Synthetic Studies on *O*-Heterocycles *via* Cycloadditions. Part 3.[1] Regiochemical and Mechanistic Questions in Reactions of Polarised Diaryl Carbonyl Ylides

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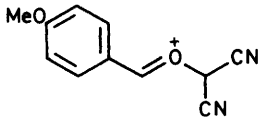
The unsymmetrical diaryloxiranes (**9**), (**24**), (**25**), and (**26**) undergo smooth cycloaddition with electron-deficient olefins under thermal or photochemical initiation, apparently *via* polarised carbonyl ylide intermediates. With unsymmetrical dipolarophiles the additions are surprisingly unregioselective; thus the oxirane (**9**) gives both adducts (**19**) and (**20**), (**24**) gives (**36**) and (**37**), (**25**) forms (**34**) and (**35**), and (**26**) affords the pairs (**38**) and (**39**), and (**40**) and (**41**). The structural variations in the intermediate series (**42**), (**43**), and (**44**) suggest a marked variation in frontier orbital levels, which is however not paralleled by changes in regioselectivity; formulation of (**42**)–(**44**) as 1,3-diradicals cannot be excluded.

In earlier work [1] we outlined the potential value of cycloaddition reactions in the synthesis of *O*-heterocycles, particularly in relation to natural lignans. We demonstrated the generation and trapping of a diaryl carbonyl ylide oxygenated in both aryl rings. However such a reaction will be of synthetic use only if the aryls are identically substituted, or if a symmetric dipolarophile is employed. If the aryls are to be different they must differ in such a way as to promote regioselectivity in the cycloaddition process. We thus set out to examine the reactions of strongly polarised ylides.

Highly polarised ylides of type (**1**) ('push-pull' ylides[2]) are readily generated from the corresponding oxiranes; in an extreme case, one such ylide (**2**) has been isolated as a solid.[3] All the cases[4] known to us at the outset of this work of intramolecular cycloaddition of carbonyl ylides to unsymmetric dipolarophiles are highly regioselective. Such regioselectivity has been rationalised in terms of control by the HOMO (dipole)–LUMO (dipolarophile) interaction.[5] We therefore expected that ylides of type (**3**) would undergo regioselective additions to electron-deficient olefins. It was envisaged that the directive nitro group could be readily transformed, for lignan synthesis, into the phenolic hydroxy group.

As a start we looked briefly at the viability of thermal and photochemical electrocyclic opening of the oxirane (**4**). This compound was obtained by the reaction of *p*-nitrobenzaldehyde with hexamethylphosphorous triamide, and on heating at 170 °C formed the ylide (**5**) which was efficiently trapped with dimethyl fumarate to afford a single adduct (**6**) (66%). The ^{1}H NMR spectrum of (**6**) shows methoxy resonances at δ($CDCl_3$) 3.82 and 3.23, *anti* and *syn* to aryl, respectively, and 2-H and 5-H signals at δ 5.49 and 5.28, demonstrating the lack of symmetry in the structure. Photochemical formation of the ylide (**5**) was also possible; irradiation of the oxirane (**4**) with 350 (max) nm light in the presence of maleic anhydride afforded the adduct (**7**) (59%), with δ($CDCl_3$) 5.58 (2-H, 5-H) and 4.40 (3-H, 4-H). Irradiation at either signal, in a nuclear Overhauser enhancement experiment (NOE), lead to strong (> 10%) enhancement of the other band. The *syn*-structure (**7**) is thus indicated, arising from *endo* selective cycloaddition of the ylide (**5**) in the more stable *exo*–*exo* conformation shown. Similar irradiation in the presence of dimethyl acetylenedicarboxylate (DMAD) afforded the *syn*-dihydrofuran (**8**) (72%).

Attention was then turned to the more interesting case of 2-(*p*-methoxyphenyl)-3-(*p*-nitrophenyl)oxirane (**9**). Both thermally and photochemically induced cycloadditions were shown to be viable using dimethyl fumarate and dimethyl acetylenedicarb-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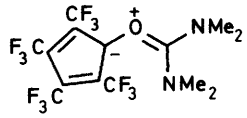
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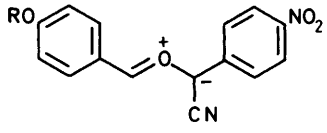
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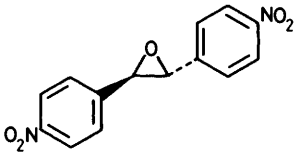
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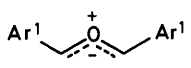
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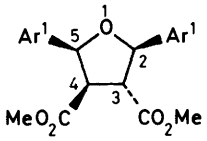
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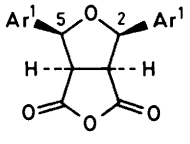
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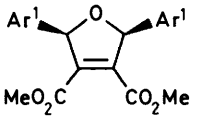
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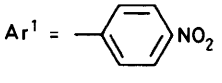

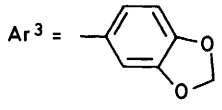

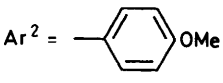

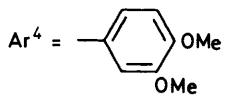

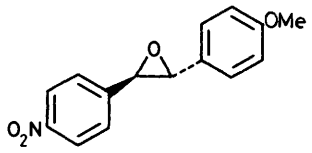
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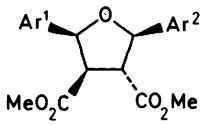
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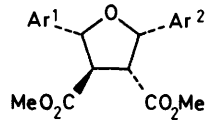
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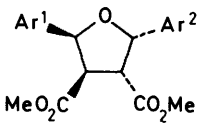
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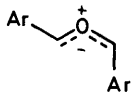
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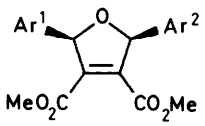
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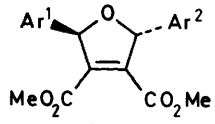
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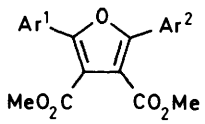
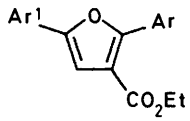
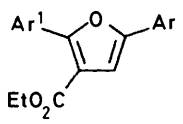

(16)

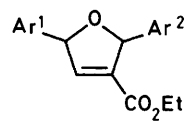
oxylate. In the first case, thermal reaction at 217 °C afforded a mixture of isomers (**10**) and (**11**) in low yield; on irradiation a mixture of three isomers (**10**), (**11**), and (**12**) was formed (total yield 62%). Although these were not separated, the ^{1}H NMR data allow clear assignments of stereochemistry; thus (**10**) and (**11**) each have one methoxycarbonyl shielded by *syn*-aryl (δ 3.24, 3.26) while (**12**) has two (δ 3.33, 3.35). The 2-H, 5-H signals indicate *cis*-aryls in (**10**) and (**11**) (δ 4.98–5.33) but *trans*-aryls in (**12**) (δ 5.70, 6.04). The ylide intermediate thus reacts in both *exo–exo* [*cf.* (**5**)] and *exo–endo* conformations (**13**), and shows little preference for Ar^1 or Ar^2 overlap with methoxycarbonyl in the transition state. The related reaction with DMAD afforded the two possible dihydrofurans (**14**) and (**15**) (44 and 28% respectively), again with 2-H, 5-H more deshielded in the *trans*-isomer. Dehydrogenation with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) afforded the diarylfuran diester (**16**) (50%).

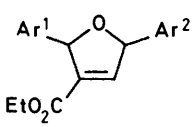
An unsymmetric dipolarophile was then investigated. The oxirane (**9**) was irradiated (350 nm) with excess of ethyl propiolate, and the product dihydrofurans were dehydrogenated (DDQ) without separation, for an expeditious solution to the regiochemical question. Both possible furans (**17**) and (**18**) were obtained, in a ratio of 9 : 11; in isomer (**18**) the four nitrophenyl ^{1}H NMR signals coincided at δ 8.31 (deshielding of the β-H_2 by (O_2Et), and furan 3-H absorbed at δ 7.00, whereas in isomer (**17**) the nitrophenyl protons appeared as two doublets, δ 7.88 and 8.24 (*J* 9 Hz), with the furan proton at δ 7.31. TLC and NMR examination of the dihydrofuran intermediates (**19**) and (**20**) suggested that both stereoisomers of each were present, although a reliable estimate of proportions could not be made. A similar experiment with 2-(3,4-methylenedioxyphenyl)-3-(4-nitrophenyl)oxirane (**21**) also gave two isomeric furans (**22**) and (**23**) (9 : 11).

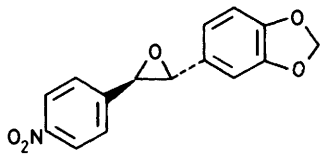
It was thus clear that the carbonyl ylides derived from (**9**) and (**14**) react non-regiospecifically with the chosen electron-deficient alkene. It appeared possible at this stage that in an


(**17**) Ar = Ar^2
(**22**) Ar = Ar^3

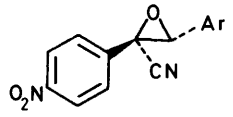

(**18**) Ar = Ar^2
(**23**) Ar = Ar^3


(**19**)

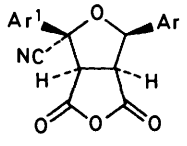

(**20**)

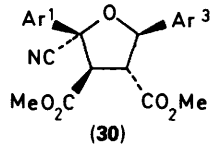

(**21**)

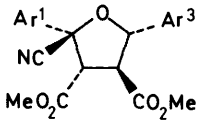
effort to induce a highly polarised ylide, the dipole frontier orbital energies had been lowered so that the HOMO (dipole) was no longer the controlling feature but was balanced by a LUMO (dipole)–HOMO (dipole) interaction, of opposite direction. We thus examined another system with a further

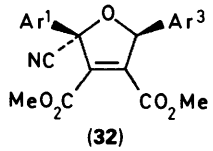

(**24**) Ar = Ar^2
(**25**) Ar = Ar^3
(**26**) Ar = Ar^4

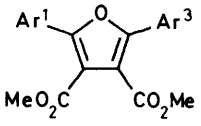

(**27**)


(**28**) Ar = Ar^3
(**29**) Ar = Ar^2


(**30**)


(**31**)


(**32**)


(**33**)

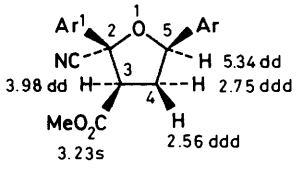
electron-withdrawing function to alter substantially the frontier orbital levels.

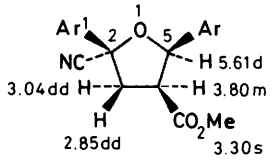
The three oxiranes (**24**)–(**26**) were prepared by epoxidation of the corresponding (*E*)-cyanostilbenes (formed by base-catalysed

condensation of 4-nitrophenylacetonitrile with the appropriate aromatic aldehyde). The related stilbene oxide (**27**) was also synthesised.

The viability of cycloadditions involving the epoxides (**24**)–(**26**) was readily demonstrated. Thus refluxing (**25**) in xylene with maleic anhydride gave one isomer only of the anhydride (**28**) (65%), and a similar reaction with (**24**) afforded adduct (**29**) (68%). Photochemical induction was also successful; irradiation of (**24**) in chloroform with 300 (max) nm light, in the presence of maleic anhydride, also gave (**29**) (65%). The structure and stereochemistry shown for (**29**) were demonstrated by NMR spectroscopy and were confirmed by a single-crystal X-ray analysis.[6] The oxirane (**25**) also reacted smoothly with dimethyl fumarate at 110 °C to yield a mixture (94%) of the adducts (**30**) and (**31**) (2:3); the stereochemistry of these isomers was deduced from their ^{1}H NMR spectra (Experimental), using similar criteria to those employed above, and by comparisons with data for the known diphenyl analogues.[4b] The thermal reaction (120 °C) of (**25**) with DMAD gave a single product (**32**) (90%), which other results indicated was probably the *syn*-isomer. Refluxing the dihydrofuran (**32**) with triethylamine in methanol led readily to the diarylfuran (**33**) with loss of hydrogen cyanide.

Stilbene oxide (**25**) was then refluxed in toluene with methyl acrylate over 68 h. HPLC analysis showed the formation of two products which were isolated chromatographically and proved to be the pair of regioisomers (**34**) and (**35**). The structures were





(**34**) Ar = Ar^3
(**36**) Ar = Ar^2
(**38**) Ar = Ar^4

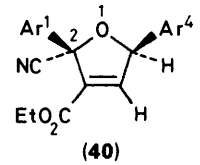
J	3,4^a	7.6
	3,4^b	8.5
	5,4^a	9.7
	4^a,4^b	13.2

(**35**) Ar = Ar^3
(**37**) Ar = Ar^2
(**39**) Ar = Ar^4

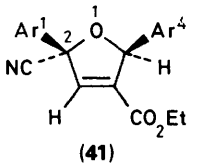
J	3^a,3^b	13.5
	3^a,4	7.6
	3^b,4	8.4
	4,5	8.5

NMR data are shown for (**34**) and (**35**) (δ_1 ppm; *J*/Hz).

assigned from the ^{1}H NMR data shown, and again confirmed by X-ray analysis of (**34**).[6] The isolated yields of (**34**) and (**35**) were 24 and 30% respectively. Each regioisomer is formed stereoselectively, from an *exo–exo* ylide conformation, with a *syn* methoxycarbonyl–aryl relation. A similar result was obtained using the oxirane (**24**), yielding a mixture (75%) of adducts (**36**) and (**37**), with similar ^{1}H NMR data to those of their analogues (**34**) and (**35**). Compound (**37**) was crystallised from the mixture; the structure followed NMR data, but was put beyond doubt by an X-ray analysis.[6] The oxirane (**26**) underwent a parallel reaction to give (**38**) and (**39**), 22 and 25% isolated yield, respectively. Using an alternative unsymmetrical dipolarophile, ethyl propiolate also led to a mixture of regioisomers (**40**) and (**41**), 30 and 36% yield after separation. The regioisomers were distinguished by the demonstration of an NOE (> 5%) between 4-H and 5-H in isomer (**40**).



(**40**)

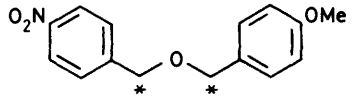


(**41**)

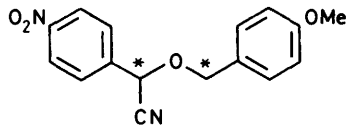
* We thank Professor W. Eberbach for bringing this to our attention.

In contrast to the facile formation of adducts from the oxiranes (**24**)–(**26**), we were unable to find any conditions, thermal or photochemical (direct irradiation, acetophenone or dicyanonaphthalene sensitisation), under which the oxirane (**27**) could be induced to yield adducts with electron-deficient alkenes.

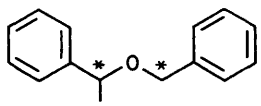
Thus in summary we have observed that neither intermediates of type (**42**) nor (**43**) undergo cycloaddition to electron-deficient alkenes with any marked degree of regioselectivity. Stereoselectivity was observed in some cases, but not all. The reactions



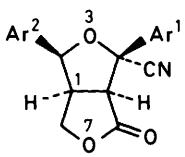
(**42**)



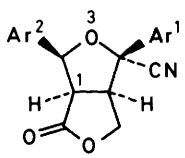
(**43**)



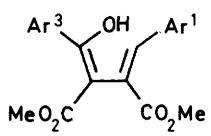
(**44**)



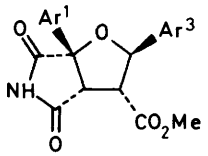
(**45**)



(**46**)



(**47**)



(**48**)

appear to be under kinetic control; thus adducts (**34**) and (**35**) do not equilibrate on heating. Non-regiospecific cycloadditions of carbonyl ylides have been described before in intramolecular cases,[7] where other factors may intervene. However, after our work we became aware of one further intermolecular case,[8] involving ylides of type (**44**).*

The variation in substitution over the three structures (**42**)–(**44**) suggests that there would be a marked variation in frontier orbital levels. It is difficult to reconcile this qualitative expectation with the lack of significant difference in regioselection between the three types, and appropriate MO calculations of HOMO/LUMO levels would clarify the situation. The present results are alternatively consonant with the formulation of intermediates (**42**)–(**44**) as 1,3-diradicals; such stereoselectivity as was observed could have arisen from (*i*) the preferred *exo–exo*-conformation of the intermediate, and (*ii*) favourable secondary interactions between aryl and ester functions, independent of the nature of the reacting sites.

Although mechanistic matters remain unsettled it is clear that our hope of obtaining a convenient and specific route to 2,5-

diaryltetrahydrofurans useful in natural product synthesis was frustrated by the unlooked for lack of regioselection.

Some preliminary investigation of the chemistry of certain adducts was made. Thus the anhydride (**29**) could be reduced to the lactones (**45**) and (**46**) with sodium borohydride, with a small preference (3:2) for the former. The diesters (**30**) and (**31**) on treatment with sodium methoxide in dimethyl sulphoxide at room temperature eliminated hydrogen cyanide to yield the dienol (**47**), but under less basic conditions (sodium methoxide–methanol) afforded the imide (**48**), with epimerisation α to the methoxy carbonyl group.

Experimental

For generalisations, see Part 1.[1] Irradiation using 350 (max) nm light was carried out in a Rayonet RPR-204 reactor, using Rul 3 500 Å lamps, and with 300 (max) nm light a Rayonet RPR-100 reactor with RPR 3 000 Å lamps was employed. NMR coupling constants are in Hz.

Dimethyl-2,5-Bis(p-nitrophenyl)tetrahydrofuran-3,4-dicarboxylate (**6**).—*trans*-2,3-Bis (*p*-nitrophenyl)oxirane[9] (3.5 g) was heated with dimethyl fumarate (4.0 g) in dry diglyme (50 cm^3) at 170 °C under nitrogen for 36 h. The solvent was evaporated off and the residue recrystallised from ethyl acetate–light petroleum to yield the title diester, stereoisomer (**6**)[10] (3.45 g, 66%), m.p. 148.5–149 °C (Found: M^+, 430.102. Calc. for $C_{20}H_{18}O_9N_2$: *M* 430.101); δ 3.23 (3 H, s, 4-CO_2Me), 3.70 (2 H, m, 3- and 4-H), 3.82 (3 H, s, 3-CO_2Me), 5.28 (1 H, d, *J* 8, 2-H), 5.49 (1 H, d, *J* 8, 5-H), 7.66 (2 H, d, *J* 9, 5-ArH$^{\beta}$), 7.86 (2 H, d, *J* 9, 2-ArH$^{\beta}$), 8.29 (2 H, d, *J* 9, 5-ArH$^{\alpha}$), and 8.36 (2 H, d, *J* 9, 2-ArH$^{\alpha}$) (throughout, H$^{\alpha}$ and H$^{\beta}$ are the 2,6 and 3,5 protons, respectively, of the aromatic substituents).

2,5-*Bis*(p-*nitrophenyl*)*tetrahydrofuran*-3,4-*dicarboxylic Anhydride*.—*trans*-2,3-Bis(*p*-nitrophenyl)oxirane (1.0 g) and maleic anhydride (1.0 g) in dry chloroform (180 cm^3) were irradiated (350 nm) through Pyrex for 36 h. The solvent was evaporated off, and the residue was recrystallised from chloroform–light petroleum to yield the *title anhydride*, stereoisomer (**7**) (0.79 g, 59%) (Found: C, 56.3; H, 3.55%; *m/z* 384.060. $C_{18}O_{12}N_2O_8$ requires C, 56.2; H, 3.2%; *M*, 384.059); ν_{max}(KBr) 1 855, 1 780, 1 610, 1 520, and 1 355 cm^{-1}; δ[$(CD_3)_3SO$] 4.40 (2 H, m, 3- and 4-H), 5.58 (2 H, d, *J* 5, 2- and 5-H), 7.81 (4 H, d, *J* 9, ArH$^{\beta}$), and 8.28 (4 H, d, *J* 9, ArH$^{\alpha}$).

Dimethyl-2,5-Bis(p-*nitrophenyl*)-2,5-*dihydrofuran*-3,4-*dicarboxylate* (**8**).—*trans*-2,3-Bis(*p*-nitrophenyl)oxirane (0.5 g) and dimethyl acetylenedicarboxylate (0.2 g) in dry acetonitrile (8 cm^3) were irradiated (350 nm) through Pyrex for 22 h. Evaporation and recrystallisation from ethanol–light petroleum gave the *title compound*, stereoisomer (**8**) (0.54 g, 72%), m.p. 183–185 °C (Found: C, 55.9; H, 3.75%; *m/z* 428.087. $C_{20}H_{16}N_2O_9$ requires C, 56.05; H, 3.75%; M^+, 428.086); ν_{max}($CHCl_3$) 1 730, 1 660, 1 605, 1 515, and 1 350 cm^{-1}; λ_{max}(dioxane) 212 (log ε 4.34) and 265 nm (4.35); δ 3.78 (6 H, s, CO_2Me), 6.29 (2 H, s, 2- and 5-H), 7.65 (4 H, d, *J* 9, ArH$^{\beta}$), and 8.31 (4 H, d, *J* 9, ArH$^{\alpha}$).

Dimethyl-2-(p-Methoxyphenyl)-5-(p-nitrophenyl)tetrahydrofuran-3,4-dicarboxylate.—(*a*) *trans*-2-(*p*-Methoxyphenyl)-3-(*p*-nitrophenyl)oxirane[11] (0.036 g) and dimethyl fumarate (0.05 g) were irradiated (350 nm) in chloroform (0.5 cm^3) for 96 h. The residue from evaporation was purified by PLC (ethyl acetate–light petroleum, 1:4), multiple elution, to yield the title compound as a mixture of stereoisomers (**10**), (**11**), and (**12**) (0.035 g, 62%) (Found: C, 60.35; H, 5.05; N, 3.25. Calc. for $C_{21}H_{21}NO_8$: C, 60.7; H, 5.1; N, 3.35%); δ 3.23, 3.24, 3.33, 3.35, 3.74, 3.83, 3.87 (all s, OMe).

(*b*) The oxirane (**9**) (0.2 g) and dimethyl fumarate (0.05 g) were refluxed together in *N,N*-diethylaniline (5 cm^3) for 24 h under argon. The cooled product was diluted with ether and washed with dilute hydrochloric acid and water. Evaporation and purification of the residue as in the preceding experiment gave a mixture of isomers (**10**) and (**11**), δ 3.24, 3.26, 3.77, 3.82 (all s, CO_2Me) and 3.86, 3.89 (both s, ArOMe).

Dimethyl-2-(p-Methoxyphenyl)-5-(p-nitrophenyl)-2,5-dihydrofuran-3,4-dicarboxylate (**14**).—*trans*-2-(*p*-Methoxyphenyl)-3-(*p*-nitrophenyl)oxirane (0.03 g) and dimethyl acetylenedicarboxylate (0.25 g) in chloroform (0.5 cm^3) were irradiated (350 nm) through Pyrex for 12 h. After evaporation the residue was purified by PLC (ethyl acetate–light petroleum, 1:4), with multiple elution, to yield the *title compound*, stereoisomer (**14**) (0.02 g, 44%), m.p. 93–94 °C (from ethanol–acetone) (Found: C, 60.75; H, 4.7; N, 2.9%; *m/z* 413.110. $C_{21}H_{19}NO_8$ requires C, 61.0; 4.65; N, 3.4%; *M*, 413.111); ν_{max}($CHCl_3$) 1 725, 1 660, 1 610, 1 510, and 1 350 cm^{-1}; λ_{max} 224 (log ε 4.30) and 265 nm (4.17); δ 3.74 (6 H, s, CO_2Me), 3.87 (3 H, s, ArOMe), 6.18 (2 H, s, 2- and 5-H), 7.0 (2 H, d, *J* 8, MeOArH$^{\alpha}$, 7.40 (2 H, d, *J* 8, MeOArH$^{\beta}$), 7.65 (2 H, d, *J* 9, O_2ArH$^{\beta}$), and 8.30 (2 H, d, *J* 9, O_2NArH$^{\alpha}$). Stereoisomer (**15**) was obtained as an oil (0.01 g, 22%) (Found: *m/z* 413.109); δ 3.74 (6 H, s), 3.87 (3 H, s), 6.39 (2 H, s), 6.97 (2 H, d, *J* 8), 7.38 (2 H, d, *J* 8), 7.64 (2 H, d, *J* 9), and 8.31 (2 H, d, *J* 9).

Dimethyl-2-(p-Methoxyphenyl)-5-(p-nitrophenylfuran-3,4-dicarboxylate (**16**).—A mixture of dihydrofurans (**14**) and (**15**) (0.14 g) was stirred with 2,3-dichloro-5,6-dicyanobenzoquinone (0.25 g) in dry benzene (5 cm^3) at room temperature for 12 h. The product was filtered through neutral alumina and evaporated, and the residue was crystallised from ethyl acetate–light petroleum to afford the *title furan* (**16**) (0.068 g, 49%), m.p. 149–150 °C (Found: C, 60.75; H, 4.15; N, 3.2%; *m/z* 411.094. $C_{21}H_{17}NO_8$ requires C, 61.3; H, 4.15; N, 3.4%; M^+, 411.095): ν_{max}($CHCl_3$) 1 725, 1 605, 1 575, 1 500, and 1 345 cm^{-1}; λ_{max} 226 (infl) (log ε 4.19), 284 (4.18), and 367 nm (4.23); δ(C_6D_6) 3.23 (3 H, s, ArOMe), 3.47 (3 H, s, CO_2Me), 3.50 (3 H, s, CO_2Me), 6.78 (2 H, d, *J* 9, MeOAr*H*$^{\alpha}$), 7.60 (2 H, d, *J* 9, ArH), 7.82 (2 H, d, *J* 9, ArH), and 7.58 (2 H, d, *J* 9, ArH).

Ethyl-5-(p-Methoxyphenyl)-2-(p-nitrophenyl)furan-3- and -4-carboxylate.*—The *trans*-oxirane (**9**) (0.05 g) and ethyl propiolate (0.46 g) in chloroform (0.5 cm^3) were irradiated (350 nm) for 12 h. The solvent was evaporated off and the residue, in dry benzene (2 cm^3), was treated with 2,3-dichloro-5,6-dicyanobenzoquinone (0.1 g) for 17 h at room temperature. The mixture was filtered through neutral alumina and evaporated, and the residue separated by PLC (chloroform–hexane, 1:1) (3 elutions) to yield, as the higher R_F band, the *isomer* (**18**) (Found: *m/z* 367.105 $C_{20}H_{17}NO_6$ requires *M*, 367.106); δ 1.47 (3 H, t, *J* 7, OCH$_2$*Me*), 3.86 (3 H, s, OMe), 4.51 (2 H, q, *J* 7, OC*H*$_2$Me), 7.00 (1 H, s, 4-H), 7.03 (2 H, d, *J* 9, MeOAr*H*$^{\alpha}$), 7.74 (2 H, d, *J* 9, MeOAr*H*$^{\beta}$), and 8.31 (4 H, s, O_2NArH). The lower R_F band gave the *isomer* (**17**) (Found: *m/z* 367.106); δ 1.45 (3 H, t, *J* 7, OCH$_2$*Me*), 3.88 (3 H, s, OMe), 4.49 (2 H, q, *J* 7, OC*H*$_2$Me), 7.05 (2 H, d, *J* 9, MeOAr*H*$^{\alpha}$), 7.31 (1 H, s, 3-H), 7.88 (2 H, d, *J* 9, O_2NArH$^{\beta}$), 8.13 (2 H, d, *J* 9, MeOAr*H*$^{\beta}$), and 8.34 (2 H, d, *J* 9, O_2NArH$^{\alpha}$).

Oxiranes (**24**), (**25**), *and* (**26**).—(*a*) (*Z*)-3-(3,4-Methylenedioxyphenyl)-2-(*p*-nitrophenyl)propenonitrile[12] (2.4 g) in pyridine (160 cm^3) was stirred at 0 °C with aqueous sodium hypochlorite (14%; 15 cm^3) for 1 h. After dilution with water the product was filtered off and recrystallised from ethanol to yield

* We thank Alan C. Spivey and Paul Stilwell for carrying out this experiment.

the *oxirane* (**25**) (2.06 g, 79%), m.p. 196.5–197.5 °C (Found: C, 62.0; H, 3.4; N, 9.25%; *m/z* 310.060. $C_{16}H_{10}N_2O_5$ requires C, 61.95; H, 3.25; N, 9.05%; M^+, 310.059); δ 4.24 (1 H, s, 3-H); ν_{max}(KBr) 2 260 cm^{-1}.

(*b*) In similar fashion were prepared the *oxirane* (**24**) (86%), m.p. 172–173 °C (Found: C, 64.6; H, 4.2; N, 9.45%; *m/z* 296.077. $C_{16}H_{12}N_2O_4$ requires C, 64.85; H, 4.05; N, 9.45%; *M*, 296.080), and the *oxirane* (**26**) (90%), m.p. 208–209 °C (Found: C, 62.75; H, 4.4; N, 8.55%; *m/z* 326.092. $C_{17}H_{14}N_2O_5$ requires C, 62.6; H, 4.3; N, 8.6%; *M*, 326.090).

2-*Cyano*-5-(3,4-*methylenedioxyphenyl*)-2-(p-*nitrophenyl*)*tetrahydrofuran*-3,4-*dicarboxylic Anhydride* (**28**).—The *trans*-oxirane (**25**) (1.0 g) and maleic anhydride (1.0 g) were heated in dry xylene (15 cm^3) at reflux for 18 h, under nitrogen. On cooling a product crystallised which on collection and recrystallisation gave the *title anhydride* (**28**) (0.86 g, 65%), m.p. 250 °C (decomp.) (Found: C, 58.6; H, 3.0; N, 6.8%; *m/z* 408.059. $C_{20}H_{12}N_2O_8$ requires C, 58.8; H, 2.95; N, 6.85%; *M*, 408.061); ν_{max}(KBr) 1 870, 1 790, 1 615, 1 530, and 1 355 cm^{-1}; δ[$(CD_3)_2SO$] 4.53 (1 H, m, 4-H), 5.04 (1 H, d, *J* 8, 3-H), 5.85 (1 H, d, *J* 8, 5-H), 6.08 (2 H, s, OCH_2O), 7.06 (3 H, m, ArH), 8.09 (2 H, d, *J* 8, ArH), and 8.43 (2 H, d, *J* 8, ArH).

2-*Cyano*-5-(p-*methoxyphenyl*)-2-(p-*nitrophenyl*)*tetrahydrofuran*-3,4-*dicarboxylic Anhydride* (**29**).—(*a*) The *trans*-oxirane (**24**) (1.0 g), maleic anhydride (1.0 g), and dry toluene (10 cm^3) were heated at reflux under nitrogen for 36 h. The product crystallised on cooling. Recrystallisation from acetone–light petroleum gave the *title anhydride* (**29**) (0.90 g, 68%), m.p. 241–242.5 °C (Found: C, 60.55; H, 3.75; N, 7.0%; *m/z* 394.078. $C_{20}H_{14}N_2O_7$ requires C, 60.9; H, 3.55; N, 7.1%; *M*, 394.080); ν_{max}(KBr) 1 865, 1 785, 1 610, 1 520, and 1 350 cm^{-1}; δ[$(CD_3)_2SO$] 3.87 (3 H, s, OMe), 4.60 (1 H, m, 4-H), 5.13 (1 H, d, *J* 9 Hz, 3-H), 7.09, 7.55, 8.16, and 8.50 (each 2 H, d, *J* 9, ArH).

(*b*) The oxirane (**24**) (0.03 g) and maleic anhydride (0.05 g) in chloroform (0.5 cm^3) were irradiated (300 nm) through Pyrex for 6 h. Evaporation and crystallisation gave the anhydride (**29**) (0.026 g, 65%), m.p. 239–241 °C.

Dimethyl-2-*Cyano*-5-(3,4-*methylenedioxyphenyl*)-2-(p-*nitrophenyl*)*tetrahydrofuran*-3,4-*dicarboxylate*.—The *trans*-oxirane (**25**) (3.5 g), dimethyl fumarate (3.0 g), and dry toluene (30 cm^3) were refluxed together for 24 h under nitrogen. After evaporation the residue was crystallised from ethyl acetate–light petroleum to yield the title compound (4.8 g, 94%) as a mixture of isomers (**30**) and (**31**) (Found: C, 57.8; H, 4.2; N, 6.05%; *m/z* 454.100. Calc. for $C_{22}H_{18}N_2O_9$: C, 58.15; H, 3.95; N, 6.15%; *M*, 454.101). Isomer (**30**) had δ 3.22 (3 H, s, OMe), 3.67 (1 H, m, 4-H), 3.74 (3 H, s, OMe), 4.30 (1 H, d, *J* 6.5, 3-H), 5.43 (1 H, d, *J* 9, 5-H), 6.02 (2 H, s, OCH_2O), 7.08 (3 H, m, ArH), 7.79 and 8.29 (both 2 H, d, *J* 9, ArH). Isomer (**31**) had δ 3.31 (3 H, s, OMe), 3.82 (3 H, s, OMe), 4.07 (2 H, m, 3- and 4-H), 5.63 (1 H, m, 5-H), 5.98 (2 H, s, OCH_2O), 6.85 (3 H, m, ArH), 8.03 and 8.37 (both 2 H, d, *J* 9, ArH).

Dimethyl-2-*Cyano*-5-(3,4-*methylenedioxyphenyl*)-2-(p-*Nitrophenyl*)-2,5-*dihydrofuran*-3,4-*dicarboxylate* (**32**).—The *trans*-oxirane (**25**) (0.5 g) and dimethyl acetylenedicarboxylate (1.0 g) were heated in dry toluene (15 cm^3) at reflux for 36 h. Evaporation and crystallisation of the residue (ethyl acetate–light petroleum) gave the *title dihydrofuran* (**32**) (0.66 g, 91%), m.p. 154–155 °C (Found: C, 58.6; H, 3.55; N, 6.2%; *m/z* 452.084. $C_{22}H_{16}N_2O_9$ requires C, 58.40; H, 3.55; N, 6.2%; *M*, 452.086); ν_{max}(KBr) 1 755, 1 730, 1 655, 1 610, 1 525, and 1 350 cm^{-1}; λ_{max}(dioxane) 245 (log ε 4.16), 264 (infl.) (4.07), and 282 (infl) nm (3.89); δ 3.66 (3 H, s, OMe), 3.70 (3 H, s, OMe), 5.94 (2 H, s, OCH_2), 6.21 (1 H, s, 5-H), 6.78 (3 H, m, ArH), 7.78, and 8.27 (both 2 H, d, *J* 9, ArH).

Dimethyl-2-(3,4-*Methylenedioxyphenyl*)-5-(p-*Nitrophenyl*)-*furan*-3,4-*dicarboxylate* (**33**).—The dihydrofuran (**32**) (2.4 g), triethylamine (1.8 g), and methanol (50 cm^3) were refluxed together for 2 h. The cooled mixture was filtered and recrystallised to yield the *title furan* (**33**) (1.83 g, 81%), m.p. 157–159 °C (from ethyl acetate–light petroleum) (Found: C, 59.2; H, 3.8; N, 3.25%; *m/z* 425.074. $C_{21}H_{15}NO_9$ requires C, 59.3; H, 3.55; N, 3.3; *M*, 425.076); ν_{max}($CHCl_3$) 1 720, 1 600, 1 555, and 1 340 cm^{-1}; λ_{max} 213 (infl.) (log ε 4.46), 237 (infl.) (4.17), 229 (infl.) (4.14), 310 (4.16), and 366 nm (4.22); δ 3.92 and 3.96 (both 3 H, s, OMe), 6.10 (2 H, s, OCH_2O), 6.96 (1 H, d, *J* 8, ArH), 7.48 (2 H, m, ArH), 8.09, and 8.27 (both 2 H, d, *J* 9, ArH).

Methyl-2-*Cyano*-5-(3,4-*methylenedioxyphenyl*)-2-(p-*nitrophenyl*)*tetrahydrofuran*-3- *and* -4-*carboxylate*.—The *trans*-oxirane (**25**) (0.5 g) and methyl acrylate (1.0 g) were refluxed in dry toluene (20 cm^3) under nitrogen for 68 h. After evaporation the residue was separated by HPLC (ethyl acetate–hexane, 2:3; μ-Porasil) to yield the title compounds. The *adduct* (**34**) (0.15 g, 24%) was eluted first, m.p. 180.5–181.5 °C (from ethanol) (Found: C, 60.35; H, 4.15; N, 7.20%; *m/z* 396.096. $C_{20}H_{16}N_2O_7$ requires C, 60.6; H, 4.05; N, 7.05%; *M*, 396.096); ν_{max}(KBr) 1 740, 1 605, 1 525, and 1 350 cm^{-1}; δ 2.56 (1 H, ddd, *J* 7.6, 9.7, and 13.2, 4-H), 2.75 (1 H, ddd, *J* 6.4, 8.5, and 13.2, 4-H), 3.24 (3 H, s, OMe), 3.98 (1 H, dd, *J* 7.6 and 8.5, 3-H), 5.34 (1 H, dd, *J* 6.4 and 9.7, 5-H), 6.02 (2 H, s, OCH_2O), 6.86 (1 H, d, *J* 8, ArH), 7.01 (1 H, br d, *J* 8, ArH), 7.14 (1 H, d, *J* 1.5, ArH), 7.78, and 8.27 (both 2 H, d, *J* 9, ArH). *Adduct* (**35**) (0.196 g, 30%) was eluted second, m.p. 185.5–186.5 °C (from ethanol) (Found: C, 60.55; H, 4.2; N, 6.95%; *m/z* 396.096); ν_{max} 1 720, 1 605, 1 520, and 1 340 cm^{-1}; δ 2.85 (1 H, dd, *J* 7.6 and 13.5, 3-H), 3.04 (1 H, dd, *J* 8.4 and 13.5, 3-H), 3.30 (3 H, s, OMe), 3.80 (1 H, m, 4-H), 5.61 (1 H, d, *J* 8.5, 5-H), 5.99 (2 H, s, OCH_2O), 6.81 (3 H, m, ArH), 7.93, and 8.36 (each 2 H, d, *J* 9, ArH).

Methyl-2-*Cyano*-5-(p-*Methoxyphenyl*-2-(p-*nitrophenyl*)*tetrahydrofuran*-4-*carboxylate* (**37**).—The *trans*-oxirane (**24**) (0.5 g) and methyl acrylate (2.0 g) were heated in dry toluene (15 cm^3) at reflux under nitrogen for 72 h. On cooling the solvent was evaporated off to yield a crystalline residue (0.48 g) containing adducts (**36**) and (**37**). Fractional crystallisation from methanol yielded *adduct* (**37**) (0.16 g, 25%), m.p. 123–125 °C (Found: C, 62.95; H, 4.9; N, 7.3%; *m/z* 382.116. $C_{20}H_{18}N_2O_6$ requires C, 62.85; H, 4.7; N, 7.3%; *M*, 382.116); δ(C_6D_6) 2.33 (1 H, dd, *J* 8 and 13, 3-H), 2.55 (1 H, dd, *J* 8 and 13, 3-H), 2.87 (3 H, s, OMe), 3.25 (1 H, m, 4-H), 3.29 (3 H, s, OMe), 5.36 (1 H, d, *J* 8.5, 5-H) 6.76 and 7.10 (each 2 H, d, *J* 8.5, ArH), 7.41 and 7.74 (each 2 H, d, *J* 9, ArH).

Methyl-2-*Cyano*-5-(3,4-*dimethoxyphenyl*)-2-(p-*nitrophenyl*)-*tetrahydrofuran*-3- *and* -4-*carboxylate*.—The *trans*-oxirane (**26**) (0.5 g) was treated with methyl acrylate as in the reaction with the oxirane (**25**). The title compounds were isolated by PLC (light petroleum–ethyl acetate, 3:1). *Adduct* (**38**) (0.139 g, 22%) had m.p. 61–63 °C (from ethanol–acetone) (Found: C, 61.05, H, 5.05; N, 6.55%; *m/z* 412.125. $C_{21}H_{20}NO_7$ requires C, 61.15; H, 4.85; N, 6.8%; *M*, 412.127); ν_{max}(KBr) 1 740, 1 610, 1 520, and 1 350 cm^{-1}; δ 2.63 (1 H, ddd, *J* 7.5, 9.8, and 13, 4-H), 2.79 (1 H, ddd, *J* 6.5, 8.6, and 13, 4-H), 3.25 (3 H, s, OMe), 3.93 (3 H, s, OMe), 3.96 (3 H, s, OMe), 3.97 (1 H, m, 3-H), 5.38 (1 H, dd, *J* 6.5 and 9.8, 5-H), 6.93 (1 H, d, *J* 8, ArH), 7.15 (1 H, m, ArH), 7.79, and 8.27 (each 2 H, d, *J* 9, ArH). *Adduct* (**39**) (0.157 g, 25%) had m.p. 112–114 °C (from ethanol–acetone) (Found: C, 61.25; H, 4.9; N, 7.05%; *m/z* 412.126); δ 2.87 (1 H, dd, *J* 7.5 and 13.5, 3-H), 3.06 (1 H, dd, *J* 8.4 and 13.5, 3-H), 3.25 (3 H, s, OMe), 3.80 (1 H,

m, 4-H), 3.88, 3.89 (each 3 H, s, OMe), 5.64 (1 H, d, *J* 8.5, 5-H), 6.90 (3 H, m, ArH), 7.94, and 8.34 (each 2 H, d, *J* 9, ArH).

Ethyl-2-Cyano-5-(3,4-dimethoxyphenyl)-2-(p-Nitrophenyl)-2,5-dihydrofuran-3-and 4-carboxylate.—The oxirane (**26**) (0.5 g) and ethyl propiolate (2.0 g) in dry toluene (20 cm^3) were heated at reflux under nitrogen for 36 h. After evaporation the products were separated by PLC (light petroleum–ethyl acetate, 3:1). The *dihydrofuran* (**40**) (0.2 g, 31%) had m.p. 138.5–140 °C (from ethanol–acetone) (Found: C, 62.55, H, 5.15; N, 6.4%; *m/z* 424.125. $C_{22}H_{20}N_2O_7$ requires C, 62.25; H, 4.7; N, 6.6%; *M*, 424.127); ν_{max}($CHCl_3$) 1 730, 1 665, 1 610, 1 515, and 1 355 cm^{-1}; λ_{max} 233 (log ε 4.26), 254 (4.08), 258 (4.09), 265 (4.06), and 283 nm (3.84); δ[$(CD_3)_2CO$] 1.19 (3 H, t, *J* 7, CH_2CH_3), 3.80 and 3.83 (both 3 H, s, OCH_3), 4.18 (2 H, q, *J* 7, CH_2CH_3), 6.38 (1 H, d, *J* 1.6, 5-H), 7.01 (3 H, br s, ArH), 7.58 (1 H, d, *J* 1.6, 4-H), 7.95, and 8.37 (both 2 H, d, *J* 9, ArH). The *dihydrofuran* (**41**) (0.239, 37%) had m.p. 69–75 °C (from ethanol–acetone) (Found: C, 60.75; H, 4.75; N, 6.25%; *m/z* 424.130); ν_{max}(film) 1 730, 1 650, 1 610, 1 525, and 1 365 cm^{-1}; λ_{max} 235 (log ε 4.20) and 258 nm (4.13); δ[$(CD_3)_2CO$)] 1.15 (3 H, t, *J* 7, CH_2CH_3), 3.70 and 3.81 (both 3 H, s, OMe), 4.13 (2 H, q, *J* 7, CH_2CH_3), 6.36 (1 H, d, *J* 2.3, 5-H), 6.83 (1 H, d, *J* 8, ArH), 6.91 (1 H, d, *J* 8, ArH), 6.93 (1 H, s, ArH), 7.42 (1 H, d, *J* 2.3, 3-H), 7.96, and 8.40 (each 2 H, d, *J* 9, ArH).

Dimethyl-(1E,3Z)-1-Hydroxy-4-(3,4-methylenedioxyphenyl)-1-(p-nitrophenyl)buta-1,3-diene-2,3-dicarboxylate (**47**).—The mixture of adducts (**30**) and (**31**) (1.0 g) in dimethyl sulphoxide (10 cm^3) was treated with a solution of sodium (0.3 g) in methanol (5 cm^3). After 18 h at ambient temperature the mixture was diluted with 4M hydrochloric acid and extracted with ether. After drying and evaporation, the solid residue was purified on a silica column (chloroform–methanol, 9:2, as eluant to yield the *title enol* (**47**) (0.6 g, 64%), m.p. 129–130 °C (from ethanol–light petroleum) (Found: C, 59.35; H, 4.2; N, 3.15%; *m/z* 427.090. $C_{21}H_{17}O_9N$ requires C, 59.0; H, 4.0; N, 3.3%; *M*, 424.090); ν_{max}($CHCl_3$) 2 950, 2 890, 1 705, 1 645, 1 620, 1 600, 1 520, and 1 340 cm^{-1}; λ_{max} 219 (infl.) (4.27), 240 (log ε) (4.31), 298 (infl.) (4.22), and 325 nm (4.27); δ 3.75 and 3.78 (each 3 H, s, OMe), 6.01 (2 H, s, OCH_2O), 6.77 (3 H, m, ArH), 7.47 and 8.07 (each 2 H, d, *J* 9, ArH), 7.50 (1 H, s, 4-H), and 13.32 (1 H, s, OH).

4-Methoxycarbonyl-5-(3,4-methylenedioxyphenyl)-2-(p-nitrophenyl)tetrahydrofuran-2,3-dicarboximide (**48**).—The adducts (**30**) and (**31**) (0.5 g) in methanol (10 cm^3) were treated with sodium (0.3 g) in methanol (5 cm^3) for 18 h at ambient temperature. On dilution with dilute hydrochloric acid the imide (**48**) (0.41 g, 85%) crystallised out, m.p. 239–240 °C; *m/z* 440; ν_{max}(KBr) 3 245, 1 720, 1 610, 1 525, and 1 355 cm^{-1}; δ[$(CD_3)_2SO$] 3.37 (1 H, br s, D_2O exchangeable, NH), 3.66 (3 H, s, OMe), 3.70 (1 H, m, 4-H), 4.61 (1 H, d, *J* 10, 3-H), 5.14 (1 H, d, *J* 11, 5-H), 6.11 (2 H, s, OCH_2O), 7.00 (3 H, m, ArH), 7.93, and 8.38 (each 2 H), d, *J* 9, ArH). On treatment of (**48**) with ethereal diazomethane, in ethanol suspension, its N-*methyl derivative* was formed, m.p. 181–183 °C (from ethyl acetate–light petroleum) (Found: C, 58.05; H, 4.3; N, 6.0%; *m/z* 454.101. $C_{22}H_{18}N_2O_9$ requires C, 58.15; H, 3.95; N, 6.15%; *M*, 454.101); δ_C($CDCl_3$) 25.82 (q, NMe), 52.67 (q, CO_2Me), 54.47 and 55.14 (both d, C-3, C-4) 82.80 (d, C-5), 86.93 (s, C-2), 168.68, 172.92, and 174.21 (all s, 3 × C=O).

Reduction of the Anhydride (**29**).—The anhydride (**29**) (0.1 g) in dry tetrahydrofuran (1 cm^3) at −15 °C was treated with a suspension of sodium borohydride (0.25 g) in dry propan-2-ol (5 cm^3), and the mixture was stirred for 48 h, the temperature being allowed to rise to ambient. The solvents were evaporated off and the residue was treated with dilute hydrochloric acid and extracted with ethyl acetate. Evaporation and chromatography (chloroform–acetone, 9:1, as eluant) yielded the (eluted first) *lactone* (**45**) (0.018 g, 19%), m.p. 204–204.5 °C (Found: C, 63.0; H, 4.35; N, 7.05%; *m/z* 380.100. $C_{20}H_{16}N_2O_6$ requires C, 63.15; H, 4.21; N, 7.35%; *M*, 380.101); ν_{max} 1 780 cm^{-1}; δ[$(CD_3)_2CO$] 3.85 (3 H, s, OMe), 3.85 (1 H, dd, *J* 4.1 and 9.1, 6-H), 4.12 (1 H, m, 5-H), 4.24 (1 H, dd, *J* 8.5 and 9.1, 6-H), 4.37 (1 H, d, *J* 8.5, 1-H), 5.85 (1 H, d, *J* 6.4, 4-H), 7.05 and 7.48 (each 2 H, d, *J* 9, ArH), 8.01, and 8.37 (each 2 H, d, *J* 9, ArH). The *lactone* (**46**) (0.031 g, 32%) was eluted second, m.p. 227–228 °C (from acetone–light petroleum) (Found: C, 62.8; H, 4.45; N, 7.1%; *m/z* 380.099); ν_{max}(KBr) 1 775 cm^{-1}; δ[$(CD_3)_2DO$] 3.70 (1 H, dd, *J* 6.6 and 10, 6-H), 3.82 (3 H, s, OMe), 4.04 (1 H, dd, *J* 8.9 and 8.9, 1-H), 4.28 (1 H, dd, *J* 9.3 and 10, 6-H), 4.55 (1 H, ddd, *J* 6.6, 8.9, and 9.3, 5-H), 5.87 (1 H, d, *J* 8.9, 2-H), 6.96 and 7.45 (each 2 H, d, *J* 8.7, ArH), 8.07, and 8.45 (each 2 H, d, *J* 9, ArH).

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