LETTERS TO THE EDITOR

Reactions of Lithium Acylates α-Carbanions with 1,2-Diiodoethane

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Abstract—The interaction of lithium acylates α -carbanions (obtained via metallation of acetic, butyric, and isobutyric acids with lithium diisopropylamide) with 1,2-diiodoethane under argon in tetrahydrofuran at 20–25°C has proceeded as oxidative cross-coupling of enolate anions to form succinic, 2,3-diethylsuccinic, and 2,2,3,3-tetramethylsuccinic acids with yields 50, 53, and 16%, respectively. The products of sequential nucleophilic substitution of iodine atoms with alkyloxycarbonyl species have not been detected.

Keywords: 1,2-diiodoethane, dicarboxylic acids, lithium acylates α -carbanions, metallation, oxidative crosscoupling

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It has been earlier shown that the reaction of dibromoalkanes containing distant bromomethylene groups with lithium acylates α -carbanions proceeds as sequential nucleophilic substitution of bromine atoms with the formation of the corresponding dicarboxylic acids [1–4]. On the contrary, we have found that the reaction of lithium acylates α -carbanions with 1,2-dibromoethane affords the products of oxidative coupling of α -carbanions (the corresponding dicarboxylic acids), except for the reaction of α -carbanion of lithium acetate, in which both nucleophilic substitution and oxidative coupling occur simultaneously, leading to adipic and succinic acids, respectively [5].

Extending the above-mentioned studies, we investigated the reaction of lithium acylates α -carbanions with 1,2-diiodoethane. It was found that the reaction of lithium acylates α -carbanions **2a**-c [prepared via metallation of acetic (**1a**), butyric (**1b**), and isobutyric (**1c**) acids with lithium diisopropyl-amide (LDA)] with 1,2-diiodoethane **3** under argon atmosphere in THF at 20–25°C in the ratio of **2** : **3** = 2 : 1 afforded succinic (**6a**), 2,3-diethylsuccinic (**6b**), and 2,2,3,3-tetramethylsuccinic (**6c**) acids with 50, 53, and 16% yield, respectively (Scheme 1). As in the case of 1,2-dibromoethane, ethylene was evolved in the course of the reaction.

The products composition suggested that, similarly to the reaction of lithium acylates α -carbanions with 1,2-dibromoethane [5], 1,2-diiodoethane was involved in the redox process with the formation of dicarboxylic acids **6a–c**, the products of oxidative coupling of lithium acylates enolates **2a–c**. 2,3-Diethylsuccinic acid **6b** was formed as a mixture of diastereomeric *meso-* and (±)-forms in 2 : 1 ratio. The formation of the reaction products could be explained by the scheme including the stage of electron transfer from lithium acylates **2a–2c** to 1,2-diiodoethane **3** (Scheme 1).

A similar scheme of the formation of the products of oxidative coupling of α -carbanions has been previously suggested for the reactions with other oxidants [5, 6].

Unlike the reaction of lithium acylates enolates with 1,2-dibromoethane, in the case of 1,2-diiodoethane, the formed iodoethyl radical **3b**, apparently, was completely eliminated yielding ethylene and iodine atom, since ethyl iodide was not detected in the reaction products; moreover, when performing the reaction in the presence of a spin trap (hex-1-ene, as described in [5, 7]), the expected spin-adduct of **3b** and hex-1-ene (octyl iodide) was not found. Iodine formed in the course of the reaction was also involved in the oxidative coupling, as described in [6, 8].



Besides, unlike the reaction of lithium acetate enolate with 1,2-dibromoethane [5], in the case of 1,2diiodoethane, the product of sequential nucleophilic substitution of the iodine atoms (adipic acid) was not found, despite higher activity of iodoalkanes in the reactions of nucleophilic substitution than bromoalkanes [9, 10].

Comparison of the yields of dicarboxylic acids formed in the reactions of lithium acylates enolates with 1,2-dibromo- and 1,2-diiodoethane showed that the dependence of the yield of dicarboxylic acids on the structure of lithium acylates α -carbanions was in general retained (**6b** > **6a** > **6c**).

Reaction of carboxylic acids with 1,2-diiodoethane. A solution of 0.01 mol of carboxylic acid 1a-1c in 20 mL of anhydrous THF was added at stirring under argon to a solution of 0.02 mol of LDA in 30 mL of anhydrous THF cooled to 0-5°C. The reaction mixture was heated to 35-40°C, stirred for 40 min, and then cooled to 20-25°C. 0.005 mol of 1,2diiodoethane 3 in 20 mL of anhydrous THF was then added, and the mixture was stirred for 2 h. During the reaction, the mixture turned dark due to the formation of iodine. 30 mL of distilled water was added to the formed mixture. The aqueous layer was treated with 10% hydrochloric acid to pH = 1 and extracted with diethyl ether (3×30 mL). The combined extracts were dried over Na₂SO₄. After evaporation of ether, the crystals of dicarboxylic acid **6a–6c** were formed.

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Ethylene was detected as 1,2-dibromoethane after trapping with bromine, as described in [5]. The solution of bromine in carbon tetrachloride was analyzed by GC and GCMS methods. Similarly, the experiments in the presence of hex-1-ene were performed, which was added in the flask together with 1,2-diiodoethane in equimolar amount.

Melting points of dicarboxylic acids coincided with the reference data [11, 12].

Succinic acid (6a). mp 188–189°C. ¹H NMR spectrum, δ , ppm: 2.40 s (4H, CH₂). ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 28.54 (CH₂), 179.63 (C=O). Mass spectrum, *m*/*z* (*I*_{rel}, %): 101 (15), 100 (49), 74 (69), 72 (18), 56 (36), 55 (95), 46 (10), 45 (100), 44 (41), 43 (15), 42 (13), 40 (15).

2,3-Diethylsuccinic acid (6b). mp 127–133°C.

meso-2,3-Diethylsuccinic acid. ¹H NMR spectrum, δ , ppm: 0.90 t (6H, CH₃), 1.52–1.70 m (2H, CH₂), 1.70– 1.87 m (2H, CH₂), 2.63–2.70 m (2H, CH). ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 11.09 (CH₃), 22.20 (CH₂), 46.79 (CH), 182.08 (C=O). Mass spectrum, *m/z* (*I*_{rel}, %): 128 (25), 101 (44), 100 (13), 99 (21), 88 (19), 87 (30), 84 (50), 83 (34), 73 (37), 70 (20), 69 (75), 57 (10), 56 (46), 55 (100), 53 (13), 45 (28), 44 (26), 43 (32), 42 (43), 41 (65), 40 (16).

(±)-2,3-Diethylsuccinic acid. ¹H NMR spectrum, δ, ppm: 1.05 t (6H, CH₃), 1.87–1.90 m (4H, CH₂), 2.70–

2.80 m (2H, CH). ¹³C NMR spectrum, δ_{C} , ppm: 13.03 (CH₃), 22.36 (CH₂), 48.48 (CH), 182.88 (C=O). Mass spectrum, *m/z* (*I*_{rel}, %): 128 (20), 101 (14), 100 (10), 99 (26), 88 (35), 87 (53), 84 (28), 83 (34), 73 (65), 70 (33), 69 (100), 56 (36), 55 (88), 53 (12), 45 (28), 44 (39), 43 (29), 42 (37), 41 (58), 40 (23).

2,2,3,3-Tetramethylsuccinic acid (6c). mp 170–171°C. ¹H NMR spectrum, δ , ppm: 1.20 s (12H, CH₃). ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 17.32 (CH₃), 48.50 (C), 179.36 (C=O). Mass spectrum, *m*/*z* (*I*_{rel}, %): 88 (100), 87 (10), 84 (49), 83 (25), 73 (52), 71 (14), 70 (46), 69 (80), 59 (34), 57 (10), 56 (15), 55 (30), 45 (19), 44 (46), 43 (43), 42 (19), 41 (88), 40 (28).

1,2-Dibromoethane. Mass spectrum, m/z (I_{rel} , %): 109 (94), 108 (4), 107 (100), 105 (3), 95 (4), 93 (5), 80 (6), 78 (6), 44 (19), 40 (3).

¹H and ¹³C NMR spectra were registered in CDCl₃ + CF₃COOH using a Bruker AM-300 spectrometer [300.13 (¹H) and 75.47 MHz (¹³C)]. Chromato–mass spectrometry analysis was performed using a GCMS-QP2010S Shimadzu instrument (electron ionization at 70 eV, the range of detected masses 33–500 Da). Capillary column HP-1MS (30 m × 0.25 mm × 0.25 µm) was used, temperature of injector – 280°C, temperature of ionization chamber – 200°C. The analysis was performed in temperature programming mode from 50 to 280°C with the rate 10 deg/min, carrier gas – helium (1.1 mL/min).

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CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

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