

EUGENOL AS STARTING MATERIAL FOR THE SYNTHESIS
OF 3-ALKYL MUONIC ACID DIMETHYL ESTERS AND
3-ALKYL ADIPIC ACID DIMETHYL ESTERS

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Compounds 1b-e prepared from eugenol (1a) were submitted to ozonation in methanol at 0°C, giving the 3-alkyl muonic acid dimethyl esters (2b-e). These were reduced to the corresponding 3-alkyl dimethyl esters of adipic acid (3b-e).

As part of a program¹ of study of abundant natural products available in Brazil we turned our attention to the transformation of eugenol (1a) into aliphatic derivatives. Compounds 1b-g were prepared by usual methods² from 1a and were submitted to ozonation in methanol.

The products from 1b-e were purified by silica gel chromatography and characterized as the 3-alkyl muonic acid dimethyl esters 2b-e³. In all cases the yield was about 45% and the ¹H NMR spectra showed the presence of a mixture of Δ^2Z , Δ^4Z and Δ^2E , Δ^4Z isomers⁴. These mixtures furnished in quantitative yield the corresponding adipates 3b-e by hydrogenation in EtOAc in the presence of Pd/C.

The derivatives 1f-g did not yield muonic acid derivatives when submitted to our ozonation condition. For 1f the main product was the methyl ester of veratric acid (20%) while for 1g a complex mixture of products was formed.

With the present method it is possible to prepare in ~ 45% yield 3-alkyl muonic acid dimethyl ester and 3-alkyl adipic acid dimethyl ester. These aliphatic compounds can be utilized as interesting intermediates in synthetic works.

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References and notes

1. P.R.R. Costa, C.C. Lopes and A.V. Pinto, *Synth. Comm.*, 13, 691 (1983); P.R.R. Costa and J.A. Rabi, *J. Chem. Research*(S), 22 (1984); P.R.R. Costa, J.A. Rabi and W.M. Queiroz, *J. Chem. Research*(S), 20 (1984); E.J. Barreiro, P.R.R. Costa, F.A.S. Coelho and F.M.C. Faria, *J. Chem. Research*(S), 220 (1985); *J. Chem. Research*(M), 2301 (1985).
2. $1a \rightarrow 1a'$, $(CH_3)_2SO_4$, NaOH, H_2O (87%); $1a' \rightarrow 1b$, H_2 , AcOEt, Pd/C (100%); $1a' \rightarrow 1c$, $BF_3 \cdot Et_2O/NaBH_4/THF$, NaOH/ H_2O_2/H_2O , $Ac_2O/DMAP$ (79%); $1a' \rightarrow 1d$, $O_2/AcOH$, 2h, $NaBH_4/CH_3OH$, $Ac_2O/DMAP$ (82%); $1a' \rightarrow 1e$, $BF_3 \cdot Et_2O/NaBH_4/THF$, Jones, CH_2N_2/Et_2O (70%); $1a' \rightarrow 1f$, KOH, CH_3OH/O_3 , HOAc/Zn (80%); $1f \rightarrow 1g$, $NaBH_4$, CH_3OH/Ac_2O , DMAP (96%).
3. For example of transformation of veratrolol systems into the muonic acid systems see: R.B. Woodward, M.P. Cava, W.D. Ollis, A. Hunger, H.U. Daeniker and K. Schenker, *Tetrahedron*, 19, 247 (1963); Paulo R.R. Costa, Sergio Pinheiro and Cláudio C. Lopes, *Tetrahedron Lett.*, 4155 (1985).
4. Depending on the experiment purified products containing slight different proportions of geometrical isomers Δ^2Z , Δ^4Z and Δ^2E , Δ^4Z were obtained. This fact permits the interpretation of the ¹H NMR spectra of the mixtures. The hydrogen atoms attached at C₄ and C₅ show identical chemical shifts and multiplicities in both geometrical isomers, while for hydrogen atom at C₂ and the methoxyl groups the chemical shifts differ. The same was observed for 2c-e. 2b (Δ^2Z , Δ^4Z) (100 MHz, $CDCl_3$) δ 7.06(1H, dd, J=12.0 and 2.0Hz, C₄-H), 5.88(1H, d, J=12.0Hz, C₅-H), 5.74 (1H, br, C₂-H), 3.70(3H, s, CO₂CH₃), 3.68(3H, s, CO₂CH₃), 2.65(2H, t, J=7.0Hz), 1.60(2H, m), 0.88(3H, t, J=7.0Hz); 2b (Δ^2E , Δ^4Z) (100MHz, $CDCl_3$) δ 7.06(1H, dd, J=12.0 and 2.0Hz, C₄-H), 6.69(1H, m, C₂-H), 5.88(1H, d, J=12.0Hz, C₅-H), 3.86(3H, s, CO₂CH₃), 3.84(3H, s, CO₂CH₃), 2.48(2H, t, J=7.0Hz), 1.60(2H, m), 0.88(3H, t, J=7.0Hz).

