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PHOTOCHEMICAL REACTION PRODUCTS OF 4-METHOXYCINNAMIC ACID-3'-METHYLBUTYL ESTER

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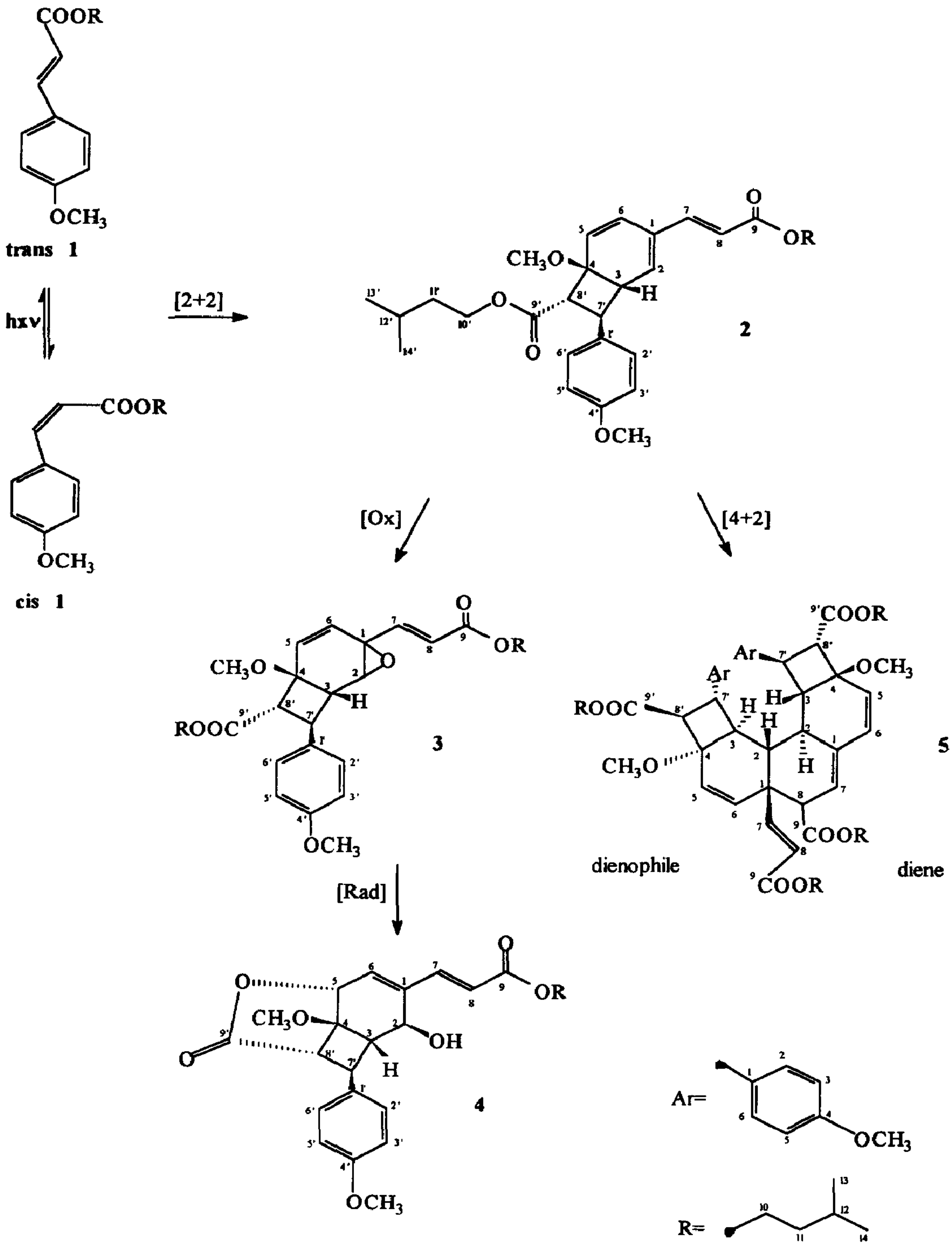
Abstract: 4-methoxycinnamic acid-3'-methylbutyl ester 1 was subjected to defined UV irradiation, resulting in the [2+2] cycloaddition products 2-4. The product 5 was also detected as a Diels-Alder adduct of 2. Nuclear magnetic resonance spectroscopy was used to identify the structures of the reaction products.

Photochemical [2+2] cycloaddition of cinnamic acid derivatives has been known for some time.[1] The formation of stereoisomeric truxinic / truxillic acid derivatives by means of irradiation with light similar to sunlight has been described in a number of publications.[2-6]

In the present study, 4-methoxycinnamic acid-3'-methylbutyl ester was irradiated in vitro by means of a solar simulator[7] used in sunscreen agent research. The wavelength of the emitted light was equivalent to that of natural sunlight up to 400 nm. Above that level, the visual/IR range was adapted so that in vivo irradiation was feasible.

Following in vitro irradiation of 1 (10% in n-hexane or propan-2-ol) the individual compounds were isolated by column chromatography and preparative TLC. ^1H and ^{13}C NMR measurements were done with the isolated fractions. The following photoproducts were determined (scheme 1):



Scheme 1. Reaction products of 4-methoxycinnamic acid-3'-methylbutyl ester after UV irradiation

After UV irradiation of trans 4-methoxycinnamic acid-3'-methylbutyl ester (1a), an equilibrium of the cis-(1b) and trans form was obtained. The ratio of trans 1 to cis 1 is 25:1.

On the basis of trans 1, compound 2 was formed as the main compound. The structure of this cyclo-adduct was determined by means of a 2-D hetero correlated COSY experiment and subsequent recording of a COLOC spectrum.[8,9] The following characteristic partial structures were detectable in the ^1H NMR spectrum of 2: One 1,4 disubstituted aromatic (AA' BB' system), one each cis and trans double bonds (10 Hz / 16 Hz), one each aromatic and aliphatic methoxyl groups, two 3-methylbutyl esters, one trisubstituted double bond (H-2) and three up field shifted displaced signals completed to form the sequence 2-3-7'-8' by means of decoupling experiments. The NOE experiments[8] established the stereochemistry.

The [2+2] cycloaddition takes place between the trans double bond of a cinnamic acid ester with the 3,4 double bond of the aromatic ring of a second cinnamic acid ester. A similar reaction was described by N. Al-Jalal et al..[10]

When compound 2 was exposed to atmospheric oxygen, it spontaneously oxidised to form epoxide 3. The ^1H NMR data are similar to those of compound 2 with the exception of the chemical shift of H-2.[11] The easy oxidisability of the material is worthy of note. The reaction mechanism is as yet unexplained. The stereochemistry of epoxide 3 is assumed due to steric hindrance by the cis-anellated cyclobutane ring. The lactone 4, probably resulting from radical formation and degradation of 3 confirms this assumption.[12] The ^1H-NMR spectrum was in part similar to those of compounds 2 and 3. However the signals for the cis double bond and one of the 3-methylbutyl ester were missing. By spin decoupling again the sequence 2-3-7'-8' was established. As the signal for H-2 was coupled with a D_2O-exchangeable signal the position of the hydroxy group was settled The chemical shift of H-5 indicated the lacton ring position and the coupling between H-5 and H-6 required a $\Delta^{1(6)}$ trisubstituted double bond. The formation of the lacton 4 from the epoxide 3 could be easily explained by conjugated addition of 9'-carboxyl group at C-5 with simultaneous migration of the double bond and opening of the epoxide ring. The compound was fully characterized by 2D-NMR spectra.[9]

A further compound 5 was detected, although in minimum concentration only. The ^1H NMR spectrum shows two sets of signals that correspond to the type-2 cyclobutane derivative. Starting with the H-8 signal in each set, decoupling experiments led to two sequences that can then be linked by means of coupling between H-2 protons.[13] The formation of a tetrameric compound 5 is thus likely. Long-range couplings between olefinic and aliphatic protons complete the structure. The Diels-Adler adduct 5 of two molecules of 2 is an endo product with respect to the side chain. In spite of minimum concentrations, the NOE effects led to the stereochemistry. It was not possible to record a ^{13}C NMR spectrum for this reason.

To summarise, the truxinic / truxillic acid derivatives do not emerge as main products of UV irradiation of 4-methoxycinnamic acid-3'-methylbutyl ester, but rather a condensed photoproduct 2 on the basic structure of which the formation of the epoxide 3, the lactone 4 and the tetrameric molecule 5 are based. Intentional thermal conversion of 2 is planned for the near future.

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8. **2** ^{1}H-NMR δ 6.34 (H-2, brd, J=6.5Hz) 3.10 (H-3, ddd, J's=9.5, 6.5, 1.5Hz) 5.82 (H-5, brd, J=10.5Hz) 6.66 (H-6, dd, J's=10.5, 1.5Hz) 7.24 (H-7, d, J=16Hz) 6.08 (H-8, d, J=16Hz) 4.20 (H10, t, J=7Hz) 1.60-1.50 (H-11, m) 1.72 (H-12, m) 0.94 (H-13 and H-14, d, J's=7Hz) 3.16 (4-OMe, s) 7.21 (H-2'/6', d) and 6.87 (H-3'/5', d, AA'BB'), 3.25 (H-7', dd) 3.55 (H-8', d, J=10Hz) 4.15 (H10', m) 1.60-1.50 (H-11', m) 1.65 (H-12', m) 0.90 (H-13' and H-14', d, J's=7Hz) 3.80 (4'-OMe, s) NOEs: H-2 with H-7(5%) and H-7'(2%), H-3 with H-8'(5%), H-2'/6'(3%) and H-2(7%), 4-OMe with H-8'(2%) and H-5(4%), H-7' with H-2'/6'(3%) and H-2(1,5%), H-8' with H-2'/6'(3%) and H-3(3%)
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11. **3** ^{1}H-NMR δ 3.545 (H-2, d, J=2Hz)
12. 4 ^{1}H-NMR δ 4.46 (H-2, brdd, J's=5.5, 2.5Hz) 3 28 (H-3, dd, J's=9, 2 5Hz) 5 14 (H-5, d, J=3 5Hz) 6.41 (H-6, d, J=3.5Hz) 7.35 (H-7, d, J=16Hz) 6.23 (H-8, d, J=16Hz) 4.21 (H-10, t, J=7Hz) 1.56 (H-11, dt, J's=7, 7Hz) 1.71 (H-12, tqq, J's=7, 7, 7Hz) 0.93 (H-13 and H-14, d, J's=7Hz) 7.18 (H-2'/6', AA') 6.89 (H-3'/5', BB') 2.66 (H-7', dd, J's=9, 7Hz) 3.21 (H-8', d, J=7Hz) 3.40 (4-OMe, s) 3.81 (4'-OMe, s) 1.84 (2-OH, d, J=5.5Hz) NOEs: H-2 with H-3(7%), H-7'(6%) and H-8(20%), H-3 with H-2'/6'(5%) and H-2(5%), H-5 with H-6(8%) and 4-OMe(5%), H-7' with H-2'/6'(5%) and H-2(4%), H-8' with H-2'/6' (5%), 4-OMe with H-5(10%) and H-8'(5%)
13. **5** ^{1}H-NMR(DP) δ 1.60 (H-2, dd, J's=11, 2Hz) 2.62 (H-3, brd, J=9Hz) 6.01 (H-5, brd, J=10.5Hz) 6.31 (H-6, d, J=10.5Hz) 6.84 (H-7, d, J=16Hz) 5.83 (H-8, d, J=16) 4.23-4.03 (H-10, m) 1.71-1.44 (H-11, H-12, m) 0.91 (H-13 and H-14, d, J's=7Hz) 6.92 (H-2'/6', AA') 6.76 (H-3'/5', BB') 3.09 (H-7' and H-8', m^{a}) 4.23-4.00 (H-10', m) 1.71-1.44 (H-11', H-12', m) 0.91 (H-13' and H-14', d, J's=7Hz) 3.01 (4-OMe, s) 3.81 (4'-OMe, s^{b}) NOEs: H-2 with H-8, H-3 with H-2'/6', 4-OMe with H-5 ^{1}H-NMR(DI) δ 2.19 (H-2, brd, J=11Hz) 2.59 (H-3, brd, J=9Hz) 5.50 (H-5, brd, J=10) 6.54 (H-6, d, J=10Hz) 6.045 (H-7, dd, J's=2.5, 4.5Hz) 3.06 (H-8, brd, J=4.5Hz) 4.23-4.03 (H-10, m) 1.71-1.44 (H-11, H-12, m) 0.88 (H-13 and H-14, d, J's=7Hz) 7.25 (H-2'/6', AA') 6.87 (H-3'/5', BB') 2.96 (H-7', dd, J's=10, 9Hz) 3.13 (H-8', d, J=10Hz) 4.23-4.00 (H-10', m) 1.71-1.44 (H-11', H-12', m) 0.88 (H-13' and H-14', d, J's=7Hz) 2.72 (4-OMe, s) 3.76 (4'-OMe, s^{b}) NOEs: H-3 with H-2'/6', H-8 with H-7 and H-6(DP), H-7' with H-2 and H-2'/6', 4-OMe with H-8' and H-5 a) not first order; when C_6H_6 H-7' 3.24 dd (J's=10, 9Hz) and H-8' 3.20 d (J=10Hz) is added ; b) possibly interchangeable

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