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Diels–Alder reaction of highly substituted 2*H*-pyran-2-ones with alkynes: reactivity and regioselectivity†

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Received (in Montpellier, France) 7th April 2005, Accepted 23rd May 2005
First published as an Advance Article on the web 28th June 2005

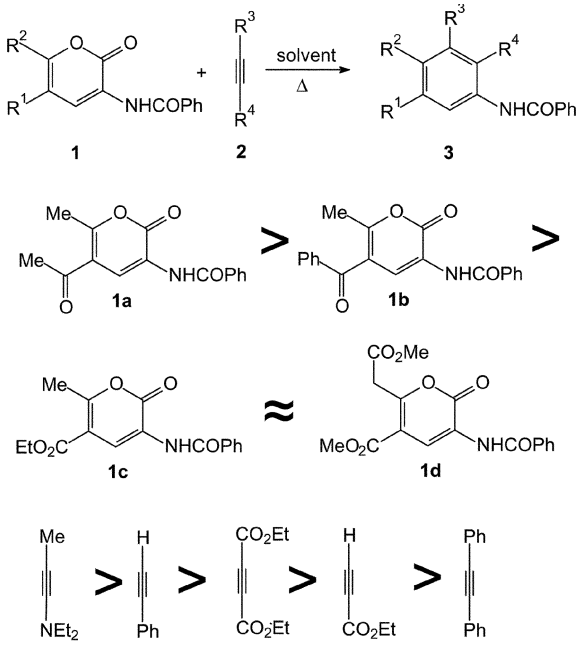
The Diels–Alder reactions of a variety of electron-rich 2*H*-pyran-2-ones **4** with alkynes **2** yielding aniline derivatives **6** under thermal conditions as well as at high pressures are presented. The effects of the substituents at the positions 3 and 5 in the 2*H*-pyran-2-one ring on the reactivity and the regioselectivity with different alkynes were qualitatively explained on the basis of electron demand and also by the formation of zwitterionic intermediates.

Introduction

The Diels–Alder [4 + 2] cycloaddition reaction[1] is one of the most powerful tools for the formation of the C–C bond, and some other bonds.[2] The reaction can take place in a concerted fashion, where the two new bonds are partially formed in the single transition state; if both bonds are formed to exactly the same extent in the transition state it is known as synchronous, otherwise it is known as asynchronous. There are also step-by-step processes, where an intermediate (diradical or zwitterion) with a single bond between the diene and dienophile is formed first, followed by the subsequent cyclization to give the final product.[3–6] The Diels–Alder reaction of various dienophiles with 2*H*-pyran-2-ones as dienes has also been widely investigated[7] and a number of articles describing the transformation with alkynes have been published.[8,9] Many dienophiles have been used, for example, electron-poor acetylenecarboxylates, where the Diels–Alder reaction with a normal electron demand usually takes place; there are also reactions starting from electron-rich phenyl-substituted acetylene,[8g,h] and even more electron-rich *N*,*N*-diethyl-1-propyn-1-amine as a dienophile,[9] where the inverse electron demand Diels–Alder reaction seems to take place.[4–6] It has also been shown that the Diels–Alder reactions can be accelerated by high-pressure conditions[10,11] due to the highly negative volume of activation; there was only one experiment described starting from 2*H*-pyran-2-ones and alkynes (namely dimethyl acetylenedicarboxylate)[12] before our investigation.

We recently published the transformation of highly substituted 2*H*-pyran-2-ones and fused pyran-2-ones with maleic anhydride[13a] and maleimides[13b] toward bicyclo[2.2.2]oct-7-enes and benz[*e*]isoindoles. In contrast, in the reaction of 2*H*-pyran-2-ones containing an electron-withdrawing group at the 5-position with various alkynes under thermal reaction conditions and at high pressures, highly substituted aniline and *o*-phenylenediamine derivatives were prepared.[13c] The effect of substituents of both reactants on the reaction rates was investigated, revealing the general reactivity order of 2*H*-pyran-2-ones **1** with dienophiles **2** as shown in Scheme 1, thus providing evidence for an inverse electron demand Diels–Alder reaction.[13c] In contrast, the reactivity order of dienophiles has shown that diethyl acetylenedicarboxylate was more reactive than ethyl propynoate, which might be evidence for the normal electron demand reaction or neutral reaction in the case of ethyl propynoate.

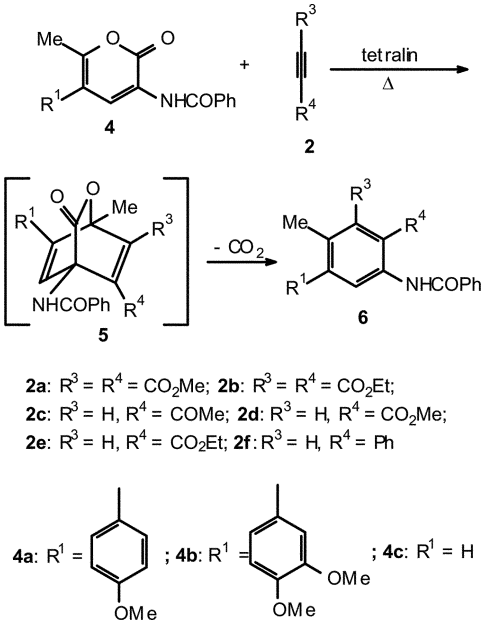
In order to determine the scope and limitations of this transformation, to clarify the above results and to elucidate the different reactivity of our substrates, we decided to investigate the Diels–Alder reaction of 2*H*-pyran-2-ones **4a,b** containing, at the 5-position, a strong electron-donating substituent (4-methoxyphenyl group in **4a** and 3,4-dimethoxyphenyl in **4b**), and for comparison at the 5-position an unsubstituted derivative **4c** (Scheme 2). With the substitution pattern of **4a,b** we expected to significantly change the reactivity and the electron demand of our compounds in comparison with **1a–d**. Namely, the substituents at the 5-position in 2*H*-pyran-2-ones **4a,b** influence the distribution of the electron density by exhibiting a strong electron-donating mesomeric



Scheme 1

† Dedicated to Professor Ľubor Fišera (Slovak University of Technology, Bratislava) on the occasion of his 60th birthday.

DOI: 10.1039/b504852d



Scheme 2

effect (and practically no inductive effect)[14] on the neighboring 6-position; this effect also combines with the relatively strong donating mesomeric (and weak inductive) effect of the benzoylamino group to the 6-position (Fig. 1). In compounds **1a–d** the effect of the substituent at the 5-position was completely different to that in compounds **4a,b** (as could be evident from the resonance structures of compounds **1**). Having in mind the above assumption and on the basis of previous experience[7–9] one could reasonably predict the highly prevailing effect of resonance forms **4a-A** and **4a-B** (with a negative charge at the 6-position) on the reactivity of derivatives **4a,b** and, most probably a concerted polarized asynchronous process or even polar reaction intermediates. It is also important to mention that 2*H*-pyran-2-ones containing such a pattern of substituents have never been investigated before in terms of reactions with alkynes, although there have been investigations of compounds containing some partially separated motifs from compounds **4**,[7–9] such as, for example, 5-phenyl-,[8c] 3-hydroxy-[8h] or 3-methoxy-2*H*-pyran-2-one derivatives,[8g,h] which have shown some regioselectivity in their transformations.

There have been many recent reports on the transformations of 2*H*-pyran-2-ones with alkenes,[7,8,13a,b,15,16] especially with halo substituted 2*H*-pyran-2-ones, published by different research groups.[16] It has been shown that 3- and 5-halo-2*H*-pyran-2-ones react with electron-rich, electron-deficient and also electron-neutral alkenes in a very regio- and stereoselective way to give oxabicyclo[2.2.2]oct-7-enes, whereas 4-halo derivatives behave completely differently.[16d,e] We believe that a comprehensive comparison with our compounds is not possible, because halogens exhibit, in contrast to the substituents in the compounds **4a,b**, a strong, positive mesomeric effect, whereas their inductive effect is strongly negative.[14]

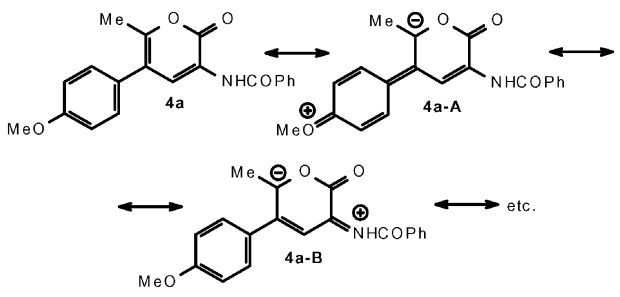


Fig. 1

Results and discussion

Cycloaddition reactions under different conditions

The above assumptions prompted us to perform cycloaddition reactions of 3-benzoylamino-6-methyl-2*H*-pyran-2-ones **4a–c** with a variety of alkynes **2a–f** as dienophiles. Upon the cycloaddition reaction and the spontaneous elimination of carbon dioxide from the intermediate **5**, we isolated multifunctional, highly substituted aniline derivatives **6a–n** (Scheme 2, Table 1).

We investigated the transformations under thermal as well as high-pressure conditions. The thermal reactions were preliminarily conducted in various solvents, including toluene, xylenes, DMF, decalin (*cis*,*trans*-decahydronaphthalene) and tetralin. In these experiments we found that the best yields for the alkynes **2a–d** were obtained using xylenes or toluene as the solvents. In the more polar solvents (DMF) or in solvents with higher boiling points (decalin and tetralin) the reaction was even faster, but because of the difficulties in evaporating those solvents, we decided to use xylenes (or alternatively toluene for the preparation of **6a,b,g,h**) as the reaction medium. Upon heating the reaction mixtures for 5.75–16.5 h and after work-up we isolated the corresponding products **6a–n** in 66–90% yield (Table 1).

Though our previous experiences[13c] with the acceleration of cycloadditions using high pressure were not completely successful, we again decided to try the reactions of **4a–c** at increased pressures (13–15 kbar). With dichloromethane as a solvent and at room temperature we successfully prepared in 2–4 weeks the products **6** (Table 1), though some of them with just low conversions (even after long reaction times), especially so with phenylacetylene (**2f**) as a dienophile and with 5-unsubstituted 2*H*-pyran-2-one **4c**. As already shown,[13c] even with very careful work-up, we were unable to detect any of the bicyclo[2.2.2]octa-1,4-diene system, thus revealing that they are really much less stable than the corresponding bicyclo[2.2.2]octenes.[7]

The cycloaddition of unsymmetrically substituted alkynes **2c–f** regioselectively led to just one type of product, as was proven by TLC and also by the ^{1}H NMR spectra of the crude reaction mixtures. The structures of the products obtained with **2c–f** (**6c–f,i–l**) containing the 1,4 arrangement of protons (2-H and 5-H) on the benzene ring were proved on the basis of their ^{1}H NMR spectra, where for 2-H and/or 5-H protons only singlet signals appeared, consistent with the smallest coupling constants existing between the 1,4 arranged protons on the benzene rings (J = 0–1 Hz). Additionally, the structures **6c–e,i–l** were further studied by means of their HMBC spectra, showing the correlation between 6-Me and 5-H (this correlation should not appear if the regioselectivity was to be reversed).

To gain more insight into the progress of the reaction, we stopped the thermal reactions after 1.5 h of heating in xylenes. After evaporating the solvent and analyzing the crude mixtures of products using ^{1}H NMR spectroscopy, we obtained the results presented in Table 1. From these results and some others given below one can conclude that the 5-(4-methoxyphenyl)- **4a** and 5-(3,4-dimethoxyphenyl)-2*H*-pyran-2-one derivatives **4b** are of similar reactivity, while the 5-unsubstituted derivative **4c** is much less reactive, as is clearly shown by the lack of reactivity with phenylacetylene (**2f**) (even upon 15 h heating in xylenes 87% of the starting **4c** was recovered), with butynone **2c** (even upon 23 h heating in xylenes 78% of the starting **4c** was recovered) and with alkyl propynoates (**2d,e**); even after a very long reaction time (28 h) with **2d** in boiling tetralin 82% of the starting **4c** was recovered.

Table 1 Reaction times, yields of products **6** and degrees of conversion

Run	Starting compounds		Product	Thermal conditions		High-pressure conditions	
	2	**4**[17]	**6**	*t*/h (yield (%))[a]	Conv. (%)[b]	*t*/h[c] (yield (%))[a]	Conv. (%)[d]
1	**2a**	**4a**	**6a**	8[e] (86)	~56	360	~69
2	**2b**	**4a**	**6b**	8[e] (72)	~60	360 (83)	~89
3	**2c**	**4a**	**6c**	5.75[f] (90)	~28	360 (95)	~100
4	**2d**	**4a**	**6d**	15[f] (76)	~13	360	~57
5	**2e**	**4a**	**6e**	15[f] (75)	~16	360	~57
6	**2f**	**4a**	**6f**	15.5[f] (75)	~13	360	~13
7	**2a**	**4b**	**6g**	9.5[e] (78)	~61	336 (92)	~95
8	**2b**	**4b**	**6h**	9[e] (74)	~65	336 (90)	~96
9	**2c**	**4b**	**6i**	6[f] (80)	~29	696 (97)	~98
10	**2d**	**4b**	**6j**	16.5[f] (87)	~14	336 (59)[g]	~74
11	**2e**	**4b**	**6k**	15[f] (68)	~17	696 (87)	~94
12	**2f**	**4b**	**6l**	15.5[f] (78)	~14	696	~7
13	**2a**	**4c**	**6m**	13.5[f] (66)	~20	360	~44
14	**2b**	**4c**	**6n**	10.5[f] (69)	~29	360	~48

[a] Yield of isolated compounds. [b] Degrees of conversion estimated from ^{1}H NMR spectra of the crude reaction mixtures after 1.5 h reflux in xylenes. [c] At 13–15 kbar in CH_2Cl_2 at room temperature. [d] Degrees of conversion estimated from ^{1}H NMR spectra of the crude reaction mixtures after high-pressure reactions. [e] Toluene as a solvent. [f] Xylenes as a solvent. [g] Yield after crystallization.

Regarding the reactivity of dienophiles **2a–f**, we can postulate the following reactivity order with 2*H*-pyran-2-ones **4a,b** for thermal reactions: both dialkyl acetylenedicarboxylates (**2a,b**) are the most reactive; they are followed by butynone **2c**, which is more reactive than both alkyl propynoates (**2d,e**) and phenylacetylene (**2f**). It also seems that ethyl propynoate (**2e**) is the most reactive amongst the last three (**2d–f**), whereas methyl propynoate (**2d**) and phenylacetylene (**2f**) exhibit nearly the same reactivity. 2*H*-Pyran-2-one **4c** reacted under our conditions only with acetylenedicarboxylates **2a,b**. These reactivity orders were also supported by many competitive experiments where we have reacted two (or more) dienophiles **2** simultaneously with 2*H*-pyran-2-ones **4a–c** or two (or more) 2*H*-pyran-2-ones **4** simultaneously with one of the dienophiles **2a–f** in boiling xylenes.

Under high-pressure conditions, the order of the reactivity is to some extent different from the thermal conditions: though there are some differences, amongst 2*H*-pyran-2-ones **4a** and **4b** have comparable reactivity, whereas **4c** is much less reactive (**4a** ≈ **4b** > **4c**). The differences might be ascribed, for example, to the stereoelectronic factors that differently influence the volume of activation;[10,11] but changes in the reaction mechanism could also not be excluded. The methoxy group in the phenyl ring is known to activate the phenyl ring for the electrophilic aromatic substitution to some extent also at the *meta* position[14] and, as a consequence, **4b** might be slightly electron-richer than **4a**; this effect could contribute slightly to the observed reactivity under high pressure (while it was not so pronounced under normal pressure, as shown from Table 1). Amongst alkynes acetylenedicarboxylates **2a,b** and butynone **2c** are the most reactive. They are followed by both propynoates **2d,e**, whereas phenylacetylene seems to be much less reactive (**2a,b,c** > **2d,e** ≫ **2f**).

Comparison of the reactivity between substrates 1 and 4

To make a useful comparison between the reactivities of **4a–c** with those of previously studied 2*H*-pyran-2-ones **1a–d**[13c] we reacted two 2*H*-pyran-2-ones (one from each set) simultaneously with one dienophile **2** in boiling xylenes. In this way the following results were obtained:

(a) In the reaction of the 5-unsubstituted 2*H*-pyran-2-one **4c** and the 5-acetyl derivative **1a** with diethyl acetylenedicarboxylate (**2b**), a conversion of 24% was found for **4c**, and 15% for **1a**. Since **4c** was the least reactive toward **2b** from all of **4a–c** and **1a** was the most reactive amongst **1a–d**[13c] the general reactivity of 2*H*-pyran-2-ones **1** and **4** with acetylenedicarboxylate **2b** is the following: **4a** ≈ **4b** > **4c** > **1a** > **1b** > **1c** ≈ **1d**.

(b) When the 5-(4-methoxyphenyl) derivative **4a** and the 5-acetyl 2*H*-pyran-2-one **1a** were simultaneously reacted with ethyl propynoate (**2e**), a conversion of 24% was found for **4a** and 14% for **1a**, thus showing the higher reactivity of the electron-richer 5-(4-methoxyphenyl) derivative **4a**. Since **4a** is more reactive than **1a** it is also more reactive than all of **1a–d**.[13c] Therefore, bearing in mind that **4c** did not react with **2e** the general reactivity of 2*H*-pyran-2-ones **1** and **4** with **2e** is the following: **4a** ≈ **4b** > **1a** > **1b** > **1c** ≈ **1d** > **4c**.

(c) The simultaneous reaction of phenylacetylene (**2f**) with the 5-methoxycarbonyl-6-methoxylcarbonylmethyl derivative **1d** and the 5-(4-methoxyphenyl) derivative **4a** resulted in a conversion of 27% for **1d** and 20% for **4a**. On this basis, and also including previous results,[13c] the following reactivity with phenylacetylene (**2f**) can be postulated for 2*H*-pyran-2-ones: **1a** > **1b** > **1c** ≈ **1d** > **4a** ≈ **4b** > **4c**.

The effect of solvent polarity on the reactivity

In order to investigate the effect of solvent polarity on the reactivity, we reacted 2*H*-pyran-2-one **4a** with an equimolar mixture of diethyl acetylenedicarboxylate (**2b**) and ethyl propynoate (**2e**) in xylenes and in DMF under the same reaction conditions (immersed in the same oil bath at 138–142 °C). Though the temperature of both reaction mixtures was identical, the reaction proceeding in DMF was faster for both dienophiles (after 1.5 h in xylenes 21% conversion for **2b** and 11% for **2e**, whereas in DMF 32% for **2b** and 15% for **2e**). These results support our assumption that the reaction involves either a polarized concerted asynchronous process or even takes place *via* polar intermediates (which are better stabilized by more polar solvents). Moreover, the changes of polarity from the starting compounds to the transition states (or eventually intermediates) seem to be comparable for both dienophiles, since the reactions are accelerated in DMF (in comparison with xylenes) to a comparable extent for both dienophiles (**2b** and **2e**). Since all the reactions were carried out at high temperatures, we were unable to isolate any intermediates to prove the eventual zwitterionic character of the intermediate. Under high-pressure conditions the reactions are perfectly clean; in the crude mixtures of products there are practically no additional products (or impurities) observable with the ^{1}H NMR technique (besides the products and starting materials) that could be ascribed to the formation of any intermediates.

Explanation of the reaction on the basis of kinetic data

Having in mind the complete regioselectivity of the reactions of unsymmetrically substituted alkynes **2c**–**f** with 2*H*-pyran-2-ones **1** and **4**, one might think that all the transformations of compounds **4** start with the nucleophilic attack of the electron-rich 2*H*-pyran-2-one derivative *via* its 6-position onto the electrophilic moiety of the dienophile either to give zwitterions as intermediates or proceeding through a concerted asynchronous transition state to the final products. Such an explanation also includes the reaction with phenylacetylene, which has been previously described as an electron-rich dienophile[8g,h] reacting with 2*H*-pyran-2-ones in an inverse electron-demand process. Our assumption is based on the fact that the phenyl moiety can stabilize either the positive or the negative character of the C-2 atom in acetylene. For this reason we propose the following pathway for the reaction of **4a,b** with **2f** (Fig. 2), which gives a highly resonance-stabilized (*via* 4-methoxyphenyl group and also *via* 3-benzoylamino moiety) zwitterionic structure **7a** as an intermediate or highly polarized transition state **7b** (where the bond between C-6 of the 2*H*-pyran-2-one moiety and C-2 of phenylacetylene is formed to a greater extent than the bond from C-3 of the 2*H*-pyran-2-one to C-1 of phenylacetylene); this process could be, in terms of electron demand, "normal" for the formation of one single bond in **7a** (by analogy with a concerted asynchronous normal electron demand Diels–Alder reaction *via* **7b**). Such a pathway (*via* **7a** or **7b**) would satisfactorily explain why compounds **4** are completely non-reactive toward electron-rich ethoxyacetylene as a dienophile (after heating **4a** or **4c** with ethoxyacetylene in xylenes at 180 °C for 15–17 h in a glass pressure tube, 85% starting **4a** or 81% of the starting **4c** were recovered).

On the other hand, the reaction between 2*H*-pyran-2-ones **1** and phenylacetylene (**2f**) takes place in a different way (Fig. 3). Phenylacetylene is here serving as a nucleophile and its attack onto **1** results in an intermediate **8a** or a transition state **8b** stabilized *via* the 5-carbonyl group. The different reactivity of compounds **1** (**1a** > **1b** > **1c** ≈ **1d**) toward **2f** can be explained by the differences in the stabilization of the negative charge in **8a** or **8b** by the group at the 5-position, the keto group being better for this purpose than an ester function. On the basis of the reactivity with phenylacetylene (**1a**–**d** > **4a,b** ≫ **4c**), and in terms of the electron demand for the asynchronous concerted transformation, for **4c** a process close to neutral, with **1a**–**d** an inverse, whereas for **4a,b** a process with normal electron demand would be expected. One might also propose for the reaction of **1a**–**d** with phenylacetylene (**2f**) a process *via* the formation of an intermediate of type **7a** or the transition state **7b** (stabilized *via* the 3-benzoylamino moiety), but such pathways do not support the observed reactivity order. The above results are qualitatively in agreement with the FMO theory,[8j] which considers only the electronic interactions between the HOMO and LUMO of the reagents in the rate-determining transition state.[4] The electron donating group at the position 5 in 2*H*-pyran-2-ones **4a,b** increases the HOMO(pyran-2-one) energy in comparison with **4c** and, as a consequence, the interaction HOMO(pyran-2-one)–LUMO(phenylacetylene) is rate determining for this normal electron demand transformation. On the other side, in the derivatives **1a**–**d** the electron-withdrawing groups are decreasing the energy of 2*H*-pyran-2-one orbitals; therefore the interaction HOMO(phenylacetylene)–LUMO(pyran-2-one) is rate determining in this inverse electron demand transformation. A detailed quantitative FMO analysis of these relatively complex 2*H*-pyran-2-ones (which is beyond the scope of the present paper) might additionally clarify our results.

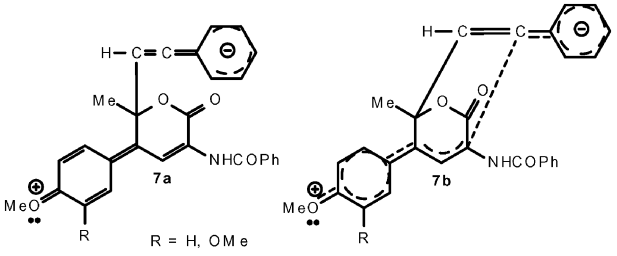


Fig. 2

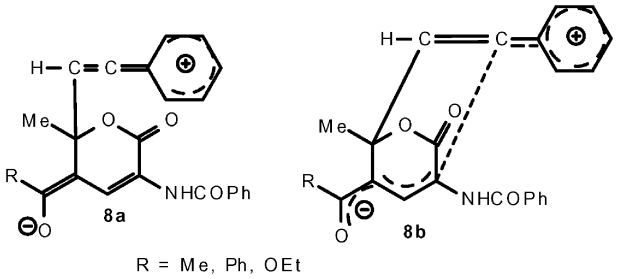


Fig. 3

For the transformation of the compounds **1** with acetylenedicarboxylates **2a,b** we propose the intermediate **9a** or the transition state **9b** (stabilized *via* 3-benzoylamino moiety) (Fig. 4). Analogously, for the conversions of compounds **4** the intermediate **10a** or the transition state **10b** (stabilized by both the methoxyphenyl moiety and the benzoylamino group) can be proposed. The general reactivity towards **2b** was shown to be **4a,b** > **4c** > **1a**–**d** and, therefore, in terms of electron demand, completely corresponds to the normal process (with the HOMO(pyran-2-one)–LUMO(acetylene) being rate determining). The differences in the reactivity of **1a**–**d** cannot be easily explained, but they might originate from stereoelectronic effects, as already briefly discussed.[13c]

On the basis of the reactivity of 2*H*-pyran-2-ones **1** and **4** with ethyl propynoate (**2e**) (**4a,b** > **1a**–**d** ≫ **4c**) one might conclude that in terms of electron demand the cycloaddition with (or around) neutral electron demand would be expected to take place with **4c**, because both an electron-donating group or a withdrawing group at the 5-position accelerated the reaction. Furthermore, a normal process *via* **10b** is expected with **4a,b** (with the smallest energy gap between HOMO(pyran-2-one)–LUMO(propynoate)), whereas with **1a**–**d** an inverse process (with the smallest energy gap between HOMO(propynoate)–LUMO(pyran-2-one)) is proposed. The latter is rather surprising for an otherwise electron-poor alkyne such as **2e**, although the inverse process (*via* a concerted asynchronous transition state with the charge distribution in a direction opposite to that

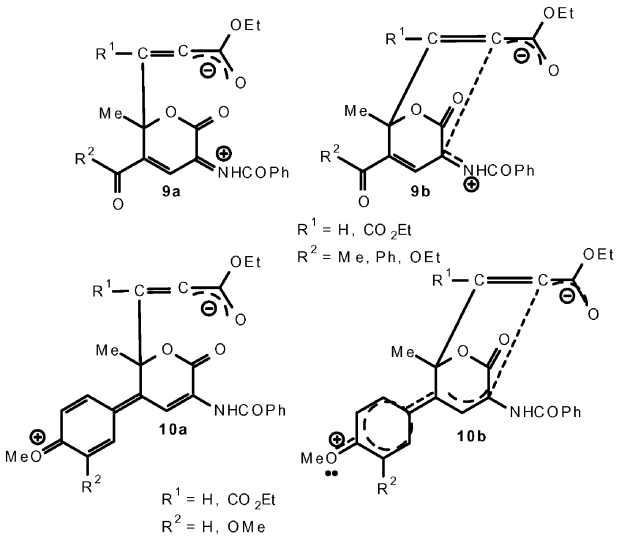


Fig. 4

in **9b**, thus exhibiting donating effect of **2e**) would give a reasonable explanation for the reactivity of 2*H*-pyran-2-ones **1a–d**, as given in Scheme 1. On the other hand, the regioselectivity could be more satisfactorily explained by the formation of the intermediate **9a**, whereas its formation would not explain the differences in the reactivity of **1a–d** with **2e**.

Substituted parent 3′-amino[1,1′-biphenyl]-4-ol derivatives have previously been prepared just in a few cases, and they do not contain additional versatile functional groups as the products **6** do. Matsumoto *et al.*[18] reported the synthesis of an unsubstituted system as well as 2′-butyl and 4′-benzyl derivatives; Brody and Finn[19] have synthesized 3′-amino-4-methoxy derivative by means of polystyrene-bound reagents, whereas Agarwal *et al.*[20] have transformed substituted 2*H*-pyran-2-ones into highly substituted aniline derivatives. Biphenyls, especially those containing derivatized 3′-amino-4-hydroxy groups, represent interesting intermediates for the late-stage introduction of amino-group modifications as well as for the synthesis of a variety of arginine mimics of vitronectin receptor ($\alpha_V\beta_3$) antagonists (*e.g.*, biphenylalanine ureas).[21] The method presented here opens up the possibility for the synthesis of novel types of highly substituted aniline derivatives.[22] In general, aromatic amines can be prepared by a wide variety of methods and represent very important compounds as the constituents of medicinally important molecules and many other industrially relevant materials.[22]

Conclusions

We have presented an efficient and completely regioselective Diels–Alder reaction of various alkynes **2** with substituted 2*H*-pyran-2-ones **4** under thermal and high-pressure conditions that leads to multifunctionally substituted aniline derivatives **6** as well as a comparison of the reactivity under high pressures and at the normal pressure. The effects of the substituents at the 3- and 5-positions in the 2*H*-pyran-2-one ring on the reactivity and the regioselectivity could be satisfactorily explained on the basis of both the electron demand *via* polarized asynchronous concerted transition states and also *via* the formation of zwitterionic intermediates (though, unfortunately, we were unable to find any proof for it). The zwitterion is, in fact, the extreme case of the transition state, where the bond between C-3 of the 2*H*-pyran-2-one unit and the dienophile does not exist. On the basis of all the results it is also clear that the reactions under high pressures are governed by different (or differently pronounced) factors than those at normal pressures.

Experimental

Materials and methods

Melting points are uncorrected. ^{1}H NMR spectra were recorded at 29 °C at 300 MHz using TMS as an internal standard. ^{13}C NMR spectra were recorded at 75 MHz and referenced against the central line of the solvent signal ($CDCl_3$ triplet at $\delta = 77.0$ ppm). The coupling constants (J) are given in Hz. Starting compounds **1a–d**[23] and **4a–c**[17] were prepared according to the published procedures. All other reagents and solvents were used as obtained from commercial suppliers. Xylene was used as a commercially available mixture of *o*-, *m*- and *p*-xylene.

General procedures

(a) Thermal conditions. A solution of 2*H*-pyran-2-one **4a–c** (1 mmol) and the corresponding acetylene **2a–f** (2 mmol) in xylenes (or toluene for **6a,b,g,h**) (3 mL) was heated under reflux for 5.75–16.5 h. The reaction mixture was evaporated under reduced pressure, the residue was treated with 2–3 mL of cold methanol, precipitated material was filtered off and washed with cold methanol (1–2 mL). For **6n** the residue was purified using column chromatography (eluent, light petroleum–ethyl acetate 5 : 3). Reaction conditions and yield are given in Table 1.

(b) High-pressure conditions. A solution of 2*H*-pyran-2-one **4a–c** (0.25 mmol) and the corresponding acetylene **2a–f** (1 mmol) in CH_2Cl_2 (2.5 mL) in a Teflon ampoule was immersed in a piston-cylinder type of pressure vessel filled with white spirit and pressurized at 13–15 kbar for the specified period of time (Table 1). Thereafter the reaction mixture was evaporated under reduced pressure, cold methanol (0.5–1 mL) was added to the residue, precipitated material was filtered off and washed with cold methanol (0.5–1 mL).

(c) Kinetic measurements. A solution of 2*H*-pyran-2-one **4a–c** (1 mmol) and the corresponding acetylene **2a–f** (2 mmol) in xylenes (3 mL) was heated under reflux for 1.5 h. Thereafter the reaction mixture was evaporated under reduced pressure and the crude mixture was analyzed by ^{1}H NMR spectroscopy. The results obtained are presented in Table 1.

(d) Thermal pressure conditions. A solution of 2*H*-pyran-2-one **4a** or **4c** (0.5 mmol) and ethoxyacetylene (40% solution in hexane) (350 mg, 2 mmol) in xylenes (4 mL) was placed in a glass pressure tube, closed with a Teflon screwed stopper and heated in an oil bath ($T = 180$ °C) for 15 h (for **4a**) or 17 h (for **4c**). The reaction mixture was cooled to the room temperature and evaporated under reduced pressure. A part of the mixture was analyzed by ^{1}H NMR spectroscopy. The residue was treated with 1–2 mL of cold methanol, precipitated material was filtered off and washed with cold methanol (1–2 mL). In this way 85% of starting **4a** and 81% of starting **4c** were recovered.

Reactions

(a) Reaction of 2*H*-pyran-2-one 4c and 5-acetyl-2*H*-pyran-2-one 1a with diethyl acetylenedicarboxylate (2b). A mixture of **4c** (114.5 mg, 0.5 mmol), **1a** (136.5 mg, 0.5 mmol) and diethyl acetylenedicarboxylate (**2b**) (340 mg, 2 mmol) in xylenes (3 mL) was refluxed for 1.5 h. Thereafter the reaction mixture was evaporated under reduced pressure and the crude mixture was analyzed by ^{1}H NMR spectroscopy: **4c** : **6n** = 0.85 : 0.27 (24% conversion) and **1a** : **3a** = 1 : 0.18 (15% conversion). For comparison, diethyl 4-acetyl-6-(benzoylamino)-3-methylphthalate (**3a**) was prepared as described previously,[13c] mp 97–99 °C (Et_2O) (mp[13c] 97–99 °C, compound number in ref. 13*c* **4a**).

(b) Reaction of 5-(4-methoxyphenyl)-2*H*-pyran-2-one 4a and 5-acetyl-2*H*-pyran-2-one 1a with ethyl propynoate (2e). A mixture of **4a** (167.5 mg, 0.5 mmol), **1a** (136.5 mg, 0.5 mmol) and ethyl propynoate (**2e**) (196 mg, 2 mmol) in xylenes (3 mL) was refluxed for 1.5 h. Thereafter, the reaction mixture was evaporated under reduced pressure and the crude mixture was analyzed by ^{1}H NMR spectroscopy: **4a** : **6e** = 0.87 : 0.28 (24% conversion) and **1a** : **3b** = 1 : 0.16 (14% conversion). For comparison, ethyl 4-acetyl-2-(benzoylamino)-5-methylbenzoate (**3b**) was prepared as described previously,[13c] mp 134–135 °C (EtOH) (mp[13c] 134–135 °C, compound number in ref. 13*c* **4b**).

(c) Reaction of 5-(4-methoxyphenyl)-2*H*-pyran-2-one 4a and 5-methoxycarbonyl-6-methoxycarbonylmethyl-2*H*-pyran-2-one 1d with phenylacetylene (2f). A mixture of **4a** (167.5 mg, 0.5 mmol), **1d** (172.5 mg, 0.5 mmol) and phenylacetylene (**2f**) (204 mg, 2 mmol) in xylenes (3 mL) was refluxed for 1.5 h.

Thereafter the reaction mixture was evaporated under reduced pressure and the crude mixture was analyzed by ^{1}H NMR spectroscopy: **4a** : **6f** = 1 : 0.25 (20% conversion) and **1d** : **3c** = 0.94 : 0.35 (27% conversion). For comparison, methyl 2-(benzoylamino)-5-[(methoxycarbonyl)methyl]-[1,1′-biphenyl]-4-carboxylate (**3c**) was prepared as described previously,[13c] mp 132.5–134.4 °C (EtOH) (mp[13c] 132.5–134.4 °C, compound number in ref. 13*c* **4l**).

Investigation of the effects of the solvent polarity

(a) In xylenes. A mixture of **4a** (335 mg, 1 mmol), diethyl acetylenedicarboxylate (**2b**) (170 mg, 1 mmol) and ethyl propynoate (**2e**) (98 mg, 1 mmol) in xylenes (3 mL) was heated for 1.5 h in an oil bath at T = 138–142 °C. Thereafter the reaction mixture was evaporated under reduced pressure and the crude mixture was analyzed by ^{1}H NMR spectroscopy: **4a** : **6b** = 1 : 0.27 (21% conversion for **2b**) and **4a** : **6e** = 1 : 0.12 (11% conversion for **2e**).

(b) In *N*,*N*-dimethylformamide (DMF). The same procedure as above; immersed in the same oil bath at T = 138–142 °C; using DMF (3 mL) instead of xylenes. Analysis by ^{1}H NMR spectroscopy: **4a** : **6b** = 1 : 0.48 (32% conversion for **2b**) and **4a** : **6e** = 1 : 0.18 (15% conversion for **2e**).

To prove the structures of products, in the above experiments authentic samples of products **3** and **6** were added to the ^{1}H NMR analyzed mixtures.

Characterization data for compounds 6a–n

Dimethyl 5-(benzoylamino)-4′-methoxy-2-methyl[1,1′-biphenyl]-3,4-dicarboxylate (6a). Mp 162.5–165.5 °C (MeOH). IR (KBr): 1721, 1698, 1676, 1608, 1584, 1510 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.19 (s, 3H, Me), 3.86 (s, 3H), 3.93 (s, 3H), 3.94 (s, 3H) (OMe, 2 × CO_2Me), 6.95 (AA′XX′, J = 8.7 Hz, 2H), 7.27 (AA′XX′, J = 8.7 Hz, 2H) (4-MeO-C_6H_4), 7.52 (m, 3H, Ph), 7.99 (m, 2H, Ph), 8.82 (s, 1H, 6-H), 11.44 (s, 1H, NH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 17.2, 52.3, 52.9, 55.3, 112.8, 113.7, 123.4, 127.2, 127.8, 128.8, 130.2, 132.0, 132.5, 134.6, 136.3, 138.4, 148.3, 159.2, 165.4, 167.9, 169.6. EI-MS: m/z (%) 433 (M^+, 57), 105 (100). Anal. Calcd for $C_{25}H_{23}NO_6$: C, 69.27; H, 5.35; N, 3.23. Found: C, 69.46; H, 5.47; N, 3.07%.

Diethyl 5-(benzoylamino)-4′-methoxy-2-methyl[1,1′-biphenyl]-3,4-dicarboxylate (6b). Mp 116.0–116.8 °C (MeOH). IR (KBr): 1730, 1709, 1672, 1604, 1580, 1509 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.39 (t, J = 7.2 Hz, 3H), 1.41 (t, J = 7.2 Hz, 3H) (2 × $CO_2CH_2CH_3$), 2.20 (s, 3H, 2-Me), 3.86 (s, 3H, OMe), 4.40 (q, J = 7.2 Hz, 2H), 4.41 (q, J = 7.2 Hz, 2H) (2 × $CO_2CH_2CH_3$), 6.96 (AA′XX′, J = 8.6 Hz, 2H), 7.27 (AA′XX′, J = 8.6 Hz, 2H) (4-MeO-C_6H_4), 7.52 (m, 3H, Ph), 7.99 (m, 2H, Ph), 8.82 (s, 1H, 6-H), 11.49 (s, 1H, NH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 13.8, 14.1, 17.1, 55.3, 61.3, 62.2, 113.0, 113.7, 123.3, 127.3, 127.8, 128.8, 130.2, 132.0, 132.7, 134.7, 136.5, 138.4, 148.2, 159.2, 165.4, 167.6, 169.1. EI-MS: m/z (%) 461 (M^+, 49), 105 (100). Anal. Calcd for $C_{27}H_{27}NO_6$: C, 70.27; H, 5.90; N, 3.03. Found: C, 70.50; H, 6.00; N, 3.23%.

***N*-(4-Acetyl-4′-methoxy-6-methyl[1,1′-biphenyl]-3-yl)benzamide (6c).** Mp 194.5–196.5 °C (xylenes). IR (KBr): 1672, 1639, 1610, 1581, 1505 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.33 (s, 3H, Me), 2.73 (s, 3H, COMe), 3.86 (s, 3H, OMe), 6.96 (AA′XX′, J = 8.8 Hz, 2H), 7.33 (AA′XX′, J = 8.8 Hz, 2H) (4-MeO-C_6H_4), 7.52 (m, 3H, Ph), 7.81 (s, 1H, 5-H), 8.06 (m, 2H, Ph), 8.90 (s, 1H, 2-H), 12.64 (s, 1H, NH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.2, 28.5, 55.2, 113.6, 120.7, 122.0, 127.3, 128.7, 129.5, 130.1, 131.8, 132.9, 133.6, 134.8, 139.1, 148.7, 159.1, 165.7, 202.8. EI-MS: m/z (%) 359 (M^+, 50), 105 (100). Anal. Calcd for $C_{23}H_{21}NO_3$: C, 76.86; H, 5.89; N, 3.90. Found: C, 77.13; H, 6.04; N, 3.88%.

Methyl 3-(benzoylamino)-4′-methoxy-6-methyl[1,1′-biphenyl]-4-carboxylate (6d). Mp 124–126 °C (MeOH). IR (KBr): 1681, 1611, 1585, 1509 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.29 (s, 3H, Me), 3.86 (s, 3H), 3.97 (s, 3H) (CO_2Me, OMe), 6.95 (AA′XX′, J = 8.8 Hz, 2H), 7.33 (AA′XX′, J = 8.8 Hz, 2H) (4-MeO-C_6H_4), 7.52 (m, 3H, Ph), 7.96 (s, 1H, 5-H), 8.03 (m, 2H, Ph), 8.85 (s, 1H, 2-H), 11.94 (s, 1H, NH). ^{13}C NMR (75.5 MHz, $CDCl_3$, 42 °C): δ 20.0, 52.2, 55.3, 113.67, 113.71, 121.8, 127.3, 128.7, 129.8, 130.1, 131.7, 132.5, 133.2, 135.0, 139.6, 148.2, 159.2, 165.4, 169.0. EI-MS: m/z (%) 375 (M^+, 24), 105 (100). Anal. Calcd for $C_{23}H_{21}NO_4$: C, 73.58; H, 5.64; N, 3.73. Found: C, 73.88; H, 5.57; N, 3.50%.

Ethyl 3-(benzoylamino)-4′-methoxy-6-methyl[1,1′-biphenyl]-4-carboxylate (6e). Mp 138.5–141.0 °C (MeOH). IR (KBr): 1686, 1671, 1612, 1582, 1508 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.45 (t, J = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 2.30 (s, 3H, Me), 3.86 (s, 3H, OMe), 4.44 (q, J = 7.2 Hz, 2H, $CO_2CH_2CH_3$), 6.96 (AA′XX′, J = 8.9 Hz, 2H), 7.33 (AA′XX′, J = 8.9 Hz, 2H) (4-MeO-C_6H_4), 7.51 (m, 3H, Ph), 7.97 (s, 1H, 5-H), 8.04 (m, 2H, Ph), 8.85 (s, 1H, 2-H), 11.99 (s, 1H, NH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.2, 20.1, 55.3, 61.4, 113.6, 113.9, 121.8, 127.3, 128.7, 129.8, 130.1, 131.7, 132.4, 133.1, 135.0, 139.5, 148.0, 159.0, 165.4, 168.6. EI-MS: m/z (%) 389 (M^+, 77), 105 (100). Anal. Calcd for $C_{24}H_{23}NO_4$: C, 74.02; H, 5.95; N, 3.60. Found: C, 74.27; H, 6.10; N, 3.43%.

***N*-{[4-Methyl-5-(4-methoxyphenyl)-2-phenyl]phenyl}benzamide (6f).** Mp 129–130 °C (EtOH). IR (KBr): 1671, 1609, 1579, 1561, 1525, 1504, 1490 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.31 (s, 3H, Me), 3.86 (s, 3H, OMe), 6.96 (AA′XX′, J = 8.7 Hz, 2H, 4-MeO-C_6H_4), 7.20 (br s, 1H, 5-H), 7.36 (m, 4H, Ph, 2H of 4-MeO-C_6H_4), 7.48 (m, 6H, Ph), 7.60 (m, 2H, Ph), 7.95 (br s, 1H, NH), 8.39 (s, 1H, 2-H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.1, 55.3, 113.5, 123.0, 126.8, 128.0, 128.7, 129.1, 129.3, 130.4, 131.3, 131.57, 131.64, 131.8, 132.4, 133.7, 134.8, 138.0, 141.6, 158.6, 164.9. EI-MS: m/z (%) 393 (M^+, 67), 105 (100). Anal. Calcd for $C_{27}H_{23}NO_2$ × 0.8 EtOH: C, 79.82; H, 6.51; N, 3.25. Found: C, 79.77; H, 6.57; N, 3.30%.

Dimethyl 5-(benzoylamino)-3′,4′-dimethoxy-2-methyl[1,1′-biphenyl]-3,4-dicarboxylate (6g). Mp 181–183 °C (MeOH). IR (KBr): 1738, 1678, 1578, 1513 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.19 (s, 3H, Me), 3.89 (s, 3H, OMe), 3.93 (s, 6H, 2 × OMe), 3.95 (s, 3H, OMe), 6.90 (m, 3H, 2′-H, 5′-H, 6′-H), 7.53 (m, 3H, Ph), 7.99 (m, 2H, Ph), 8.84 (s, 1H, 6-H), 11.44 (s, 1H, NH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 17.2, 52.3, 52.9, 55.89, 55.92, 111.0, 112.2, 112.9, 121.4, 123.3, 127.2, 127.8, 128.8, 132.0, 132.8, 134.5, 136.3, 138.3, 148.4, 148.60, 148.68, 165.4, 167.8, 169.5. EI-MS: m/z (%) 463 (M^+, 75), 105 (100). Anal. Calcd for $C_{26}H_{25}NO_7$: C, 67.38; H, 5.44; N, 3.02. Found: C, 67.66; H, 5.50; N, 3.04%.

Diethyl 5-(benzoylamino)-3′,4′-dimethoxy-2-methyl[1,1′-biphenyl]-3,4-dicarboxylate (6h). Mp 109–111.5 °C (Et_2O). IR (KBr): 1722, 1705, 1677, 1603, 1578 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.40 (t, J = 7.2 Hz, 3H), 1.41 (t, J = 7.2 Hz, 3H) (2 × $CO_2CH_2CH_3$), 2.21 (s, 3H, Me), 3.89 (s, 3H, OMe), 3.93 (s, 3H, OMe), 4.40 (q, J = 7.2 Hz, 2H), 4.41 (q, J = 7.2 Hz, 2H) (2 × $CO_2CH_2CH_3$), 6.90 (m, 3H, 2′-H, 5′-H, 6′-H), 7.51 (m, 3H, Ph), 7.99 (m, 2H, Ph), 8.83 (s, 1H, 6-H), 11.49 (s, 1H, NH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 13.8, 14.0, 17.1, 55.87, 55.89, 61.3, 62.2, 111.0, 112.2, 113.1, 121.4, 123.1, 127.2, 127.7, 128.7, 131.9, 132.9, 134.6, 136.5, 138.3, 148.2, 148.57, 148.63, 165.3, 167.5, 169.0. EI-MS: m/z (%) 491 (M^+, 62), 105 (100).

Anal. Calcd for $C_{28}H_{29}NO_7$: C, 68.42; H, 5.95; N, 2.85. Found: C, 68.68; H, 6.04; N, 2.87%.

***N*-(4-Acetyl-3′,4′-dimethoxy-6-methyl[1,1′-biphenyl]-3-yl)-benzamide (6i).** Mp 172.5–174 °C (EtOH). IR (KBr): 1670, 1649, 1573, 1510 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.34 (s, 3H, Me), 2.74 (s, 3H, COMe), 3.91 (s, 3H, OMe), 3.94 (s, 3H, OMe), 6.93 (m, 3H, 2′-H, 5′-H, 6′-H), 7.52 (m, 3H, Ph), 7.82 (s, 1H, 5-H), 8.06 (m, 2H, Ph), 8.91 (s, 1H, 2-H), 12.64 (s, 1H, NH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.2, 28.5, 55.89, 55.94, 110.9, 112.2, 120.7, 121.4, 121.9, 127.3, 128.7, 129.6, 131.8, 133.2, 133.5, 134.8, 139.0, 148.57, 148.61, 148.8, 165.8, 202.8. EI-MS: *m*/*z* (%) 389 (M^+, 62), 105 (100). Anal. Calcd for $C_{24}H_{23}NO_4$: C, 74.02; H, 5.95; N, 3.60. Found: C, 73.92; H, 6.13; N, 3.61%.

Methyl 3-(benzoylamino)-3′,4′-dimethoxy-6-methyl[1,1′-biphenyl]-4-carboxylate (6j). Mp 185.5–188 °C (MeOH). IR (KBr): 1692, 1668, 1612, 1579, 1509 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.30 (s, 3H, Me), 3.91 (s, 3H, OMe), 3.93 (s, 3H, OMe), 3.99 (s, 3H, CO_2Me), 6.92 (m, 3H, 2′-H, 5′-H, 6′-H), 7.52 (m, 3H, Ph), 7.97 (s, 1H, 5-H), 8.04 (m, 2H, Ph), 8.86 (s, 1H, 2-H), 11.94 (s, 1H, NH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.0, 52.2, 55.83, 55.88, 110.9, 112.2, 113.6, 121.3, 121.6, 127.2, 128.6, 129.7, 131.7, 132.4, 133.4, 134.8, 139.4, 148.2, 148.46, 148.49, 165.3, 168.9. EI-MS: *m*/*z* (%) 405 (M^+, 64), 105 (100). Anal. Calcd for $C_{24}H_{23}NO_5$: C, 71.10; H, 5.72; N, 3.45. Found: C, 71.28; H, 5.92; N, 3.35%.

Ethyl 3-(benzoylamino)-3′,4′-dimethoxy-6-methyl[1,1′-biphenyl]-4-carboxylate (6k). Mp 166–168.5 °C (MeOH). IR (KBr): 1684, 1665, 1603, 1578, 1510 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.46 (t, $J = 7.1$ Hz, 3H, $CO_2CH_2CH_3$), 2.30 (s, 3H, Me), 3.91 (s, 3H, OMe), 3.93 (s, 3H, OMe), 4.45 (q, $J = 7.1$ Hz, 2H, $CO_2CH_2CH_3$), 6.93 (m, 3H, 2′-H, 5′-H, 6′-H), 7.52 (m, 3H, Ph), 7.97 (s, 1H, 5-H), 8.04 (m, 2H, Ph), 8.86 (s, 1H, 2-H), 11.99 (s, 1H, NH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.3, 20.1, 55.97, 56.01, 61.4, 111.0, 112.3, 114.1, 121.5, 121.7, 127.3, 128.8, 129.9, 131.8, 132.4, 133.5, 135.0, 139.5, 148.2, 148.55, 148.60, 165.5, 168.6. EI-MS: *m*/*z* (%) 419 (M^+, 77), 105 (100). Anal. Calcd for $C_{25}H_{25}NO_5$: C, 71.58; H, 6.01; N, 3.34. Found: C, 71.77; H, 6.16; N, 3.41%.

***N*-{[4-Methyl-5-(3,4-dimethoxyphenyl)-2-phenyl]phenyl}benzamide (6l).** Mp 206–208 °C (MeOH). IR (KBr): 1638, 1578, 1553, 1515 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.32 (s, 3H, Me), 3.92 (s, 3H, OMe), 3.94 (s, 3H, OMe), 6.96 (m, 3H, 2′-H, 5′-H, 6′-H), 7.21 (s, 1H, 5-H), 7.49 (m, 8H), 7.61 (m, 2H) (2 × Ph), 7.95 (br s, 1H, NH), 8.41 (s, 1H, 2-H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.0, 55.87, 55.88, 110.9, 112.7, 121.5, 122.9, 126.7, 128.0, 128.6, 129.1, 129.2, 131.4, 131.5, 131.6, 131.8, 132.4, 134.1, 134.7, 137.9, 141.8, 148.1, 148.5, 164.9. EI-MS: *m*/*z* (%) 423 (M^+, 88), 105 (100). Anal. Calcd for $C_{28}H_{25}NO_3$: C, 79.41; H, 5.95; N, 3.31. Found: C, 79.47; H, 6.03; N, 3.28%.

Dimethyl 3-(benzoylamino)-6-methylphthalate (6m). Mp 110–113 °C (Et_2O). IR (KBr): 1733, 1685, 1673, 1598, 1526 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.33 (s, 3H, Me), 3.911 (s, 3H, CO_2Me), 3.912 (s, 3H, CO_2Me), 7.44 (d, $J = 8.7$ Hz, 1H, 4-H or 5-H), 7.53 (m, 3H, Ph), 7.99 (m, 2H, Ph), 8.78 (d, $J = 8.7$ Hz, 1H, 4-H or 5-H), 11.26 (s, 1H, NH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 19.0, 52.3, 52.9, 114.7, 122.2, 127.2, 128.8, 130.3, 132.0, 134.5, 135.0, 135.6, 138.4, 165.4, 168.0, 169.1. EI-MS: *m*/*z* (%) 327 (M^+, 49), 105 (100). Anal. Calcd for $C_{18}H_{17}NO_5$: C, 66.05; H, 5.23; N, 4.28. Found: C, 66.17; H, 5.29; N, 4.11%.

Diethyl 3-(benzoylamino)-6-methylphthalate (6n). Mp 54–57 °C (PE : EtOAc = 5 : 3). IR (KBr): 1733, 1699, 1686, 1596, 1526 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.37 (t, $J = 7.3$ Hz, 3H), 1.39 (t, $J = 7.3$ Hz, 3H) (2 × $CO_2CH_2CH_3$), 2.34 (s, 3H, Me), 4.38 (q, $J = 7.3$ Hz, 4H, 2 × $CO_2CH_2CH_3$), 7.42 (d, $J = 8.8$ Hz, 1H, 5-H), 7.52 (m, 3H, Ph), 7.99 (m, 2H, Ph), 8.76 (d, $J = 8.8$ Hz, 1H, 4-H), 11.32 (s, 1H, NH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 13.7, 14.1, 18.9, 61.2, 62.2, 114.8, 122.0, 127.2, 128.7, 130.1, 131.9, 134.6, 135.2, 135.4, 138.4, 165.4, 167.7, 168.6. EI-MS: *m*/*z* (%) 355 (M^+, 39), 105 (100). Anal. Calcd for $C_{20}H_{21}NO_5 \cdot 0.25\ H_2O$: C, 66.75; H, 6.02; N, 3.89. Found: C, 66.85; H, 6.12; N, 3.61%.

Acknowledgements

We thank the Ministry of Higher Education, Science and Technology of the Republic of Slovenia for financial support (P1-0230-0103 and J1-6693-0103). Dr B. Kralj and Dr D. Žigon (Center for Mass Spectroscopy, "Jožef Stefan" Institute, Ljubljana, Slovenia) are gratefully acknowledged for mass measurements.

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