

Synthesis and antimicrobial activity of new 2-azetidinones from *N*-(salicylidene)amines and 2-diazo-1,2-diarylethanones

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Dedicated to Professor Berhanu M. Abegaz on the occasion of his 60th birthday

Abstract

This paper describes the reactions of *N*-salicylideneamines with diarylketenes generated from thermal decomposition of the 2-diazo-1,2-diarylethanones. An equimolar reaction of the *N*-salicylidenebenzhydramine with diphenylketene affords a mixture of 2-[(benzhydrylimino)methyl]phenyl-2,2-diphenylacetate as a major product and 1-benzhydryl-3,3-diphenyl-4-[2'-(*O*-diphenylacyl)hydroxyphenyl]-2-azetidinone as a minor product. The reactions of various *N*-salicylideneamines with 2.2 molar equivalents of 2-diazo-1,2-diarylethanones have been carried out to afford 1-substituted-3,3-diaryl-4-[2'-(*O*-diarylacyl)hydroxyphenyl]-2-azetidinones as sole product in excellent yields. The products, characterized on the basis of satisfactory analytical and spectral data, have shown moderate to good antimicrobial activity against some bacteria and fungi. Among the fourteen compounds in the series, the 2-azetidinone **4I** with a 4-chlorophenyl group on β -lactam ring nitrogen and 4-methylphenyl groups on β -lactam ring C-3 position is the most active compound.

Keywords: 2-Azetidinones, diarylketenes, iminophenols, cycloaddition, antimicrobial

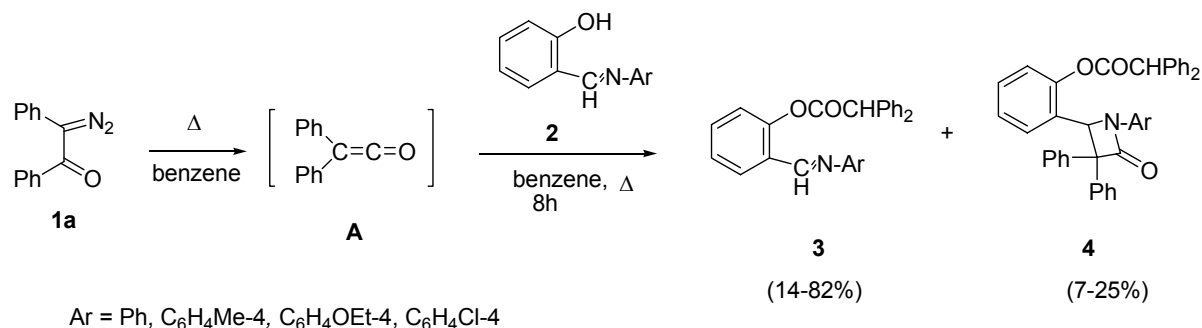
Introduction

2-Azetidinones, commonly known as β -lactams, are well-known heterocyclic compounds among the organic and medicinal chemists.¹ The activity of the famous antibiotics such as penicillins, cephalosporins and carbapenems are attributed to the presence of 2-azetidinone ring in them. Recently, some other types of biological activity besides the antibacterial activity have been reported in compounds containing 2-azetidinone ring.^{2,3} Such biological activities include antifungal, antitubercular, antitumor, cholesterol absorption inhibition and enzyme inhibition activity. The β -lactams also serve as synthons for many biologically important classes of organic

compounds.⁴ Due to this, the investigation of chemistry and biology of these compounds continue to appeal the synthetic and medicinal organic chemists.¹⁻⁴

The most common method for the synthesis of 2-azetidinones is the Staudinger ketene-imine cycloaddition, which involves the reaction of imines with acid chloride in the presence of a tertiary base.⁵ This reaction, however, depends, on many factors including temperature, which often needs to be optimized.⁶ We have been using α -diazoketones as precursors of diarylketenes and carbenoids, and investigating the reactions of these intermediates with organic compounds containing nitrogen atom in different structural environments.⁷ These reactions are simple to carry out, versatile and do not require the use of any acidic or basic reagent. Using 2-diazoketones as precursors of the diarylketenes, we have recently reported the synthesis of 2-azetidinones and spiro-2-azetidinones from the imines of the thiophene-2-carbaldehyde and indoline-2,3-dione, respectively, as possible antimicrobial agents.^{8,9} The 2-azetidinones, obtained from the imines of thiophene-2-carbaldehyde and diarylketenes, showed moderate antibacterial and antifungal activity.⁸ The reactions of ketenes with ambident substrates, however, depend on the structural environment of the particular functional group. For example, diphenylketene adds on to the carbon-nitrogen double bond of the benzil monoimines and camphor monoimines leaving the carbon-oxygen double bond on these compounds.^{10,11} The reaction of diphenylketene with isatin imines has been observed to occur at the amido nitrogen and not at imino nitrogen.¹²

Our group has recently undertaken a project on the reactions of salicylaldehyde derivatives with α -diazocarbonyl compounds in quest for new aspirin analogs. We have carried out an equimolar reaction of the 2-diazo-1,2-diphenylethanone **1a** with *N*-salicylideneanilines **2** and observed that the regiochemistry of the reaction depended significantly on the substituents on aniline moiety (Scheme 1).¹³ The reaction of diphenylketene (**A**), generated *in situ* from thermal decomposition of the 2-diazo-1,2-diphenylethanone **1a**, with **2** having an electron withdrawing chloro group on the phenyl ring attached to imino nitrogen occurred mainly at phenolic hydroxyl group giving rise to [(4-chlorophenylimino)methyl]phenyl-2,2-diphenylacetate **3** whereas the reaction with substrates **2** having an electron-donating groups afforded a mixture of 2-[(arylimino)methyl]phenyl-2,2-diphenylacetates **3** and 1-substituted-3,3-diphenyl-4-[2'-(*O*-diphenylacyl)hydroxyphenyl]-2-azetidinones **4**; the latter being in appreciable amounts. In continuation of this study, the present paper reports an equimolar reaction of the 2-diazo-1,2-diphenylethanone **1a** with an *N*-alkylimine, *N*-salicylidenebenzhydramine **2g**, and a 2.2:1 molar reaction of the 2-diazo-1,2-diarylethanones **1a,b** with various *N*-salicylideneamines **2a-h** affording new 1-substituted-3,3-diaryl-4-[2'-(*O*-diarylacyl)hydroxyphenyl]-2-azetidinones **4a-n** in excellent yields. The products, characterized on the basis of satisfactory analytical and spectral data, have been screened for their antibacterial and antifungal activity.

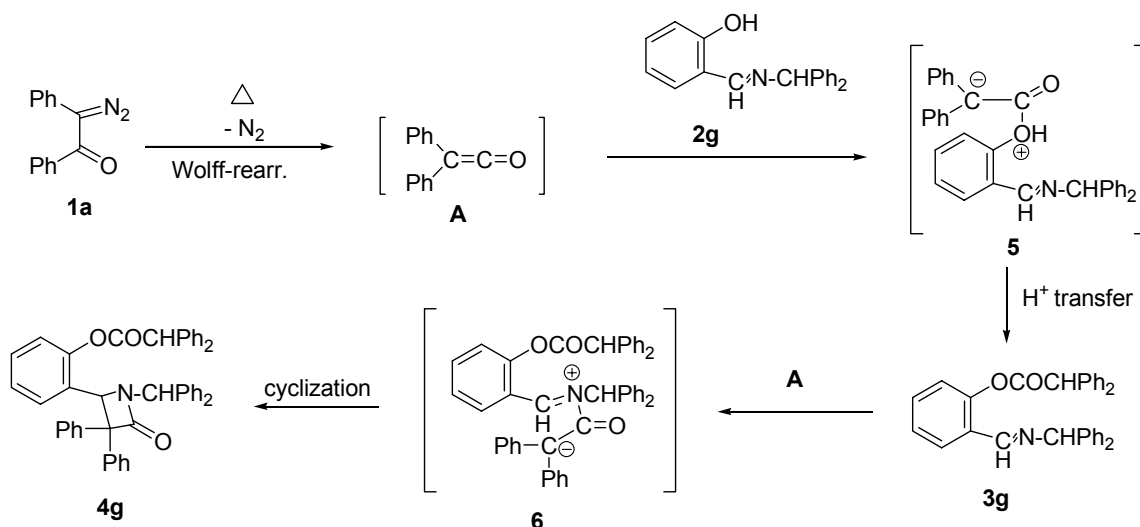


Scheme 1

Results and Discussion

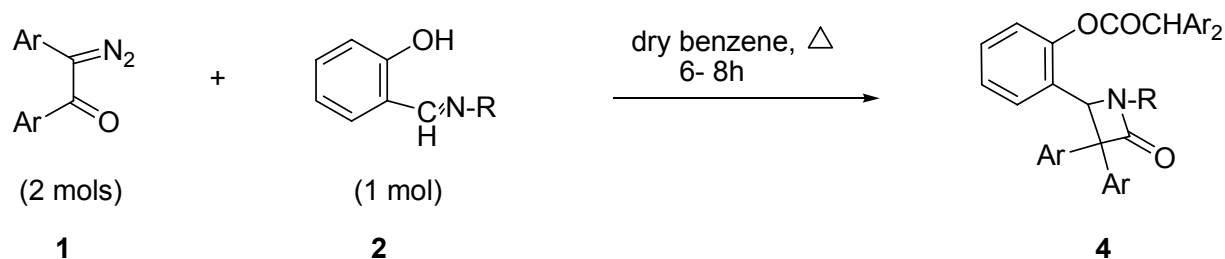
An equimolar reaction of the 2-diazo-1,2-diphenylethanone **1a** with *N*-salicylidenebenzhydramine **2g** afforded two products, which were separated by fractional crystallization from ethanol. The major product (85 % from ¹H NMR) has been characterized as 2-[(benzhydrylimino)methyl]phenyl-2,2-diphenylacetate **3g** and the minor product (7 % from ¹H NMR) as 1-benzhydryl-3,3-diphenyl-4-[2'-(*O*-diphenylacetyl)hydroxyphenyl]-2-azetidinone **4g** on the basis of satisfactory analytical and spectral data (see experimental section). Thus, the product distribution in this reaction is almost parallel to the ratio obtained from the similar reaction of **1a** with *N*-salicylidene-4-chloroaniline **2e**.¹³ Similar to previous reactions of the *N*-salicylideneanilines with diphenylketene no 1:1 molar diphenylketene-azomethine cycloaddition product, the 1-benzhydryl-3,3-diphenyl-4-(2-hydroxyphenyl)-2-azetidinone, was obtained in this reaction as well.

The results of the 1:1 molar reaction of the diphenylketene with *N*-salicylideneamines led us to infer that the hydroxy group had higher reactivity in comparison to imino group towards diphenylketene. However, the imines with strong electron-donating ethoxy group competed efficiently with the hydroxyl group to afford the 2-azetidinone in appreciable amount. Diphenylketene, formed from thermal decomposition of the 2-diazo-1,2-diphenylethanone, reacted first with the hydroxyl group forming an intermediate **5** (Scheme 2). A 1,3-proton transfer in the latter intermediate afforded the product **3g**. A second mole of diphenylketene then reacted with imino nitrogen of the **3g** forming the *zwitterionic* intermediate **6**. Similar *zwitterionic* intermediates have been proposed earlier in the reactions of ketenes with imines. These intermediates may cyclize to form the product **4g**.



Scheme 2

The reaction of imine **2a** with 2.2 molar equivalents of 2-diazo-1,2-diphenylethanone **1a** afforded a white crystalline compound as the sole product in good yield (Table 1) (Scheme 3). This product has been identified as the 2-azetidinone **4a** on the basis of similar spectral data (see experimental) and undepressed mixed melting point with the sample obtained from an equimolar reaction of the **1a** with **2a**.¹³ Similar reactions of **1a** with **2b-h**, and of 2-diazo-1,2-bis(4-methylphenyl)ethanone **1b** with **2** also afforded the 2-azetidinones **4b-m** in good to excellent yields (Table 1). The significant features of the spectra are described briefly in the succeeding paragraph.



Scheme 3

The IR spectra of the compounds showed strong absorption band at $1750-1765\text{ cm}^{-1}$ characteristic of the β -lactam and ester carbonyl groups. The broad band around 3400 cm^{-1} observed in the IR spectra of imines **2a-h** also disappeared in the IR spectra of the products indicating that the reaction has occurred at the hydroxyl group. The 1H NMR spectra of **4** showed the disappearance of the singlet azomethine signal at around δ 8.0 ppm observed in the 1H NMR spectra of the substrates **2** indicating the reaction of the diarylketenes with the

azomethine group. In most of the products, the β -lactam ring methine proton and *O*-acyl proton appeared respectively at around δ 5.8 and 5.3 ppm. These assignments were confirmed by ^1H - ^{13}C correlation studies by HMBC (Figure 1). A typical HMBC spectrum is shown in Figure 2. The ^{13}C NMR spectra showed two downfield signals at around δ 171.0 and 166.0 ppm corresponding to the ester and amido carbonyl carbons, respectively. The other four membered ring carbons appeared at around 72.0 (C-3) and 56.0 ppm (C-4).

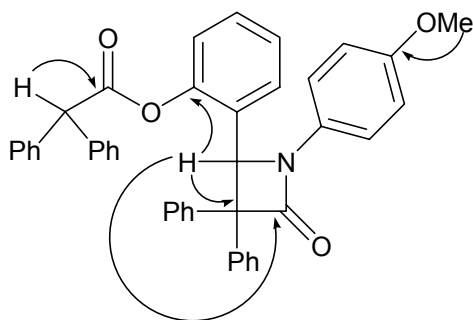


Figure 1. Selected HMBC correlations in **4b**

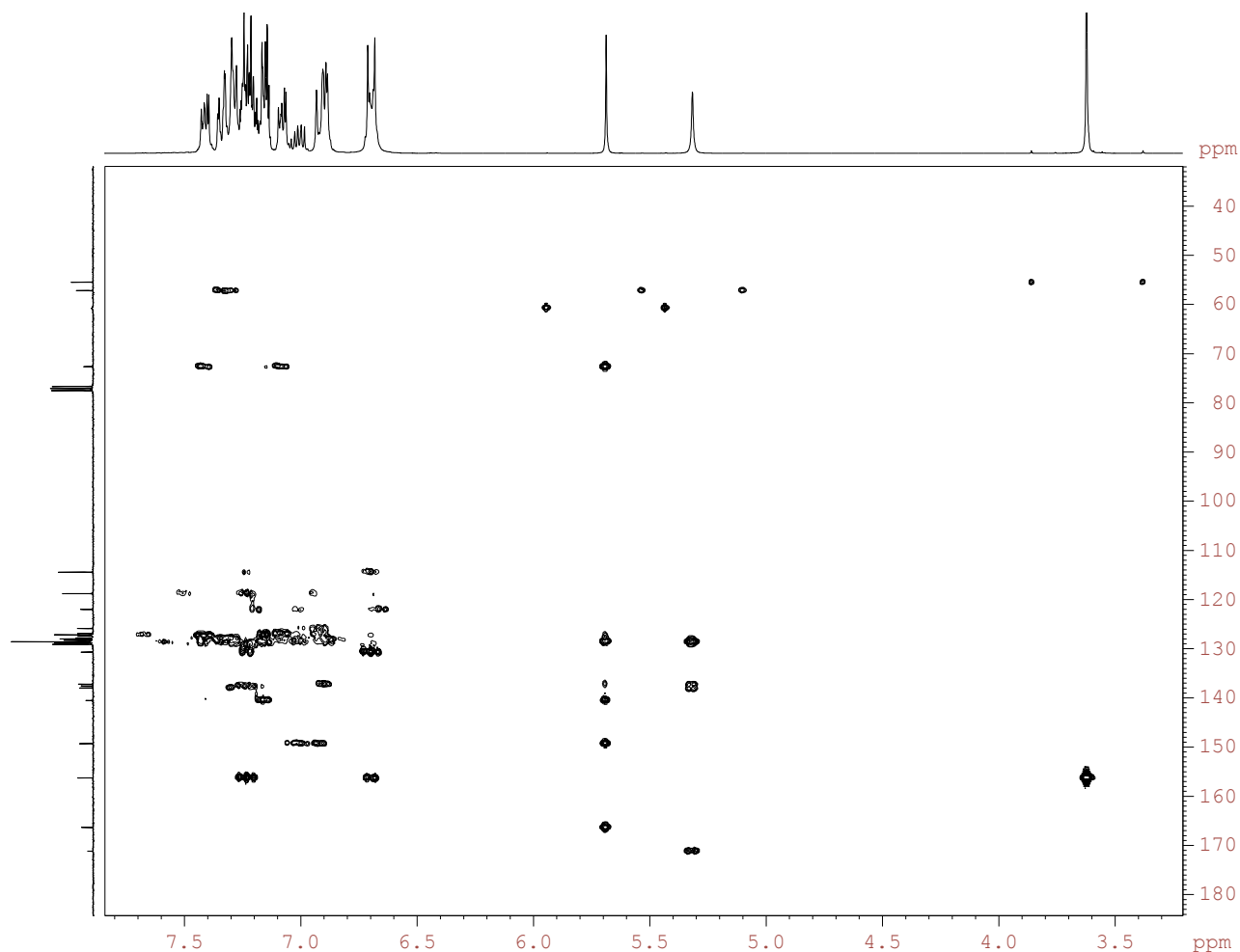


Figure 2. HMBC spectrum of the 2-azetidinone **4b**.

The formation of the products can be explained by same path as shown in Scheme 2. However, in case of imines with electron donating groups, the product 2-azetidinones might not be formed only from the reaction of diarylketenes with 1:1 molar product **3**. In these cases the imino group can compete with the phenolic group for the diarylketenes and reaction at both sites can occur simultaneously.

Ten of the fourteen 2-azetidinones **4** have been screened for their antibacterial and antifungal activity. The compounds exhibited moderate activity (Table 2). Usually the monocyclic 2-azetidinones show better activity against Gram (-) bacteria. These compounds, however, showed almost parallel activity against Gram (-) bacteria and Gram (+) *B. subtilis*. Although no significant effect of substituents on the 2-azetidinone ring was observed on the activity of the compounds the product **4l** with 4-chlorophenyl group on ring nitrogen was the most active compound in the series. The 2-azetidinones **4j** and **4m** with methoxy and benzhydryl group, respectively, paralleled the antibacterial activity of **4l** but their activity on fungi was lower. The compounds having 4-methylphenyl groups on C-3 position of the azetidinone ring

showed significantly higher activity in comparison to those with phenyl rings on C-3 position of the 2-azetidiones against *S. aureus*. All the compounds showed better antifungal activity against *C. mycoderma* compared to *S. cerevisiae*.

Table 1. Physical data of 2-azetidiones 4a-n

Compd No.	Ar	R	Mol. Formula*	m. p. (°C)	Yield (%)
4a	Ph	Ph	C ₄₁ H ₃₁ NO ₃	152	65
4b	Ph	4-CH ₃ OC ₆ H ₄	C ₄₂ H ₃₃ NO ₄	160	78
4c	Ph	4-C ₂ H ₅ OC ₆ H ₄	C ₄₃ H ₃₅ NO ₄	140	75
4d	Ph	4-CH ₃ C ₆ H ₄	C ₄₂ H ₃₃ NO ₃	173	70
4e	Ph	4-ClC ₆ H ₄	C ₄₁ H ₃₀ NO ₃ Cl	172	63
4f	Ph	4-NO ₂ C ₆ H ₄	C ₄₁ H ₃₀ N ₂ O ₅	160	58
4g	Ph	4-CHPh ₂	C ₄₈ H ₃₇ NO ₃	128	48
4h	Ph	4-CH ₂ Ph	C ₄₂ H ₃₃ NO ₃	130	65
4i	4-CH ₃ C ₆ H ₄	Ph	C ₄₅ H ₃₉ NO ₃	184	69
4j	4-CH ₃ C ₆ H ₄	4-CH ₃ OC ₆ H ₄	C ₄₆ H ₄₁ NO ₄	112	75
4k	4-CH ₃ C ₆ H ₄	4-CH ₃ C ₆ H ₄	C ₄₆ H ₄₁ NO ₃	150	70
4l	4-CH ₃ C ₆ H ₄	4-ClC ₆ H ₄	C ₄₅ H ₃₈ ClNO ₃	120	87
4m	4-CH ₃ C ₆ H ₄	4-CHPh ₂	C ₅₂ H ₄₅ NO ₃	200	50
4n	4-CH ₃ C ₆ H ₄	4-CH ₂ Ph	C ₄₆ H ₄₁ NO ₃	164	69

* All the compounds gave satisfactory elemental analysis for C, H and N.

Table 2. Antibacterial and antifungal activity of **4** (MIC µg/mL)

No.	Ar	R	<i>E. coli</i>	<i>P. aeruginosa</i>	<i>B. subtilis</i>	<i>S. aureus</i>	<i>C. mycoderma</i>	<i>S. cerevisiae</i>
4a	Ph	Ph	5	5	5	50	5	10
4b	Ph	4-CH ₃ OC ₆ H ₄	5	5	5	50	5	10
4e	Ph	4-ClC ₆ H ₄	5	5	5	50	5	10
4g	Ph	4-CHPh ₂	5	5	5	50	0.5	5
4h	Ph	4-CH ₂ Ph	10	5	5	100	5	100
4i	4-CH ₃ C ₆ H ₄	Ph	5	5	10	50	10	10
4j	4-CH ₃ C ₆ H ₄	4-CH ₃ OC ₆ H ₄	5	5	0.5	5	10	100
4l	4-CH ₃ C ₆ H ₄	4-ClC ₆ H ₄	5	5	0.5	0.5	0.5	5
4m	4-CH ₃ C ₆ H ₄	4-CHPh ₂	5	5	0.5	5	5	50
4n	4-CH ₃ C ₆ H ₄	4-CH ₂ Ph	10	5	5	5	10	10
Chloramphenicol			0.1	0.1	0.1	0.1	0.1	0.1
Miconazole			0.1	0.1	0.1	0.1	0.1	0.1

Experimental Section

General Procedures. Melting points have been recorded on a Stuart Scientific melting point apparatus and are uncorrected. The IR spectra were recorded on a Perkin-Elmer-781 IR spectrophotometer using KBr disc of the sample. The ^1H and ^{13}C NMR spectra were recorded in a CDCl_3 solution at 300 MHz and 75.4 MHz, respectively, on a BrukerTM 300 MHz spectrometer.

Benzil, 4,4'-dimethylbenzil, hydrazine hydrate, salicylaldehyde and amines were Aldrich products. Benzene was dried by refluxing over sodium hydride.

2-Diazo-1,2-diarylethanones were prepared by oxidation of the benzil monohydrazones.¹⁴ The latter compounds were synthesized by the condensation of benzils with hydrazine hydrate by reported method.¹⁴ *N*-(2-Salicylidene)amines were prepared by reacting an equimolar amount of salicylaldehyde and amines.¹⁵

General procedure for the reaction of 2-diazoketones with *N*-salicylideneamines

A solution of either equimolar amount (1 mmol of each of **1a** and **2g**) or 2.2 mmol of **1** and 1 mmol of the imines **2** in dry benzene (10 ml) was refluxed for 6-8 hrs under continuous stream of nitrogen. The solvent was removed under reduced pressure and the residual matter was purified by fractional crystallization with ethanol to afford white crystalline products.

Antimicrobial activities

Using microlitre syringes, different amounts (0.05 μg , 0.1 μg , 0.5 μg , 5 μg , 10 μg , 50 μg and 100 μg) of each compound and standards were spotted on different glass-backed plates coated with silica-gel (Merck) 60 F₂₅₄. Nutrient agar was inoculated with respective pure microbial cultures, overlaid on the above plates and incubated appropriately. Inhibition of the bacterial and fungal growth was evaluated based on a simple and rapid bioautographic agar overlay method using procedures described earlier.¹⁶⁻¹⁸

3g. Mp: 110 °C; Yield: 65%; IR (KBr, cm^{-1}): 1764 (C=O), 1636 C=N); ^1H NMR (CDCl_3 , δ ppm): 8.20 (dd, 1H, aromatic proton), 8.09 (s, 1H, azomethine proton), 7.40-7.13 (23H, aromatic), 5.31 (s, 1H, CH), 5.11 (s, 1H, CH); ^{13}C NMR (CDCl_3 , δ ppm): 170.54, 155.14, 150.13, 143.64, 137.93, 131.45, 128.87, 128.76, 128.36, 128.25, 127.68, 127.60, 126.95, 126.26, 122.47, 78.26, 57.08.

4a. IR (KBr, cm^{-1}): 1754 (C=O); ^1H NMR (CDCl_3 , δ ppm): 7.34-6.84 (29H, aromatic), 5.84 (s, 1H, ring CH), 5.42 (s, 1H, COCH); ^{13}C NMR (CDCl_3 , δ PPM): 170.0, 166.9, 149.2, 140.33, 137.9, 137.5, 137.1, 137.0, 129.1, 129.0, 128.9, 128.7, 128.5, 128.2, 127.9, 127.8, 127.7, 127.3, 127.1, 126.9, 125.8, 124.2, 121.9, 117.4, 72.6, 60.6, 57.9

4b. IR (KBr, cm^{-1}): 1746 (C=O); ^1H NMR (CDCl_3 , δ ppm): 7.52-6.80 (28H, aromatic), 5.79 (s, 1H, ring CH), 5.42 (s, 1H, COCH), 3.76 (s, 3H, CH₃); ^{13}C NMR (CDCl_3 , δ ppm): 171.07, 166.26, 156.28, 149.29, 140.51, 137.95, 137.56, 137.19, 130.68, 129.07, 129.02, 128.94, 128.72, 128.56 (two C), 128.25, 127.96, 127.89, 127.74, 127.32, 127.28, 127.15, 126.84, 125.84, 121.97, 118.76, 114.41, 72.6, 60.80, 57.17, 55.43.

4c. IR (KBr, cm^{-1}): 1747 (C=O); ^1H NMR (CDCl_3 , δ ppm): 7.52-6.79 (28H, aromatic), 5.79 (s, 1H, ring CH), 5.42 (s, 1H, COCH), 3.99 (q, 2H, $J_1=6.9$ Hz, CH_2), 1.38 (t, 3H, $J=6.9$ Hz, CH_3); ^{13}C NMR (CDCl_3 , δ ppm): 171.05, 166.21, 155.61, 149.23, 140.46, 137.93, 137.52, 137.17, 130.52, 129.05, 128.97, 128.92, 128.69, 128.53 (two C), 128.23, 127.93, 127.87, 127.72, 127.29, 127.25, 127.13, 126.81, 125.81, 121.92, 118.72, 114.98, 72.6, 63.66, 60.78, 57.14, 14.8.

4d. IR (KBr, cm^{-1}): 1748 (C=O); ^1H NMR (CDCl_3 , δ ppm): 7.46-6.93 (28H, aromatic), 5.85 (s, 1H, ring CH), 5.45 (s, 1H, COCH), 2.30 (s, 3H, CH_3); ^{13}C NMR (CDCl_3 , δ ppm): 171.03, 166.60, 149.19, 140.40, 137.95, 137.54, 137.12, 134.66, 133.86, 129.63, 129.08, 128.98, 128.94, 128.72, 128.55, 128.35 (two C), 128.25, 127.96, 127.88, 127.74, 127.33, 127.24, 127.15, 126.85, 125.84, 121.94, 117.41, 72.55, 60.0, 57.15, 20.91.

4e. IR (KBr, cm^{-1}): 1750 (C=O); ^1H NMR (CDCl_3 , δ ppm): 7.29-6.76 (28H, aromatic), 5.79 (s, 1H, ring CH), 5.43 (s, 1H, COCH); ^{13}C NMR (CDCl_3 , δ ppm): 171.14, 166.80, 149.26, 140.17, 137.86, 137.47, 136.89, 135.58, 129.36, 129.30, 129.23, 129.10, 128.98, 128.82, 128.53, 128.35 (two C), 128.11, 128.06, 127.96, 127.81, 127.49, 127.06, 127.00, 126.80, 125.97, 122.12, 118.73, 72.94, 60.69, 57.14.

4f. IR (KBr, cm^{-1}): 1760 (C=O); ^1H NMR (CDCl_3 , δ ppm): 7.45-6.66 (28H, aromatic), 5.86 (s, 1H, ring CH), 5.45 (s, 1H, COCH); ^{13}C NMR (CDCl_3 , δ ppm): 171.26, 167.46, 149.35, 143.64, 142.07, 139.75, 137.74, 137.38, 136.52, 129.65, 129.11, 129.01, 128.93, 128.69, 128.50, 128.47, 128.19, 128.00, 127.93, 127.86, 127.70, 127.20, 126.93, 126.35, 126.12, 125.22, 122.31, 117.47, 73.52, 60.96, 57.15.

4g. IR (KBr, cm^{-1}): 1759 (C=O); ^1H NMR (CDCl_3 , δ ppm): 7.11-6.68 (34H, aromatic), 5.64 (s, 1H, ring CH), 5.52 (s, 1H, COCH), 5.23 (s, 1H, CH); ^{13}C NMR (CDCl_3 , δ ppm): 170.8, 169.9, 149.4, 140.8, 138.7, 138.4, 137.9, 137.8, 137.6, 129.3, 128.95, 128.90, 128.7, 128.67, 128.62, 128.55, 128.51, 128.48 (2C), 128.41, 128.2, 127.9, 127.7, 127.68, 127.63, 127.59, 127.10, 127.06, 126.65, 125.24, 121.66, 72.34, 62.62, 61.12, 57.08.

4h. IR (KBr, cm^{-1}): 1759 (C=O); ^1H NMR (CDCl_3 , δ ppm): 7.25-6.79 (29H, aromatic), 5.27 (s, 1H, ring CH), 5.19 (s, 1H, COCH), 4.93 (d, 1H, $J=14.7$ Hz, CH_2), 3.89 (d, 1H, $J=14.7$ Hz, CH_2); ^{13}C NMR (CDCl_3 , δ ppm): 169.60, 168.46, 148.51, 139.44, 136.92, 136.53, 136.39, 134.00, 127.81, 127.76, 127.63, 127.48, 127.43, 127.39, 127.23, 126.84, 126.75, 126.53, 126.23, 125.92, 125.85, 125.62, 124.53, 121.01, 72.4, 59.2, 55.95, 43.51.

4i. IR (KBr, cm^{-1}): 1750 (C=O); ^1H NMR (CDCl_3 , δ ppm): 7.40-7.02 (25H, aromatic), 5.81 (s, 1H, ring CH), 5.35 (s, 1H, COCH), 2.38 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 2.16 (s, 3H, CH_3); ^{13}C NMR (CDCl_3 , δ ppm): 171.37, 167.31, 149.31, 137.77, 137.45, 137.30, 137.22, 136.81, 136.33, 135.23, 134.82, 134.27, 129.67, 129.56, 129.33, 129.05, 128.89, 128.62, 128.52, 128.38, 128.33, 128.00, 127.36, 126.94, 125.77, 124.05, 121.94, 117.49, 72.0, 60.75, 56.42, 21.05, 21.01, 20.92.

4j. IR (KBr, cm^{-1}): 1751 (C=O); ^1H NMR (CDCl_3 , δ ppm): 7.39-6.79 (24H, aromatic), 5.76 (s, 1H, ring CH), 5.35 (s, 1H, COCH), 3.76 (s, 3H, OCH_3), 2.38 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 2.18 (s, 3H, CH_3); ^{13}C NMR (CDCl_3 , δ ppm): 171.4, 166.8, 156.1, 149.4, 137.9, 137.5, 137.3, 136.7, 136.3, 135.2, 134.8, 134.4, 130.8, 130.7, 129.7, 129.6, 129.3, 128.9,

128.6, 128.4(2C), 128.3, 128.0, 127.5, 126.9, 125.9, 125.8, 121.9, 118.7, 114.3, 56.4, 72.0, 60.8, 55.4, 21.1, 21.0 (2C), 20.9.

4k. IR (KBr, cm^{-1}): 1756 (C=O); ^1H NMR (CDCl_3 , δ ppm): 7.45-6.80 (24H, aromatic), 5.77 (s, 1H, ring CH), 5.32 (s, 1H, COCH), 2.37 (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 2.28 (s, 3H, CH_3), 2.15 (s, 3H, CH_3); ^{13}C NMR (CDCl_3 , δ ppm): 171.4, 167.0, 149.3, 137.8, 137.4, 137.3, 136.7, 136.3, 135.2, 134.8, 134.7, 134.3, 133.6, 129.6, 129.5, 129.3, 128.8, 128.6, 128.5, 128.4, 128.0, 127.5, 126.9, 125.8, 121.9, 117.4, 72.0, 60.7, 56.4, 21.1, 21.0 (two C), 20.9, 20.8.

4l. IR (KBr, cm^{-1}): 1753 (C=O); ^1H NMR (CDCl_3 , δ ppm): 7.38-6.78 (24H, aromatic), 5.77 (s, 1H, ring CH), 5.35 (s, 1H, COCH), 2.37 (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 2.16 (s, 3H, CH_3); ^{13}C NMR (CDCl_3 , δ ppm): 171.5, 167.2, 149.4, 137.6, 137.5, 137.4, 136.9, 136.5, 135.7, 135.1, 134.7, 134.1, 129.7, 129.6, 129.4, 129.2, 128.7, 128.4 (2C), 127.9, 127.0, 126.8, 125.9, 122.1, 118.7, 72.9, 60.5, 56.40, 21.07, 21.04 (2C), 20.94.

4m. IR (KBr, cm^{-1}): 1749 (C=O); ^1H NMR (CDCl_3 , δ ppm): 7.27-6.69 (30H, aromatic), 5.61 (s, 1H, ring CH), 5.49 (s, 1H, COCH), 5.15 (s, 1H, CH), 2.37 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 2.15 (s, 3H, CH_3); ^{13}C NMR (CDCl_3 , δ ppm): 171.17, 170.31, 149.57, 139.02, 138.59, 138.24, 137.17, 137.13, 136.33, 136.05, 135.26, 135.05, 134.92, 129.55, 129.49, 129.22, 128.60, 128.53, 128.45, 128.40, 128.39, 128.33, 128.04, 127.97, 127.51, 127.46, 126.86, 125.14, 121.62, 71.79, 62.63, 61.26, 56.35, 21.05, 21.02 (2C), 20.92.

4n. IR (KBr, cm^{-1}): 1753 (C=O); ^1H NMR (CDCl_3 , δ ppm): 7.13-6.78 (25H, aromatic), 5.25 (s, 1H, ring CH), 5.13 (s, 1H, COCH), 4.90 (d, 1H, $J=14.7$ Hz, CH_2), 3.87 (d, 1H, $J=14.7$ Hz, CH_2), 2.36 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 2.29 (s, 3H, CH_3), 2.16 (s, 3H, CH_3); ^{13}C NMR (CDCl_3 , δ ppm): 171.17, 170.31, 149.6, 137.9, 137.14, 137.09, 136.3, 136.7, 135.3, 135.2, 134.9, 134.7, 129.5, 129.4, 129.2, 128.9, 128.8, 128.6, 128.34, 128.30, 128.1, 127.7, 127.4, 126.7, 125.5, 122.9, 72.9, 60.5, 56.2, 44.5, 21.07, 21.0 (2C), 20.95.

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