Photosensitized Oxidation of Furans. X [1]. Solvent Effect in the Nuclear Magnetic Resonance of Functionalized Diacyloxiranes

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A simple, rapid method to determine the configuration of 2-alkoxycarbonyl-2,3-diacyloxiranes and 2-alkoxycarbonyl-2,3-diacyl-3-methyloxiranes is described. The method is based on the observation of the solvent effect on the chemical shifts of the proton or the methyl group linked to the oxirane ring.

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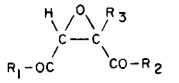
Alkoxycarbonyl-2,3-diacyloxiranes are interesting multifunctional compounds which can be obtained by thermal conversion of the *endo*-peroxides of furans, this route leading stereospecifically to the *cis*-isomers [1,2]. Moreover, a non-stereospecific synthesis has been described which includes a treatment of functionalized 2-ene-1,4-diones with *t*-butyl hydroperoxide in the presence of triethylamine [1].

Intramolecular nuclear Overhauser effect (NOE) is a tool particularly suited to ascertaining configuration of the synthetized products [3,4] but it cannot be applied if protons which may interact are not present in the molecule. In consideration that the solvent effects in the nuclear magnetic resonance have been used for the determination of the configuration of several alkenes [5] and cyclopropane derivatives [6], we inquire whether a similar method could be applied to oxirane compounds.

We wish to report here that in the case of trisubstituted compounds, the solvent effect on the chemical shifts of the oxirane proton can be used to assist in the determination of configuration. In fact, when nmr spectra of a trisubstituted oxirane are successively measured in deuteriochloroform and in hexadeuteriobenzene the algebraic difference of shielding $\Delta\delta = \delta$ deuteriochloroform - δ hexadeuteriobenzene results to be specific of the position of the oxirane proton with respect to the carbonyl group linked to the adjacent carbon atom.

The couples of *cis/trans* isomeric oxiranes **1a-d/2a-d** have been synthetized from the corresponding 2-ene-1,4-diones according to the described procedure [1]. The distinction between the two isomers for each couple has been effected by comparison of the products with the *cis* isomers obtained by the alternate route [1]. The δ values in deuteriochloroform and hexadeuteriobenzene for the oxirane proton of compounds **1a-d** and **2a-d** are reported in Table 1. The most signficant feature which appears from the data is that the upfield shift $\Delta\delta$ for the oxirane proton is constantly higher than 0.45 ppm in *trans*-isomer **2a-d** where it is on the same side of the acyl group, with a maximum of 0.67 for compound **2c**; conversely, this value is much lower ($\leq$0.20 ppm) when *cis*-isomers **1a-d** are concerned. A further confirmation that a high upfield shift is connected with the position of the oxirane proton as regards to the acyclic function comes from the values (Table 1) observed for the triacyloxiranes **1e-f** and **2e-f** where, in any case, the proton is on the same side of an acyl group. The configuration of the triacyloxiranes **1e-f** and **2e-f** has



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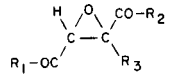

2

a, $R_1 = R_2 = C_6H_5$, $R_3 = CO_2CH_3$
b, $R_1 = R_2 = C_6H_5$, $R_3 = CO_2C_2H_5$
c, $R_1 = C_6H_5$, $R_2 = CH_3$, $R_3 = CO_2CH_3$
d, $R_1 = CH_3$, $R_2 = C_6H_5$, $R_3 = CO_2C_2H_5$
e, $R_1 = R_2 = C_6H_5$, $R_3 = COCH_3$
f, $R_1 = CH_3$, $R_2 = C_6H_5$, $R_3 = COCH_3$

Table 1

Solvent Effect on the Chemical Shift of Oxirane Proton of Compounds **1a-f** and **2a-f**

Compound	Solvent: Deuteriochloroform (δ)	Solvent: Perdeuteriobenzene (δ)	$\Delta\delta$
1a	4.86	4.72	0.14
1b	4.83	4.75	0.08
1c [a]	4.82	4.62	0.20
1d	4.10	3.95	0.15
1e	4.62	4.08	0.54
1f	3.92	3.38	0.54
2a	4.55	4.00	0.55
2b	4.54	4.07	0.47
2c [a]	4.48	3.81	0.67
2d	3.85	3.40	0.45
2e	4.69	4.20	0.49
2f	3.96	3.40	0.56

[a] The chemical shifts of **1c** and **2c** reported in ref [3,4] were measured with a Perkin Elmer R12A spectrometer.

been deduced on the basis of the formation of **1e-f** *via* thermal conversion of the corresponding *endo*-peroxides and confirmed by NOE difference experiments.

With the aim of extending the above rule to tetrasubstituted alkoxycarbonyl-2,3-diacyloxiranes bearing a methyl group instead of a hydrogen atom, we synthetized the two new pairs of isomeric compounds **3a-b** and **4a-b**, the former *via* thermal conversion of *endo*-peroxides **5a-b** obtained by singlet oxidation of furans **6a-b**, the latter by reaction of diacylethylenes **7a-b** with *t*-butylhydroperoxides in the presence of triethylamine [7] (Scheme). The δ values in deuteriochloroform and hexadeuteriobenzene for the methyl groups of oxiranes **3a-b** and **4a-b** are reported in Table 2. Again the upfield shifts $\Delta\delta$ for the methyl resonances are higher when this group is on the same side of the acyl group even if the differences are not so remarkable as in the case of the proton of trisubstituted oxiranes; however, before a systematic generalization can be made, further confirmations are required.

Scheme

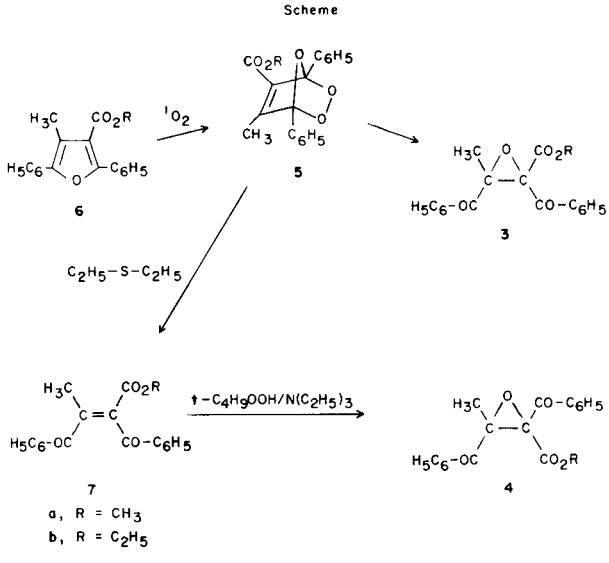

Table 2

Solvent Effect on the Chemical Shift of Methyl Group of Compounds **3a-b** and **4a-b**

Compound	Solvent: Deuteriochloroform (δ)	Solvent: Perdeuteriobenzene (δ)	$\Delta\delta$
3a	1.81	1.71	0.10
3b	1.82	1.72	0.10
4a	1.99	1.75	0.24
4b	2.01	1.74	0.27

EXPERIMENTAL

Melting points are uncorrected. The ir spectra were recorded on a Perkin Elmer 157 spectrometer using chloroform as solvent. The ^{1}H nmr spectra were recorded on a Bruker WH 270 Fourier transform using tetramethylsilane as internal standard. Nuclear Overhauser effects of compounds **1e-f** and **2e-f** were measured with the aid of an ASPECT 2000 microprogram which allowed direct automatic accumulation of NOE difference FID's; 3% deuteriochloroform degassed solutions were used. The chemical shifts in deuteriochloroform and hexadeuteriobenzene of compounds **1-4** were measured on 2% solutions at normal temperature. Silica gel 0.05-0.2 mm (Merck) and light petroleum bp 30-50 were used for column chromatography.

Preparation of *cis*-Oxirane **3a** by Thermal Conversion of *endo*-Peroxide **5a**.

Methyl 2,5-diphenyl-4-methylfuran-3-carboxylate (**6a**) was prepared by saponification of the ethyl ester [8] followed by methylation with diazomethane of the acid obtained. Silica gel chromatography (elution with light petroleum/ether 9:1) gave **6a** (95%), mp 97-98°; ir: ν max 1712 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.43 (3H, s, CH_3), 3.82 (3H, s, OCH_3), and 7.25-7.90 (10H, m, aromatic H).

Anal. Calcd. for $C_{19}H_{16}O_3$: C, 78.06; H, 5.52. Found: C, 78.12; H, 5.51.

The singlet oxidation of furan **6a**, according to the procedure used for **6b** [9], leads in quantitative yields to the *endo*-peroxide **5a** as a colourless oil; ir: ν max 1720, 1675 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.15 (3H, s, CH_3), 3.62 (3H, s, OCH_3), 7.40-7.85 (10H, m, aromatic H).

Anal. Calcd. for $C_{19}H_{16}O_5$: O_{act}, 4.9. Found: O_{act}, 4.6.

The *endo*-peroxide **5a** (324 mg, 1 mmole) was kept under anhydrous conditions at 50° [10]. After 2 hours **5a** was completely transformed (^{1}H nmr) and the mixture was chromatographed on silica gel (15 g). Elution with light petroleum/ether (4:1) gave a mixture of oxirane **3a** and hitherto unidentified products (150 mg). This mixture, by further chromatography on silica gel (20 g), eluent benzene, afforded pure oxirane **3a** (35 mg, 10%) as a colourless oil; ir: ν max 1748, 1690 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.81 (3H, s, CH_3), 3.80 (3H, s, OCH_3), and 7.40-8.15 (10H, m, aromatic H).

Anal. Calcd. for $C_{19}H_{16}O_5$: C, 70.36; H, 4.98. Found: C, 70.35; H, 4.99.

Preparation of *trans*-Oxirane **4a** from Diacylethylene **7a**.

The ethylene **7a** was obtained by deoxygenation of *endo*-peroxide **5a** with diethyl sulfide and isolated in 90% yield by column chromatography on silica gel by the procedure used for **7b** [11]. The ethylene **7a**, recrystallized from light petroleum (bp 40-70°), gave white crystals, mp 102-103°; ir: ν max 1725, 1670, 1600 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.32 (3H, s, CH_3), 3.62 (3H, s, OCH_3), 7.20-7.90 (10H, m, aromatic H).

Anal. Calcd. for $C_{19}H_{16}O_4$: C, 74.01; H, 5.23. Found; C, 74.00; H, 5.25.

To a 4% solution of the ethylene **7a** (308 mg, 1 mmole) in chloroform triethylamine (3 mmoles) and *t*-butylhydroperoxide (3 mmoles) were added and the resulting solution was kept at room temperature. After 24 hours the reaction was complete (^{1}H nmr), the solvent and the unchanged reactants were removed under reduced pressure and the residue chromatographed on silica gel (15 g). Elution with light petroleum/ether (4:1) gave the pure oxirane **4a** in 60% yield. The oxirane **4a**, recrystallized from light petroleum (bp 40-70°) gave white crystals, mp 136-138°; ir: ν max 1725, 1675 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.99 (3H, s, CH_3), 3.50 (3H, s, OCH_3), and 7.40-8.15 (10H, m, aromatic H).

Anal. Calcd. for $C_{19}H_{16}O_5$: C, 70.36; H, 4.98. Found: C, 70.38; H, 4.99.

Preparation of *cis*-Oxirane **3b** by Thermal Conversion of *endo*-Peroxide **5b**.

endo-Peroxide **5b** (338 mg, 1 mmole) [9] was kept under anhydrous conditions at 50° [10]. After 2 hours the conversion was complete (^{1}H nmr) and the mixture was chromatographed on silica gel (15 g). Elution with light petroleum/ether (4:1) gave a mixture of oxirane **3b** and hitherto unidentified products (160 mg). This mixture by further chromatography on silica gel (20 g), eluent benzene, afforded pure oxirane **3b** (36 mg, 10%) as a colourless oil; ir: ν max 1745, 1690 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.22 (3H, t, J = 7 Hz, CH_3), 1.82 (3H, s, CH_3), 4.33 (2H, q, J = 7 Hz, CH_2), and 7.35-8.15 (10H, m, aromatic H).

Anal. Calcd. for $C_{20}H_{18}O_5$: C, 70.99; H, 5.36. Found: C, 70.96; H, 5.38.

Preparation of *trans*-Oxirane **4b** from Diacylethylene **7b**.

To a 4% solution of the ethylene **7b** (322 mg, 1 mmole) [11] in chloroform, triethylamine (3 mmoles) and *t*-butylhydroperoxide (3 mmoles) were added and the resulting solution was kept at room temperature. After 24 hours the reaction was complete (^{1}H nmr), the solvent and the unchanged reactants were removed under reduced pressure and the residue chromatographed on silica gel (15 g). Elution with light petroleum/-ether (4:1) gave the pure oxirane **4b** in 75% yield as a colorless oil; ir: ν max 1719, 1675 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 0.90 (3H, t, J = 7 Hz, CH_3), 2.01 (3H, s, CH_3), 3.96 (2H, q, J = 7 Hz, CH_2), and 7.40-8.15 (10H, m, aromatic H).

Anal. Calcd. for $C_{20}H_{18}O_5$: C, 70.99; H, 5.36. Found: C, 71.02; H, 5.35.

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