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The Photochemistry of N-Phenyl Phthalonimide: Formation of Substituted Dihydroisocoumarins in the Presence of Tertiary Amines.

Rafael Suau* and Ezequiel P. de Inestrosa Villatoro

Departamento de Química Orgánica. Facultad de Ciencias.
Universidad de Málaga, E-29071 Málaga, Spain.

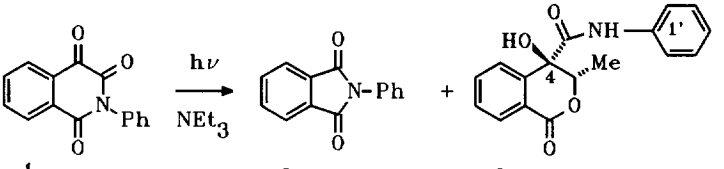
Abstract: N-Phenyl phthalimide and 3,4-Dihydroisocoumarins were obtained by irradiation of N-phenyl phthalonimide in the presence of tertiary amines. The δ-lactone structure was demonstrated via an alternative synthesis that gave the isomeric γ-lactone as well. The key steps of the photoreaction, and the role of the amine, oxygen and several potential intermediates are discussed.

INTRODUCTION

The reactivity of molecules bearing several photochemically active functional groups is, frequently, difficult to predict as it often involves unexpected processes. Thus, the photochemical behaviour of aliphatic imides[1] is similar to that of related amides and ketones and includes α-cleavage, type-II processes and oxetane formation. In addition, phthalimide the archetypal aromatic imide, exhibits intra- and inter-molecular photocycloaddition of alkenes[2] leading to benzazepinediones (a process of promising synthetic value) or undergoes dearomatization[3] to give a wide array of products via *ortho* and *para* photoadducts. The photochemistry of imides with additional functionalities such as phthalonimide, bis(phenylglyoxylolyl)-alkylamines,[4] N,N-dialkylpiperazinetetrones[5] and imidazolidinetriones[6] is lesser known, this substances can be considered α-oxoimides with an interesting reactivity. Recently, we described several processes that take place when the α-ketoimide phthalonimide is irradiated under different conditions.[7] The C-4 carbonyl group behaves as expected, giving oxetanes with alkenes and photoaddition products with hydrogen donors. N-photoarylation of phthalonimide is observed in aromatic solvents and triethylamine; the reaction is explained on the basis of the formation of an electrophilic phthalonimidyl radical. Under such conditions, formation of N-aryl phthalimide, a by-product ascribed to the photochemical decarbonylation of the N-aryl phthalonimide initially produced, is observed. In this context, the photochemical behaviour of N-phenyl phthalonimide in benzene/triethylamine/oxygen was carefully studied. This paper shows that, contrary to the expectations, neither decarbonylation to N-phenyl phthalimide nor photoreduction to N-phenyl homophthalimide are the exclusive processes involved in the photochemistry of N-phenyl phthalonimide in the presence of tertiary amines. Rather,the competitive uptake of one alkyl radical of the amine by the α-ketoimide occurs, and a δ-lactone is obtained after oxidation.

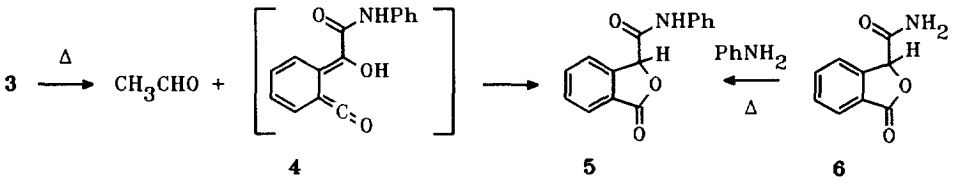
RESULTS AND DISCUSSION

Irradiation of a partially deoxygenated benzene solution of **1** and triethylamine (in a 1:3 mole ratio) was monitored by GC/MS until almost complete disappearance of the imide. Chromatographic separation of the reaction products allowed the two major components, N-phenyl phthalimide (**2**) and the lactone **3**, to be isolated. The elemental analysis of **3** (C_{17} H_{15} N O_4) required the attachment of a two-carbon fragment (C_2 H_6 O) to the phthalonimide. The ^{13}C-NMR spectrum was consistent with two carbonyl groups bonded to heteroatoms (δ 168.3 and 165.2), 12 aromatic carbons (9 methines) and 3 aliphatic carbons, a quaternary (δ 75.3), a low field methine (δ 79.2), and a methyl group (δ 14.4). The ^{1}H-NMR spectrum revealed the aliphatic hydrogens to be coupled and two exchangeable protons (δ 9.20 and 4.64) to be present. The high field signal was typical of a vicinally uncoupled hydroxyl proton; the other was ascribed to an amide proton, which suggested the disappearance of the imide function. These inferences were confirmed by the IR spectrum, which included an amide carbonyl band at 1678 cm^{-1}, the amide band-II at 1529 cm^{-1} and a distinct signal for a δ-lactone at 1720 cm^{-1}. Meaningful information was also obtained from the mass spectra. Introduction by GC showed the M^+ ion at *m/z* 253, while introduction by DIP gave a M^+ ion at *m/z* 297, consistent with the recorded molecular formula. This data indicated that **3** lost 44 amu thermally prior to ionization. DTA/TG test confirmed this assumption (an endothermic peak was observed at 193°C associated to a mass loss of 14.8%).



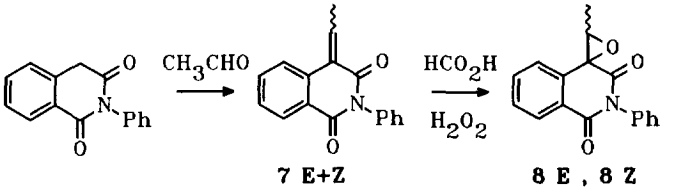
Heating **3** in a NMR tube caused it to disappear at the same time a proton signal (δ 9.83, quartet, J= 3Hz) coupled to one for a methyl group (δ 2.2, doublet) started to appear; both signals were unambiguously assigned to acetaldehyde. The structure of a 3,4-dihydro-1*H*-2-benzopyran-1-one, possessing a quaternary carbon at position-4 and bearing a -OH and a phenylcarbamoyl group was proposed for compound **3**. This structure is consistent with a retro Diels-Alder reaction under heating to give acetaldehyde and the *ortho*-quinodimethane intermediate (**4**), which must undergo cyclization, either through the -NH to the 4-hydroxy-N-phenyl homophthalimide or through the -OH to 3-phenylcarbamoyl phthalide (**5**). When the thermal reaction of **3** was carried out on a preparative scale and under nitrogen stream to remove the acetaldehyde, a single compound was isolated that was identified as **5**. Two carbonyl bands at 1774 and 1669 cm^{-1} (γ-lactone and amide, respectively) in the IR spectrum and one methine singlet (δ 5.89) in the ^{1}H-NMR spectrum that correlates with a carbon atom at δ 78.3 support the proposed structure.

The structure of **5** was definitely established by independent synthesis from homophthalic acid by reaction with



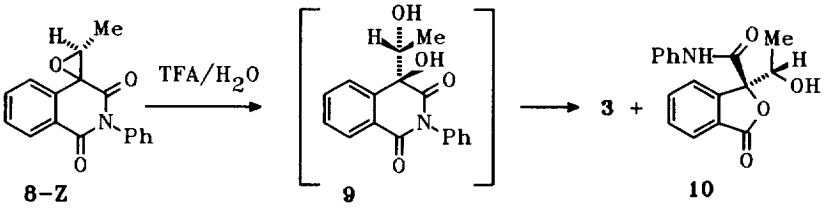
sodium azide in sulfuric acid to the 3-carbamoyl phthalide (**6**),[8] followed by transamidation with aniline.

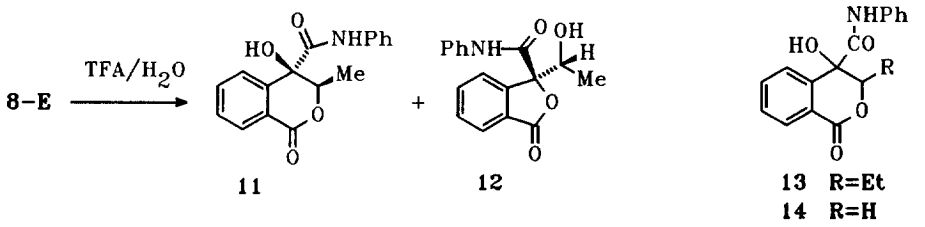
The relative configuration of the lactone **3** at C-3 and C-4 was derived from proton-coupled ^{13}C-NMR spectra, selective heteronuclear decoupling experiments and three-bond coupling constant measurements. Thus, the coupled ^{13}C-NMR spectrum of **3** included, the signals for the amide and the lactone carbonyls as doublets, with a coupling constant of 6.1 Hz and 3.0 Hz, respectively. Both doublets are the result of three-bond coupling to H-3, and merge into a singlet when the proton was irradiated. As seen in structurally related dihydroisocoumarins,[9] a twist conformation for the pyran ring was assumed and so was Karplus-type relationship to hold for the H-C vicinal coupling constants. The $^3J_{H3\text{-}CO(amide)}$ value, 6.1 Hz, is consistent with a H_3-C_3-C_4-C=O dihedral angle of *ca.* 180°, while the $^3J_{H3\text{-}CO(lactone)}$ value, 3.0 Hz, must be close to 40°. This data is consistent with a *cis* arrangement of the H-3 proton and the hydroxyl group at C-4, so the 3R,4R/3S,4S configuration for compound **3** was advanced. However, the assigned structure was still somewhat uncertain, so an independent synthesis of **3** was attempted. Condensation of N-phenyl homophthalimide and acetaldehyde gave **7** as a 2:1 mixture of the **E** and **Z** isomers that were resolved for structural analysis. From the chemical shift of the olefine proton and the methyl group in the ^{1}H-NMR spectrum recorded in C_6D_6, the geometry of the double bond in **7-E** and **7-Z** was derived. Because separating the two isomers proved rather difficult, the epoxidation reaction (95% HCO_2H/35% H_2O_2) was carried out on the alkene mixture. The epoxides obtained, **8-E** and **8-Z**, were readily resolved by column chromatography. As predicted, the **8-Z** isomer exhibited the aliphatic proton signals at δ 3.37 and 1.60, while the methyl doublet for the **8-E** isomer shifted downfield (δ 3.71) and the proton quartet upfield (δ 1.4).



On the assumption of stereospecific opening of the epoxides, it was anticipated that hydration of **8-Z** would lead to the racemic diol of configuration R,R/S,S (**9**)[10]. The attack of the exocyclic hydroxyl group on the C-1 carbonyl should give the lactone **3** with its exact stereochemistry. Unfortunately, any attempt at opening **8-Z** with hydroxide ion as the nucleophile proved fruitless, so acid catalysed opening was mandatory. The reaction of **8-Z** with TFA/H_2O gave **3** as the major product and the phthalide **10**, formed by attack of the tertiary hydroxyl group on

the C-1 carbonyl. The γ-lactone ring was realized from the carbonyl band in the IR spectrum (1762 cm^{-1}), in addition to the amide carbonyl and the band-II amide (1668 and 1532 cm^{-1}). On the other hand, the chemical shift of the aliphatic carbons, quaternary at δ 89.9 and tertiary at δ 72.2, are consistent with an exocyclic position of the latter. Under identical conditions, the opening of the epoxide **8-E** was a more complex reaction. From the mixture, a δ-lactone (**11**) and a γ-lactone (**12**) were isolated, their structures being established from spectroscopic data that correlated with those of their respective isomers (**3** and **10**).

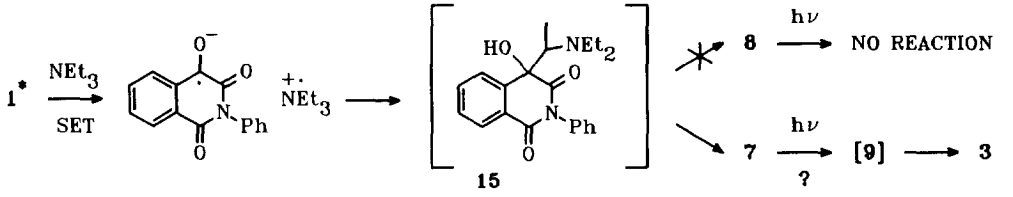




An ethyl radical of the triethylamine was assumed to be the source of the two carbon fragment incorporated into compound **3**, and molecular oxygen that of its additional oxygen atom. Confirmation of this assumption was obtained by irradiation of **1** under variable conditions: i) in the absence of amine, phthalimide **2** was the sole product obtained; ii) under strictly deoxygenated conditions, the reaction did no take place; iii) when tri-*n*-propyl amine was used instead of triethylamine, the expected δ-lactone **13** was isolated; iv) with N-methyl piperidine as the tertiary amine, the simplest δ-lactone **14** was isolated. Compound **13** was readily characterized from the loss of propionaldehyde under heating, as well as from the appearance of the -OCH-CH_2-CH_3 sequence in the ^{13}C-NMR (δ 84.2, 22.4 and 9.9) and ^{1}H-NMR spectra (δ 4.90, 1H, dd; 2.00 1H, and 1.68, 1H, m; and 1.08, 3H, t). The stereochemistry of **13** was established by analogy with **3**. The spectroscopic data for compound **14** were consistent with a methylene group at position 3 of the δ-lactone ring (GC/MS, parent peak at *m/z* 253, M^+ - H_2CO). In the IR spectrum, the band for the lactone carbonyl group was shifted to 1728 cm^{-1}, which can be attributed to the more planar heterocyclic ring occurring in the absence of the substituent at C-3.

The photochemical reaction of **1** to give the 3,4-dihydroisocoumarins **3**, **13** and **14** is obviously a complex process that evades detailed explanation. However, three key steps can be anticipated *viz.* i) C-C bond formation between the phthalonimide and the amine; ii) cleavage of the C-N bond to release a radical from the amine; iii) oxygenation and rearrangement to the lactone.

From available knowledge on the photochemistry of carbonyls in the presence of amines, an initial single-electron transfer step can be assumed.[11] The usual deprotonation of the acidic amine cation radical to the α-carbon radical may be followed by radical coupling to an intermediate such as **15**. Consistent with this mechanism, only the exocyclic α-radical seems to be formed in the asymmetrically substituted N-methyl piperidine.[12] This type of addition process is rarely observed in carbonyl compounds,[13] in contrast to aromatic hydrocarbons, particularly in intramolecular reactions.[14] The tendency of phthalimides and phthalonimide to undergo photoaddition under photoreductive conditions, however, is not exhibited by **1**. Since irradiation in methanol solution gives the double reduction product, N-phenyl homophthalimide, almost quantitatively.



The intermediate **15** can be regarded as a ß-amino carbonyl compound and its photochemistry to be relevant in the sense that it forms cyclopropane derivatives, which are rather unstable.[15] We considered the cleavage of the C-N bong potentially taking place via some type of displacement or elimination involving the hydroxyl group at C-4. Consequently, either the epoxide **8** or the ethylidene homophthalimide **7** could be a reaction intermediate. In fact, while **8** was found to be considerably photostable, the δ-lactone **3** was formed in the irradiation of **7-Z** in the presence of triethylamine/oxygen. Oxygenation of the double bond, via dioxetane, may lead to the dihydroxy derivative **9**, a common intermediate in the acid-catalyzed opening of **8**, which cyclizes thermally to **3**. Further work is required in order to confirm the participation of these intermediates in this intricate and unique photochemical reaction and to improve the yields of isocoumarins as to make the reaction synthetically valuable.

EXPERIMENTAL

General. All compounds were racemic. Melting points are given uncorrected. IR spectra (KBr) were recorded on a Perkin-Elmer IR-883 or a FT-IR 1760X spectrometer. ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker WP-200 SY spectrometer. Chemical shifts are given in ppm and referred to internal TMS. Mass spectra (70 eV, direct insertion) were obtained on a Hewlet-Packard 5988A instrument equipped with electron impact ionization. DTA-TG analyses were carried out on a Rigaku Thermoflex TG8110 using calcined Al_2O_3 as the internal standard reference and 10 K/min as a heating rate. Elemental analyses were performed at the CHN Service of the University of Málaga, Spain. Preparative irradiations were conducted by using a 125 W medium-pressure mercury lamp (General Electric H125/27) in a Pyrex immersion well reactor at near-room temperature. Prior to irradiation, solutions were bubbled with argon for 10 min.

General procedure for irradiation of N-phenyl phthalonimide (1) in benzene/tertiary amines: A solution of **1** (1 mmol) and amine (3 mmol) in benzene (150 ml) was irradiated at near room temperature. The reaction was monitored by GC/MS and allowed to proceed to over 80% conversion (2.5 h). The solvent was then removed *in vacuo* and the residue column chromatographed over silica gel (eluent: 2:3 EtOAc/Hexane). Further purification was achieved by preparative tlc (silica gel, 1:1 EtOAc/Hexane) with the following results: **from triethylamine**: **1** (38 mg, 15%), **2** (100 mg, 45%) and **3** (83 mg, 28%); **from tri-*n*-propylamine**: **1** (15 mg, 6%), **2** (89 mg, 40%) and **13** (62 mg, 20%); **from N-methyl piperidine**: **1** (25 mg, 10%), **2** (109 mg, 49%) and **14** (34 mg, 12%).

N-phenyl phthalimide (**2**): mp 199-200 °C (EtOH) (lit.[16], 205-206°C).

(3*RS*,4*RS*)-3,4-dihydro-4-hydroxy-3-methyl-4-(phenylcarbamoyl)-1*H*-2-benzopyran-1-one (**3**): Mp 193-5°C (dec) (Cl_4C). ^{1}H-NMR ($CDCl_3$) δ 9.20 (bs, 1H, NH), 7.92 (dd, 1H, J = 7.6 and 1.5Hz, H-8), 7.67 (m, 2H, H-2' and H-6'), 7.64 (dt, 1H, J = 7.6, 7.6 and 1.5Hz, H-6), 7.45 (dt, 1H, J = 7.6, 7.6 and 1.3Hz, H-7), 7.40 (m, 3H, H-5, H-3' and H-5'), 7.19 (m, 1H, H-4'), 5.16 (q, 1H, J = 6.5Hz, H-3), 4.64 (bs, 1H, OH) and 1.47 (d, 3H, J = 6.5Hz, CH_3). ^{13}C-NMR ($CDCl_3$) δ 168.3 (CO amide), 165.2 (C-1), 140.9 (C-4a), 136.8 (C-1'), 135.1 (C-6), 130.3 (C-8), 129.9 (C-7), 129.2 (C-3' and C-5'), 126.4 (C-5), 125.2 (C-4'), 123.9 (C-8a), 119.9 (C-2' and C-6'), 79.2 (C-3), 75.3 (C-4) and 14.4 (CH_3). IR(ν, cm^{-1}) 3482, 3329, 1720, 1683, 1529. EI-MS, m/z(%) 297 (M^+, 14), 253 (8), 178 (46), 160 (100), 134 (53), 105 (57). Anal. Calcd. for C_{17} H_{15} N O_4: C, 68.69; H, 5.05; N, 4.71. Found: C, 68.73; H, 5.00; N, 4.67.

(3*RS*,4*RS*)-3,4-dihydro-4-hydroxy-3-ethyl-4-(phenylcarbamoyl)-1*H*-2-benzopyran-1-one (**13**): Mp 191-195°C (dec) (Cl_4C). ^{1}H-NMR ($CDCl_3$) δ 9.23 (bs, 1H, NH), 7.93 (dd, 1H, J = 7.7 and 1.4Hz, H-8), 7.65 (m, 2H, H-2' and H-6'), 7.61 (dt, 1H, J = 7.7, 7.7 and 1.4Hz, H-6), 7.43 (dt, 1H, J = 7.7, 7.7 and 1.4Hz, H-7), 7.40 (m, 3H, H-5, H-3' and H-5'), 7.19 (m, 1H, H-4'), 4.90 (dd, 1H, J = 10.3 and 2.7Hz, H-3), 4.78 (bs, 1H, OH), 2.00 (m, 1H, CH_2), 1.68 (m, 1H, CH_2) and 1.08 (t, 3H, J = 7.3Hz, CH_3). ^{13}C-NMR ($CDCl_3$) δ 168.4 (CO amide), 164.9 (C-1), 141.1 (C-4a), 136.8 (C-1'), 135.0 (C-6), 130.5 (C-8), 130.0 (C-7), 129.3 (C-3' and C-5'), 126.3 (C-5), 125.3 (C-4'), 124.4 (C-8a), 120.0 (C-2' and C-6'), 84.2 (C-3), 75.5 (C-4), 22.4 (CH_2) and 9.9 (CH_3). IR(ν, cm^{-1}) 3343, 1704, 1678, 1526. EI-MS, m/z(%) 311 (M^+, 8), 253 (16), 224 (3), 192 (54), 174 (88), 134 (100), 105 (88). Anal. Calcd. for C_{18} H_{17} N O_4: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.58; H, 5.61; N, 4.50.

3,4-dihydro-4-hydroxy-4-(phenylcarbamoyl)-1*H*-2-benzopyran-1-one (**14**): Mp 189-192 °C (dec) (Cl_4C). ^{1}H-NMR ($CDCl_3$) δ 9.14 (bs, 1H, NH), 7.93 (d, 1H, J = 7.5Hz, H-8), 7.57 (m, 3H, H-6, H-2' and H-6'), 7.35 (m, 4H, H-5, H-7, H-3' and H-5'), 7.15 (m, 1H, H-4'), 5.65 (bs, 1H, OH), 4.85 (d, 1H, J = 11.5Hz, CH_2), 4.45 (d, 1H, J = 11.5Hz, CH_2). ^{13}C-NMR (Cl_3CD) δ 168.5 (CO amide), 166.7 (C-1), 141.2 (C-4a), 137.0 (C-1'), 135.1 (C-6), 131.0 (C-8), 130.4 (C-7), 129.3 (C-3' and C-5'), 126.6 (C-5), 125.5 (C-4'), 124.3 (C-8a), 120.2 (C-2' and C-6'), 83.9 (C-3) and 76.0 (C-4). IR(ν, cm^{-1}) 3360, 1728, 1676, 1531. EI-MS, m/z(%) 283 (M^+, 10), 253 (5), 164 (60), 146 (100), 134 (64), 105 (79). Anal. Calcd. for C_{16} H_{13} N O_4: C, 67.84; H, 4.59; N, 4.95. Found: C, 67.56; H, 4.41; N, 5.11.

Photoreduction of N-phenyl phthalonimide in methanol. A solution of **1** (1 mmol) in methanol was irradiated until complete decolorization (2 h). Tlc analysis of the reaction products revealed a single component. Removal of the solvent and crystallization from EtOAc gave N-phenyl homophthalimide in a 86% yield. Mp 174-178 °C (lit.[17], mp 188).^{1}H-RMN ($CDCl_3$) δ 8.23 (dd, J=7.7 and 1.5 Hz, H-8), 7.64 (dt, J=7.7, 7.7 and 1.5 Hz, H-6), 7.48 (m, H-7, H-2', H-4' and H-6'), 7.34 (d, J=7.7 Hz, H-5), 7.20 (m, H-3' and H-5') and 4.22 (s, 2H, H-4). ^{13}C-RMN (Cl_3CD) δ 169.7 (C-3), 164.9 (C-1), 135.0 (C-4a) , 134.4 (C-1'), 133.8 (C-6), 129.3 (C-8), 129.2 (C-3' and C-5'), 128.5 (C-4'), 128.4 (C-2' and C-6'), 127.7 (C-7), 127.2 (C-5), 125.4 (C-8a) and 36.8 (C-4). EI-MS m/z(%) 237 (M^+; 100), 209 (31). IR(ν, cm^{-1}) 1715, 1670. Anal. Calcd. for $C_{15}H_{11}NO_2$: C, 75.94; H, 4.67; N, 5.90. Found: C, 75.74; H, 4.81; N, 5.88.

(Z,E)-4-ethylidene-N-phenyl-homophthalimide (7): To a suspension of N-phenyl-homophthalimide (0.07 mol) and acetaldehyde (0.14 mol) a catalytic amount of piperidine (1 μl) was added. The mixture was refluxed for 4 h; after cooling, a thick precipitate was obtained, characterized as a mixture of **7-E** and **Z** in a 1:2 ratio (84% yield). IR(ν, cm^{-1}) 1733, 1712, 1685, 1670. EI-MS, m/z(%) 263 (M^+, 100), 235 (29), 115 (57). Anal. Calcd. for $C_{17}H_{13}NO_2$: C, 77.57; H, 4.94; N, 5.32. Found: C, 77.51; H, 4.87; N, 5.28.
For analytical purposes the isomers were separated on a small scale by preparative tlc (silica gel) after several elutions with 1:6 EtOAc/Hexane. The upper band was extracted and crystallized from EtOH (**7-Z**); the lower band contained the mixture of isomers, were **7-E** was prevalent.

Z-4-ethylidene-N-phenyl-homophthalimide (7-Z): Mp 260-262 °C (EtOH). ^{1}H-NMR (C_6D_6) δ 8.37 (d, 1H, J=8.0 Hz, H-8), 7.12 (m, 8H, ar-H), 6.62 (q, 1H, J=7.5, H-1") and 2.17 (d, 3H, J=7.5 Hz, H-2"). ^{13}C-NMR (Cl_3CD) δ 164.4 and 164.3 (C-1 and C-3), 146.0 (C-1"), 135.4 (C-4a), 134.8 (C-1'), 133.8 (C-6), 129.5, 129.3, 128.7, 128.5), 128.2 (C-7, C-8, C-2', C-3', C-4', C-5', C-6'), 126.0 (C-8a), 124.1 (C-4), 121.9 (C-5) and 17.3 (C-2").

E-4-ethylidene-N-phenyl-homophthalimide (7-E): ^{1}H-NMR (C_6D_6) δ 8.40 (d, 1H, J=7.8 Hz, H-8), 7,38 (q, 1H, J=7.5 Hz, H-1"), 7.14 (m, 8H, ar-H) and 1.70 (d, 3H, J=7.5 Hz, H-2").

Epoxidation of 7: To a stirred solution of the mixture of alkenes **7-E** and **Z** (2.63 g, 0.01 mol) in 10 ml of 98% formic acid, 2 ml of 35% H_2O_2 was added, and the mixture was warmed gently at 45°C for 8 h. After addition of a saturated aqueous NaCl solution, the mixture was extracted with Cl_3CH and the organic layer washed with aqueous $NaHCO_3$. Open column chromatography (silica gel, 3:7 EtOAc/Hexane) followed by preparative tlc was used to separate the epoxides, that were crystallized from EtOAc (**8-Z**, 27%, and **8-E** 13%).

(Z)-4,1"-epoxy-4-ethyl-N-phenyl-homophthalimide (8-Z): Mp 189-191 °C (EtOAc). ^{1}H-NMR ($CDCl_3$) δ 8.23 (dd, 1H, J=7.7 and 1.5Hz, H-8), 7.69 (dt, 1H, J=7.7, 7.7, and 1.5Hz, H-6), 7.53 (dt, 1H, J=7.7, 7.7 and 1.5Hz, H-7), 7.45 (m, 3H, H-2', H-4' and H-6'), 7.34 (dd, 1H, J=7.7 and 1.5Hz, H-5), 7.20 (m, 2H, H-3' and H-5'), 3.37 (q, 1H, J=5.2Hz, H-1"), 1.60 (d, 3H, J=5.2Hz, H-2"). ^{13}C-NMR (Cl_3CD) δ 167.4 (C-3), 163.8 (C-1), 136.3 (C-4a), 134.8

(C-1'), 134.5 (C-6), 129.3 (C-8, C-3' and C-5'), 129.0 (C-7), 128.8 (C-4'), 128.5 (C-2' and C-6'), 126.8 (C-8a), 122.4 (C-5), 69.3 (C-1"), 59.0 (C-4) and 12.4 (C-2"). IR(ν, cm^{-1}) 1735, 1690. EI-MS, m/z(%) 279 (M^+, 81), 263 (6), 224 (19), 174 (15), 132 (29), 104 (100).

(E)-4,1"-epoxy-4-ethyl-N-phenyl-homophthalimide (8-E): Mp 199-201 °C (EtOAc). ^{1}H-NMR ($CDCl_3$) δ 8.29 (dd, 1H, J=7.6 and 1.4Hz, H-8), 7.72 (dt, 1H, J=7.6, 7.6, and 1.4Hz, H-6), 7.58 (dt, 1H, J=7.6, 7.6 and 1.4Hz, H-7), 7.47 (m, 3H, H-2', H-4' and H-6'), 7.40 (dd, 1H, J=7.6 and 1.4Hz, H-5), 7.22 (m, 2H, H-3' and H-5'), 3.71 (q, 1H, J=5.4Hz, H-1"), 1.40 (d, 3H, J=5.4Hz, H-2"). ^{13}C-NMR (Cl_3CD) δ 169.3 (C-3), 163.9 (C-1), 134.6 (C-1'), 133.2 (C-6), 132.9 (C-4a), 129.7 (C-8), 129.2 (C-3' and C-5'), 129.0 (C-7), 128.8 (C-4'), 128.4 (C-2' and C-6'), 128.0 (C-8a), 125.7 (C-5), 66.0 (C-1"), 59.4 (C-4) and 11.8 (C-2"). IR(ν, cm^{-1}) 1730, 1685. EI-MS, m/z (%) 279 (M^+, 93), 263 (9), 224 (17), 174 (15), 132 (30), 104 (100). Anal. Calcd. for $C_{17}H_{13}NO_3$ (Mixture of **8Z/8E**): C, 73.11; H, 4.69; N, 5.01. Found: C, 72.91; H, 4.75; N, 4.92.

Hydrolysis of 8-Z. A solution of **8-Z** (70 mg, 0.25 mmol) in 10:1 TFA/H_2O was refluxed for 12 h. After removal of the solvent and preparative tlc (silica gel, 35:65 EtOAc/hexane), **3** (11 mg; 14%) and **10** (19 mg; 26%) were isolated.

(3*RS*,1"*RS*)-3-(1"-hydroxyethyl)-3-(phenylcarbamoyl)-1(3*H*)-benzofuranone (10): Mp 188-9° C. ^{1}H-RMN (Cl_3CD) δ 8.38 (bs, 1H, N-H), 7.94 (dd, 1H, J=7.5 and 2.3Hz, H-7), 7.89 (dd, 1H, J=7.5 and 2.3Hz, H-4), 7.72 (dt, 1H, J=7.5, 7.5Hz and 2.3Hz, H-5), 7.59 (dt, 1H, J=7.5, 7.5 and 2.3Hz, H-6), 7.51 (m, 2H, H-2'and H-6'), 7.29 (m, 2H, H-3' and H-5'), 7.12 (m, 1H, H-4'), 4.48 (q, 1H, J=6.4Hz, H-1"), 3.03 (bs, 1H, OH) and 1.09 (d, 3H, J=6.4Hz, H-2"). ^{13}C-RMN (Cl_3CD) δ 168.9 (CO amide), 166.7 (C-1), 146.6 (C-3a),136.4 (C-1'), 135.1 (C-5), 130.3 (C-7), 129.0 (C-3' and C-5'), 125.9 (C-4), 125.3 (C-4'), 124.3 (C-6), 120.4 (C-2' and C-6'), 89.9 (C-3), 72.2 (C-1") and 17.1 (C-2"). IR(ν, cm^{-1}) 3454, 3279, 1762, 1668, 1532. EI-MS m/z(%) 297 (M^+ ;4), 253 (67), 235 (4), 178 (23), 160 (79), 134 (95), 105 (70), 93 (100). Anal. Calcd. for $C_{17}H_{15}NO_4$: C, 68.69; H, 5.05; N, 4.71. Found: C, 68.49; H, 5.24; N, 4.67.

Hydrolysis of 8-E: Was carried out as above to obtain **11** (10 mg; 13%) and **12** (19 mg; 25%).

(3*RS*,4*SR*)-3,4-dihydro-4-hydroxy-3-methyl-4-(phenylcarbamoyl)-1*H*-2-benzopyran-1-one (11): Amorphous powder, ^{1}H-NMR ($CDCl_3$) δ 8.18 (dd, 1H, J=7.5 and 2.3Hz, H-8), 7.8-7.2 (m, 8H, ar-H), 4.79 (q, 1H, J=6.5Hz, H-3), 3.6 (bs, 1H, OH) and 1.53 (d, 3H, J=6.5Hz, CH_3). ^{13}C-NMR ($CDCl_3$) δ 168.3 (C=O amide), 166.4 (C-1), 149.5 (C-4a), 136.7 (C-1'), 135.4 (C-6), 130.9 (C-8), 129.6 (C-7), 129.2 (C-3' and C-5'), 125.6 (C-5), 125.2 (C-4'), 123.9 (C-8a), 120.6 (C-2' and C-6'), 79.9 (C-3), 74.0 (C-4) and 15.3 (CH_3). IR(ν, cm^{-1}) 3373, 1717, 1680, 1528. EI-MS, m/z(%) 297 (M^+, 7), 253 (3), 178 (42), 160 (100), 105 (30). Anal. Calcd. for $C_{17}H_{15}NO_4$: C, 68.69; H, 5.05; N, 4.71. Found: C, 68.49; H, 5.24; N, 4.67.

(3*RS*,1"*SR*)-3-(1"-hydroxyethyl)-3-(phenylcarbamoyl)-1(3*H*)-benzofuranone (12): Oil, ^{1}H-RMN (Cl_3CD) δ 8.26 (bs, 1H, N-H), 7.97 (d, 1H, J=8.0Hz, H-7), 7.90 (d, 1H, J=8.0Hz, H-4), 7.74 (dt, 1H, J=8.0, 8.0 and 1.6Hz, H-5), 7.59 (t, 1H, J=8.0Hz, H-6), 7.50 (m, 2H, H-2' and H-6'), 7.30 (m, 2H, H-3' and H-5'), 7.12 (m, 1H, H-4'), 4.63 (q, 1H, J=6.3Hz, H-1") and 1.31 (d, 3H, J=6.3Hz, CH_3). ^{13}C-RMN (Cl_3CD) δ 168.9 (CO amide), 166.5 (C-1), 145.9 (C-3a), 136.1 (C-1'), 135.1 (C-5), 130.3 (C-7), 129.2 (C-3' and C-5'), 125.7 (C-4), 125.5 (C-4'), 124.2 (C-6), 120,4 (C-2' and C-6'), 89.0 (C-3), 71.2 (C-1") and 17.3 (CH_3). IR(ν, cm^{-1}) 1760, 1667, 1539. EI-MS, m/z(%) 297 (M^+, 6), 253 (100), 224 (15), 178 (22), 160 (69), 134 (32), 105 (50), 93 (96). Anal. Calcd. for C_{17} H_{15} N O_4: C, 68.69; H, 5.05; N, 4.71. Found: C, 68.52; H, 5.17; N, 4.69.

Synthesis of 3-phenylcarbamoyl phthalide (5)[8]. To a cooled solution (0°C) of homophthalic acid (500 mg, 2.8 mmol) in 4ml of conc. H_2SO_4, NaN_3 (202 mg, 3.1 mmol) was added in several portions. After 12 h the reaction was extracted with Et_2O. Removal of the solvent afforded 3-carbamoyl phtalide (**6**) that was crystallized from EtOH (222 mg, 45%). Mp 184-186°C (lit.[8], mp 185°C) ^{1}H-RMN ($CDCl_3$:CD_3OD) δ 7.81 (d, 1H, J=7.3Hz, H-7), 7.79 (d, 1H, J=7.5Hz, H-4), 7.66 (dd, 1H, J=7.5 and 7.3Hz, H-5), 7.51 (t, 1H, J=7.3Hz , H-6) and 5.69 (s, 1H, H-3). ^{13}C-RMN ($CDCl_3$:CD_3OD) δ 170.0 (CO amide), 169.4 (C-1), 145.0 (C-3a), 134.9 (C-5), 130.0 (C-7), 125.5 (C-4), 123.8 (C-7a), 123.5 (C-6) and 78.3 (C-3). IR(ν, cm^{-1}) 1769, 1677, 1611. EI-MS, m/z(%) 177 (M^+, 1), 134 (100), 133 (93), 105 (87).

A mixture of **6** (44 mg, 0.25 mmol), aniline (0.035 ml, 0.4 mmol) in 3 ml of xylene were refluxed for 4 h. Removal of the solvent and preparative tlc (silica gel, 7:3 EtOAc/Hexane) gave **5** (10 mg). Mp 165-168°C (EtOH). ^{1}H-RMN ($CDCl_3$) δ 8.18 (bs, 1H, N-H), 7.97 (dd, 1H, J=7.8 and 1.5Hz, H-7), 7.91 (d, 1H, J=7.8Hz, H-4), 7.74 (dt, 1H, J=7.8, 7.8 and 1.5Hz, H-5), 7.58 (t, 1H, J=7.8Hz, H-6), 7.52 (m, 2H, H-2' and H-6'), 7.30 (m, 2H, H-3' and 5'), 7.12 (m, 1H, H-4') and 5.89 (s, 1H, H-3). ^{13}C-RMN ($CDCl_3$) δ 169.2, 164.4 (CO), 145.1 (C-3a), 139.7 (C-1'), 135.1 (C-5), 130.2 (C-7), 129.1 (C-3' and C-5'), 125.8 (C-4), 125.3 (C-4'), 124.0 (C-6 and C-7a), 120.2 (C-2' and C-6') and 78.3 (C-3). IR(ν, cm^{-1}) 1774, 1669, 1536. EI-MS, m/z(%) 253 (M^+, 19), 134 (100), 105 (31).

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