponding pure acetyl derivative.

4.7 General procedure for the oximination reactions:

10 mg of the compound was dissolved in dry pyridine (1 mL) and hydroxylamine hydrochloride (1.5 eqv.) was added to it and allowed to heat at100^{0}C for 4h. The reaction mixture was cooled, poured into ice cold water (10 mL), filtered and washed with water repeatedly and the solid was vacuum dried. The residue was recrystallized from chloroform-ethanol or ethanol to obtain the corresponding pure oxime derivative.

4.8 Hydrolysis with KOH/ MeOH:

Friedel-3-oxo-4α-acetate (**11**, 17 mg, 0.035 mmol) was dissolved in aqueous methanol (MeOH: H_2O= 9:1, 5 mL) and solid KOH (3eqv.) was added to it. The reaction mixture was refluxed for 30 minutes, cooled and then methanol was evaporated out (rota vac.). Chloroform (10 mL) was

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added to the residue, washed with water (2x 10 mL), brine (1x 10 mL) and again with water (1x 10 mL) and was dried (Na_2SO_4). The solvent was removed by distillation to obtain pale yellowish solid which after column chromatography furnished the pure product friedelan-3-oxo-4α-ol (**21**, 13 mg, 84%).

4.9 General procedure for the reduction with $NaBH_4$:

Substrate (10 mg) was dissolved in CH_2Cl_2-MeOH (1:1, 2 mL) and $NaBH_4$ (1.2 equivalent) was added. The solution was stirred for 4 hours at room temperature. Sodium hydroxide (1 M, 2 mL) was added and the reaction mixture was extracted with $CHCl_3$and after usual work-up (washed, dried, solvent evaporated), silica gel column chromatography furnished the expected pure products.

4.10 Procedure for the synthesis of compound 19:

Cerin (**3**, 100 mg) was dissolved in dry isopropanol (4 mL), and sodium (small pieced-cut, 20 mg) was added to it. The reaction mixture was refluxed for 2 hours and then cooled. The content was then added drop wise to 100 mL of ice-cold water and the reaction mixture was extracted with $CHCl_3$ and after usual work-up (washed, dried, solvent evaporated), silica gel column chromatography furnished compound **19** as pure white solid.

4.11 General procedure for the Vilsmeier-Haack reaction of friedelin (2):

A solution of friedelin (**2**, 1 g, 2.34 mmol) in dry chloroform (25 mL) was added drop wise to a cold and stirred solution of phosphorus oxychloride (5 mL) and dry dimethylformamide (5 mL). The mixture was allowed to attain room temperature and then refluxed under nitrogen for 6h. It was then concentrated under reduced pressure and poured onto ice followed by extraction with chloroform (3 × 20 mL). The combined extracts were washed with brine (3 × 25 mL) and dried (Na_2SO_4), and solvent was removed to give a yellowish solid. Purification by column chromatography yielded the four products- 3-chlorofriedel-3-ene (**27**), 3-chloro-2-formylfriedel-2-ene (**28**), 2-formyl-3-hydroxyfriedel-2-ene (**29**) and 3-chloro-2-formyl-4α-hydroxyfriedel-2-ene (**30**).

4.12 Procedure for the synthesis of 3-chlorofriedel-2-ene-2-carboxamide 39 from oxime 34:

In a solution of oxime **34** (20 mg, 0.04 mmol) in dry DMF (5 mL) was added anhydrous $FeCl_3$ (5 eqv.) and the mixture was allowed to reflux for 5h. The reaction was cooled and water (15 mL) was added. It was then extracted with diethyl ether (3 × 15 mL) and the combined organic solvent was washed successively with water (2 × 15 mL) and brine solution (2 × 15 mL), dried

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(Na_2SO_4), and solvent was removed at reduced pressure to give a yellowish solid. Finally, column chromatography furnished the 2-carboxamide friedelane derivative **37** as a pure compound.

4.13 Allylic hydroxylation by selenium dioxide:

To a solution of **28** (or, **35**, 0.1 mmol) in dioxane (10 mL) was added selenium dioxide (0.15 mmol), the mixture was heated at 100^0C for 24h. The reaction mixture was then cooled and the black selenium deposited was filtered off through Whatman 41. To the filtrate chloroform (20 mL) was poured and was washed successively with water and then with saturated brine solution, dried over Na_2SO_4 and concentrated *in vacuo* to give a reddish gummy residue. The residue was then column chromatographed to isolate the pure product.

4.14 General procedure for the syntheses of heterocycle-linked 2-*homo*friedelanes:

A mixture of compound **28 (**0.1 mmol), suitable heterocycle (0.25 mmol), and K_2CO_3 (0.5 mmol) in dry DMF (2 mL) was heated at 80 °C under N_2 for 3 h. After cooling to room temperature, the reaction mixture was poured onto ice-cold water (30 mL), and was extracted with chloroform (3 × 15 mL) and the combined organic solvent was washed successively with water (2 × 25 mL) and brine solution (2 × 25 mL), dried (Na_2SO_4), and solvent was removed at reduced pressure to give a yellowish solid. Finally, column chromatography furnished the heterocycle-linked 2-*homo*friedelane derivatives.

4.15 Characterization of the products

4.15.1 Friedelin (2): Eluent in column chromatography: 2% ethyl acetate in petroleum ether. White crystalline solid, m.p. 262-263 ^{o}C (pet. ether- ethyl acetate, lit.[26a] 262-263 ^{o}C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.73 (s, 3H, Me-24), 0.87 (s, 3H, Me-25), 0.89 (s, 3H, Me-23), 0.95(s, 3H, Me-30), 1.00 (s, 6H, Me-26 and Me-29), 1.05 (s, 3H, Me-27), 1.18(s, 3H, Me-28), 1.91- 2.02 (m, 1H, H-1), 2.20-2.47 (m, 3H, H-2 and H-4). ^{13}C NMR (75 MHz, $CDCl_3$): δ 6.80 (C-23), 14.61 (C-24), 17.91 (C-25), 18.18 (C-7), 18.64 (C-27), 20.22 (C-26), 22.24 (C-1), 28.12 (C-20), 29.93 (C-17), 30.45 (C-12), 31.74 (C-29), 32.04 (C-28), 32.35 (C-21), 32.69 (C-15), 34.99 (C-30), 35.28 (C-19), 35.55 (C-11), 35.94 (C-16), 37.37 (C-9), 38.23 (C-14), 39.20 (C-22), 39.63 (C-13), 41.21 (C-6), 41.49 (C-2), 42.11 (C-5), 42.70 (C-18), 53.03 (C-8), 58.15 (C-4), 59.38 (C-10), 213.37 (C-3). FTIR (nujol, cm^{-1}): *v* 1714, 1380, 1302, 1257, 1103, 1071, 1046, 1004, 795, 719.

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4.15.2 Cerin (3): Eluent in column chromatography: ethyl acetate. White crystalline solid, m.p. 231 ^{o}C (ethyl acetate, lit.[41] 230 ^{o}C).^{1}H NMR (300 MHz, $CDCl_3$): δ 0.73 (s, 3H, Me-24), 0.87 (s, 3H, Me-25), 0.89 (d, J=6.0 Hz, 3H, Me-23), 0.95 (s, 3H, Me-30), 1.01 (s, 6H, Me-27 and Me-28), 1.05 (s, 3H, Me-26), 1.18 (s, 3H, Me-29), 1.57 (d, J= 4.8Hz), 2.18 (d, J= 5.1Hz, 1H, OH), 3.60 (m, 1H, H-3α), 3.89 (m, 1H, 2β).

4.15.3 Friedel-2-ene (4): Eluent in column chromatography: petroleum ether. Yield: 7-16%, white prism like crystals, m.p. 246 ^{o}C (chloroform-methanol, lit.[15a] 246-248 ^{o}C).^{1}H NMR (300 MHz, $CDCl_3$): δ 0.75 (s, 3H, Me-24), 0.80 (s, 3H, Me-25), 0.86 (s, 3H, Me-23), 0.94 (s, 3H, Me-30), 1.03 (s, 3H, Me-26 and Me-29), 1.09 (s, 3H, Me-27), 1.15 (s, 3H, Me-28), 2.27 (d, *J*=13.8 Hz, 2H, H-1), 2.65 (d, *J*=10.5 Hz, 1H, H-4), 4.86 (s, 1H, H-2), 5.13-5.21 (m, 1H, H-3).^{13}C NMR (75 MHz, $CDCl_3$): δ 16.36, 17.80, 18.72, 18.79, 21.43, 21.69 (2), 23.83, 24.14, 25.17, 26.55, 32.38, 33.27, 33.34, 33.47, 34.61, 34.87, 35.53, 36.74, 37.66, 38.71, 39.47, 40.51, 41.29, 42.14, 44.77, 50.87, 56.50, 133.02 (C-2), 134.67 (C-3). FTIR (nujol, cm^{-1}): *v* 1376, 1363, 1343, 1257, 1166, 1142, 1085, 1036, 967, 820, 803, 720.

4.15.4 Friedel-3-enol-acetate (**5**): Eluent in column chromatography: 2% ethyl acetate in petroleum ether. Yield: 8-60%, white crystalline solid, m.p. 262 ^{o}C (chloroform-methanol). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.85 (s, 3H, Me-25), 0.95 (s, 3H, Me-30), 1.00 (s, 6H, Me-26 and Me-29), 1.01 (s, 3H, Me-27), 1.02 (s, 3H, Me-24), 1.18 (s, 3H, 28-Me), 1.59 (s, 3H, Me-23), 2.12 (s, 3H, -CH_3 of -OAc). ^{13}C NMR (75 MHz, $CDCl_3$): δ 9.55, 17.46, 18.16, 18.26, 18.67, 20.10, 20.69, 20.88, 28.20, 28.39, 30.07, 30.61, 31.83, 32.16, 32.39, 32.90, 35.04, 35.25, 35.42, 36.11, 37.08, 38.22, 38.39, 38.66, 39.31, 39.84, 42.95, 52.75, 56.10, 130.57 (C-4), 141.31 (C-3), 168.98 (>C=O of -OAc). FTIR (nujol, cm^{-1}): *v* 667, 759, 1070, 1222, 1382, 1456, 1749 (>C=O of -OAc), 2337. LRESIMS m/z (%): 491.3 (33) $[M+ Na]^{+}$, 489.3 (100). Analysis calcd: C, 81.99; H, 11. 18. Found: C, 81.56; H, 10.89.

4.15.5 Friedel-2-oxo-3-enol acetate (6): Eluent in column chromatography: 5% ethyl acetate in petroleum ether. Yield: 22-32%, yellowish-white solid, m.p. 280-282 ^{o}C (chloroform-methanol, lit.[26b] 283-285 ^{o}C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.93 (s, 3H, Me-25), 0.95 (s, 3H, Me-30), 0.99 (s, 6H, Me-26 and Me-29), 1.01 (s, 3H, Me-27), 1.16 (s, 3H, Me-24), 1.18 (s, 3H, Me-28), 1.76 (s, 3H, Me-23), 2.24 (s, 3H, CH_3 of -OAc). ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.46, 17.64, 17.95, 18.59, 19.11, 20.13, 20.37, 28.14, 29.99, 30.21, 31.76, 32.10, 32.19, 32.73, 34.04, 34.52, 35.01, 35.31, 35.88, 36.89, 37.83, 38.23, 39.22, 39.72, 40.54, 42.74, 52.41, 54.55, 140.87 (C-4),

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157.02 (C-3), 168.58 (-CH_3 of -OAc), 191.89 (C-2). FTIR (neat, cm^{-1}): *v* 752, 916, 1006, 1089, 1219, 1325, 1383, 1462, 1523, 1682, 1761, 2862, 2929. LRESIMS m/z (%): 483.25 (32) $[M+H]^+$, 465.26 (65), 413.16 (47), 315.09 (51), 301.08 (100). Analysis calcd: C, 79.62; H, 10.44. Found: C, 79.78; H, 10.52.

4.15.6 Friedelane-3-hydroxyimino (7): Yellowish-white solid, m.p. 283-284 ^oC (chloroform-methanol, lit.[1a] 280-282 ^oC). ^1H NMR (300 MHz, $CDCl_3$): δ 0.67 (s, 3H, Me-25), 0.77 (s, 3H, Me-30), 0.88 (s, 3H, Me-26), 0.89 (s, 3H, Me-29),0.93 (s, 6H, Me-23 and Me-24), 0.98 (s, 3H, Me-27), 1.10 (s, 3H, Me-28), 1.70 (m, 1H, H-2_{eq}), 1.97 (m, 1H), 2.11 (s, 1H, H-4), 3.36 (d, J=12Hz, H-2_{ax}). ^{13}C NMR (75 MHz, $CDCl_3$): δ 7.34, 13.20, 16.94, 17.32, 17.65, 19.22, 19.55, 23.47, 27.15, 28.68, 28.99, 29.52, 30.76, 31.08, 31.38, 31.78, 34.01, 34.31, 34.55, 35.04, 36.30, 37.27, 38.24, 38.64, 40.12, 41.76, 49.92, 52.07, 58.96, 159.61.

4.15.7 Friedelan-3β–ol (8): Eluent in column chromatography: 5% ethyl acetate in petroleum ether. Yield: 72%, white crystalline solid, m. p. 290 ^oC (pet. ether- ethyl acetate, lit.[26c] 290-291 ^oC). ^1H NMR (300 MHz, $CDCl_3$): δ 0.86(s, 3H, Me-25), 0.93 (s, 3H, Me-24), 0.95 (d, *J*=1.2 Hz, 3H, Me-23), 0.96 (s, 3H, Me-30), 0.99 (s, 6H, Me-26 and Me-29), 1.00 (s, 3H, Me-27), 1.17 (s, 3H, Me-28), 1.75 (dt, *J*=12.8 and 3.2 Hz, 1H, H-6,), 3.75 (m, 1H, H-3). **^{13}C** NMR (75 MHz, $CDCl_3$): δ 11.63 (C-23), 15.76 (C-1), 16.39 (C-24), 17.52 (C-7), 18.24 (C-25), 18.66 (C-26), 20.12 (C-27), 28.17 (C-20), 30.00 (C-17), 30.62 (C-15), 31.78 (C-29), 32.07 (C-28), 32.29 (C-21), 32.76 (C-12), 35.03 (C-30), 35.13 (C-2), 35.31 (C-19), 35.52 (C-11), 36.04 (C-16), 37.06, 37.79 (C-9), 38.33 (C-13), 39.26 (C-22), 39.64 (C-14), 41.67 (C-5), 42.76 (C-6), 49.12 (C-4), 53.16 (C-8), 61.29 (C-10), 72.75 (C-3). FTIR (nujol, cm^{-1}): *v* 3474, 1381, 1174, 1044, 999, 943, 916, 719.

4.15.8 Lactam 9: Eluent in column chromatography: 35% ethyl acetate in petroleum ether. Yield: 67%, yellow amorphous solid, m.p. 266-267 ^0C (lit[1a] 266-268 ^0C). ^1H NMR (300 MHz, $CDCl_3$): δ 0.81 (s, 3H, Me-24), 0.81 (s, 3H, Me-25), 0.95 (s, 3H, Me-30), 0.98 (s, 3H, Me-27), 0.99 (s, 3H, Me-29), 1.00 (s, 3H, Me-26), 1.04 (d, *J*=6.6Hz, 3H, Me-23), 1.17 (s, 3H, Me-28), 1.73 (brs, 1H, H-10), 2.38 (m, 2H, H-2), 3.26 (q, *J*=6.6 Hz, 1H, H-4), 5.28 (brs, 1H, N-H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.88 (C- 24), 16.03 (C-23), 17.95 (C-25), 18.35 (C-1), 18.44 (C-7), 18.58 (C-26), 20.21 (C-27), 28.17 (C-20), 29.99 (C-17), 30.66 (C-12), 31.75 (C-29), 32.04 (C-15), 32.40 (C-28), 32.76 (C-21), 35.03 (C-30), 35.29 (C-11), 35.50 (C-19), 36.01 (C-16), 36.52 (C-2), 38.43 (C-9), 38.51 (C-14), 39.24 (C-22), 39.27 (C-5 and C-6), 39.86 (C-13), 42.72 (C-18),

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52.77 (C-8), 59.02 (C-4), 65.24 (C-10), 177.07 (C-3). FTIR (nujol, cm^{-1}): *v* 2928, 2867, 1672 (C=O), 1458 (N-H), 1362 (C-N), 734 (N-H).

4.15.9 Friedelane-3β-acetate (10): Eluent in column chromatography: 1% ethyl acetate in petroleum ether. Yield: 30%, white crystalline solid, m. p. 298 ^{o}C (chloroform-methanol, lit.[26c] 299 ^{o}C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.75 (s, 3H, Me-24), 0.77 (s, 3H, Me-25), 0.82 (s, 3H, Me-23), 0.95 (s, 3H, Me-30), 0.99 (s, 6H, Me-26, Me-29), 1.01 (s, 3H, Me-27), 1.17 (s, 3H, Me-28), 1.78 (dt, *J*=12.8 and 3.2 Hz, 1H, H-6), 2.01 (s, 3H, -$OCOCH_3$), 2.03- 2.12 (m, 3H, H-2 and H-4), 4.62 (m, 1H, H-3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 9.93 (C-23), 14.50 (C-24), 17.85 (C-25), 18.12 (C-7), 18.65 (C-27), 19.33 (-CH_3 of -OAc), 20.16 (C-26), 21.36 (C-1), 28.18 (C-20), 30.01 (C-17), 30.57 (C-12), 31.80 (C-29), 32.10 (C-28), 32.35 (C-15), 32.71 (C-2), 32.80 (C-21), 35.02 (C-30), 35.32 (C-19), 35.53 (C-11), 36.05 (C-16), 37.00 (C-9), 38.30 (C-14), 38.39 (C-5), 39.27 (C-22), 39.68 (C-13), 41.33 (C-6), 42.81 (C-18), 50.03 (C-4), 52.98 (C-8), 59.89 (C-10), 75.19 (C-3), 170.99 (>C=O of -OAc). FTIR (nujol, cm^{-1}): *v* 1736, 1379, 1049, 1019, 972, 754, 721. Analysis calcd: C, 81.64; H, 11.56. Found: C, 81.55; H, 11.43.

4.15.10 Friedel-3-oxo-4α-acetate (11): Eluent in column chromatography: 2% ethyl acetate in petroleum ether. Yield: 12-41%, white crystalline solid, m.p. 174-176 ^{o}C (chloroform-methanol). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.80 (s, 3H, Me-25), 0.86 (s, 3H, Me-24), 0.96 (s, 3H, Me-30), 1.00 (s, 6H, Me-26 and Me-29), 1.07 (s, 3H, Me-27),1.18 (s, 3H, Me-28),1.30 (s, 3H, Me-23), 1.93- 2.02 (m, 1H, H-1), 2.26-2.52 (m, 2H, H-2), 2.14 (-CH_3 of -OAc).^{13}C NMR (75 MHz, $CDCl_3$): δ 12.64, 15.68, 17.95, 18.13, 18.73, 20.19, 21.50, 22.98, 28.20, 30.03, 30.55, 31.84, 32.12, 32.38, 32.85, 34.29, 35.00, 35.34, 35.95, 36.05, 37.29, 38.03, 38.32, 39.28, 39.70, 42.88, 46.05, 50.34, 52.47, 89.09 (C-4), 170.11 (-CH_3 of -OAc), 208.30 (C-3). FTIR (nujol, cm^{-1}): *v* 722, 1119, 1245, 1377, 1508, 1736, 2345. LRESIMS m/z (%): 507.5 (100) $[M+ Na]^{+}$, 508.5 (46). Analysis calcd: C, 79.29; H, 10.81. Found: C, 79.38; H, 10.73.

4.15.11 Friedel-3-oxo-4β-acetate (12): Eluent in column chromatography: 5% ethyl acetate in petroleum ether Yield: 35%, white crystalline solid, m.p. 228-230 ^{o}C (chloroform-methanol). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (s, 3H, Me-25), 0.91 (s, 3H, Me-24), 0.96 (s, 3H, Me-30), 1.00 (s, 3H, Me-26), 1.01 (s, 3H, Me-29), 1.05 (s, 3H, Me-27), 1.18 (s, 3H, Me-28), 1.84 (s, 3H, Me-23), 2.08 (-CH_3 of -OAc), 2.29-2.40 (m, 1H, H_α-2), 2.51-2.59 (m, 1H, H_β-2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.02, 17.64, 17.99, 18.73, 19.18, 20.33, 21.71, 22.84, 28.18, 30.02, 30.49, 31.76, 32.12, 32.49, 32.80, 33.22, 35.05, 35.39, 36.02, 36.08, 37.40, 37.45, 38.34, 39.29, 39.73,

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42.85, 47.00, 51.98, 53.23, 89.83 (C-4), 169.69 (-CH_3 of -OAc), 205.79 (C-3). FTIR (nujol, cm^{-1}): *v* 1755, 1723, 1462, 1377, 1235, 1192, 1118, 1090, 1017, 605, 500. Analysis calcd: C, 79.29; H, 10.81. Found: C, 79.41; H, 10.65.

4.15.12 Friedel-3β-ol-4α-acetate (13): Eluent in column chromatography: 2% ethyl acetate in petroleum ether. Yield: 27%, pale yellow solid, m.p. 230 ^oC.^1H NMR (300 MHz, $CDCl_3$): δ 0.83 (s, 3H, Me-25), 0.94 (s, 3H, Me-30), 0.99 (s, 6H, Me-26 and Me-29), 1.14 (d, *J*= 1.2 Hz, 3H, Me-27), 1.15 (s, 3H, Me-24), 1.16 (s, 3H, Me-28), 1.20 (d, *J*=1.5 Hz, 3H, Me-23), 1.75-1.78 (m, 1H, H-10), 2.07 (q, *J*=1.5 Hz, -CH_3 of -OAc), 2.15 (t, *J*=3.9 Hz, H-3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.18 (C-23), 15.25 (C-24), 17.70 (C-25), 17.82 (C-1), 18.04 (C-7), 18.71 (C-27), 20.17 (C-26), 21.02 (CH_3 of -OAc), 27.86 (C-6), 28.15 (C-20), 30.00 (C-17), 30.49 (C-12), 31.76 (C-29), 32.10 (C-28), 32.33 (C-15), 32.77 (C-21), 35.05 (C-30), 35.34(C-11),35.52 (C-16), 36.00 (C-22), 36.46 (C-19), 36.66 (C-9), 38.27 (C-14), 38.36 (C-5), 39.25 (C-2), 39.70 (C-13), 42.78 (C-18), 48.10 (C-8), 52.36 (C-10), 71.65 (C-3), 88.05 (C-4), 169.51 (>C=O of -OAc). FTIR (nujol, cm^{-1}): *v* 615,722, 838, 1041, 1148, 1213, 1241, 1377, 1560, 1654, 1742. Analysis calcd: C, 78.96; H, 11.18. Found: C, 78.83; H, 10.97.

4.15.13 Friedelin-2,3-lactone (14): Eluent in column chromatography: 5% ethyl acetate in petroleum ether. Yield: 81%, white crystalline solid, m.p. 287-289 ^oC (lit.[1a] 288-290 ^oC).^1H NMR (300 MHz, $CDCl_3$): δ 0.85 (s, 3H, Me-25), 0.89 (s, 3H, Me-24), 0.91 (s, 3H, Me-26), 0.96 (s, 6H, Me-27 and Me-30), 1.01 (s, 3H, Me- 29), 1.15 (s, 3H, Me-28), 1.23 (d, 3H, *J* = 6.3 Hz, Me-23), 1.95 (m, 1H, H-1_{ax}), 2.55 (td, 1H, *J*= 1.5, 13.0 and 13.0 Hz, H-2_{ax}), 2.65 (ddd, 1H, *J* = 1.5, 7.0 and 13.0 Hz, H-2_{eq}), 4.24 (q, 1H, *J* = 6.3 Hz, H-4). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.45 (C-23), 16.22 (C-24), 17.90 (C-25), 18.03 (C-7), 18.55 (C-1), 18.58 (C-26), 20.20 (C-27), 28.17 (C-20), 29.99 (C-17), 30.61 (C-12), 31.76 (C-29), 32.06 (C-28), 32.37 (C-15), 32.75 (C-21), 34.36 (C-2), 35.03 (C-30), 35.31 (C-11), 35.42 (C-16), 35.97 (C-19), 38.20 (C-9), 38.39 (C-14), 38.47 (C-6), 39.23 (C-22), 39.35 (C-13), 40.79 (C-5), 42.73 (C-18), 52.73 (C-8), 63.99 (C- 10), 84.92(C-4), 175.59 (C3). FTIR: (KBr, cm^{-1}): ν 2945, 1734 (C=O), 1072 (CO), 752.

4.15.14 3,4-*Seco*-friedelane-3,4-diol (15): Eluent in column chromatography: 35% ethyl acetate in petroleum ether. Yield 72%, white powdered solid, m.p. 249 ^oC.^1H NMR (300 MHz, $CDCl_3$): δ 0.88 (s, 3H, Me-24), 0.93 (s, 3H, Me-25), 0.95 (s, 3H, Me-30), 0.98 (s, 3H, Me-23), 1.00 (s, 6H, Me-26 and Me-29), 1.01 (s, 3H, Me-27), 1.18 (s, 3H, Me-28), 3.51-3.65 (m, 3H, H-3 and H-4). ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.37 (C-23), 17.81 (C-24), 18.02, 18.65 (C-27), 18.79(C-25),

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20.16 (C-26), 21.98, 28.16, 30.00, 30.23, 31.85 (C-29), 32.10 (C-28), 32.26, 32.82, 34.94 (C-30), 35.07, 35.29, 36.06, 38.30, 39.28, 39.56, 41.91, 42.81, 52.84, 58.53, 63.25 (C-3), 75.87 (C-4). FTIR (neat, cm^{-1}): *v* 3392, 2937, 2868, 1652, 1458, 1388, 1068. Analysis calcd: C, 80.65; H, 12.18. Found: C, 80.20, H, 12.01.

4.15.15 Friedelane-3-oximino-4α–ol (16): Yield: 88%, pale yellow solid, m.p. 227 ^{o}C.^{1}H NMR (300 MHz, DMSO-d_6): δ 0.73 (s, 3H, Me-24), 0.81 (s, 3H, Me-25), 0.96 (s, 3H, Me-30), 0.99 (s, 6H, Me-26 and Me-29), 1.12 (s, 3H, Me-27), 1.17 (s, 3H, Me-28), 1.26 (s, 3H, Me-23), 1.70-2.01 (m, 3H, H-2 and H-10), 4.39 (br s, 1H, -OH), 10.38 (br s, 1H, -NOH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 17.16, 18.12, 18.67, 18.93, 19.85, 20.36, 28.32, 30.06, 30.59, 32.16, 32.35, 32.99, 33.75, 35.24, 35.80, 36.11, 36.97, 38.25, 39.50, 39.77, 40.05, 40.33, 40.61, 40.89, 42.90, 43.47, 49.44, 52.37, 76.62 (C-4), 161.14 (C-3). FTIR (nujol, cm^{-1}): *v* 3442, 3301, 2723, 1378, 1302, 1178, 1045, 992, 944, 919, 769, 725, 572.

4.15.16 Friedelan-3β-amine-4α-ol (17): Yield: 63%, pale yellow small-flower-like crystals, m.p. 242 ^{o}C (chloroform-ethanol).^{1}H NMR (300 MHz, $CDCl_3$): δ 0.84 (s, 3H, Me-24), 0.88 (s, 3H, Me-25), 0.93 (s, 3H, Me-30), 0.95 (s, 6H, Me-29), 1.10 (s, 3H, Me-27), 1.14 (s, 3H, Me-26), 1.18 (s, 3H, Me-28), 2.08 (m, 3H, Me-23), 2.17- 2.28 (m, 1H, H-10), 2.47- 2.56 (m, 1H, H-2), 3.61- 3.83 (br hump, -OH), 5.01- 5.29 (br hump, $-NH_2$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.44 (CH_3-24), 16.81 (CH_3-25), 16.94 (CH_3-23), 17.66 (CH_3-27), 19.15 (CH_3-26), 23.78, 24.78, 27.14, 28.68, 28.96, 29.02, 30.80, 31.11, 31.32, 31.79 (CH_3-29), 33.94 (CH_3-28), 34.29, 34.36, 34.93 (CH_3-30), 37.27, 37.33, 38.23, 38.62, 41.81, 51.36, 52.26, 52.94, 54.8 (C-3), 76.20 (C-4). Analysis calcd: C, 81.20; H, 12.04; N, 3.16 Found: C, 81.40; H, 11.95; N, 3.09.

4.15.17 Friedelane-2α,3β-diol (18): Eluent in column chromatography: 50% ethyl acetate in petroleum ether. Yield: 68%, white crystalline solid, m.p. 288-290 ^{o}C (ethyl acetate, lit[15a] 287-290 ^{o}C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.85 (s, 3H, Me-24), 0.88 (s, 3H, Me-25), 0.93 (s, 3H, Me-23), 0.95 (s, 3H, Me-30), 0.99 (s, 3H, Me-26), 1.01 (s, 3H, Me-29), 1.07 (s, 3H, Me-27), 1.17 (s, 3H, Me-28), 3.55 (s, 1H, H-2), 3.99 (d, *J*=2.7 Hz, 1H, H-3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.90, 15.93, 17.54, 18.17, 18.74, 20.15, 23.96, 28.19, 30.05, 30.63, 31.80, 32.14, 32.36, 32.84, 35.05, 35.37, 35.52, 36.09, 36.55, 37.82, 38.42, 39.30, 39.73, 41.41, 42.87, 43.71, 52.31, 53.27, 71.43 (C-2), 77.22 (C-3). FTIR (nujol, cm^{-1}): *v* 3443, 3300, 2724, 1377, 1301, 1179, 1045, 992, 943, 918, 768, 724, 572. Analysis calcd: C, 81.02; H, 11.79. Found: C, 81.32; H, 11.35.

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4.15.18 3-*Epi*pachysandiol A (19): Eluent in column chromatography: 50% ethyl acetate in petroleum ether. Yield: 62%, white needle-shaped crystals, m.p. 282-283 ^{o}C (ethyl acetate, lit.[15a] 281- 283 ^{o}C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.80 (d, *J*= 6.3 Hz, 3H, CH_3-24), 0.90 (d, *J*= 6.6 Hz, 3H, CH_3-25), 0.95 (s, 1H, CH_3-30), 0.99 (s, 6H, CH_3-26 and CH_3-29), 1.00 (s, 1H, CH_3- 2), 1.17 (s, 1H, CH_3-28), 1.26 (s, 1H, CH_3-23), 3.18 (dd, *J*= 9 Hz and 10.5 Hz, C-3), 3.38- 3.47 (m, 1H, C-2). ^{13}C NMR (75 MHz, CDCl3): δ 9.71, 14.76, 17.77, 18.15, 18.60, 20.13, 27.91, 28.15, 29.34, 30.00, 30.55, 31.76, 32.09, 32.37, 32.81, 35.00, 35.35, 35.53, 36.04, 36.96, 38.26, 38.32, 39.26, 39.70, 41.17, 42.83, 49.78, 53.12, 57.41, 77.19, 77.50. FTIR (KBr, cm^{-1}): *ν* 3416, 2934, 2866, 1702, 1635, 1461, 1386, 1034, 592. LRESIMS m/z (%): 467.5 (100) $[M + Na]^+$, 468.5 (42).Analysis calcd: C, 81.02; H, 11.79. Found: C, 81.40, H, 11.92.

4.15.19 Friedelane-3β,4α-diacetate (20): Eluent in column chromatography: petroleum ether. Yield: 95%, white solid, m.p. 209-210 ^{o}C.^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (s, 3H, Me-24), 0.91 (s, 3H, Me-25), 0.95 (s, 3H, Me-30), 1.00 (s, 6H, Me-26 and Me-29), 1.06 (d, *J*=1.8 Hz, 3H, Me-27), 1.18 (s, 3H, Me-28), 1.26 (s, 3H, Me-23), 2.07 (s, 3H, -CH_3 of -OAc), 2.08 (s, 3H, -CH_3 of -OAc), 2.90-3.06 (m, 1H, H-3). FTIR (nujol, cm^{-1}): *ν* 1749, 1734, 1717, 1459, 1375, 1233, 1112, 1014, 955, 800, 719, 599.

4.15.20 Friedelan-3-oxo-4α-ol (21): Eluent in column chromatography: 10% ethyl acetate in petroleum ether. Yield: 84%, needle shaped crystals, m.p. 268-270 ^{o}C (lit.[15e] 269-271 ^{o}C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.81 (s, 3H, Me-25), 086 (s, 3H, Me-24),0.95 (s, 3H, Me-30), 0.99 (s, 6H, Me-26 and Me-29), 1.06 (d, *J*=3.9 Hz, 3H, Me-27), 1.16 (s, 3H, Me-23), 1.17 (s, 3H, Me-28), 2.11 (d, *J*=12.6 Hz, 1H, H-10), 2.22 (d, *J*= 14.1 Hz, 1H, H-2), 2.95 (m, 1H, H-2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.74 (Me-23), 16.91 (Me-24),17.86 (C-1), 18.02 (Me-25), 18.77 (Me-27), 20.29 (Me-26), 21.72 (C-7), 28.21 (C-20), 30.06 (C-17), 30.57 (C-12), 31.79 (Me-29), 32.13 (Me-28), 32.51(C-15), 32.86 (C-21), 33.50 (C-19), 35.05 (Me-30), 35.42 (C-11), 35.83 (C-16), 36.09 (C-22), 37.08 (C-6), 37.25 (C-9), 38.33 (C-14), 39.31 (C-2), 39.77 (C-13), 42.89 (C-18), 44.63 (C-5), 49.38 (C-8), 52.45 (C-10), 81.08 (C-4), 212.92 (C-3). FTIR (nujol, cm^{-1}): *ν* 3447, 1702, 1377, 1108, 1068, 746, 722. Analysis calcd: C, 81.39; H, 11.38. Found: C, 88.45; H, 11.43.

4.15.21 Friedelane-3β,4α-diol (22): Eluent in column chromatography: 20% ethyl acetate in petroleum ether. Yield: 62%, m.p. 241-242 ^{o}C (lit[15e] 240-241^{o}C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.84 (s, 3H, Me-25), 0.87 (s, 3H, Me-29),0.94 (s, 3H, Me-26), 0.99 (s, 3H, Me-30), 1.05 (s, 3H,

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Me-27),1.17 (s, 3H, Me-28),1.26 (d, J= 13.2 Hz, 6H, Me-23& Me-24), 1.77 (m, 1H, H-2_{eq}), 2.07 (s, 1H, OH), 2.18 (s, 1H, OH), 3.57 (br s, 1H, H-2_{ax}) 4.74 (s, 1H, H-4). ^{13}C NMR (75 MHz, $CDCl_3$): δ12.19, 15.28, 17.73, 17.84, 18.70, 18.76, 20.18, 27.88, 28.18, 30.04, 30.52, 31.78, 32.12, 32.39, 32.84, 35.05, 35.39, 35.56, 36.06, 36.50, 36.72, 38.31, 38.40, 39.29, 39.75, 42.86, 48.16, 52.41, 81.04 (C-3), 88.09 (C-4). FTIR (nujol, cm^{-1}): *v* 3443, 3300, 2724, 1377, 1301, 1179, 1045, 992, 943, 918, 768, 724, 572. Analysis calcd: C, 81.02; H, 11.79. Found: C, 81.32; H, 11.35.

4.15.22 Cyclic amine 23: Eluent in column chromatography: methanol. Yield: 63%, white crystalline solid, m.p. 228 °C (aqueous ethanol). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.84 (s, 3H, Me-24), 0.87 (s, 3H, Me-25), 0.92 (d, *J*= 3 Hz, 3H, Me-23), 0.94 (s, 3H, Me-30), 0.97 (s, 3H, Me-27), 0.99 (s, 3H, Me-26), 1.00 (s, 3H, Me-29), 1.17 (s, 3H, Me-28),1.79-1.86 (m, 1H, H_β-3), 2.13 (dd, *J*=12 Hz, 6 Hz; 1H, H-4), 2.71-2.81 (m, 1H, H_α-3), 3.07-3.14 (m, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.94 (C-24), 17.55 (C-23), 17.76 (C-25), 18.30 (C-7), 18.69 (C-27), 20.22 (C-26), 21.08 (C-1), 28.18 (C-20), 28.99 (C-2), 30.04 (C-17), 30.57 (C-12), 31.81 (C-29), 32.09 (C-28), 32.43 (C-15), 32.87 (C-21), 34.88 (C-11), 35.01 (C-30), 35.33 (C-19), 36.16 (C-16), 38.38 (C-14), 38.73 (C-9), 39.28 (C-22), 39.46 (C-13), 40.24 (C-6), 41.67 (C-5), 42.85 (C-18), 47.94 (C-3), 52.78 (C-8), 60.28 (C-10), 70.52 (C-4). FTIR (nujol, cm^{-1}): *v* 669, 786, 1145 (br., C-N str.), 1384, 1510, 1558, 1651 (N-H, def.), 2337, 2362, 3340, 3423 (N-H, str.). Analysis calcd: C, 84.24; H, 12.49. Found: C, 83.93; H, 12.25.

4.15.23 Friedelan-3-oxo-2α–acetate (24): Eluent in column chromatography: 2% ethyl acetate in petroleum ether. Yield: 78%, white solid, m.p. 268-269 °C (lit.[15a] 269.5-271 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.71 (s, 3H, Me-24), 0.84 (s, 3H, Me-25), 0.89 (d, *J*= 6.6 Hz, 3H, Me-23), 0.96 (s, 3H, Me-30), 1.00 (s, 6H, Me-26 and Me-29), 1.07 (s, 3H, Me-27), 1.18 (s, 3H, Me-28), 2.13 (s, 3H, -CH_3 of -$COCH_3$), 2.67 (q, *J*= 6.6 Hz, 1H, H-4), 4.94 (d, *J*= 3.3 Hz, 1H, H-2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 6.50, 14.13, 17.91, 18.28, 18.63, 20.14, 21.12, 28.19, 28.26, 30.04, 30.38, 31.77, 31.89, 32.16, 32.41, 32.90, 34.97, 35.35, 35.58, 36.09, 36.99, 38.41, 39.28, 39.77, 41.14, 42.93, 43.24, 53.10, 53.40, 54.47, 169.69 (-CH_3 of -OAc), 207.98 (C-3). FTIR (nujol, cm^{-1}): *v* 1744, 1720, 1377, 1365, 1257, 1229, 1184, 1164, 1041, 1023, 997, 933, 795, 758, 722. Analysis calcd: C, 79.29; H, 10.81. Found: C, 77.42; H, 11.03.

4.15.24 Friedelan-3-oximino-2α–ol (25): Yield: 95%, pale yellow plate-like crystals, m.p. 265-271 °C (ethanol, lit.[26d] 266-272 °C). ^{1}H NMR (300 MHz, DMSO-d_6): δ 0.71 (s, 3H, Me-24), 0.74

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(s, 3H, Me-25), 0.84 (d, *J*=2.7 Hz, 3H, Me-23), 0.95 (s, 3H, Me-30), 1.00 (s, 3H, Me-26 and Me-29), 1.03 (s, 3H, Me-27), 1.18 (s, 3H, Me-28), 1.92-2.10 (m, 2H, H-2), 2.50-2.58 (m, 1H, H-4), 3.62- 3.80 (m, 1H, H-2).). ^{13}C NMR (75 MHz, DMSO-d_6): δ 8.37, 13.25, 17.69, 17.93, 18.47, 19.86, 27.82 (2-carbons), 28.55, 28.97, 29.54, 30.08, 31.66, 31.77, 31.86, 32.44, 34.76 (2-carbons), 35.56, 36.19, 37.79, 39.46, 39.77, 40.02, 42.35, 44.80, 51.68, 52.60, 57.48, 160.06. FTIR (nujol, cm^{-1}): *v* 3286, 3168, 2724, 1380, 1261, 1147, 1093, 1023, 943, 801, 724.

4.15.25 Friedelane-2α,3β-diacetate (26): Eluent in column chromatography: 1% ethyl acetate in petroleum ether. Yield: 97%,white crystalline solid, m.p. 226-228 ^{o}C (lit[15a] 226-227 ^{o}C).^{1}H NMR (300 MHz, $CDCl_3$): δ 0.84 (s, 3H, Me-24), 0.88 (s, 3H, Me-25), 0.91 (s, 3H, Me-23), 0.94 (s, 3H, Me-30), 0.99 (s, 3H, Me-26 and Me-29), 1.01 (s, 3H, Me-27), 1.17 (s, 3H, Me-28), 2.06 (s, 3H, -CH_3 of -OAc), 2.08 (s, 3H, -CH_3 of -OAc), 4.02-4.4.33 (m, 1H, H-2), 4.84 (dd, *J*=21.3 Hz and 2.4 Hz, 1H, H-3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.49, 15.32, 17.67, 18.04, 18.52, 20.06, 21.00, 21.73, 21.29, 28.18, 30.07, 30.41, 31.47, 31.87, 32.14, 32.34, 32.91, 34.97, 35.43, 36.13, 36.50, 37.55, 38.45, 39.29, 39.70, 41.36, 42.93, 43.86, 53.04, 53.17, 70.90, 73.97, 169.63 (-CH_3 of C_2-OAc), 169.95 (-CH_3 of C_3-OAc). FTIR (nujol, cm^{-1}): *v* 1734, 1717, 1464, 1376, 1243, 1227, 1201, 1032, 965, 891, 719.

4.15.26 3-Chlorofriedel-3-ene (27): Eluent in column chromatography: petroleum ether. Yield: 12%, white cube-like crystals, m.p. 260-262 ^{o}C.^{1}H NMR (300 MHz, $CDCl_3$): δ 0.77 (s, 3H, Me-24), 0.87 (m, 3H, Me-25), 0.93 (m, 12H, Me-26, Me-27, Me-29, Me-30), 1.10 (s, 3H, Me-28) 1.63 (d, 3H, *J*=2.1 Hz, Me-23), 1.80 (dd, 1H, *J*= 3 Hz, 12 Hz H-1), 2.23-2.36 (br m, 2H, H-2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.03 (C-24), 17.27 (C-23), 17.27, 17.54 (C-25), 17.80 (C-27), 19.04, 19.51(C-26), 27.18, 29.06, 29.55, 30.82, 31.13, 31.32 (C-29), 31.88 (C-28), 33.99, 34.26, 34.38, 34.49 (C-30), 35.07, 36.02, 37.34, 38.06, 38.27, 38.78, 39.66, 41.94, 51.72, 55.21, 125.83 (C-3), 138.20 (C-4). FTIR (neat, cm^{-1}): *v* 3409, 2926, 2847, 1444, 1380, 1072, 973.

4.15.27 3-Chlorofriedel-2-ene-2-carbaldehyde (28): Eluent in column chromatography: 5% ethyl acetate in petroleum ether. Yield: 52%, white crystalline solid, m.p. 218 ^{o}C.^{1}H NMR (300 MHz, $CDCl_3$): δ 0.77 (s, 3H, Me-24), 0.93 (s, 3H, Me-25) 0.94 (s, 3H, Me-30), 0.99 (s, 6H, Me-26 and Me-29), 1.01 (s, 3H, Me-27), 1.14 (s, 3H, Me-28), 1.16 (d, 3H, J=2.4 Hz Me-23), 1.91-2.05 (m, 2H, H_{ax}-1 and H-10) 2.39-2.45 (m, 2H, H_{eq} and H-4). ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.77 (C-23), 14.43 (C-24), 17.39 (C-25), 18.31, 18.61 (C-27), 20.41 (C-26), 21.53, 28.18, 30.03, 30.27, 31.79 (C-29), 32.12 (C-28), 32.43, 32.80, 35.03 (C-30), 35.17, 35.31, 35.99, 36.79,

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38.17, 38.17, 39.27, 39.66, 41.84, 42.75, 52.88, 53.21, 54.23, 133.08 (C-2), 155.10 (C-3), 192.18 (-CHO). FTIR (neat, cm^{-1}): *v* 2932, 2855, 1675, 1611, 1394, 1232, 953.

4.15.28 Friedel-2-en-3-ol-2-carbaldehyde (29): Eluent in column chromatography: 7% ethyl acetate in petroleum ether. Yield: 10%, white powdered solid, m.p. 258-260 ^{o}C.^{1}H NMR (300 MHz, $CDCl_3$): δ 0.93 (s, 3H, Me-24), 0.94 (s, 3H, Me-25), 0.986 (s, 3H, Me-26), 0.994 (s, 3H, Me-29), 1.01 (s, 3H, Me-30), 1.14 (s, 3H, Me-27), 1.18 (s, 3H, Me-28), 1.79-1.85 (m, 1H, H_{ax}-1), 1.99- 2.07 (m, 3H, Me-23), 2.37- 2.52 (m, 1H, H_{eq}1), 2.64 (dd, 1H, *J*= 3 Hz and 18 Hz, H-4), 9.97 (d, 1H, *J*= 4.8 Hz, -CHO). ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.52 (CH_3-23), 17.63 (CH_3-24), 18.10 (CH_3-25), 18.51, 18.78 (CH_3-27), 20.10 (CH_3-26), 28.14, 28.14, 30.01, 30.20, 31.79 (CH_3-29), 32.11, 32.16, 32.74 (CH_3-28), 34.60, 34.64, 34.99 (CH_3-30), 35.31, 35.88, 36.85, 38.23, 38.42, 39.21, 39.70, 42.76, 42.76, 52.44, 54.59, 129.02 (C-2), 166.02 (C-3), 192.02 (-CHO). FTIR (KBr, cm^{-1}): *v* 3443, 2933, 2863, 1687, 1587, 1462, 1383, 1282, 1177, 972, 675, 628, 573. Analysis calcd: C, 81.88; H, 11.08. Found: C, 81.40, H, 11.05.

4.15.29 3-Chlorofriedel-2-en-4α-ol-2-carbaldehyde (30): Eluent in column chromatography: 10% ethyl acetate in petroleum ether. Yield: 7-65%, white powdered solid, m.p. 195 ^{o}C.^{1}H NMR (300 MHz, $CDCl_3$): δ 0.90 (s, 3H, Me-25), 0.94 (s, 3H, Me-30), 0.97 (s, 3H, Me-24), 1.00 (s, 6H, Me-26 and Me-29), 1.01 (s, 3H, Me-27), 1.18 (s, 3H, Me-28), 1.40 (s, 3H, Me-23), 1.94- 2.14 (m, 3H, H-6 and H-10), 2.41 (dd, *J*= 4.2 Hz & 18.3 Hz, 2H, H-1), 10.24 (s, 1H, -CHO). ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.42 (CH_3-24), 17.89 (CH_3-25), 17.98 (CH_3-23), 18.70 (CH_3-27), 20.43 (CH_3-26), 20.66, 22.03, 28.16, 30.02, 30.26, 31.74 (CH_3-29), 32.09 (CH_3-28), 32.39, 32.76, 33.59, 35.03 (CH_3-30), 35.32, 35.40, 35.96, 36.61, 38.13, 39.26, 39.66, 42.60, 42.71, 46.43, 52.04, 78.4 (C-4), 133.7 (C-2), 153.2 (C-3) 192.8 (-CHO). FTIR (neat, cm^{-1}): *v* 3480, 2926, 2855, 1675, 1373, 1113, 945.

4.15.30 Friedel-3-en-23-al (31): Eluent in column chromatography: petroleum ether. Yield: 56%, white small-needle-shaped crystals, m.p. 232 ^{o}C. (petroleum ether-ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (s, 3H, Me-25), 0.95 (s, 3H, Me-30), 1.00 (s, 6H, Me-26 and Me-29), 1.01 (s, 3H, Me-27), 1.15 (s, 3H, Me-24), 1.18 (s, 3H, Me-28), 2.26- 2.52 (m, 3H, H-1 and H-10), 2.72 (td, *J*= 3Hz and 15 Hz, 1H, H_{eq}-2), 6.55 (d, *J*=2.7 Hz, 1H, H-3), 9.30 (s, 1H, -CHO). ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.73 (C-24), 17.96 (C-25), 18.33 (C-27), 18.62, 20.05 (C-26), 21.12, 28.19, 28.87, 30.07, 30.57, 31.83 (C-29), 32.14 (C-28), 32.27, 32.86, 35.03 (C-30), 35.39, 35.51, 36.07, 37.28, 37.54, 37.93, 38.37, 39.29, 39.77, 42.93, 53.09, 56.95, 151.84 (C-3), 151.98

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(C-4), 194.23 (-CHO). FTIR (KBr, cm^{-1}): *v* 3449, 2929, 2862, 2713, 1680, 1628, 1455, 1384, 1170, 1042, 991, 825, 690. LRESIMS m/z (%): 447.3 (87) $[M+ Na]^+$, 413.2 (64), 301.1 (100). Analysis calcd: C, 84.84; H, 11.39. Found: C, 84.38, H, 11.17.

4.15.31 Friedelan-3α,4α-epoxide(32): Eluent in column chromatography: petroleum ether. Yield: 56%, white powdered solid, m.p. 276 ^oC.^1H NMR (300 MHz, $CDCl_3$): δ 0.82 (s, 3H, CH_3-25), 0.934 (s, 3H, CH_3-24), 0.944 (s, 3H, CH_3-30), 0.99 (d, *J*= 1.8 Hz, 3H, CH_3-26), 1.00 (s, 3H, CH_3-29), 1.02 (s, 3H, CH_3-27), 1.17 (s, 3H, CH_3-28), 1.26 (s, 3H, CH_3-23), 2.19 (q, *J*= 6.6 Hz, 1H, H_{ax}-2), 2.89 (br s, 1H, H_{eq}-2), 4.221 (t, *J*= 3 Hz, 1H, H-3).^{13}C NMR (75 MHz, $CDCl_3$): δ 9.52 (CH_3-23), 15.23 (CH_3-24), 17.68 (CH_3-25), 18.20 (CH_3-7), 18.64 (CH_3-27), 20.00 (CH_3-26), 23.81 (C-1), 28.16 (C-20), 30.01 (C-17), 30.51 (C-12), 31.79 (CH_3-29), 32.13 CH_3-28), 32.29 (C-21), 32.83 (C-15), 34.99 (CH_3-30), 35.24 (C-19), 35.31 (C-11), 36.03 (C-16), 36.41 (C-9), 38.36 (C-14), 39.25 (C-22), 39.72 (C-13), 40.73 (C-6), 41.78 (C-2), 42.87 (C-18), 50.42 (C-5), 52.83 (C-10), 53.36 (C-8), 76.88 (C-3), 102.35 (C-4). FTIR (KBr, cm^{-1}): *v* 2919, 2850, 1466, 1376, 1309, 723, 655. Analysis calcd: C, 84.44; H, 11.81. Found: C, 84.66, H, 11.95.

4.15.32 24-*Nor*friedel-1, 3, 5 (10), 6-tetraene (33): Eluent in column chromatography: petroleum ether. Yield: 42%, colourless sticky gum.^1H NMR (300 MHz, $CDCl_3$): δ 0.97 (s, 3H, CH_3-30), 1.02 (s, 6H, Me-26 and CH_3-29), 1.03 (s, 3H, CH_3-27), 1.21 (d, *J*= 2.4 Hz, CH_3-28), 1.25 (d, *J*= 4.2 Hz, CH_3-25), 2.25 (d, *J*= 3Hz, CH_3-23), 6.06 (dd, 1H, *J*= 2.7Hz and 9.9 Hz, H-7), 6.83 (dd, 1H, *J*= 3.0 Hz and 9.9 Hz, H-6), 6.92-7.17 (m, 3H, H-1, H-2 and H-3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.01 (C-25), 18.81 (C-27), 20.45 (C-26), 21.80, 21.85, 21.22 (C-23), 30.29, 30.96, 31.49, 31.61 (C-29), 32.09 (C-28), 32.22, 33.02, 34.77, 35.37 (C-30), 35.73, 37.69, 38.00, 38.94, 39.36, 42.83, 47.93, 119.14, 124.95, 128.98, 130.95, 131.13, 131.84, 133.87, 147.12. LRESIMS m/z (%): 413.4 (95) $[M+ Na]^+$. Analysis calcd: C, 89.16; H, 10.84. Found: C, 88.97; H, 11.01.

4.15.33 3-Chlorofriedel-2-ene-2-carboxaldoxime (34): Yield: 96%, off-white needle-shaped crystals, m.p. 164 ^oC (chloroform-methanol). ^1H NMR (300 MHz, $CDCl_3$): δ 0.78 (s, 3H, Me-24), 0.93 (s, 3H, Me-25), 0.94 (s, 3H, Me-30), 0.99 (s, 6H, Me-26 and Me-29), 1.01 (s, 3H, Me-27), 1.09 (d, *J*= 7.2 Hz, 3H, Me-23), 1.17 (s, 3H, Me-28), 1.92 (d, *J*= 13.2 Hz, 1H, H-1), 2.13 (dt, *J*= 3.3 Hz & 12.9 Hz, 1H, H-4), 2.31-2.45 (m, 2H, H-10), 8.40 (s, 1H, -C<u>H</u>=NOH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.47 (CH_3-23), 14.28 (CH_3-24), 17.39 (CH_3-25), 18.33, 18.63 (CH_3-27), 20.43 (CH_3-26), 23.09, 28.17, 30.02, 30.35, 31.77 (CH_3-29), 32.10, 32.41, 32.77 (CH_3-28), 35.06

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(CH_3-30), 35.15, 35.35, 35.97, 36.73, 38.04, 38.18, 39.26, 39.65, 41.81, 42.74, 52.32, 52.87, 54.32, 126.29 (C-2), 141.69 (C-3), 150.28 (-C=NOH). FTIR (KBr, cm^{-1}): *v* 3353, 2931, 2862, 1623, 1458, 1386, 1294, 1182, 1135, 985, 958, 749, 549. LRESIMS m/z (%): 488.5 (68) $[M+H]^+$, 474.5 (100). Analysis calcd: C, 76.27; H, 10.32; N, 2.87. Found: C, 76.47; H, 10.41; N, 2.77.

4.15.34 3-Chlorofriedel-2-ene-2-methanol (35): Eluent in column chromatography: 15% ethyl acetate in petroleum ether. Yield 92%, white crystalline solid, m.p. 244-246 ^oC (chloroform-methanol). ^1H NMR (300 MHz, $CDCl_3$): δ 0.77 (s, 3H, Me-24), 0.79 (s, 3H, Me-25), 0.93 (s, 3H, Me-23), 0.94 (s, 3H, Me-30), 0.99 (s, 3H, Me-27), 1.01 (d, *J*=2.1 Hz, 6H, Me-26 and 29), 1.17 (d, *J*= 3 Hz, 3H, Me-28), 1.90 (dd, *J*= 3 Hz and 10.5 Hz, 1H, H-1), 2.07-2.27 (m, 3H, H-1, H-4 and H-10), 4.25 (dd, *J*= 12 Hz and 26.7 Hz, 2H, -C$\underline{H_2}$OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.43 (CH_3-23), 14.09 (CH_3-24), 17.49 (CH_3-25), 18.37, 18.64 (CH_3-27), 20.39 (CH_3-26), 26.05, 28.19, 30.04, 30.35, 31.80 (CH_3-29), 32.12 (CH_3-28), 32.42, 32.82, 35.04 (CH_3-30), 35.33, 36.01, 36.69, 37.97, 38.20, 39.28, 39.68, 41.87, 42.77, 51.31, 52.87, 54.96, 64.07 (-CH_2OH), 132.14 (C-2), 133.10 (C-3). FTIR (KBr, cm^{-1}): *v* 3384, 2938, 2864, 1662, 1461, 1385, 1183, 1133, 1045, 1007, 948, 755, 696. LRESIMS m/z (%): 499.5 (40) $[M + Na + 2H]^+$, 497.5 (100) $[M + Na]^+$, 413.4 (44), 301.2 (75). Analysis calcd: C, 78.35; H, 10.82. Found: C, 78.47, H, 10.91.

4.15.35 3-Chlorofriedel-2-ene-2-methanol acetate (36): Eluent in column chromatography: 2% ethyl acetate in petroleum ether. Yield 98%, white crystalline solid, m.p. 180-182 ^oC (pet. ether-ethyl acetate). ^1H NMR (300 MHz, $CDCl_3$): δ 0.77 (s, 3H, Me-24), 0.92 (s, 3H, Me-25), 0.94 (s, 3H, Me-23), 1.00 (s, 3H, Me-30), 1.01 (s, 6H, Me-26 and Me-29), 1.06 (s, 3H, Me-27), 1.17 (s, 3H, Me-28), 1.90 (d, *J*= 13.2 Hz, 1H, H-1), 2.09 (s, 3H, -CH_3 of -OAc), 4.75 (s, 2H, -C$\underline{H_2}$OH**).** ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.38 (CH_3-23), 14.09 (CH_3-24), 17.45 (CH_3-25), 18.33, 18.58 (CH_3-27), 20.33 (CH_3-26), 20.87, 25.67, 28.15, 30.03, 30.26, 31.82 (CH_3-29), 32.10 (CH_3-28), 32.38, 32.83, 34.96 (CH_3-30), 35.20, 35.32, 35.99, 36.66, 37.89, 38.20, 39.23, 39.67, 41.83, 42.82, 51.39, 52.83, 54.75, 65.30 (-$\underline{C}H_2$OAc), 127.69 (C-2), 134.98 (C-3), 171.02 (-OCO$\underline{C}H_3$). FTIR (KBr, cm^{-1}): *v* 3444, 2933, 2866, 1745, 1459, 1383, 1225, 1026, 954, 910, 759. LRESIMS m/z (%): 541.5 (40) $[M + Na + 2H]^+$, 539.5 (100) $[M + Na]^+$, 301.3 (38).Analysis calcd: C, 76.63; H, 10.33; O, 6.19. Found: C, 76.67; H, 10.25; O, 6.05.

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4.15.36 3-Chlorofriedel-2-ene-2-carboxamide (37): Eluent in column chromatography: 10% ethyl acetate in petroleum ether. Yield: 58%, pale yellow crystals, m.p. 233-236 ^{o}C (pet. ether-ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.94 (s, 3H, Me-24), 0.96 (s, 3H, Me-25), 0.97 (s, 3H, Me-23), 0.99 (s, 3H, Me-30), 1.005 (s, 3H, Me-27), 1.014 (s, 6H, Me-26 and Me-29), 1.17 (s, 3H, Me-28), 1.99 (d, *J*= 12.3 Hz, 1H, H-1), 5.08 (s, 1H, -$CONH_2$), 5.48 (s, 1H, -$CONH_2$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.7 (CH_3-24), 17.49 (CH_3-25), 17.53 (CH_3-23), 19.35 (CH_3-27), 21.57 (CH_3-26), 26.58, 27.16, 28.69, 29.03, 29.25, 30.84, 31.12, 31.37, 31.87 (CH_3-29), 33.95 (CH_3-28), 34.04, 34.29, 35.02 (CH_3-30), 36.16, 37.24, 38.24, 38.65, 38.65, 39.38, 41.83, 44.05, 51.82, 52.20, 132.02 (C-2), 153.58 (C-3), 161.70 (-$CONH_2$). Analysis calcd: C, 76.27; H, 10.32; N, 2.87; O, 3.28. Found: C, 75.57; H, 10.66; N, 2.90; O, 3.35.

4.15.37 3-Chlorofriedel2-en-4α-ol-2-carboxaldoxime (38): Yield 97%, pale yellow crystals, m.p. 240 ^{o}C (chloroform-methanol). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.92 (s, 3H, Me-25), 0.94 (s, 3H, Me-30), 0.98 (s, 3H, Me-24), 1.00 (s, 3H, Me-27), 1.01 (s, 6H, Me-26 and Me-29), 1.18 (s, 3H, Me-28), 1.35 (s, 3H, Me-23), 1.95- 2.19 (m, 4H, H-6 and H-10), 2.46 (dd, *J*= 4.5 Hz and 17.7 Hz, 2H, H-1), 8.37 (s, 1H, -C<u>H</u>=NOH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.43 (CH_3-24), 17.89 (CH_3-25), 18.04 (CH_3-23), 18.72 (CH_3-27), 20.43 (CH_3-26), 21.30, 23.50, 28.17, 30.03, 30.30, 31.75 (CH_3-29), 32.09 (CH_3-28), 32.37, 32.75, 33.59, 35.03 (CH_3-30), 35.32, 35.47, 35.96, 36.59, 38.15, 39.25, 39.67, 42.56, 42.72, 46.56, 52.05, 77.97 (C-4), 128.70 (C-2), 141.20 (C-3), 150.15 (C=NOH). FTIR (KBr, cm^{-1}): *v* 3422, 2939, 2868, 1627, 1459, 1385, 1295, 1181, 1073, 992, 972, 751, 696. LRESIMS m/z (%): 526.5 (100) $[M + Na]^+$, 413.5 (48).Analysis calcd: C, 73.85; H, 10.00; N, 2.78; O, 6.35. Found: C, 73.87; H, 10.16; N, 2.90, O, 6.01.

4.15.38 3-Chlorofriedel-2-en-4α-ol-2-methanol (39): Eluent in column chromatography: 25% ethyl acetate in petroleum ether. Yield 78%, pale yellow crystals, m.p. 160 ^{o}C.^{1}H NMR (300 MHz, $CDCl_3$): δ 0.87 (s, 3H, Me-25), 0.91 (s, 3H, Me-24), 0.95 (s, 3H, Me-30), 1.00 (s, 9H, Me-26, Me-27 and Me-29), 1.15 (s, 3H, Me-28), 1.26 (s, 3H, Me-23), 1.75 (s, 3H, Me-23), 1.87-1.91 (m, 3H, H-1 and H-10), 4.19 (s, 2H, -C<u>H</u>$_2$OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.15 (CH_3-24), 18.14 (CH_3-25), 18.62 (CH_3-27), 19.04 (C-23), 20.05 (CH_3-26), 27.13, 28.16, 29.71, 30.02, 30.45, 31.81 (CH_3-29), 32.13 (CH_3-28), 32.26, 32.78, 35.01 (CH_3-30), 35.16, 35.30, 35.98, 36.48, 38.30, 38.47, 39.24, 39.77, 41.55, 42.83, 50.43, 52.59, 70.27 (-CH_2OH), 77.21 (C-4), 128.95 (C-2), 144.11 (C-3).

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4.15.39 2-Formyl-3-(1*H*-piperidin-1-yl)-friedel-2-ene (40): Eluent in column chromatography: 10% ethyl acetate in petroleum ether. Yield: 72%, pale yellow solid, m.p. 167 ^{o}C.^{1}H NMR (300 MHz, $CDCl_3$): δ 0.95 (s, 6H, Me-24 and CH_3-30), 1.01 (s, 6H, CH_3-26 and CH_3-29), 1.03 (s, 3H, Me-25), 1.16 (s, 3H, Me-27), 1.18 (s, 3H, Me-28), 1.27 (d, *J*= 3.3 Hz, CH_3-23), 1.50- 1.55 (m, 6H, H-3′, H-4′ and H-6′), 3.25- 3.80 (m, 4H, H-2′ and H-6′). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.06 (CH_3-24), 17.64 (CH_3-25), 18.26 (CH_3-27), 18.51, 18.72 (CH_3-23), 20.12 (CH_3-26), 22.68, 24.50, 26.45, 28.17, 29.71, 30.04, 30.25 31.79 (CH_3-29), 32.14 (CH_3-28), 32.32, 32.81, 34.66, 35.00 (CH_3-30), 35.36, 35.96, 35.96, 38.12, 38.30, 38.44, 39.25, 39.74, 42.84, 46.51, 46.86, 52.53, 53.18, 54.66, 142.95, 165.84, 199.80. Analysis calcd: C, 82.85; H, 11.40; N, 2.68. Found: C, 82.10; H, 10.99; N, 2.26.

4.15.40 2-Formyl-3-(1*H*-morpholin-4-yl)-friedel-2-ene (41): Eluent in column chromatography: 10% ethyl acetate in petroleum ether. Yield: 70%,pale yellow solid, m.p. 170 ^{o}C.^{1}H NMR (300 MHz, $CDCl_3$): δ 0.91 (s, 3H, CH_3-24), 0.94 (s, 3H, CH_3-30), 1.00 (s, 6H, CH_3-26 and CH_3-29), 1.01 (s, 6H, CH_3-25 and CH_3-27), 1.07 (s, 3H, CH_3-23), 1.18 (s, 3H, CH_3-28), 1.91-2.06 (m, 4H, H-1, H-2), 2.33-2.37 (t, *J*= 6 Hz, 1H, H-4), 2.96 (br s, 4H, H-3′ and H-5′), 3.71 (br s, 4H, H-2′ and H-6′). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.13 (CH_3-24), 17.60 (CH_3-25), 18.14, 18.54 (CH_3-27), 19.04 (CH_3-23), 20.13 (CH_3-26), 28.14, 29.68, 30.02, 30.24, 31.76 (CH_3-29), 32.11 (CH_3-28), 32.23, 32.78, 34.60, 35.00 (CH_3-30), 35.34, 35.64, 35.95, 36.90, 38.22, 38.63, 39.24, 39.80, 40.50, 42.81, 50.34 (2), 52.54, 54.80, 66.78 (2), 141.22 (C-2), 166.66 (C-3), 198.38 (-CHO). Analysis calcd: C, 80.25; H, 10.97; N, 2.67. Found: C, 80.46; H, 11.12; N, 2.32.

4.15.41 2-Formyl-3-(1*H*-piperazin-1-yl)-friedel-2-ene (42): Eluent in column chromatography: 20% ethyl acetate in petroleum ether. Yield: 65%, white powdered solid, m.p. 156 ^{o}C.^{1}H NMR (300 MHz, $CDCl_3$): δ 0.87 (s, 3H, CH_3-24), 0.92 (s, 6H, CH_3-26 and CH_3-29), 0.93 (s, 3H, CH_3-30), 1.01 (s, 3H, Me-25), 1.11 (s, 3H, CH_3-27), 1.19 (s, 6H, CH_3-23, CH_3-28), 3.25- 3.70 (m, 8H, H-2′, H-3′, H-5′ and H-6′). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1, 18.1, 18.6, 18.7, 20.5, 22.7, 27.3, 28.2 (2), 29.4, 29.7 (2), 30.0, 30.3, 30.8, 31.8, 32.1, 32.7, 33.8, 35.0, 35.3, 35.9, 38.2, 39.2, 39.8, 42.8, 50.6 (2), 51.6 (2), 53.4, 54.9, 142.9, 167.0, 199.0.

4.15.42 2-Formyl-3-(1*H*-imidazol-1-yl)-friedel-2-ene (43): Eluent in column chromatography: 50% ethyl acetate in petroleum ether. Yield 72%, pale yellow crystals, m.p. 210 ^{o}C (decomp.). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.95 (s, 3H, CH_3-30), 0.99 (s, 3H, CH_3-26), 1.00 (s, 3H, CH_3-29), 1.03 (s, 3H, CH_3-27), 1.04 (s, 3H, CH_3-25), 1.19 (s, 3H, CH_3-28), 1.26 (s, 3H, CH_3-24), 1.74 (s,

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3H, CH_3-23), 1.91- 2.03 (m, 1H, H-10), 2.48- 2.85 (m, 3H, H-2 and H-4), 6.83 (br s, 1H, H-4′), 7.27 (m, associated with the $CHCl_3$ peak (from $CDCl_3$), 1H, H-5′), 7.72 (br s, 1H, H-2′). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.16 (CH_3-24), 17.69 (C-25), 18.00, 18.56 (C-27), 19.05 (C-23), 20.15 (CH_3-26), 28.15, 29.68, 30.03, 30.19, 31.75 (CH_3-29), 32.11 (CH_3-28), 32.23, 32.75, 34.04, 34.65, 34.98 (CH_3-30), 35.36, 35.89, 37.08, 38.03, 38.29, 39.23, 39.76, 41.42, 42.81, 52.49, 54.66, 121.20, 130.49, 130.53, 130.57, 168.52, 193.35. Analysis calcd: C, 80.90; H, 10.38; N, 5.55. Found: C, 80.79; H, 10.29; N, 5.71.

4.15.43 2-Formyl-3-(1*H*-benzimidazol-1-yl)-friedel-2-ene (44): Eluent in column chromatography: 25% ethyl acetate in petroleum ether. Yield 68%, pale yellow crystals, m.p. 220 ^{o}C.^{1}H NMR (300 MHz, $CDCl_3$): δ 0.96 (s, 3H, CH_3-30), 1.01 (s, 3H, CH_3-29), 1.03 (s, 3H, CH_3-26), 1.06 (s, 3H, CH_3-27), 1.20 (s, 3H, CH_3-28), 1.26 (d, *J*= 3.3 Hz, 3H, CH_3-25), 1.38 (s, 3H, CH_3-24), 1.65 (s, 3H, CH_3-23). 7.20- 7.91 (m, 4H, H-4′, H-5′, H-6′andH-7′), 8.13 (d, *J*= 5.1 Hz, 1H, H-2′). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.39 (CH_3- 24), 17.78 (CH_3- 25), 18.09, 18.59 (CH_3- 27), 19.47 (CH_3- 23), 20.19 (CH_3- 26), 28.20, 29.70, 30.09, 30.25, 31.81 (CH_3- 29), 32.16 (CH_3- 28), 32.30, 32.83, 34.35, 34.74, 35.01 (CH_3- 30), 35.40, 35.95, 37.23, 37.98, 38.36, 39.27, 39.81, 41.77, 42.89, 52.55, 54.86, 109.86, 120.08 (2), 124.14, 127.96 (2), 134.50 (C-2), 145.24, 171.95 (C-3), 192.97 (-CHO). Analysis calcd: C, 82.26; H, 9.81; N, 5.05. Found: C, 82.11; H, 9.72; N, 5.13.

4.15.44 2-Formyl-3-(1*H*-1, 2, 3-Benzotriazol-1-yl)-friedel-2-ene (45): Eluent in column chromatography: 50% ethyl acetate in petroleum ether. Yield: 70%, pale yellow crystalline solid, m.p. 237 ^{o}C (decomp.). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.76 (d, *J*= 4.5 Hz, 3H, CH_3-25), 0.93 (s, 3H, CH_3-24), 0.95 (s, 3H, CH_3-30), 1.00 (s, 3H, Me-26), 1.01 (d, *J*= 1.5 Hz, CH_3- 29), 1.03 (s, 3H, CH_3-27), 1.18 (d, 3H, *J*= 2.7 Hz CH_3-28), 1.95 (s, 3H, CH_3-23), 6.84 (t, *J*= 7.5 Hz, 1H), 7.02 (d, *J*= 7.8 Hz, 1H), 7.22- 7.28 (m, 1H), 7.98 (s, 1H), 10.22 (-CHO). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.39 (CH_3-24), 17.56 (CH_3-25), 18.24, 18.35 (CH_3-23), 18.46 (CH_3-27), 20.39 (CH_3-26), 28.19, 30.07, 30.29, 31.81 (CH_3-29), 31.90, 32.15 (CH_3-28), 32.48, 32.88, 34.99 (CH_3-30), 35.37, 35.96, 36.05, 36.81, 38.30, 39.29, 39.76, 42.87, 42.94, 52.39, 52.98, 54.34, 112.70, 120.02, 129.17, 129.26, 137.66 (C-2), 144.77, 155.01 (C-3), 192.12 (-CHO). Analysis calcd: C, 79.95; H, 9.61; N, 7.56. Found: C, 80.06; H, 9.48; N, 7.62.

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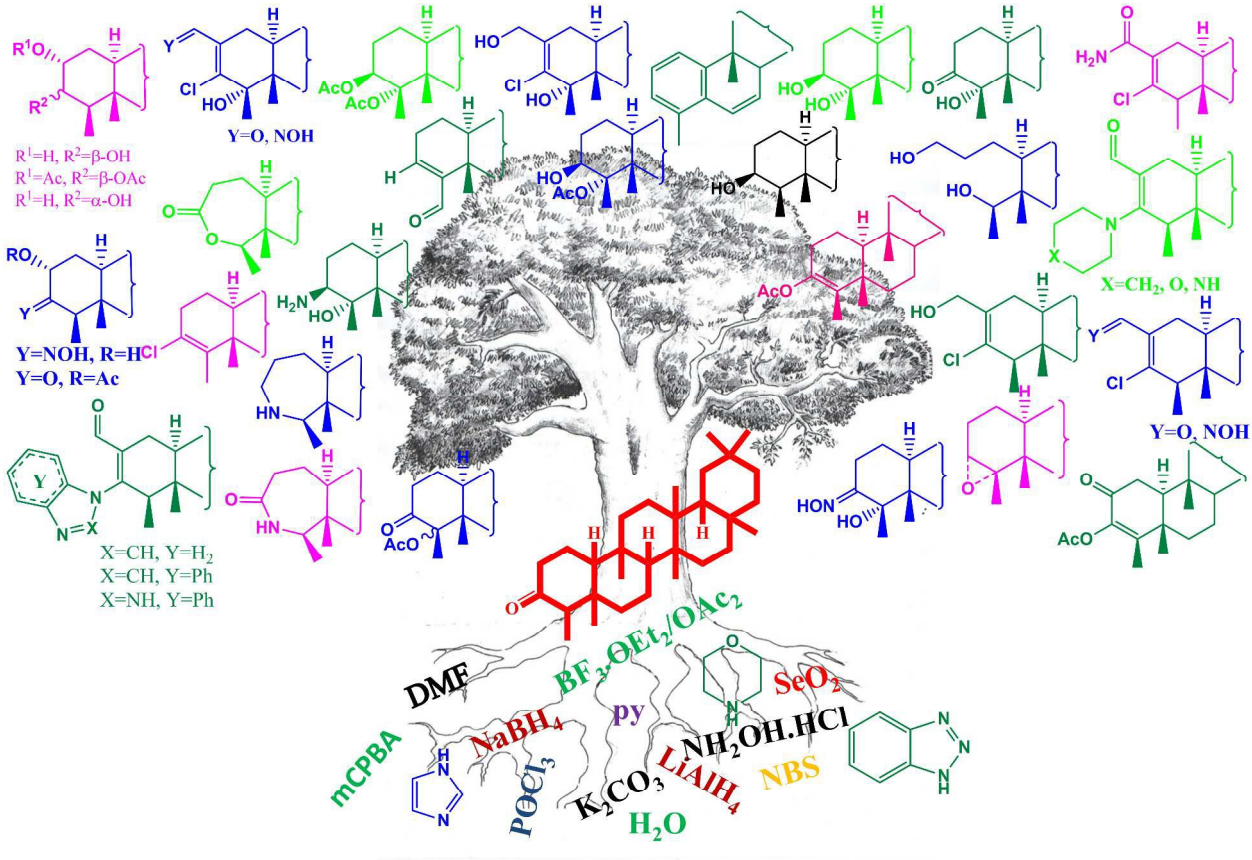
Friedelane triterpenoids: transformations toward A-ring modifications including 2-*homo*derivatives†

Jayanta Das, Antara Sarkar and Pranab Ghosh*

Common reaction strategies were employed on suitable substrates to achieve a series of C2,C3-; C3,C4-; and C2,C3,C4- functionalized (including 2-*homo*-) friedelane triterpenoids just within one to four efficient steps.



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