Regioselective Epoxidation of 3-(3-Oxo-3-arylpropenyl)chromen-4-ones by Dimethyldioxirane

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Dedicated to Professor Dr. Antal Tungler on the occasion of his 60th birthday.

Regioselective epoxidation of 3-(3-oxo-3-arylpropenyl)chromen-4-ones **1a-h** by isolated dimethyldioxirane provided epoxides **2a-h** as sole detectable and isolable products in good (75-86%) yields.

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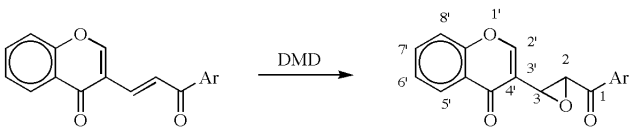
Several representatives of the 3-(3-oxo-3-arylpropenyl)-chromen-4-ones have been described in the literature [1-3]. However, the investigation of their chemical transformations has hitherto received less attention although these compounds possess two moieties, *víz.* a 3-chromonyl group and an α,β-unsaturated ketone unit which are prone to a wide variety of chemical transformations. Recently, we have started a systematic study of the chemical transformations of these interesting chromone derivatives. Their 1,3-dipolar cycloaddition with diazomethane provided 2-pyrazolines [4,5] similarly to the related α,β-unsaturated ketones. As another group of heterocyclic compounds, 4-aryl-2-(3-chromonyl)-2,3-dihydro-1,5-benzothiazepines were synthesized by the reaction of 3-(3-oxo-3-arylpropenyl)chromen-4-ones and 2-aminothiophenol [6,7]. To our knowledge, epoxidation of these compounds with two sites of epoxidation has not yet been published. For this reason, it appeared expedient to investigate their epoxidation and to search for oxidation method(s) capable of their regioselective epoxidation without decomposition and the formation of by-product(s).

The isolated dimethyldioxirane (DMD) [8] was found to be the oxidant of choice both for the epoxidation of various chromone derivatives [9-14] and α,β-unsaturated ketones [15-22]. As far as the utility of the dimethyldioxirane is concerned, the 3-(3-oxo-3-arylpropenyl)chromen-4-ones are especially challenging compounds since they possess two electron deficient olefinic double bonds. Therefore, the question is whether one of these carbon-carbon double bonds can be seletively epoxidized with such an electrophilic oxidant as the dimethyldioxirane is. In this paper we report on the regioselective epoxidation of the α,β-unsaturated ketone moiety of these chromene derivatives.



1a-h **2a-h**

a: Ar = phenyl
b: Ar = 4-Me-phenyl
c: Ar = 4-MeO-phenyl
d: Ar = 4-F-phenyl
e: Ar = 4-Cl-phenyl
f: Ar = 4-Br-phenyl
g: Ar = 1-naphthyl
h: Ar = 2-naphthyl

E-3-(3-Oxo-3-arylpropenyl)chromen-4-ones **1a-h** dissolved in anhydrous dichloromethane were allowed to react with isolated dimethyldioxirane (DMD) at ambient temperature. The progress of the oxidation was monitored by thin-layer chromatography (tlc) until a complete conversion of starting materials **1a-h** was achieved. It is worth mentioning that in the reaction mixture only one product was detected even if high amount of the oxidant (20 equivalents) was added for a prolonged reaction time (20 days). Epoxides **2a-h** (Scheme) have been isolated after evaporation of the solvent followed by crystallization form methanol.

Structure elucidation of the isolated oxidized products **2a-h** has been performed by elemental analyses and spectroscopic methods. Elemental analyses and mass spectroscopic data unequivocally prove that one oxygen atom was inserted into the molecules of the starting materials **1a-h**. Electron impact (70 eV) mass spectra of epoxides **2a-h** are relatively simple and very similar. Molecular ion could be observed in all cases (3-6%) and the base peak is mainly the Ar-CO^+ ion. The initial step in the fragmentation involves loss of CO and Ar-CO from the molecular ion resulting in M-28 (2-4%) and intense *m/z* 187 ions. Two characteristic C=O bands between 1680-1700 and 1640-1660 cm^{-1} and cyclic ether bands around 1230 and 880-900 cm^{-1} are found in their ir spectra. In the ^1H nmr spectra two narrow doublets of the 2-H (δ = 4.32-4.53) and 3-H (δ = 4.18-4.28) prove the presence of the epoxide functionality. The low coupling constant values (J = 1.4-2.1 Hz) refer to the *trans* stereochemistry of the oxirane ring as observed in the case of the epoxidation of the *E*-diastereomers of α,β-unsaturated ketones [15-22]. In their ^{13}C nmr spectra, chemical shift values of the C-2 (59-61) and C-3

(53-54) atoms corroborate the presence of an epoxide moiety originated from an α,β-unsaturated ketone. The spectral data also prove that the 3-chromonyl group remained unchanged in the course of the epoxidation.

In summary, we have succeeded in the regioselective epoxidation of *E*-3-(3-oxo-3-arylpropenyl)chromen-4-ones **1a-h** with dimethyldioxirane to obtain hitherto unknown epoxides **2a-h** of chromone type compounds. It should be emphasized that this procedure provides the above-mentioned epoxides in good (75-86%) yields under strictly neutral conditions without the formation of any by-product. Our results also prove that this highly effective electrophilic oxidant can be advantageously used for a regioselective epoxidation of compounds with several electron deficient olefinic double bonds.

EXPERIMENTAL

Melting points were determined with a Koffler hot-stage apparatus and are uncorrected. ^{1}H and ^{13}C nmr spectra were recorded on a Varian Gemini 200 spectrometer at 200/50 MHz in deuteriochloroform (internal standard TMS, δ = 0.0) at room temperature. The ir spectra (KBr discs) were obtained with a Perkin-Elmer 16 PC instrument. Mass spectra were recorded on a VG Trio-2 instrument. Elemental analyses were measured in-house with a Carlo Erba 1106 EA instrument. Tlc was performed on Kieselgel 60 F_{254} (Merck) layer using 1,2-dichloroethane as eluent. Dimethyldioxirane (as an acetone solution) was prepared as described [8] by using Caroat received as a generous gift from Perixid-Chemie GmbH (München, Germany) and its peroxide content was determined iodometrically. Starting materials **1a-h** were synthesized according to known procedures [1-3].

General Procedure for the Epoxidation of Compounds **1a-h**.

The required amount of isolated dimethyldioxirane in acetone (0.05-0.10 *M*) was added to a solution of the appropriate 3-(3-oxo-3-arylpropenyl)chromen-4-one (**1a-h**; 0.50 g, 1.5-1.8 mmoles) in anhydrous dichloromethane (100 ml) at room temperature. The mixture was left to stand at room temperature and another equivalent of dimethyldioxirane was added every day until the complete conversion of the starting materials into the appropriate epoxides **2a-h** was achieved by using seven equivalents of dimethyldioxirane in 7 days. The solvent was evaporated under reduced pressure (*ca*. 20 Torr) and the residue was crystallized from methanol to afford white crystalline epoxides **2a-h**.

3-(3-Chromonyl)-2,3-epoxy-1-phenylpropan-1-one (**2a**).

This compound was isolated as white needles in 75% yield, mp 135-137°; ir: ν 1682, 1661, 1470, 1408, 1232, 896, 766, 667 cm^{-1}; ^{1}H nmr ($CDCl_3$): δ 4.22 (d, J = 1.4 Hz, 3-H), 4.50 (d, J = 1.4 Hz, 2-H), 7.46-8.27 (m, 2'-H + 9 arom. H); ^{13}C nmr ($CDCl_3$): δ 53.7, 59.3, 118.4, 120.0, 123.8, 125.8, 125.9, 128.6, 128.9, 134.1, 134.3, 135.6, 153.9, 156.5, 176.8, 193.3; ms: *m/z* = 292 (M^+, 4), 264 (4), 187 (29), 105 (100).

Anal. Calcd for $C_{18}H_{12}O_4$: C, 73.96; H, 4.14. Found: C, 73.91; H, 4.16.

3-(3-Chromonyl)-2,3-epoxy-1-(4-methylphenyl)propan-1-one (**2b**).

This substance was obtained as white needles in 76% yield, mp 127-128°; ir: ν 1691, 1655, 1645, 1618, 1607,1573, 1466, 1410, 1233, 898, 830, 773, 767, 669 cm^{-1}; ^{1}H nmr ($CDCl_3$): δ 2.43 (s, 3H, Me), 4.20 (d, J = 1.8 Hz, 3-H), 4.49 (d, J = 1.8 Hz, 2-H), 7.30-8.27 (m, 2'-H, + 8 arom. H); ^{13}C nmr ($CDCl_3$): δ 21.6, 53.6, 59.3, 118.4, 120.1, 123.8, 125.7, 125.8, 128.7, 129.7, 133.2, 134.3, 145.2, 153.9, 156.6, 176.8, 192.8; ms: *m/z* = 306 (M^+, 4), 278 (3), 187 (38), 119 (100).

Anal. Calcd for $C_{19}H_{14}O_4$: C, 74.50; H, 4.61. Found: C, 74.54; H, 4.63.

3-(3-Chromonyl)-2,3-epoxy-1-(4-methoxyphenyl)propan-1-one (**2c**).

This compound was obtained as white plates in 81% yield, mp 138-139°; ir: ν 1690, 1657, 1620, 1606, 1568, 1412, 900, 835, 768, 668 cm^{-1}, ^{1}H ($CDCl_3$): δ 3.89 (s, 3H, Me), 4.20 (d, J = 2.1 Hz, 3-H), 4.36 (d, 2.1 Hz, 2-H), 6.70-8.27 (m, 2'-H + 8 arom. H); ^{13}C nmr ($CDCl_3$): δ 53.5, 55.4, 59.3, 114.2, 118.4, 120.2, 123.9, 125.8, 125.9, 128.7, 131.0, 134.3, 153.9, 156.6, 164.5, 176.9, 191.5. ms: *m/z* = 322 (M^+, 3), 294 (2), 187 (29), 135 (100).

Anal. Calcd for $C_{19}H_{14}O_5$: C, 70.80; H, 4.38. Found: C, 70.83; H, 4.36.

3-(3-Chromonyl)-2,3-epoxy-1-(4-fluorophenyl)propan-1-one (**2d**).

This compounds was prepared as white needles in 85% yield, mp 136-137°; ir: ν 1679, 1617, 1598, 1509, 1467, 1434, 1414, 1349, 1230, 1164, 883, 778, 758, 629 cm^{-1}; ^{1}H nmr ($CDCl_3$): δ 4.20 (d, J = 1.9 Hz, 3-H), 4.36 (d, J = 1.9 Hz, 2-H), 7.14-8.25 (m, 2'-H + 8 arom. H); ^{13}C nmr ($CDCl_3$): δ 53.6, 59.3, 116.0, 116.4, 118.4, 120.0, 123.8, 125.8, 131.3, 131.5, 132.0, 134.4, 154.0, 156.6, 163.9, 169.1, 176.9, 191.8; ms: *m/z* = 310 (M^+, 4), 282 (3), 187 (34), 123 (100).

Anal. Calcd for $C_{18}H_{11}FO_4$: C, 69.67; H, 3.57. Found: 69.71; H, 3.55.

1-(4-Chlorophenyl)-3-(3-chromonyl)-2,3-epoxypropan-1-one (**2e**).

This material was obtained as pale yellow plates in 81% yield, mp 151-152°; ir: ν 1679, 1642, 1588, 1466, 1430, 1221, 1169, 1090, 1006, 882, 814, 777, 759, 696, 668 cm^{-1}. ^{1}H nmr ($CDCl_3$): δ 4.19 (d, J = 1.9 Hz, 3-H), 4.36 (d, J = 1.9 Hz, 2-H), 7.47-8.25 (m, 2'-H + 8 arom. H); ^{13}C nmr ($CDCl_3$): δ 53.7, 59.3, 118.4, 119.9, 123.8, 125.8, 129.4, 130.0, 133.8, 134.4, 140.7, 154.0, 156.6, 176.9, 192.3; ms: *m/z* = 326 (M^+, 3), 298 (2), 187 (39), 171 (100).

Anal. Calcd for $C_{18}H_{11}ClO_4$: C, 66.21; H, 3.40. Found: C, 66.18; H, 3.42.

1-(4-Bromophenyl)-3-(3-chromonyl)-2,3-epoxypropan-1-one (**2f**).

This compound was isolated as yellow needles in 86% yield, 175-176°; ir: ν 1680, 1644, 1590, 1468, 1418, 1230, 1092, 882, 810, 760, 670 cm^{-1}; ^{1}H nmr ($CDCl_3$): δ 4.18 (d, J = 1.7 Hz, 3-H), 4.34 (d, J = 1.7 Hz, 2-H), 7.42-8.25 (m, 2'-H + 8 arom. H); ^{13}C nmr ($CDCl_3$): δ 53.7, 59.3, 118.4, 119.9, 123.8, 125.8, 129.5, 130.1, 132.4, 134.2, 134.4, 154.0, 156.6, 176.6, 192.5; ms: *m/z* = 370/372 (M^+, 4/4), 342/344 (3/3), 187 (100), 183 (71).

Anal. Calcd for $C_{18}H_{11}BrO_4$: C, 58.24; H, 2.99. Found: C, 58.27; H, 2.97.

3-(3-Chromonyl)-2,3-epoxy-1-(1-naphthyl)propan-1-one (**2g**).

This substance was prepared as white needles in 77% yield, 66-167°; ir: ν 1700, 1678, 1592, 1436, 1401, 1346, 1222, 1178,

1069, 888, 784, 757, 632 cm^{-1}; ^1H nmr ($CDCl_3$): δ 4.23 (d, J = 2.0 Hz, 3-H), 4.32 (d, J = 2.0 Hz, 2-H), 7.47-8.71 (m, 2'-H + 11 arom. H); ^{13}C nmr ($CDCl_3$): δ 54.1, 61.0, 118.4, 120.3, 123.8, 124.7, 125.8, 125.9, 126.9, 128.6, 128.7, 129.4, 130.4, 133.1, 133.9, 134.0, 134.3, 153.7, 156.6, 176.9, 196.3; ms: *m/z* = 342 (M^+, 6), 314 (2), 187 (34), 155 (100).

Anal. Calcd for $C_{22}H_{14}O_4$: C, 77.18; H, 4.12. Found: 77.21; H, 4.14.

3-(3-Chromonyl)-2,3-epoxy-1-(2-naphthyl)propan-1-one (**2h**).

This compound was obtained as white needles in 79% yield, 170-171°; ir: ν 1685, 1651, 1617, 1573, 1470, 1404, 1349, 1316, 1221, 906, 860, 773, 751 cm^{-1}; ^1H nmr ($CDCl_3$): δ 4.28 (d, J = 2.0 Hz, 3-H), 4.53 (d, J = 2.0 Hz, 2-H), 7.43-8.72 (m, 2'-H + 11 arom. H); ^{13}C nmr ($CDCl_3$): δ 53.8, 59.4, 118.4, 120.2, 123.8, 123.9, 125,8, 125.9, 127.1, 127.9, 128.9, 129.1, 130.0, 130.1, 132.6, 133.0, 134.3, 136.1, 154.0, 156.6, 176.7, 193.3. ms: *m/z* = 342 (M^+, 6), 314 (4), 187 (39), 155 (100).

Anal. Calcd for $C_{22}H_{14}O_4$: C, 77.18; H, 4.12. Found: C, 77.14; H, 4.10.

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