

Reactions of Aromatic Dithiols with Diethyl 2-Alkyl-2-(oxiran-2-ylmethyl)malonates

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Abstract—New sulfur-containing butano-4-lactones were synthesized by reaction of diethyl 2-alkyl-2-(oxiran-2-ylmethyl)malonates with biphenyl-4,4'-dithiol, (biphenyl-4,4'-diyl)dimethanethiol, and (2,4,6-trimethylbenzene-1,3-diyl)dimethanethiol. Opening of the oxirane ring in the initial ester followed the Krasuskii rule.

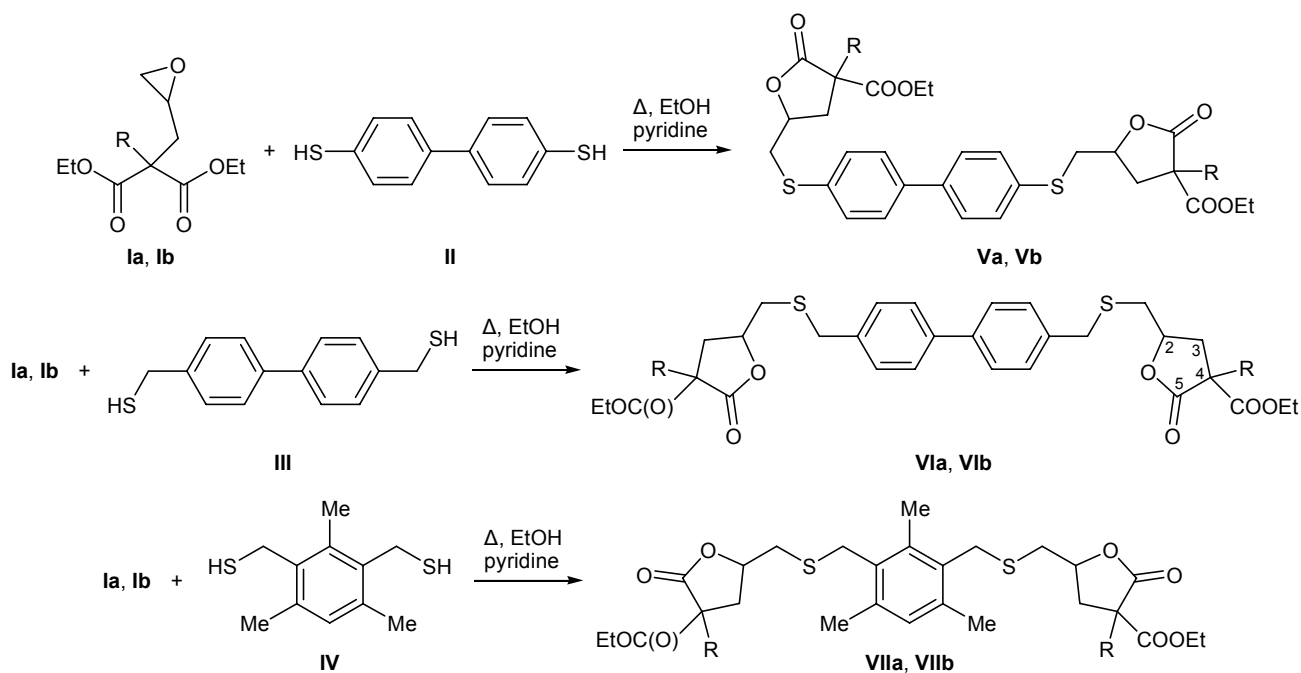
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Functionally substituted butano-4-lactones constitute a promising class of organic compounds. They are widely used in fine organic synthesis and in synthesis of medicinal agents [1–3]. Therefore, development of new methods of synthesis of oxygen-, nitrogen-, and especially sulfur-containing butano-4-lactone derivatives seems to be a quite important problem, and it

could considerably extend the synthetic potential and scope of application of this class of compounds [3–7].

We previously showed that the use of alkyl(oxiran-2-ylmethyl)malonic and acetoacetic acid esters [6–9] ensures wide variation of structural fragments in butano-4-lactones and one-step syntheses of various polyfunctionalized butano-4-lactones. Reactions of

Scheme 1.



[†] Deceased.

dithiols with oxiranes underlie procedures for the preparation of artificial fibers [10], branched transport molecules [11, 12], molecular glasses [13, 14], potential biologically active substances [15, 16], etc.

The present communication reports on the reaction of diethyl 2-alkyl-2-(oxiran-2-ylmethyl)malonates **Ia** and **Ib** with sulfur-containing nucleophiles, biphenyl-4,4'-dithiol (**II**), (biphenyl-4,4'-diyl)dimethanethiol (**III**), and (2,4,6-trimethylbenzene-1,3-diyl)dimethanethiol (**IV**). The effects of different factors, such as temperature, solvent, reaction time, and reactant ratio, on the process were studied with a view to optimize the reaction conditions. The oxirane ring in compounds **Ia** and **Ib** was opened according to the Krasuskii rule [17] with formation of the corresponding alcohols which underwent cyclization under reduced pressure to form butano-4-lactones **V–VII** (Scheme 1). The reactions were carried out on heating in ethanol in the presence of pyridine, the reactant ratio **I**-to-(**II–IV**) being 2:1. Insofar as the initial oxiranes were racemates, compounds **V–VII** were formed as mixtures of diastereoisomers; in addition, the cyclization gave rise to new chiral centers. As a result, overlapping multiplet signals were observed in their ^1H NMR spectra. The structure of compounds **V–VII** was confirmed by the IR and ^1H NMR spectra and elemental analyses.

EXPERIMENTAL

The ^1H NMR spectra were recorded from solutions in $\text{DMSO}-d_6$ on a Varian Mercury-300 spectrometer (300 MHz) using hexamethyldisiloxane as internal reference. The IR spectra were measured on UR-20 and Nicolet FTIR NEXUS spectrometers from thin films. Initial diethyl 2-alkyl-2-(oxiran-2-ylmethyl)malonates **Ia** and **Ib** were synthesized according to the procedure described in [18].

Butano-4-lactones V–VII (general procedure). A mixture of 5.9 mmol of dithiol **II–IV**, 12 mmol of ester **Ia** or **Ib**, 0.01 ml of pyridine, and 10 ml of ethanol was heated for 5 h at 75–80°C. The solvent was removed under reduced pressure, and the residue was heated at 50–60°C to complete cyclization, dissolved in 20 ml of diethyl ether, and reprecipitated with hexane. The viscous material was separated from the solution, dried under reduced pressure, and purified by column chromatography on Al_2O_3 using ethanol as eluent. All compounds **V–VII** were isolated as undistillable viscous substances.

4,4'-Bis(4-ethoxycarbonyl-5-oxo-4-pentyltetrahydrofuran-2-ylmethylsulfanyl)biphenyl (Va). Yield

2.9 g (70%), $n_D^{20} = 1.5780$. IR spectrum, ν , cm^{-1} : 3010, 1605 ($\text{C}=\text{C}_{\text{arom}}$), 1770 ($\text{C}=\text{O}$, lactone), 1740 ($\text{C}=\text{O}$, ester). ^1H NMR spectrum, δ , ppm: 0.88 m (6H, CH_3 , pentyl), 1.10–2.25 m (22H, $\text{CH}_3\text{CH}_2\text{O}$, CH_2), 2.46 m and 2.67 m (2H each, 3-H), 3.10–3.40 m (4H, CH_2S), 4.20 m (4H, OCH_2), 4.63 m (2H, 2-H), 7.40–7.60 m (8H, H_{arom}). Found, %: C 65.03; H 54.10; S 8.99. $\text{C}_{38}\text{H}_{50}\text{O}_8\text{S}_2$. Calculated, %: C 65.30; H 18.31; S 9.18.

4,4'-Bis(4-ethoxycarbonyl-4-isopentyl-5-oxotetrahydrofuran-2-ylmethylsulfanyl)biphenyl (Vb). Yield 2.7 g (65%), $n_D^{24} = 1.5736$. IR spectrum, ν , cm^{-1} : 3010, 1605 ($\text{C}=\text{C}_{\text{arom}}$), 1770 ($\text{C}=\text{O}$, lactone), 1740 ($\text{C}=\text{O}$, ester). ^1H NMR spectrum, δ , ppm: 0.96 m [12H, (CH_3) $_2\text{CH}$], 1.23 m (6H, $\text{CH}_3\text{CH}_2\text{O}$), 1.10–1.80 m (6H, CHCH_2CH_2), 1.90–2.20 m (4H, 4- CH_2), 2.45 m and 2.68 m (2H each, 3-H), 3.15–3.45 m (4H, CH_2S), 4.19 m (4H, OCH_2), 4.61 m (2H, 2-H), 7.40–7.60 m (8H, H_{arom}). Found, %: C 65.59; H 18.44; S 8.91. $\text{C}_{38}\text{H}_{50}\text{O}_8\text{S}_2$. Calculated, %: C 65.30; H 18.21; S 9.18.

4,4'-Bis(4-ethoxycarbonyl-5-oxo-4-pentyltetrahydrofuran-2-ylmethylsulfanylmethyl)biphenyl (VIa). Yield 3.5 g (85%), $n_D^{25} = 1.5603$. IR spectrum, ν , cm^{-1} : 3010, 1605 ($\text{C}=\text{C}_{\text{arom}}$), 1780 ($\text{C}=\text{O}$, lactone), 1735 ($\text{C}=\text{O}$, ester). ^1H NMR spectrum, δ , ppm: 0.90 m (6H, CH_3 , pentyl), 1.05–2.15 m (22H, $\text{CH}_3\text{CH}_2\text{O}$, CH_2), 2.40 m and 2.64 m (2H each, 3-H), 2.77 m (4H, 2- CH_2), 3.81 s (4H, SCH_2), 4.20 m (4H, OCH_2), 4.59 m (2H, 2-H), 7.30–7.60 m (8H, H_{arom}). Found, %: C 65.81; H 7.79; S 9.09. $\text{C}_{40}\text{H}_{54}\text{O}_8\text{S}_2$. Calculated, %: C 66.09; H 7.49; S 8.82.

4,4'-Bis(4-ethoxycarbonyl-4-isopentyl-5-oxotetrahydrofuran-2-ylmethylsulfanylmethyl)biphenyl (VIb). Yield 3.7 g (88%), $n_D^{25} = 1.5643$. IR spectrum, ν , cm^{-1} : 3010, 1605 ($\text{C}=\text{C}_{\text{arom}}$), 1780 ($\text{C}=\text{O}$, lactone), 1735 ($\text{C}=\text{O}$, ester). ^1H NMR spectrum, δ , ppm: 0.96 m [12H, (CH_3) $_2\text{CH}$], 1.29 m (6H, $\text{CH}_3\text{CH}_2\text{O}$), 1.10–1.80 m (6H, CHCH_2CH_2), 1.80–2.17 m (4H, 4- CH_2), 2.39 m and 2.63 m (2H each, 3-H), 2.76 m (4H, 2- CH_2), 3.80 s (4H, SCH_2), 4.19 m (4H, OCH_2), 4.58 m (2H, 2-H), 7.30–7.60 m (8H, H_{arom}). Found, %: C 66.31; H 7.77; S 9.11. $\text{C}_{40}\text{H}_{54}\text{O}_8\text{S}_2$. Calculated, %: C 66.09; H 7.49; S 8.82.

2,6-Bis(4-ethoxycarbonyl-5-oxo-4-pentyltetrahydrofuran-2-ylmethylsulfanylmethyl)-1,3,5-trimethylbenzene (VIIa). Yield 2.1 g (51%), $n_D^{20} = 1.5300$. IR spectrum, ν , cm^{-1} : 3010, 1605 ($\text{C}=\text{C}_{\text{arom}}$), 1790 ($\text{C}=\text{O}$, lactone), 1750 ($\text{C}=\text{O}$, ester). ^1H NMR spectrum, δ , ppm: 0.89 m (6H, CH_3 , pentyl), 1.10–2.20 m (22H, $\text{CH}_3\text{CH}_2\text{O}$, CH_2), 2.43 m and 2.66 m (2H

each, 3-H), 2.40 s (9H, CH₃), 2.83 m (4H, 2-CH₂), 3.82 s (4H, SCH₂), 4.20 m (4H, OCH₂), 4.62 m (2H, 2-H), 6.78 s (1H, H_{arom}). Found, %: C 64.25; H 8.38; S 9.51. C₃₇H₅₆O₈S₂. Calculated, %: C 64.13; H 8.15; S 9.25.

2,6-Bis(4-ethoxycarbonyl-4-isopentyl-5-oxotetrahydrofuran-2-ylmethylsulfanylmethyl)-1,3,5-trimethylbenzene (VIIb). Yield 1.8 g (41%), $n_D^{22} = 1.5320$. IR spectrum, ν , cm⁻¹: 3010, 1605 (C=C_{arom}), 1790 (C=O, lactone), 1750 (C=O, ester). ¹H NMR spectrum, δ , ppm: 0.96 m [12H, (CH₃)₂CH], 1.25 m (6H, CH₃CH₂O), 1.10–2.20 m (10H, CHCH₂CH₂), 2.45 m and 2.65 m (2H, 3-H), 2.38 s (9H, CH₃), 2.83 m (4H, 2-CH₂), 3.85 s (4H, SCH₂), 4.19 m (4H, OCH₂), 4.63 m (2H, 2-H), 6.79 s (1H, H_{arom}). Found, %: C 64.29; H 8.41; S 9.44. C₃₇H₅₆O₈S₂. Calculated, %: C 64.13; H 8.15; S 9.25.

REFERENCES

- Collins, I., *J. Chem. Soc., Perkin Trans. 1*, 1999, p. 1377.
- Kuroyan, R.A., Pogosyan, S.A., and Grigoryan, N.P., *Khim. Zh. Arm.*, 1998, vol. 51, p. 34.
- Mesropyan, E.G. and Avetisyan, A.A., *Arm. Khim. Zh.*, 1993, vol. 46, p. 32.
- Kochikyan, T.V., Samvelyan, M.A., Haroutyunyan, V.S., and Avetissyan, A.A., *Synth. Commun.*, 2006, vol. 36, p. 1613.
- Kochikyan, T.V., Arutyunyan, E.V., Arutyunyan, V.S., and Avetisyan, A.A., *Khim. Geterotsikl. Soedin.*, 2005, p. 1625.
- Mesropyan, E.G., Ambartsumyan, G.B., Galstyan, A.S., and Avetisyan, A.A., *Khim. Zh. Arm.*, 2003, vol. 56, p. 64.
- Mesropyan, E.G., Ambartsumyan, G.B., Avetisyan, A.A., Melikyan, G.S., and Galstyan, A.S., *Khim. Zh. Arm.*, 2003, vol. 56, p. 97.
- Mesropyan, E.G., Ambartsumyan, G.B., Buniyatyanyan, Yu.A., and Dangyan, M.T., *Arm. Khim. Zh.*, 1976, vol. 29, p. 944.
- Mesropyan, E.G., Karapetyan, Z.T., and Dangyan, M.T., *Arm. Khim. Zh.*, 1977, vol. 30, p. 604.
- Carpenter, A.S., Reeder, F., and Waters, D.J., UK Patent no. 678576, 1952.
- Getautis, V., Paliulis, O., Degutyte, R., and Paulauskaite, I., *Khim. Geterotsikl. Soedin.*, 2004, p. 96.
- Matoliukstyte, A., Grazulevicius, J.V., and Jankauskas, V., *Mol. Cryst. Liq. Cryst.*, 2007, vol. 466, p. 85.
- Gaidelis, V., Gavutiene, J., Getautis, V., Grazulevicius, J.V., Jankauskas, V., Kavaliunas, R., Lazauskaite, R., Paliulis, O., Rossman, M.A., Sidoravicius, D.J., Smith, T.P., and Stanishauskaite, A., US Patent no. 6214503, 2001.
- Sinkeviciute, G., Stanishauskaite, A., Gaidelis, V., Jankauskas, V., and Montrimas, E., *Mol. Cryst. Liq. Cryst.*, 2007, vol. 468, p. 515.
- Mesropyan, E.G., Galstyan, A.S., Avetisyan, A.A., and Ter-Vardanyan, L.R., *Izv. Ross. Akad. Nauk, Ser. Khim.*, 2009, p. 1483.
- Nikitina, L.E., Plemenkov, V.V., Startseva, V.A., Artemova, N.P., and Fedyunina, I.V., Abstracts of Papers, *II Vserossiiskaya konferentsiya "Khimiya i tekhnologiya rastitel'nykh veshchestv"* (IInd All-Russian Conf. "Chemistry and Technology of Vegetable Substances"), Kazan, June 24–27, 2002, p. 13.
- Krasuskii, K.A., *Zh. Obshch. Khim.*, 1936, vol. 6, p. 460.
- Mesropyan, E.G., Karapetyan, Z.T., and Dangyan, M.T., *Arm. Khim. Zh.*, 1969, vol. 22, p. 904.