

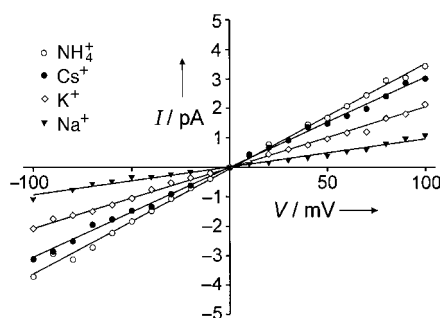


Figure 3. Current–voltage relationships for single channels of **1** in soybean lecithin membranes in the presence of various electrolytes. Only the highest conductance levels were considered.

The present work reports on the synthesis and functional characterization of a novel cation channel. The structural characterization of the active conformation of the THF-gramicidin hybrids in the membrane by isotope labeling and solid-phase NMR is currently under investigation and will be reported elsewhere.

Experimental Section

Planar lipid membranes were prepared by painting a solution of soybean lecithin (45% Avanti Polar Lipids) in *n*-decane (25 mg mL⁻¹) over a cuvette aperture with a diameter of 0.15 mm.^[1c] The membrane surface was 0.01 to 0.02 mm² assuming a specific membrane capacity of 0.4 μF cm⁻². All experiments were performed at ambient temperature. The electrolyte solutions with a concentration of 1 M each were unbuffered. The probes, dissolved in methanol, were added to the *trans* side, to give a final concentration of 0.01–0.03 μM. Current detection and recording was performed using a patch-clamp amplifier Axopatch 200, a DigiData A/D converter, and the pClamp 6 software (Axon Instruments). The acquisition frequency was 5 kHz. The data were filtered with an analogue filter at 100 Hz for further analysis.

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Simple Synthesis of Tetra-Acceptor-Substituted Alkenes by the Formal Dehydrodimerization of Malonates**

Torsten Linker* and Ursula Linker

Dedicated to Professor Bernd Giese
on the occasion of his 60th birthday

Acceptor-substituted alkenes are important precursors for Diels–Alder reactions, Michael additions, or polymerizations. Due to their electronic properties, ethylenetetracarboxylates exhibit an especially high reactivity, but are difficult to prepare. Traditional syntheses start from halomalonates and sodium or mesoxalic acid,^[1] whereas modern methods by the dimerization of malonates require an excess of oxidant or the use of expensive azo compounds.^[2] Furthermore, disadvantages of all methodologies are the moderate yields. Herein we describe a simple new access to tetra-acceptor-substituted alkenes by the formal dehydrodimerization of malonates in only two steps. The synthesis is characterized by cheap reagents and high yields.

During the course of our investigations on transition metal mediated radical reactions,^[3] we succeeded in the addition of dimethyl malonate (**1a**) to various alkenes. To further improve the yields and due to the mild conditions, we became

[*] Prof. Dr. T. Linker, Dr. U. Linker
Institut für Organische Chemie der Universität
Pfaffenwaldring 55, 70569 Stuttgart (Germany)
Fax: (+49) 711-685-4269
E-mail: torsten.linker@po.uni-stuttgart.de

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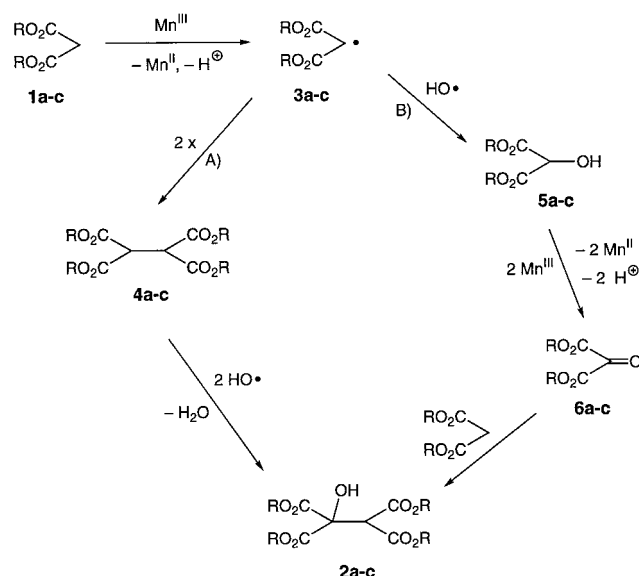
interested in reactions under ultrasonic irradiation. Such reactions have attracted much attention in organic synthesis^[4] and were recently applied for transition metal mediated radical reactions.^[5] However, our experiments did not afford the expected addition products, but instead the alcohol **2a** in high yield. To further optimize this surprising reaction, dimethyl malonate (**1a**) was irradiated without alkenes under various conditions (Table 1).

The initial experiments were performed in the presence of ceric(IV) ammonium nitrate (CAN; entries 1 and 2), the reagent of choice for the radical reactions we investigated recently.^[3c-e] However, the desired alcohol **2a** was isolated in only moderate yield at low conversion, which can be rationalized by the direct oxidation of the solvents.^[4] Manganese(III) acetate dihydrate (abbreviated here as Mn(OAc)₃) in acetic acid afforded better results (entry 3), although the conversions were not satisfactory. Finally, the optimal conditions were found by the addition of acetic anhydride and potassium acetate, which accelerate the enolization of CH-acidic compounds and, therefore, the generation of radicals (entry 4).^[3] Furthermore, reactions with catalytic amounts of oxidant were realized (entries 5–7), since manganese(II) can be reoxidized to manganese(III) in acetic acid during ultrasonic irradiation.^[5a] With only 0.05 equiv of Mn(OAc)₃, the conversion dropped remarkably (entry 7), but unconverted malonate **1** could be reisolated by distillation. Besides manganese(III) acetate, CAN and potassium permanganate can serve as cheap oxidants, but again for such reactions the conversion is lower (entries 8 and 9). Finally, control experiments clearly indicated that both manganese salts and ultrasound are essential for the formation of the alcohol **2a** (entries 10 and 11). After the successful optimization of the reaction conditions with dimethyl malonate (**1a**), the diethyl ester **1b** and the sterically more hindered diisopropyl ester **1c** afforded the desired products **2b** and **2c** in excellent yields as well (entries 12 and 13).

Table 1. Ultrasonic reactions of the malonates **1**.^[a]

Entry	Ester (R =)	Oxidant [equiv]	Solvent	Conversion [%] ^[b]	Yield of 2 [%] ^[c]
1	1a (Me)	CAN [1.0]	MeOH ^[d]	20	45
2	1a (Me)	CAN [1.0]	CH ₃ CN ^[d]	20	43
3	1a (Me)	Mn(OAc) ₃ [1.0]	HOAc	40	90
4	1a (Me)	Mn(OAc) ₃ [1.0]	HOAc/Ac ₂ O ^[e]	85	96
5	1a (Me)	Mn(OAc) ₃ [0.4]	HOAc/Ac ₂ O ^[e]	90	98
6	1a (Me)	Mn(OAc) ₃ [0.1]	HOAc/Ac ₂ O ^[e]	90	98
7	1a (Me)	Mn(OAc) ₃ [0.05]	HOAc/Ac ₂ O ^[e]	60	93
8	1a (Me)	CAN [0.1]	HOAc/Ac ₂ O ^[e]	60	90
9	1a (Me)	KMnO ₄ [0.1]	HOAc/Ac ₂ O ^[e]	65	98
10	1a (Me)	–	HOAc/Ac ₂ O ^[e]	–	–
11	1a (Me)	Mn(OAc) ₃ [0.1]	HOAc/Ac ₂ O ^[e,f]	–	–
12	1b (Et)	Mn(OAc) ₃ [0.1]	HOAc/Ac ₂ O ^[e]	85	98
13	1c (iPr)	Mn(OAc) ₃ [0.1]	HOAc/Ac ₂ O ^[e]	80	98

[a] Reaction of 5.0 mmol of malonate **1** in 40 mL of solvent at 80 °C for 3 h, irradiation with a BANDELIN sonotrode HD 200 (50 % intensity). [b] Unconverted malonate **1** was reisolated by distillation. [c] Yield based on converted malonate **1**. [d] Reaction at 50 °C. [e] Addition of 3.0 g of potassium acetate. [f] Reaction without ultrasound.

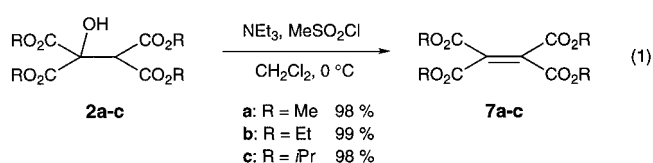


Scheme 1. Proposed mechanism for the formation of alcohols **2**.

The formation of the alcohols **2** can be rationalized by two different mechanistic pathways (Scheme 1). In the first step, the malonyl radicals **3** are generated from the malonates **1**, an electron transfer reaction that is strongly accelerated by ultrasound.^[4, 5] The resulting high concentration of radicals might lead to a dimerization (pathway A). Finally, the oxidation of the dimers **4** to the observed products **2** by hydroxy radicals, which are always formed by ultrasonic reactions,^[4] is conceivable. Alternatively, the malonyl radicals **3** might be trapped directly by hydroxy radicals to form the alcohols **5** (pathway B), which are further oxidized to the mesoxalic esters **6** under the reaction conditions. This hypothesis is in accordance with examples for the acceleration of the oxidation of alcohols by manganese salts and ultrasound.^[6] Finally, the excess of malonates **1** and ketones **6** should afford the products **2** by a Knoevenagel reaction.

To differentiate between these two mechanistic pathways, the dimer **4b** was synthesized independently^[1a] and then irradiated in acetic acid/acetic anhydride in the presence of Mn(OAc)₃. Even after 6 h no conversion was obtained, which excluded pathway A. Further evidence for pathway B was found by control experiments with diethyl malonate (**1b**) and diethyl mesoxalate (**6b**), which react smoothly to the alcohol **2b** under irradiation. Therefore, ultrasound not only accelerates the generation of radicals and the oxidation to the mesoxalates **6**, but also the Knoevenagel reaction, which is in accordance with literature results.^[7]

To demonstrate the potential of the herein described ultrasonic reactions for the synthesis of tetra-acceptor-substituted alkenes, we investigated the dehydration of the alcohols **2**. Triethylamine and methanesulfonyl chloride were found to be the reagents of choice; they afforded the desired alkenes **7** quantitatively under mild conditions [Eq. (1)].



In summary, malonates, which are cheap and commercially available C_3 building blocks, were transformed into tetra-acceptor-substituted alkenes in only two steps in excellent yields. The procedure is characterized by simple reagents, especially since only a catalytic amount of $Mn(OAc)_3$ is required. Ultrasonication was the method of choice as it accelerates the radical reactions as well as the Knoevenagel reactions. Since radicals can be generated from various CH-acidic substrates by manganese(III), the present methodology offers promising prospects for the synthesis of other acceptor-substituted alkenes.

Experimental Section

A solution of malonate **1** (5.0 mmol), potassium acetate (3.0 g, 31 mmol), and acetic anhydride (1.0 mL, 11 mmol) in acetic acid (40 mL) was heated to 80 °C. Manganese(III) acetate dihydrate (270 mg, 1.0 mmol) was added, and the mixture was irradiated (BANDELIN sonotrode HD200, 50 % intensity) for 3 h. After dilution with water (200 mL), the solution was extracted with dichloromethane (3 × 50 mL) and the combined organic phases were washed with a saturated sodium hydrogen carbonate solution (2 × 50 mL) and brine (50 mL). After drying (sodium sulfate) and concentration under vacuum, the unconverted malonate was removed by Kugelrohr distillation. The remaining alcohol **2** can directly be used for the next step or recrystallized from ethanol. A solution of the alcohol **2** (10.0 mmol) in dichloromethane (40 mL) was cooled to 0 °C, and triethylamine (3.0 g, 30 mmol) and a solution of methanesulfonyl chloride (2.3 g, 20 mmol) in dichloromethane (10 mL) were added dropwise at this temperature. After 2 h 10 % hydrochloric acid (50 mL) was added carefully and the combined organic phases were washed with a saturated sodium hydrogen carbonate solution (2 × 50 mL) and brine (50 mL). After drying (sodium sulfate) and concentration under vacuum the residue was crystallized from isopropanol. The alkenes **7** were isolated in analytically pure form in 98–99 % yield.

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Direct Evidence for Trivalent Cationic Conduction in Nd^{3+} - β'' - Al_2O_3 **

Joachim Köhler, Nobuhito Imanaka, Werner Urland, and Gin-ya Adachi*

Dedicated to Prof. Arndt Simon
on the occasion of his 60th birthday

The ionic conduction properties of monovalent M^{+} - β'' - Al_2O_3 compounds ($M = Na, Ag, Cu$) have been known for decades.^[1, 2] Also the migration of ions in oxides with divalent metals, M^{2+} - β'' - Al_2O_3 ($M = Ca, Sr, Pb$), has been confirmed and identified.^[3–5] On the other hand, the issue of whether or not M^{3+} - β'' - Al_2O_3 crystals behave as conductors with mobile M^{3+} cations as charge carriers has not yet been clarified and is still being controversially discussed. The main point of the criticism concerns the high charge of the trivalent cations. It is assumed that the resulting high Columbic interaction with the surrounding anionic host lattice prevents a corresponding current transport. Here, new experiments and results are presented for Nd^{3+} - β'' - Al_2O_3 crystals which directly identify and confirm the trivalent cation transport in M^{3+} - β'' - Al_2O_3 .

About two decades ago, the Na^{+} ions in Na^{+} - β'' - Al_2O_3 crystals were replaced by trivalent lanthanide cations (Ln^{3+}).^[6] The realization of these ion-exchange experiments already indicates that the trivalent cations are capable of noticeable diffusive migration at comparatively low temperatures.^[7] However, the final evidence that these cations behave as charge carriers in an electric potential gradient and migrate macroscopic distances within the crystal could not be given.

Previous characterizations of Ln^{3+} - β'' - Al_2O_3 compounds are mainly based on impedance spectroscopy^[8–11] or X-ray diffraction experiments^[12–15] in which the measured impedances and electron density distributions are interpreted as the mobility of the trivalent cations. However, critics have often expressed doubt that these methods actually convey con-

[*] Prof. G.-y. Adachi, Dr. N. Imanaka
Department of Applied Chemistry
Faculty of Engineering, Osaka University
2-1 Yamadaoka, Suita, Osaka 565-0871 (Japan)
Fax: (+81)6-6879-7352
E-mail: adachi@chem.eng.osaka-u.ac.jp
Dr. J. Köhler
Department of Applied Chemistry
Faculty of Engineering, Osaka University (Japan)
Present address:
Kansai Research Institute (KRI)
Advanced Materials Research Center
Inorganic Fine Laboratory
Kyoto Research Park
17 Chudoji Minami-machi, Shimogyo, Kyoto 600-8813 (Japan)
Prof. Dr. W. Urland
Institut für Anorganische Chemie
Universität Hannover
Callinstrasse 9, 30167 Hannover (Germany)

[**] The fully ion exchanged Nd^{3+} - β'' - Al_2O_3 crystals were prepared at the Universität Hannover. The electrochemical investigations were conducted at Osaka University. J.K. gratefully acknowledges the financial support for his postdoctoral fellowship for foreign researchers in Japan by the Japan Society for the Promotion of Science (JSPS).