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2D ^{1}H and ^{13}C NMR studies of the adducts obtained by cyclostereoselective oligomerization of α,β-unsaturated arylidenketones promoted by 6 amino-1,3-dimethyl uracil

E. Díaz [a,*], H. Barrios [a], A. Gúzman [a], D. Corona [a], R. Díaz [b], A. Fuentes [b] and C.K. Jankowski [c]

[a] *Instituto de Química, Universidad Nacional Autónoma de México, Circuito Exterior, Ciudad Universitaria Coyoacán, 04510 Mexico D.F., Mexico*

[b] *Facultad de Química de la Universidad Autónoma del Estado de México, Paseo Colón y Tollocan, Toluca 50000 Toluca, E. de México, Mexico*

[c] *Département de Chimie et Biochimie, U. de Moncton, Moncton N.B., Canada, E1A 3E9*

Dedicated to the memory of Dr. Piet Leclercq

Abstract. The reaction of the 6-amino-1,3-dimethyl uracil with the arylidenketones **1**–**4**, enabled us to obtain adducts whose structures result from nucleophilic attack and self condensation, yielding with monomeric, dimeric or trimeric derivatives obtained with moderate (40–50%) yields. The reaction was induced by the uracil derivative and the role of this reagent was that of a nucleophile and oligomerization promoter. The structures obtained in this study were mainly elucidated with 1D and 2D high resolution NMR experiments.

1. Introduction

The oligomerizations of α,β-unsaturated ketones have shown to be an interesting transformation in organic synthesis. Unfortunately, most of these reactions give considerable resinification [1–3] and consequently the isolation and structural determination of the differents oligomers obtained is difficult.

In order to overcome this drawback for this type of transformations, the electro-assisted reactions using metallic cations such as Cr(III) and Mn(II) were performed, these usually give good yields and suppress completely the resinification [4,5].

The electro-assisted oligomerization reactions have shown to be an efficient way to obtain from α,β-unsaturated ketones dimerization, and dehydrodimerization products. Several years ago, the electrochem-

*Corresponding author.

ical reduction of 1,3-diphenylpropenone (chalcone) was described. This reaction provided new trimer compound or some known electrodimers, whose structures and configurations were well established [6].

On the other hand, since the pioneering studies of samarium diiodide (SmI_2), as homogeneus one-electron transfer agent by Kagan [7,8] and coworkers there have been several examples of the use of lanthanoid reagents in organic synthesis. Recently, it has been described the intramolecular cycloreductive coupling of α,β-unsaturated ketones leading to cyclopentanol derivatives [9].

We have recently described the use of 6-amino-1,3-dimethyl uracil as another nuclophile tested in Michael addition on sesquiterpene γ-lactones yielding different pyrimidine derivatives [10,11]. In some cases we also observed the formation of lactames [12]. New ring transformations of 6-amino-1,3-dimethyl uracil with acetylenedicarboxylates moieties to pyridinedionates and pyrrolo(3,4-c) pyridines have been fully discussed several years ago [13].

From these findings it seemed interesting to explore the Michael addition of the 6-amino-1,3 dimethyl-2,4 pyrimidinedione to the α,β-unsaturated systems **1**–**4** and undertake the structural determination of the adducts obtained, using 2D NMR spectroscopy (COSY [14], NOESY [15], HMQC [16] and HMBC [17] experiments).

2. Results and discussion

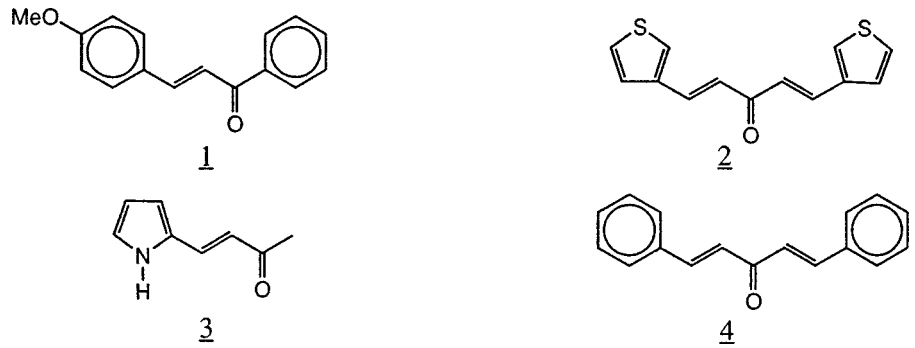
In this paper we report on the Michael addition of the 6-amino-1,3-dimethyl uracil to α,β-unsaturated ketones, with a particular emphasis on the role of the uracil derivative as nucleophile and promoter of a stereocontrolled oligomerization reactions. We also present correct stereochemistry at different carbons as well as the complete proton assignment from a detailed analysis of the ^{1}H–^{1}H dipolar correlations spectra of the obtained adducts. Likewise, we report the ^{13}C assignment of the products and a disscusion of the probable mechanisms involved.

In order to obtain evidences for the unambiguous structure and configuration assignment of the adducts we used a 2D NMR studies. The assignments given in the Experimental part are self consistent, unambiguous an they will be fully disscused.

The ketones **1**–**4** were prepared [18] by known general methods. The reaction of the α,β-unsaturated ketones with the 6-amino-1,3-dimethyl uracil was performed under phase transfer conditions using Triton B/CH_2Cl_2/H_2O (see Experimental).

The ketone **1** when treated with the 6-amino-1,3-dimethyl uracil yielded compounds **5** and **6**. In the proton NMR spectrum of compound **5** new signals at $\delta = 2.94$ (dd, $J = 9.6, -17.1$), 3.57 (dd, $J = 0.5, -17.1$) and 4.31 (dd, $J = 0.5, 9.6$) were observed, instead of the well identified signals of the trans α,β-unsaturated moiety of the starting material ($\delta = 7.79$, d, $J = 15.6$; 7.42, d, $J = 15.6$). In addition, we were able to identify two singlets (3H each) assigned to N-methyl groups at $\delta = 3.38$ and 3.72. These data suggest that the enolate of the p-methoxychalcone **1** was functionalized with the pyrimidine derivative. Compound **5** showed an AA′XX′ pattern on the proton NMR at $\delta = 6.72$ (2H) and 7.09 (2H) which were assigned to the p-metoxyphenyl ring protons. In addition, we also observed the signals of the phenyl ring moiety at $\delta = 8.00$ (2H), 7.47 (2H) and 7.55 (1H).

On the other hand, the full evidences about the structure **5** were obtained by the ^{13}C NMR spectra (1D NMR, DEPT, HMQC and HMBC). For instance, the protons at $\delta = 3.57$ and 2.94 correlate with the methylene carbon at $\delta = 32.8$. The methine proton at $\delta = 4.31$ correlates with the carbon at $\delta = 32.1$. The N-methyl groups at $\delta = 30.1$ and 28.2 were correlated with the singlets at $\delta = 3.72$ and 3.38, respectively. The carbonyls of the uracil moiety appear at $\delta = 162.7$ and 152.2. Additional assignments are presented in Scheme 5.



Scheme 1. α, β-unsaturated ketones used in this study.

The assignment of the structure of compound **6** which was isolated as a yellow solid was supported by the MS, where the molecular ion (M^+) correspond to a molecular formula of $C_{38}H_{35}N_3O_5$.

The ^{1}H NMR spectrum shows four singlets (3H each) at $\delta = 3.66$, 3.73, 3.45 and 3.31 assigned to the methoxy and the two N-Me groups, respectively. From the COSY spectrum we were able to observe a proton sequence as –CH_2–CH_x–CH_y–CH_z–. The chemical shifts of the methylene protons at $\delta = 3.40$ and 3.81, as an ABX pattern ($J_{AB} = -17.1$, $J_{AX} = 4.5$, $J_{BX} = 8.4$ Hz) and the large geminal coupling suggest the vicinity of a carbonyl group [19]. The proton H_x was assigned to be a methine proton at $\delta = 3.85$. The protons H_y and H_z were observed at $\delta = 3.70$ and 4.28, respectively. The small vicinal coupling between H_y–H_z (0.5 Hz) suggests a close to 100° dihedral relationship and this arrangement can be explained only when both protons are in *anti* geometry, based on the known Karplus equation [20, 21].

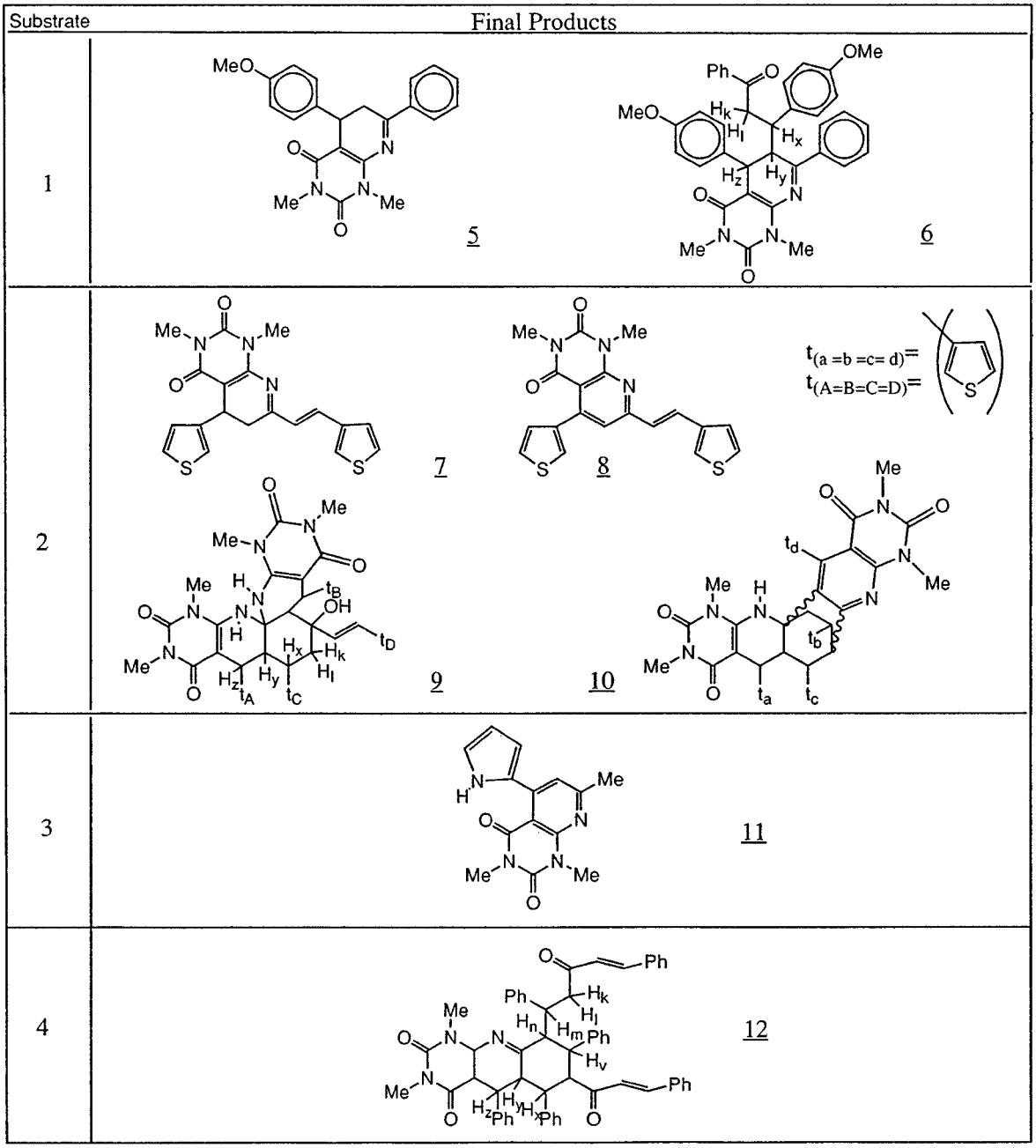
The full NMR assignment of both protons and carbons was performed using HMQC and HMBC experiments. Three carbonyl carbons were observed at $\delta = 197.9$, 162.7 and 151.7 which were assigned to a keto group and those corresponding to the pyrimidine moiety respectively. The non protonated carbons at $\delta = 175.4$, 97.1 and 148.9 were assigned to the sp^2 carbons of the dihydropyridine moiety. The methoxy protons at $\delta = 3.66$ correlates with the carbon at $\delta = 55.1$. The carbon at $\delta = 55.3$ was correlated with the methoxy singlet at $\delta = 3.73$.

Both N-Me groups at $\delta = 3.31$ and 3.45 were correlated with the signals at $\delta = 29.7$ and 28.0, respectively. The assignment of the remaining carbons was unambiguously achieved by the 2σ and 3σ proton-carbon correlations (HMBC) and they are resumed in Scheme 5. The key element in the assignment of these carbons was the correlation between the doublet at $\delta = 4.28$ (H_z) and signals at $\delta =$ 175.4, 162.7, 148.9, 133.6, 127.6, 97.1 and 46.6.

Compounds **5** and **6** were probably formed through the mechanism presented in Schemes 3 and 4. With regard to compound **5**, we assumed that it was formed by the Michael addition of one molecule of uracil which react with the unsaturated double bond and then attack of the amino group to the carbonyl function by the well known Schiff base mechanism to form the dihydropyridine (Scheme 3).

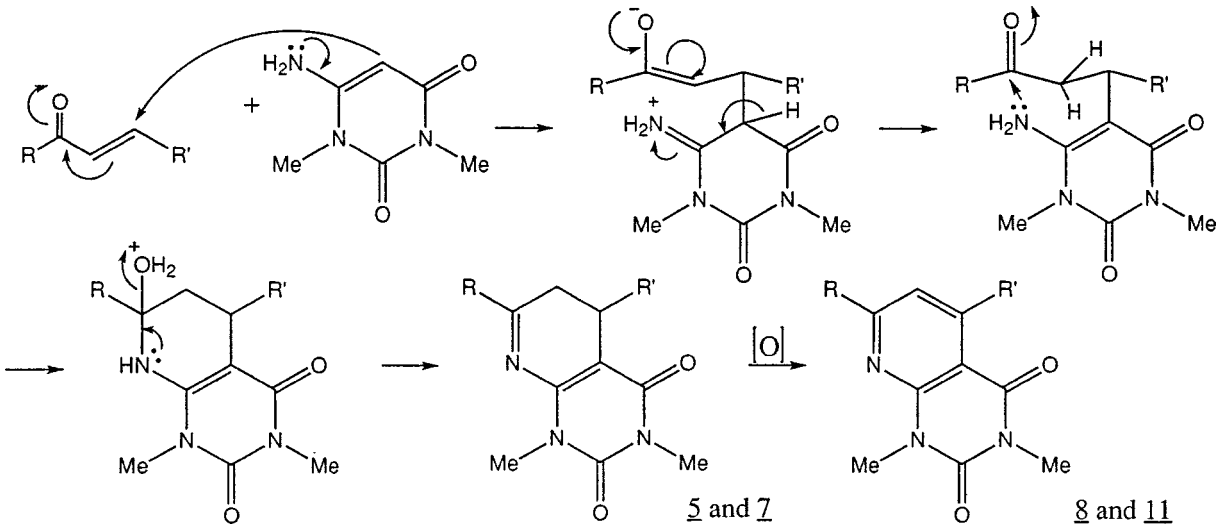
The formation of compound **6** appears more elaborated and involves two molecules of p-methoxy chalcone. One of them accept the addition of the uracil as was mentioned before, then the anionic intermediate **1a** attack a second molecule of unsaturated ketone in order to form the oligomer **6** as it is shown in Scheme 4.

On the other hand, from the reaction of 3′-dithiophenylidenacetone **2** with the 6-amino-1,3-dimethyl uracil under the same phase transfer conditions, we were able to isolate four adducts identified as **7**, **8**, **9** and **10** (Scheme 2).

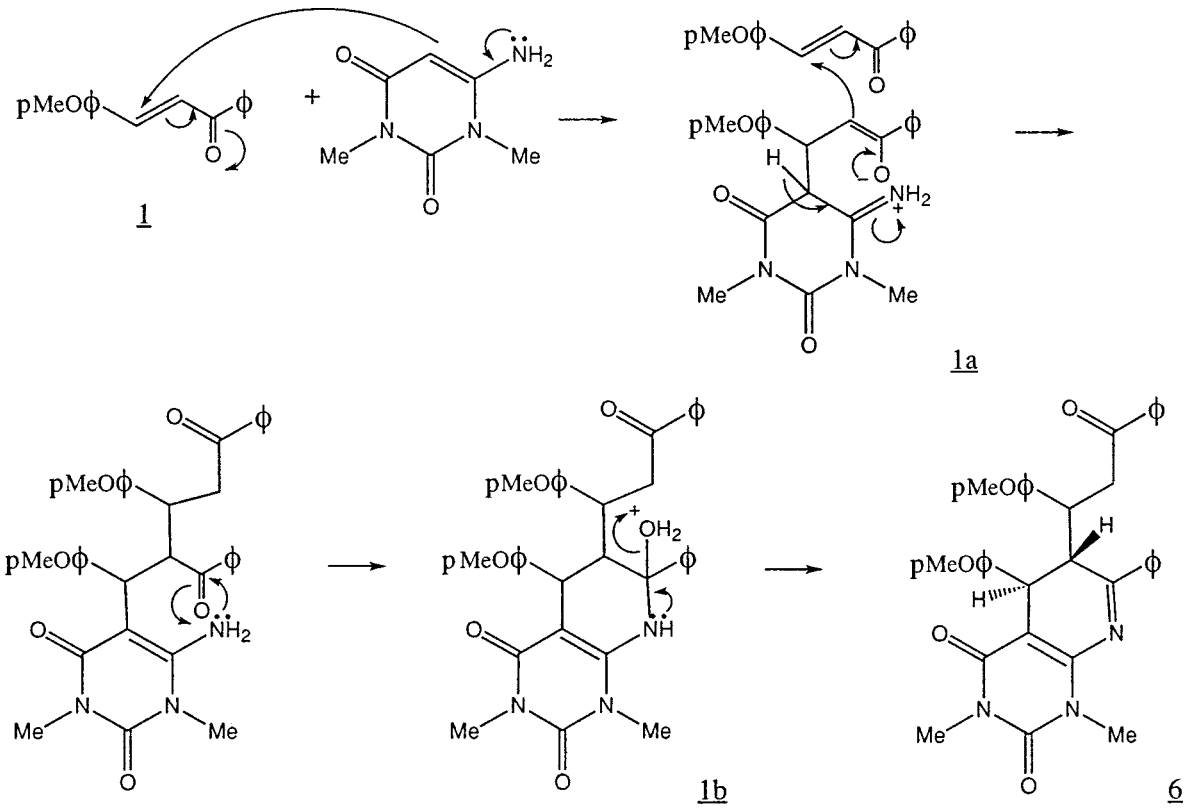


Scheme 2. Addition products of 6-amino-1,3-dimethyluracil with α,β-unsaturated ketones **1** to **4**.

Derivatives **7** and **8** were obtained by the usual attack of uracil on one of the trans double bonds available on the starting material **2** followed by cyclization, as it is shown in the mechanistic approach depicted on Scheme 3. The structures of the adducts **7** and **8** were well supported by their spectroscopic features. For instance, compound **7** displaied in its ^{1}H NMR spectrum an ABX pattern observed at high field ($\delta = 2.67$ 1H, $J = 9.0, -16.7$; 3.35 1H, $J = 0.5, -16.7$ and 4.41 1H, $J = 0.5, 9.0$) and assigned



Scheme 3. Mechanism of formation of compounds **8** and **11**.



Scheme 4. Formation of product **6**.

to the dihydropyridine moiety. We also detected the usual doublets assigned to the trans double bond localized at $\delta = 7.54$ and 6.96. The formation of this adduct was also established by the observation of two singlets (3H each) at $\delta = 3.39$ and 3.60 which identify unambiguously both N-Me groups on the uracil moiety. The molecular weight obtained from MS matched molecular formula $C_{19}H_{17}S_2N_3O_2$ (M^+ m/z 383).

The oxidated product **8** shown in MS a molecular ion m/z 381 which was assigned to a molecular formula $C_{19}H_{15}S_2N_3O_2$. The structure **8** was well supported by both ^{1}H and ^{13}C NMR spectra. While the proton resonance enabled us to observe mainly the typical chemical shift of the N-Me groups of the uracil moiety at $\delta = 3.40$ and 3.83 as well as the usual AB pattern for the *trans* double bond at $\delta = 7.83$ (d, $J = 15.6$) and 6.98 (d, $J = 15.6$), the ^{13}C NMR spectrum through the HMQC and HMBC experiments allowed the unambiguous assignment of the protonated and the non-protonated carbons respectively (Scheme 5).

The N-Me groups at $\delta = 3.83$ and 3.40 were correlated with the carbons at $\delta = 30.1$ and 28.4, respectively. The *trans* double bond protons were correlated with carbons at $\delta = 128.7$ and 131.0. On the low field chemical shift range we observed the usual signals for the carbonyl carbons at 162.0 and 151.8 while those assigned to the pyridine moiety were observed at $\delta =$ 106.3, 151.5, 149.6, 126.2 and 158.1. Additional observed signals are displayed in Scheme 5 and in the Experimental.

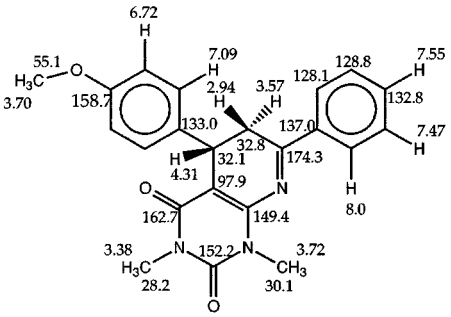
The structure of the spiro adduct **9** as depicted on Scheme 2, is well supported by its spectroscopic features and by mechanistic considerations (Scheme 6).

The MS of adduct **9** has a molecular ion M^+ at m/z 784 which corresponded to a molecular formula of $C_{38}H_{36}O_5N_6S_4$.

In the proton NMR spectrum, we observed three singlets at $\delta = 6.15$ (1H), 5.46 (1H) and 2.45 (1H). All of them were exchanged with deuterium oxide (singlet at $\delta = 5.45$ exchanges very slowly). These observations enabled us to assume the presence of two amino and one hydroxyl groups. We also observed the AB pattern for a *trans* double bond at $\delta =$ 6.30 (1H, d, $J = 16.0$) and 5.40 (1H, d, $J = 16$). At higher field ($\delta_A = 4.42$ 1H, d, $J = 10.5$ and $\delta_B = 2.72$ 1H, d, $J = 10.5$) we detected a new isolated AB pattern. The large vicinal coupling between these protons suggested an usual anti-dihedral relationship in agreement with Karplus predictions [20]. From the COSY spectrum (Fig. 1) we were able to detect a proton network (see Scheme 2) H_k–C–H_l–CH_x–CH_y–CH_z– where the methylene protons shown a characteristic pattern at $\delta = 1.84$ (1H, dd, $J = 3.5, -14.5$) and 2.05 (1H, dd $J = 13.0, -14.5$). The diagonal peaks of these protons correlated well with the cross peaks of the signal at 2.99 (H_x, ddd, $J = 3.5$, 11.0, 13.0). This later proton was also correlated with the proton H_y at $\delta = 2.83$ (1H, dd, $J = 0.5$, 11.0). The large vicinal coupling observed between H_x and H_y suggested a dihedral angle [21] of about 180° between both protons. Finally, the proton H_z was observed at $\delta = 4.10$ (1H, d, $J = 0.5$).

The presence of two units of the 6-amino-1,3-dimethyl uracil was infered from the observation of four N-Me singlets at $\delta = 3.42$, 3.39, 3.11 and 2.58. The configuration of different stereogenic centers on adduct **9** was established using the useful ^{1}H–^{1}H dipolar spatial correlations which were achieved through NOESY experiment (see Fig. 2). Here, the diagonal peak of the doublet at $\delta = 2.72$ correlates with the cross peak of the doublet of doublet at $\delta = 2.83$. This proton also shown a dipolar correlation with the NH at $\delta = 5.45$. The doublet at $\delta = 4.42$ correlates with the NH group at $\delta = 6.15$ and with the hydroxyl proton at $\delta = 2.38$ and the N-Me group at $\delta = 2.58$ with the NH at $\delta = 5.45$. The doublet at $\delta = 4.10$ displays dipolar correlation with the multiplet at $\delta = 2.99$ and with the doublet of doublet at $\delta = 2.83$. The full dipolar interactions are described in Fig. 2.

5,6,Dihydro-5-(*p*-anisoyl)-1,3-dimethyl-7-phenyl-(1H,3H)pyrido[2,3-d]pyrimidin-2,4-dione.



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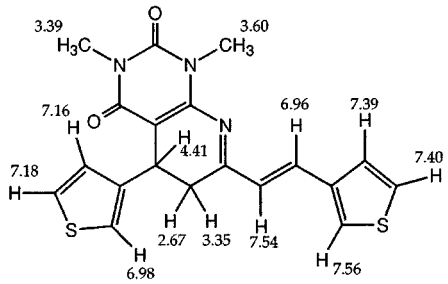
5,6-Dihydro-1,3-dimethyl-5-(3-thienyl)ethenyl (1H,3H)pyrido[2,3-d]pyrimidin-2,4-dione



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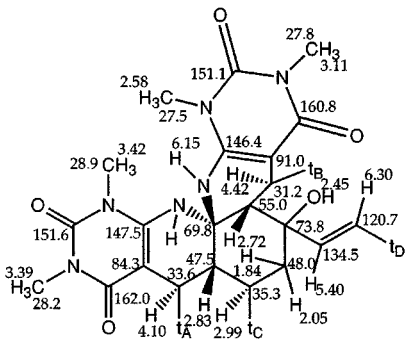
5,5a,7,8,8a,9,14,15,-Octahydro-1,3,11,13-tetramethyl-6-hydroxi-5,8,9-tri(3-thienyl) -6-[2-(3-thienyl)ethenyl]-2,4,10,12-tetraoxo. 1,3,8-triazanaftalene[6,7-k]quinopyrimidine



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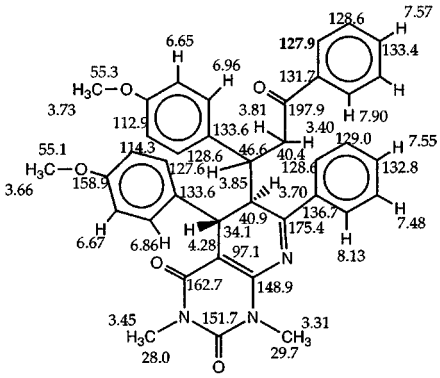
5,5a,6,7,8,9-Hexahydro-1,3-dimethyl-5,6,8-triphenyl-7-(3-phenyl-2-propenoyl) -9-(1,5-diphenyl-3-oxo-4-pentenyl)-(1H,3H)pyrimido[4,5-b]quinoline-2,4-dione

5,6,Dihydro-5-(*p*-anisoyl)-6-[(*p*-anisoyl)-2-benzoyletil-1,3-dimethyl-7-phenyl-(1H,3H) pyrido[2,3-d] pyrimidin-2,4-dione.



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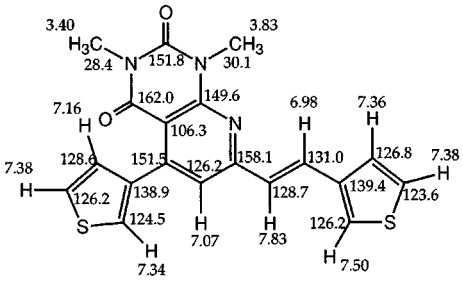
1,3-Dimethyl-5-(3-thienyl)-7-[2-(thienyl)ethenyl] (1H,3H)pyrido[2,3-d]pyrimidin-2,4-dione



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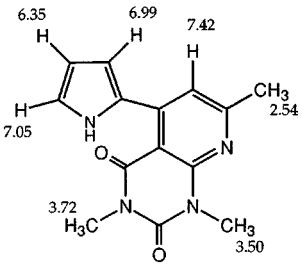
1,3,7-Trimethyl-5-(2-pirrolil)-(1H,3H)pyrido-[2,3-d]pyrimidin-2,4-dione



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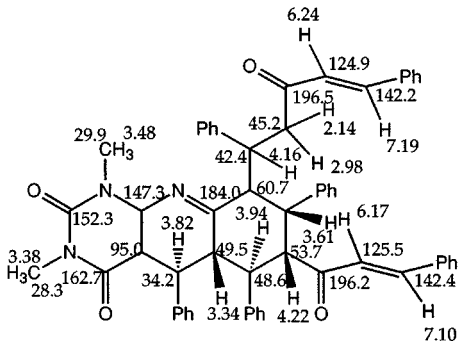

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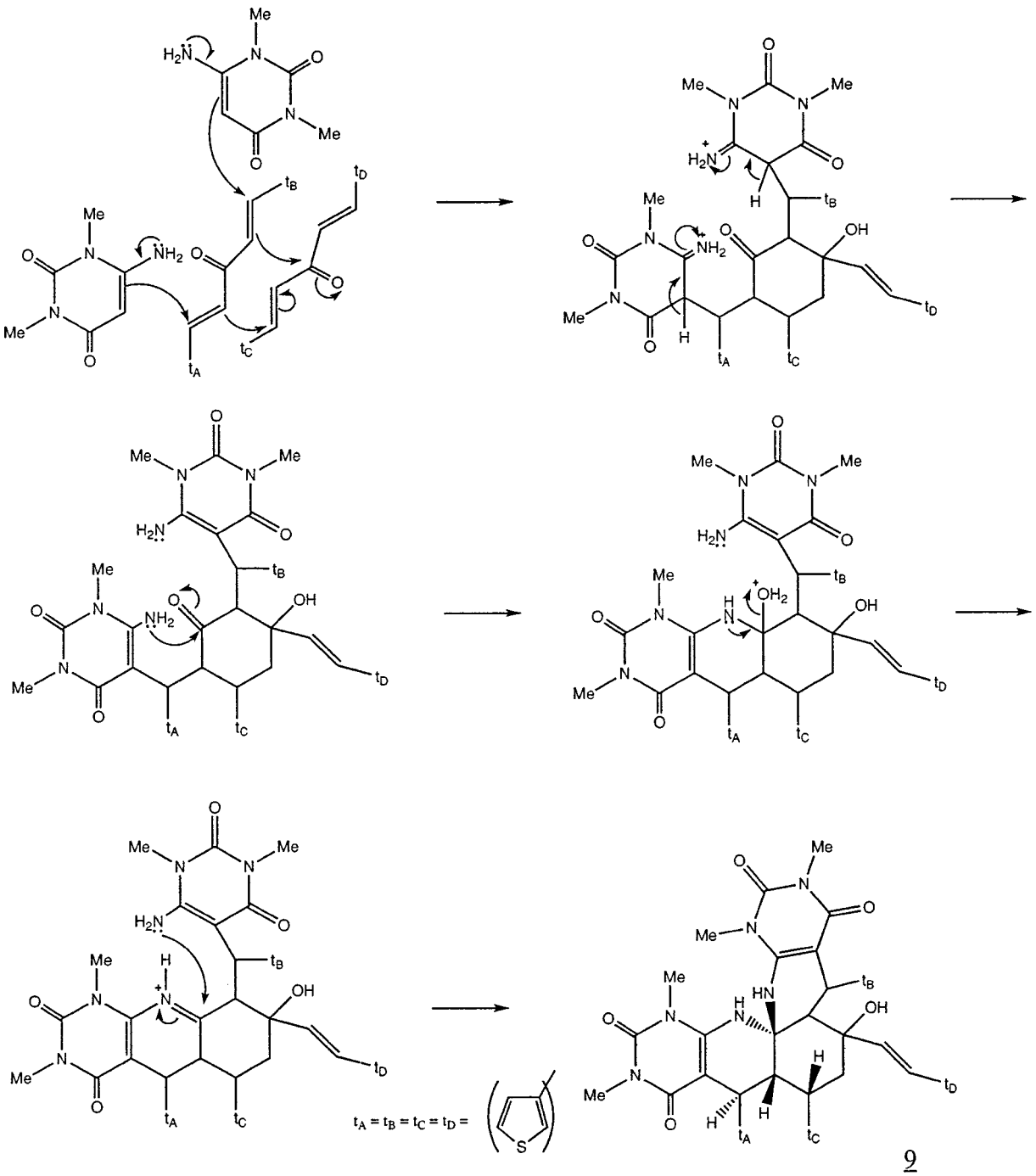
Scheme 5. NMR spectroscopic data for compounds **5**–**9**, **11** and **12**.



Scheme 6. Formation of product **9**.

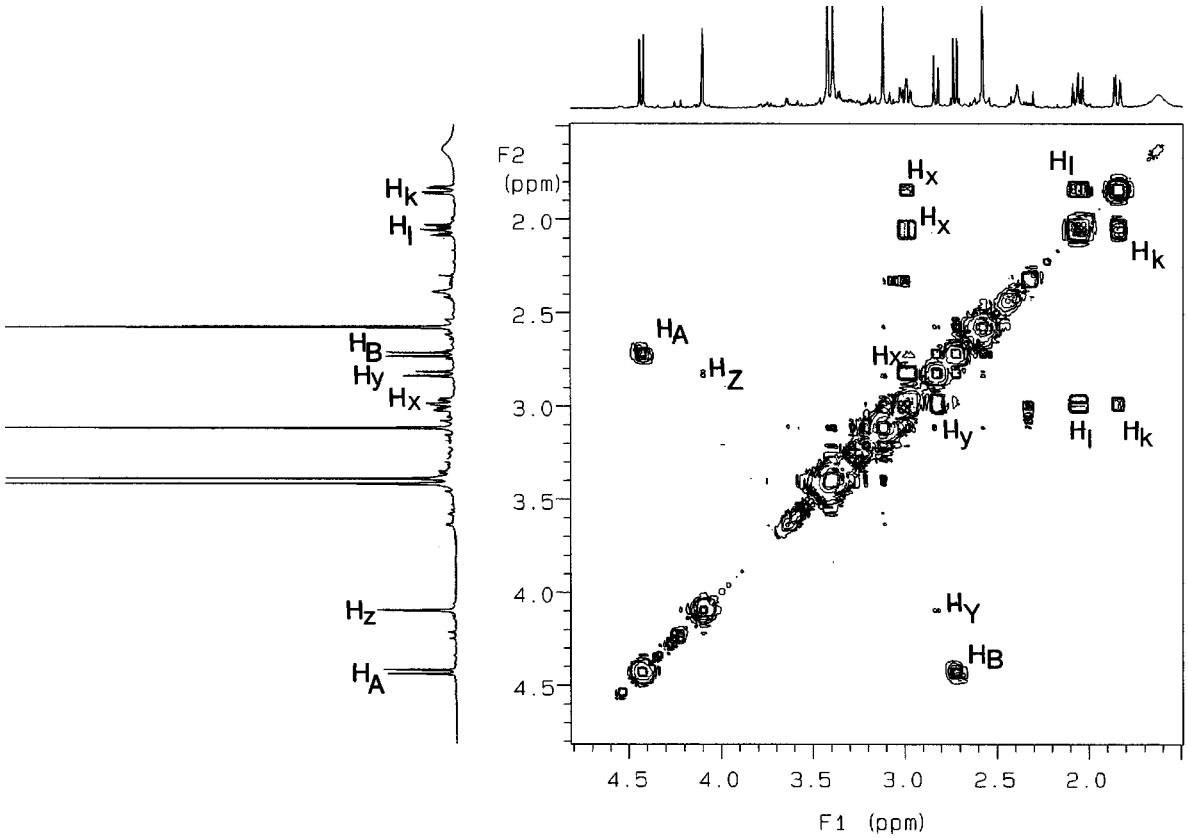


Fig. 1. COSY 500 MHz of compound **9**.

With regards to ^{13}C NMR, the chemical shifts assignment of the protonated carbons was performed using the HMQC experiment. For example, the doublet for H_A at $\delta = 4.42$ is correlated to the methine carbon at $\delta = 31.2$ and the doublet at $\delta = 4.10$ with the carbon signal at $\delta = 33.6$.

The N-Me group singlet at $\delta = 3.42$ correlate with the signal at $\delta = 28.9$. Similarly, the N-Me singlet at $\delta = 3.39$ correlates with the signal at $\delta = 28.2$. The remaining N-Me at $\delta = 3.11$ and 2.58 shown correlation with the carbon signals at $\delta = 27.8$ and 27.5, respectively. The assignment of the methylene carbon and the remaining saturated methine carbons was achieved by the correlation of protons at $\delta = 1.84$ and 2.05 with the methylene carbon at $\delta = 48.0$. H_B (d, $\delta = 2.72$) was correlated with the carbon signal at $\delta = 55.0$. Finally the methine carbons at $\delta = 35.3$ and 47.5 were correlated with the proton signals for H_x at $\delta = 2.99$ and for H_y (2.83), respectively. Details of additional assignments are presented in Scheme 5 and in Experimental. The non-protonated carbons of the structure **9**, were assigned using the HMBC spectrum. Here we detected that the *trans* double bond protons at $\delta = 6.30$ were correlated through 2σ and 3σ bonds with the carbon at $\delta = 73.8$ and the methine proton at $\delta = 4.42$ also with the same carbon. The NH proton at $\delta = 6.15$ showed through 3σ bond the correlation with the non-protonated sp^2 carbon at $\delta = 84.3$, while the NH at $\delta = 5.45$ and the doublet at $\delta = 4.42$ correlated with the carbon at $\delta = 91.0$. The spiro carbon (NH–C–NH) at $\delta = 69.8$ was correlated with the protons H_z (4.10), H_y (2.83) and the doublet at $\delta = 2.72$.

The signals of the N-Me protons have shown to be a key element for the assignment of the carbonyls of the uracil moieties as well as to predict the magnetic enviroment of the non-protonated sp^2 carbons.

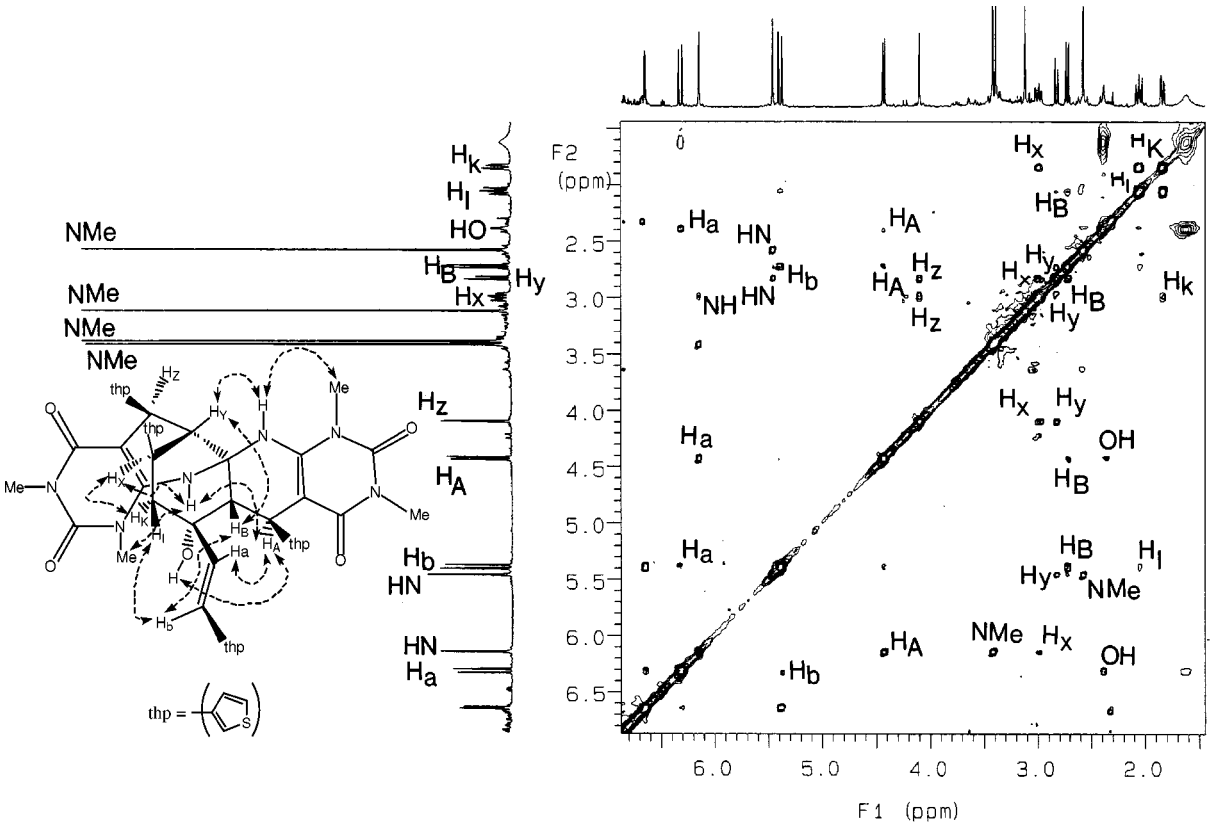


Fig. 2. NOESY 500 MHz of compound **9**.

Thus, the N-Me protons at $\delta = 3.42$ correlate with the carbonyl at $\delta = 151.6$ and with the sp^2 carbon at $\delta = 147.5$. The N-Me protons at $\delta = 3.39$ correlate with both carbonyls at $\delta = 151.6$ and 162.0. On the other hand, the N-Me protons at $\delta = 3.11$ correlate with the carbonyl carbons at $\delta = 160.8$ and 151.1, while the N-Me at $\delta = 2.58$ correlate with the carbonyl at $\delta = 151.1$ as well as the carbon at 146.4. The proton H_z at $\delta = 4.10$ also correlates with the carbonyl at $\delta = 162.0$ as well as the signals at $\delta = 147.5$, 143.5 and 122.1 (belonging to the thiophene ring "T_A"). The doublet at $\delta = 4.42$ correlates with the signals of non-protonated carbons at $\delta = 146.4$ and 144.8 and with methines at $\delta = 128.9$ and 122.2 (thiophene ring "T_B"). Proton H_x at $\delta = 2.99$ correlates with the carbons at $\delta = 142.3$ (C), 125.7 (CH) and 122.3 (CH) (thiophene ring "T_C"). Finally the trans double bond protons at $\delta = 6.30$ and 5.40 correlates with the carbons at $\delta = 125.5$, 122.3 and 138.0 (thiophene ring "T_D"). The signals of remaining carbons are described in detail in Experimental. The NOESY spectrum of the adduct **9** is presented in Fig. 2.

The fourth adduct isolated from the reaction was a compound **10**, obtained as white solid, which after the spectroscopic evaluation showed to be a 1 : 1 mixture of two isomers (10A and 10B, see Scheme 7). The full evidence of structure **10** was established by the spectroscopic features as follows.

The high resolution MS (FAB) shown a molecular ion (M^+) at m/z 765, which corresponds well to a molecular formula of $C_{38}H_{32}O_4N_6S_4$. The proton NMR spectrum (500 MHz) shown the presence of two singlets at $\delta = 4.21$ and 4.19, both exchangable rapidly with deuterium oxide, suggesting the presence of

two NH groups. The observation of six singlets signals (3H each) and one singlet (6H) due to eigth NMe groups at $\delta = 3.746$, 3.742, 3.30 (6H), 3.218, 3.214, 3.04 and 3.00, as well as the full ^{13}C NMR, where we observed the spectrum with duplicated signals, which indicated the presence of two configurational isomers at c.a. 1 : 1 ratio. The structural elucidation was carried out using a combination of 500 MHz NMR including COSY, NOESY, HMQC and HMBC experiments.

From DEPT experiments ten methine carbons at $\delta = 50.6$, 50.4, 50.0, 49.3, 43.9, 44.5, 41.0 (2C), 32.0 and 31.7; two methylenes at $\delta = 44.5$ and 43.9 and the previously mentioned eight methyls at $\delta = 30.2$ (2C), 30.3, 28.7, 28.6 (3C) and 27.75 as well as two non-protonated sp^3 carbons at $\delta = 58.5$ and 58.4 enabled us to assume the existence of a mixture of two bis-dimeric adduct **10**. At lower field we also observed four non-protonated carbons $\delta = 89.1$ and 88.8 (from the uracil moiety) and 108.4 and 108.0 (for the pyridine moiety) of both isomers.

The mechanistic approach for the formation of such bis-dimeric adduct is depicted on Scheme 7 where the key element that support this structure was suggested by the above mentioned ^{13}C NMR chemical shifts. Furthermore, we observed several sp^2 carbons (carbonyl included) which appeared with the chemical shift range of 166–120 ppm as duplicated signals.

There are four carbonyl signals at $\delta = 160.4$ (2C), 160.0 (2C), 151.0 and 150.7 which identify the carbonyls of both units of the uracil present in both isomers. The signals at $\delta = 165.1$ and 164.0 were assigned to the non-protonated carbons of pyridine rings. For the remaining protonated carbons, sp^2 methines described in experimental section showed eigth 3′(thiophenyl) fragments originated from both isomers. From the data presented, we concluded that compound **10** is a mixture of two stereoisomers having different chemical shifts for carbons and protons and consequently does slightly different spectra in ^{13}C and ^{1}H NMR. The structures 10A and 10B (Scheme 7) were then proposed for the two isomers.

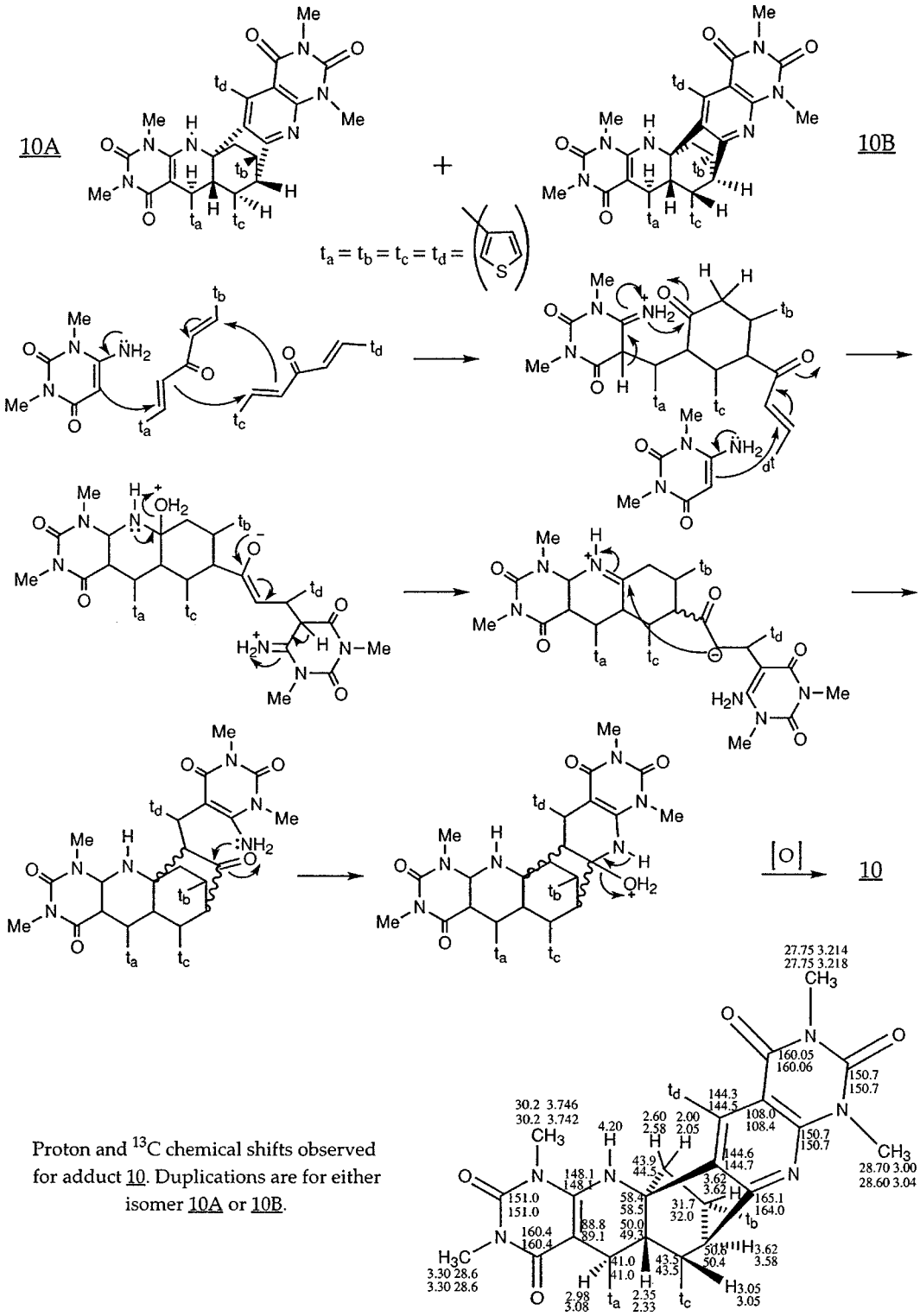
Finally, when the dibenzalacetone **4** react under phase transfer conditions with the 6-amino-1,3-dimethyl uracil as nucleophile, we were able to isolate only the adduct **12**. The chemical structure support for this trimeric derivative mainly come from the 2D NMR ^{1}H and ^{13}C NMR as well as from the HRMS data.

Compound **12** was obtained as a white solid and shown in HRMS (FAB) a molecular ion ($M^+ + 1$) m/z 840 (formula $C_{57}H_{49}N_3O_4$).

The 1D proton NMR shows several signals at high field $\delta = 3.48$ (s, 3H) and 3.38 (s, 3H) which can be related to the presence of one uracil unit only. The observation of the multiplets in the chemical shift range of the aromatic and vinylic protons, together with the integration, enabled us to confirm the presence of 34 protons, where 30 belong to the six phenyl rings, with the remaining protons (4H) splitted in two different AB patterns. Because of the coupling constant observed between each doublet we assumed that two trans double bonds did not react ($\delta = 6.17$, d, $J = 16.5$; 7.10, d, $J = 16.5$; 6.24, d, $J = 16.0$; 7.19, d, $J = 16.0$). From this observation we can assume that three units of the dibenzalacetone and one of the uracil were involved in the reaction.

From the COSY spectrum we were able to detect a proton network as –H_k–C–H_l–CH_m–CH_n–CH_v–CH_w–CH_x–CH_y–CH_z– (see Scheme 2).

The methylene protons were observed as part of an ABX pattern where $\delta H_k = 2.14$ dd, $J = 2.0$, -17.0 and $\delta H_l = 2.98$, dd, $J = 10.5$, -17.0. The large geminal coupling between H_k and H_l and their chemical shift suggest again the vicinity of a carbonyl group [19]. Through their diagonal peaks on the COSY spectrum we observed that both methylene protons correlated with the cross peak of the proton H_m ($\delta H_m = 4.16$, ddd, $J = 2.0$, 10.5, 12.0). This later proton is also correlated with H_n ($\delta H_n = 3.21$, dd, $J = 1.5$, 12.0).



Proton and ^{13}C chemical shifts observed for adduct 10. Duplications are for either isomer 10A or 10B.

Scheme 7. Formation of product **10**.

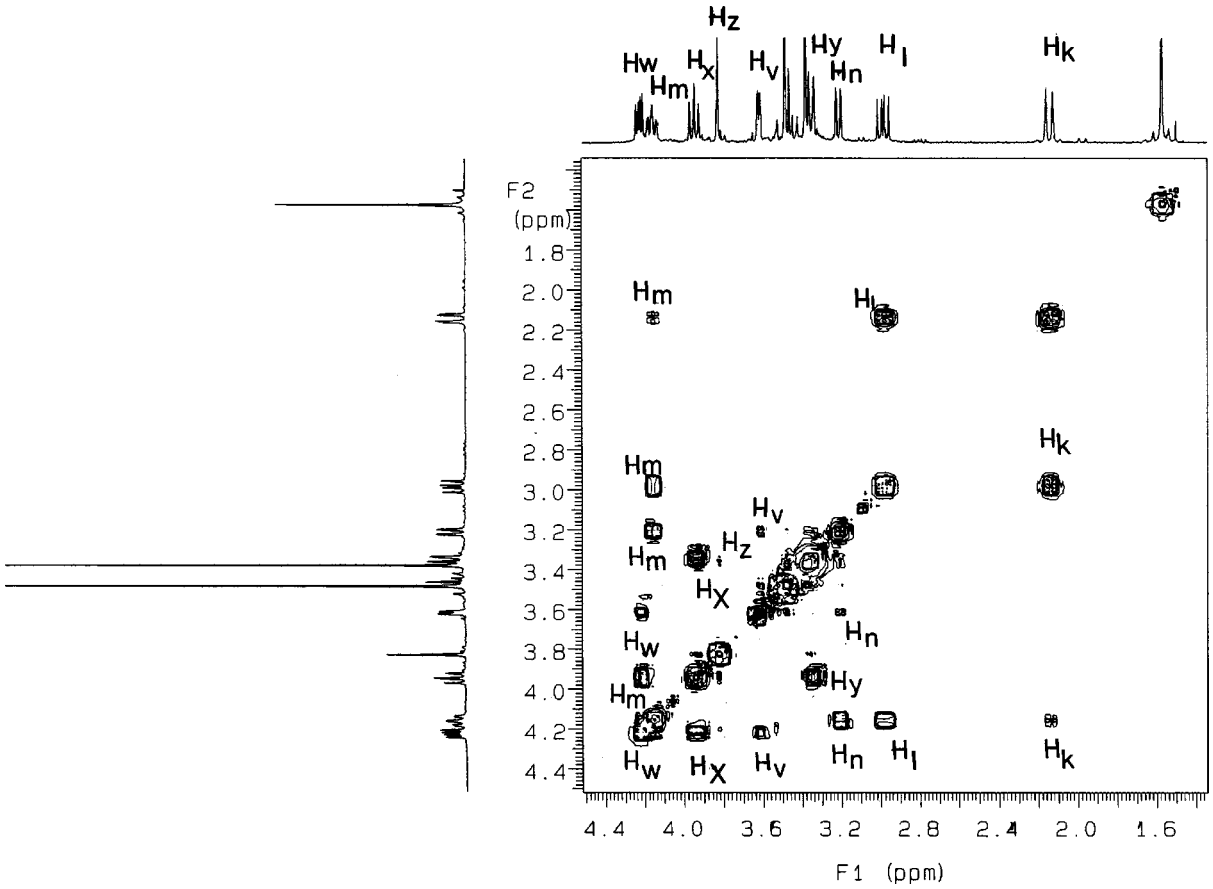


Fig. 3. COSY 500 MHz of compound **12**.

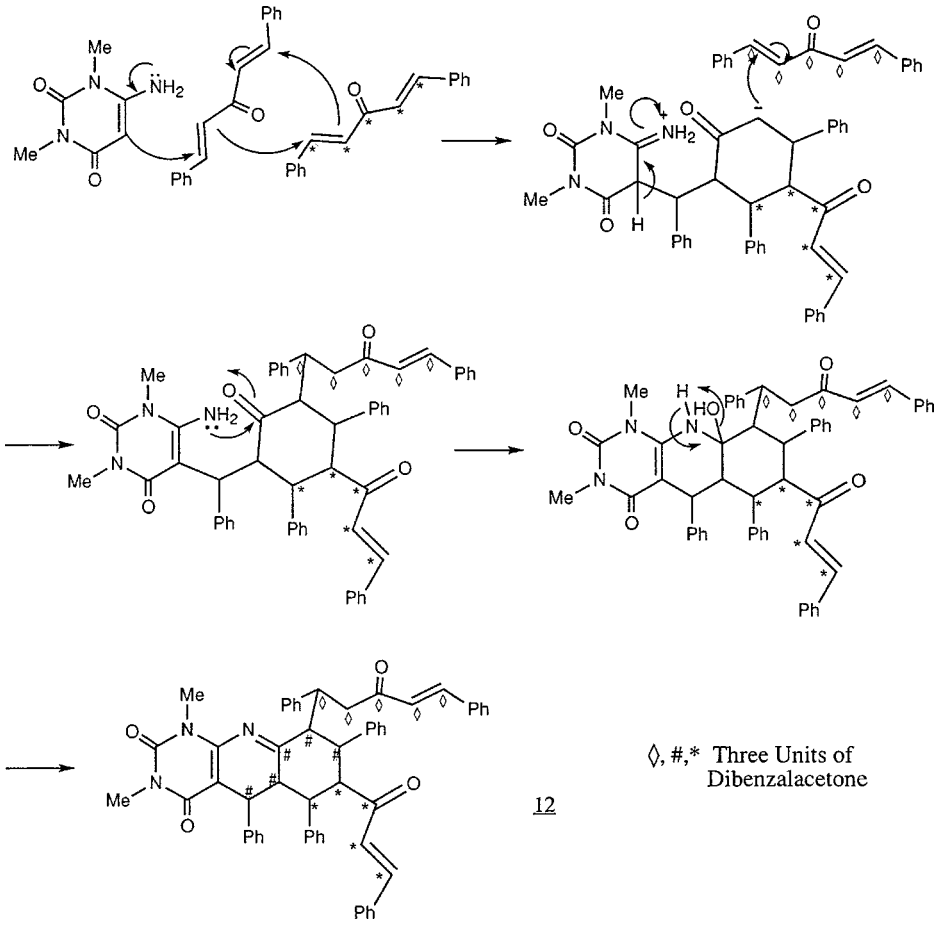
Following the COSY spectrum (see Fig. 3), we localized the proton H_v at $\delta = 3.61$ (dd, $J = 1.5, 6.0$). Then next protons H_w at $\delta = 4.22$ (dd, $J = 6, 11.0$), H_x ($\delta = 3.94$, dd, $J = 11.0, 12.0$), H_y, $\delta = 3.34$ (dd, $J = 0.5, 12.0$) and finally H_z at $\delta = 3.82$, d, $J = 0.5$.

The mechanism presented in Scheme 8 justified the structure **12** for this compound.

The full support for such a structure was obtained again through 1D ^{13}C NMR as well as from the HMQC and HMBC spectra.

The noise decoupling ^{13}C NMR and the DEPT experiments enabled us to detect in the chemical shift range of the sp^3 carbons, the presence of methines at $\delta = 34.2, 49.5, 48.6, 53.7, 49.3, 60.7, 42.4$ as well as the methylene carbon at $\delta = 45.2$. Using HMQC experiment the before mentioned carbons were correlated respectively to the protons H_z (3.82); H_y (3.34); H_x (3.94); H_w (4.22); H_v (3.61); H_n (3.20) and H_m (4.16). Methylene carbon correlates with protons at $\delta = 2.14$ and 2.98 (H_k and H_l). The carbons of the *trans* double bonds were correlated as follow: proton at $\delta = 6.17$ to the methine carbon at $\delta = 125.5$; and proton doublet at $\delta = 7.10$ with the carbon at $\delta = 142.4$. In addition the protons at $\delta = 6.24$ and 7.19 were correlated with the carbon signal at $\delta = 124.9$ and 142.2, respectively.

In order to determinate the dipolar ^{1}H–^{1}H correlations, we recorded a NOESY spectrum which suggested the configurations of assymetric centers in adduct **12** as in Scheme 5. The key feature of this identification was the correlation observed between the diagonal peak from H_m at $\delta = 4.16$ and the cross



Scheme 8. Formation of product **12**.

peak of H_y at $\delta = 3.34$. Both protons are separated by five σ bonds, however they keep a close spatial relationship that enabled the assignment of H_y and the bond CH_n–CH_m-space orientation to be in β position (see Fig. 4). This later assumtion explained the unusual chemical shift observed for the –C=N– ($\delta = 184.0$) and is supported by the well known axial β deshielding [22] described several years ago. In addition we observed the dipolar correlation between H_z with H_x where both protons were assigned as being of α orientation. Other less relevant correlations are presented in Fig. 4.

Finally, adduct **11** was obtained from the unsaturated ketone **3** under the same desribed conditions. Its NMR characteristics (Scheme 5) are self consistent and they will not be disscused in detail (see Experimental).

3. Conclusion

The structures of the adducts described herein are self consistent and do not held further rationalization. As was suggested in the title of this paper, the reaction is stereocontroled and consequently the stereogenic centers observed on the adducts obtained conserve the same geometric relationship that the double bond of the starting material from which they come from.

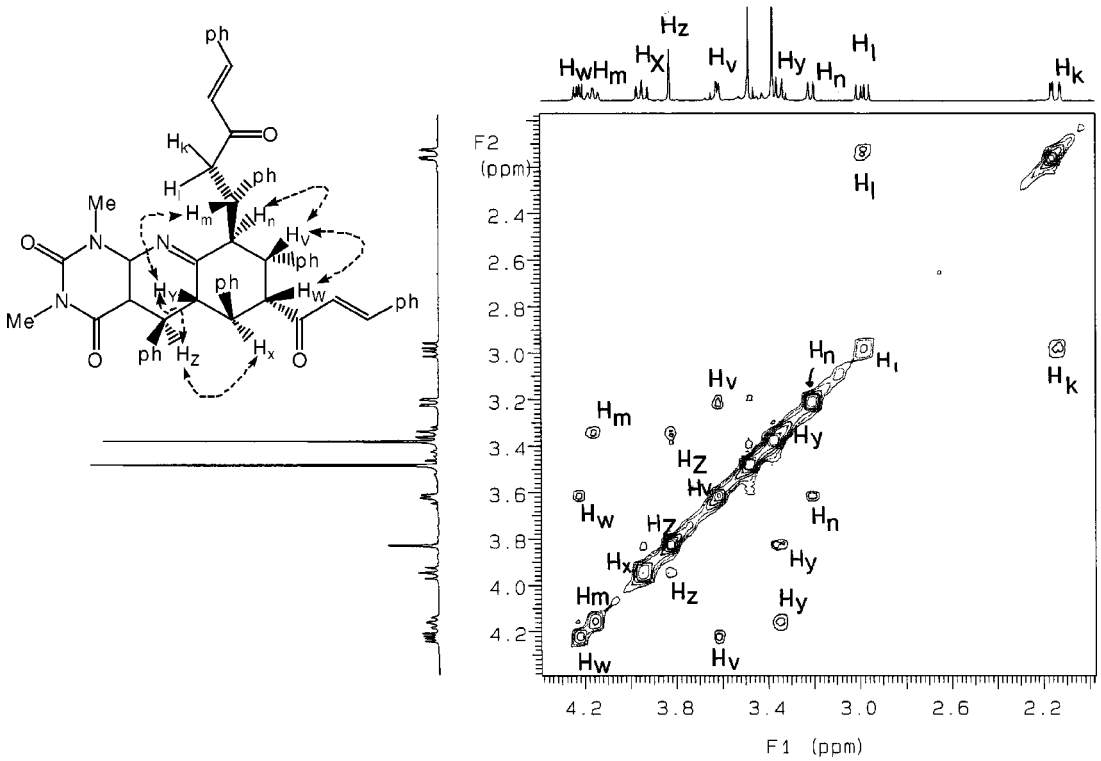


Fig. 4. 500 MHz partial NOESY spectrum of adduct **12**.

4. Experimental

Melting points were determined with a Kofler Hot Stage Apparatus-and and were not corrected. The NMR ^{1}H and ^{13}C spectra were recorded using Varian Unity 300 spectrometer operating at observation frequency of 300.0 MHz for ^{1}H and 75.0 MHz for ^{13}C. The ^{1}H and ^{13}C chemical shifts (δ) are given in ppm relative to tetramethylsilane (TMS).

High resolution spectra were recorded on a Varian Unity 500 operating at 500.3 MHz for ^{1}H and 125.0 MHz for ^{13}C. The experiments were performed using an inverse detection 5 mm probe. The COSY, NOESY, HMQC and HMBC spectrum were recorded using usual Varian Unity softwares.

Mass spectra were recorded on instruments using standard FAB or CI/EI sources in glycerol or with CH4 gas respectively JEOL-JMS-AX505 HA and JEOL-JMS-10217. The IR spectra were performed on Nicolet FX-SX and Nicolet 55-X in film mode.

The arylidenacetones used as starting material were prepared following the procedure described for the dibenzalacetone [18].

The 6-amino-1,3-dimethyluracil, dichloromethane and Triton B were purchased from Aldrich Chemical and they were used as received.

General procedures of synthesis of the adducts

To a suspention of 2 mM of 6-amino-1,3-dimethyl uracil in 3 ml of CH_2Cl_2, 1 ml of TRITON B(MeOH soln) and 1 ml of destillated water were added, followed by 1 mM of the corresponding arylidenacetone

in 5 ml of CH_2Cl_2. The mixture was stirred at room temperature until the starting material was consumed (reaction was monitored by TLC).

Usual work up followed by flash column chromatography (silica gel, Kieselgel 60, 230–400 mesh, Merck) or by preparative Thin Layer Chromatography (silicagel GF-254, plates 20 × 20 2 mm thin) yields the adducts which were recrystallized from a mixture of CH_2Cl_2/hexane.

*Compound **5**.* Obtained from p-methoxy-chalcone **1** as a yellowish-green solid yield after crystallization from dichloromethane/hexane m.p. 209–211°C, MW = 375 ($C_{22}H_{21}N_3O_3$); MS EI, M^+ m/z 375 374 (100), 268 (M- ϕOCH_3). IR ν_{max}/cm^{-1} 3020, 2945, 1693, 1644, 1245.

δ_H ($CDCl_3$, 300 MHz) 8.00, 7.47, 7.55 (5H); 6.72 (2H), 7.09 (2H), 3.70 s (3H), 3.72 s (3H), 3.38 s (3H), 4.31 (1H, dd, $J = 0.5, 9.6$), 3.57 (1H, dd, $J = 0.5, -17.1$), 2.94 (1H, dd, $J = 9.6, -17.1$).

δ_C ($CDCl_3$, 75.0 MHz) 174.3, 162.7, 158.7, 152.2, 149.4, 137.0, 133.0, 132.8, 128.1, 127.7, 114.2, 97.9, 55.1, 32.8, 32.1, 30.1, 28.2.

*Compound **6**.* Obtained as a yellow solid m.p. 216–217°C MW 613, $C_{38}H_{35}N_3O_5$ MS m/z: 613 (M^+), 374, 239, 105 (100) IR ν_{max}/cm^{-1}, 3010, 2939, 1693, 1644, 1248.

δ_H ($CDCl_3$, 300 MHz) 8.13, 7.55, 7.48, 7.90, 7.57, 6.67, 6.96, 6.65, 6.86, 4.28 (d, 1H, $J = 0.5$), 3.70 (1H), 3.85 (1H), 3.85, 3.40, 3.66 (s, 3H), 3.73 (s, 3H), 3.45 (s, 3H), 3.31 (s, 3H).

δ_C ($CDCl_3$, 75.0 MHz) 197.9, 175.4, 162.7, 158.9, 158.5, 151.7, 148.9, 136.7, 133.6, 133.4, 132.8, 131.7, 129.0, 132.8, 128.6, 127.6, 114.3, 122.9, 112.9, 55.3, 55.1, 46.6, 40.9, 34.1, 29.7, 28.0.

*Compound **7**.* Obtained as orange-yellowish solid. m.p. dec. MW 383 $C_{19}H_{17}S_2N_3O_2$. δH ($CDCl_3$ 300 MHz) 7.56, 7.54 (d), 7.40, 7.39, 7.18, 7.16, 6.98, 6.96 (d), 4.41 (dd), 3.60 s (3H), 3.39 s (3H), 3.35 dd, 2.67 dd.

*Compound **8**.* Obtained as yellow solid m.p. 221–223°C. MW 381 $C_{19}H_{15}S_2N_3O_2$ MS CI ($M^+ + 1$) m/z 382, 307, 289, 154 (100), 136.

δ_H ($CDCl_3$ 300 MHz) 7.83 (d), 7.50, 7.38 (2H), 7.36, 7.34, 7.16, 7.07 (s), 6.98 (d), 3.83 s (3H), 3.40 s (3H).

δ_C ($CDCl_3$ 75 MHz) 162.0, 158.1, 151.8, 151.5, 149.6, 139.4, 138.9, 131.0, 128.7, 128.6, 126.8, 126.2, 124.5, 123.6, 124.5, 30.1, 28.4.

*Compound **9**.* Obtained as yellow light solid m.p. 250–252°C MW 784 $C_{38}H_{36}O_5N_6S_4$ MS (FAB) m/z: M^+ 785, 630, 382, 307, 250, 154 (100), 136.

δ_H ($CDCl_3$ 500 MHz) 7.40 dd (1H), 7.35 dd (1H), 7.14 dd (1H), 6.90 m (2H), 7.05–6.94 m (6H), 6.63 (1H), 6.30 d ($J = 16.0$), 6.15 (NH), 5.46 s (NH), 5.38 d ($J = 16.0$), 4.42 d ($J = 10.5$), 4.10 d ($J = 0.5$), 3.42 s (3H), 3.39 s (3H), 3.11 s (3H), 2.99 ddd ($J = 3.5, 11.0, 13.0$), 2.83 dd ($J = 0.5, 11.0$), 2.72 d ($J = 10.5$), 2.58 s (3H), 2.45 (OH), 2.05 dd ($J = 13.0 - 14.5$), 1.84 dd ($J = 3.5, -14.5$).

δ_C ($CDCl_3$ 125.0 MHz) 162.1, 160.8, 151.6, 151.1, 147.5, 146.4, 144.8, 143.5, 142.3, 138.5, 134.6, 131.6, 128.9, 127.9, 127.4, 126.9, 125.7, 125.5, 125.1, 124.3, 122.3 (2C), 122.2, 122.0, 120.7, 91.0, 84.3, 73.8, 69.8, 55.0, 48.0, 47.5, 35.3, 33.6, 31.2, 28.9, 28.2, 27.8, 27.5.

*Compound **10**.* Obtained as mixture of enantiomers 10A and 10B (1 : 1 ratio).

It was observed as white solid mp 284–286°C MW 764, $C_{38}H_{32}O_4N_6S_4$. HRMS (FAB) MW estimated 765.1446; observed 765.1433 MS: m/z 765 ($M^+ + 1$), 681, 382, 154 (100) IR ν_{max}/cm^{-1} 3440, 3010, 2940, 1707, 1662, 1634, 1284.

δ_H ($CDCl_3$ 500 MHz) 7.46 dd (1H), 7.17 dd (1H), 7.15 dd (1H), 7.14 dd (2H), 7.00 dd (1H), 6.96 dd (1H), 6.93 m (2H), 6.84 m (3H), 6.80 dd (1H), 6.78 dd (1H), 6.74 dd (1H), 6.70 dd (1H), 6.67 m (5H),

6.66 dd (1H), 6.48 m (2H), 6.63 dd (1H), 4.20 (NH), 3.746 s (3H), 3.742 s (3H), 3.30 s (6H), 3.218 s (3H), 3.214 s (3H), 3.00 s (3H), 3.04 s (3H), 3.08 d (1H), 2.98 d (1H), 2.35 dd (1H), 2.33 dd (1H), 3.05 (2H), 3.62 m (3H), 3.58 (1H), 2.60 dd (1H), 2.58 dd (1H), 2.00 dd (1H), 2.05 dd (1H).

δ_C ($CDCl_3$ 125.0 MHz) 165.1, 164.9, 160.4 (2C), 160.05, 160.06, 151.1, 150.7, 148.1 (2C), 144.7, 144.6, 144.5, 144.3, 141.7, 141.5, 141.2, 141.0, 137.5, 135.0 (all non-protonated carbons); 128.1, 127.3, 126.9, 126.8, 126.6, 126.5, 126.2, 126.17 (3C), 125.7, 125.6, 125.4, 125.3, 125.2, 125.0, 121.9, 121.1, 121.0, 120.9, 120.8, 120.4, 120.0 (2C), (all sp^2 methine carbons) 108.4 (C), 108.1 (C), 89.1 (C), 88.8 (C), 58.5 (C), 58.4 (C), 50.6 (CH), 50.4 (CH), 50.0 (CH), 49.3 (CH), 44.5 (CH2), 43.9 (CH), 43.9 (CH2), 43.5 (CH), 41.0 (CH), 32.0 (CH), 31.7 (CH), 30.2 (Me), 28.7 (Me), 28.6 (Me), 27.7 (Me).

*Compound **11***. It was obtained as yellow crystals m.p. 197–199°C MW 270 $C_{14}H_{14}N_4O_2$ MS EI m/z M^+ 270 (100), 269, 241. IR ν_{max}/cm^{-1} 3250, 3015, 2966, 1698, 1645.

δ_H ($CDCl_3$ 300 MHz) 12.8 (NH), 6.99 dd (1H), 6.35 dd (1H), 7.05 dd (1H), 7.42 s (1H), 3.72 s (3H), 3.50 s (3H), 2.54 s (3H).

*Compound **12***. It was obtained as white solid mp 228–230°C MW 839 $C_{57}H_{49}N_3O_4$ HRMS (FAB) MW estimated 840.3801, observed 840.3879. MS: m/z 761, 737, 606, 370. IR ν_{max}/cm^{-1} 3086, 3064, 2960, 1696, 1653.

δ_H ($CDCl_3$ 500 MHz) 7.65–6.35 m (30H), 6.17d (1H), 7.10 d (1H), 6.24 d (1H), 7.19 d (1H), 3.48 s (3H), 3.38 s (3H), 3.82 d (1H), 3.34 dd (1H), 3.94 dd (1H), 4.22 dd (1H), 3.61 dd (1H), 3.20 dd (1H), 4.16 ddd (1H), 2.98 dd (1H), 2.14 dd (1H).

δ_C ($CDCl_3$ 125.0 MHz)196.6 (C=O), 196.3 (C=O), 184.4 (C=N), 162.7 (C=O), 152.3 (C=O), 147.3, 142.8, 142.5, 142.4, 141.7, 140.2, 139.6, 134.2, 134.1, 130.6, 130.5, 129.2, 129.1, 129.0, 128.8, 128.3, 128.2, 128.1, 127.8, 127.1, 126.0, 125.5, 124.9,95.0, 60.7, 53.7, 49.5, 49.3, 48.7, 45.3, 42.4, 34.2, 30.0, 28.3.

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