140. Construction of Highly Substituted Nitroaromatic Systems by Cyclocondensation. Part I. Synthesis of 4-Nitro-3-oxobutyrate[1])

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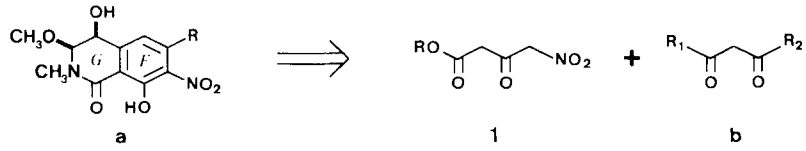
Summary

Methyl 4-nitro-3-oxobutyrate (**1**) is prepared by substitution of 4-bromo- and 4-iodo-3-oxobutyrate enol ether or enol acetate derivatives with nitrite and deprotection of the keto function (*Schemes 2* and *3*). A much more convenient access to **1** is, however, the nitration of acetoacetate dianion with alkyl nitrates *(Scheme 4)*. Compound **1** is stable and storable, and can be handled safely. Its use in cyclocondensations is established by the reaction with acetylacetone *(Scheme 5)*, affording 4,6-dimethyl-3-nitrosalicylate **48** in 70% yield. The halogen-substitution method for the synthesis of **1** gives also access to the crystalline (*E*)-enol ether **18** of **1**, as well as to its dimethyl acetal **25**, (*Z*)-enol acetate **32**, and (*E*)-enol acetate **33**. The 3-substituted 4-bromobutenoates **15**, **16** and **26** have been prepared from 4-bromo-3-oxobutyrate **12**, a useful alternative to existing methods applying *N*-bromosuccinimide.

1. Introduction. – The methods of classical aromatic chemistry are frequently too harsh and not selective enough to be useful for total syntheses of complex natural products. Alternatives are provided by biomimetic processes like cyclocondensations of polyketide chains [1]. Highly substituted phenols are efficiently constructed by the *Prelog* condensation [2] and closely related reactions [3]. In the course of devising total synthetic schemes for the novel antibiotic Lysolipin I [4], the concept of constructing a suitably substituted precursor of ring F (**a**) by cyclocondensation of 4-nitro-3-oxobutyrate **1** and a β-dicarbonyl compound **b** seemed very attractive *(Scheme 1)*. Methyl 4-nitro-3-oxobutyrate (**1**) is the mononitro analogue of 3-oxoglutarate **2**, a most

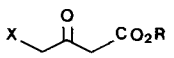
Scheme 1



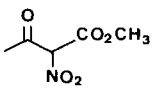
[1]) Parts of these results were presented at the «Herbstversammlung der Schweizerischen Chemischen Gesellschaft», October 15, 1982, in Bern.

useful synthetic unit, which – in addition to the *Prelog* condensation [2] [3] – found use in other important processess like the *Robinson-Schöpf* reaction [5], the *Weiss* reaction [6], and related annelations [7].

Despite of the additional synthetic potential due to the NO_2-function [8] and the current synthetic activities in the field of 4-hetero-substituted 3-oxobutyrates [9] (s. **3**–**9**), 4-nitro-3-oxobutyrate **1** as well as related compounds have not appeared in the literature[2]). Known are, however, the isomeric 2-nitro-3-oxobutyrate **10** [10] and the dipotassium 1,3-dinitro-2-oxopropane-1,3-diide (**11**) [11], the dinitro analogue of doubly deprotonated 3-oxoglutarate **2**.



$X = NO_2$	**1**	
$X = CO_2R$	**2**	
$X = CN$	**3**	[9a]
$X = (C_6H_5)_3P^{\oplus}$	**4**	[9b]
$X = (C_6H_5)_2P(O)$	**5**	[9c]
$X = (EtO)_2P(O)$	**6**	[9d]
$X = RO$	**7**	[9a] [9e]
$X = RS$	**8**	[9a] [9e] [9f]
$X = R_2N$	**9**	[9a] [9g]



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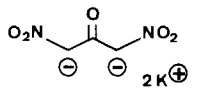

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2. Synthesis of *1* from *12* *via* enol ether *18* *(Scheme 2).* – The first approach to the synthesis of 4-nitro-3-oxobutyrate **1** is based upon substitution of halogen by nitrite [12], starting from the readily available 4-bromo-3-oxobutyrate **12** [13]. The bromide **12** was first converted to the rather unstable iodide **13** [14][3]) by treatment with NaI in acetone [15]. However, the subsequent substitution with $AgNO_2$ [12b] gave an unstable brown oil containing none of the desired **1**[3]). Since the failure to substitute a primary α-halo ketone by nitrite is not without precedence [12]; it was decided to circumvent this problem by forming a derivative of the β-keto ester **12**. Treatment of **12** with trimethyl orthoformate gave, in analogy to the corresponding chloro-keto ester [16], the dimethyl acetal **14**, which was isolated in 71% yield by column chromatography together with 12% of (*E*)-enol ether **15**. Pyrolysis and distillation of the crude mixture in the presence of ethyldiisopropylammonium *p*-toluenesulfonate [17] yielded 78% of the known [18] (*E*)-4-bromo-3-methoxy-2-butenoate **15** purified by chromatography *(Scheme 2)*[4]).

Compound **15** is frequently used as a synthetic unit in alkylations [18j-m] and *Reformatzky* reactions [19]. The preparation described herein is a good alternative to the existing method [18]. The yields are comparable for both processes. The new method uses a cheaper bromination agent and affords, after distillation, a somewhat purer product.

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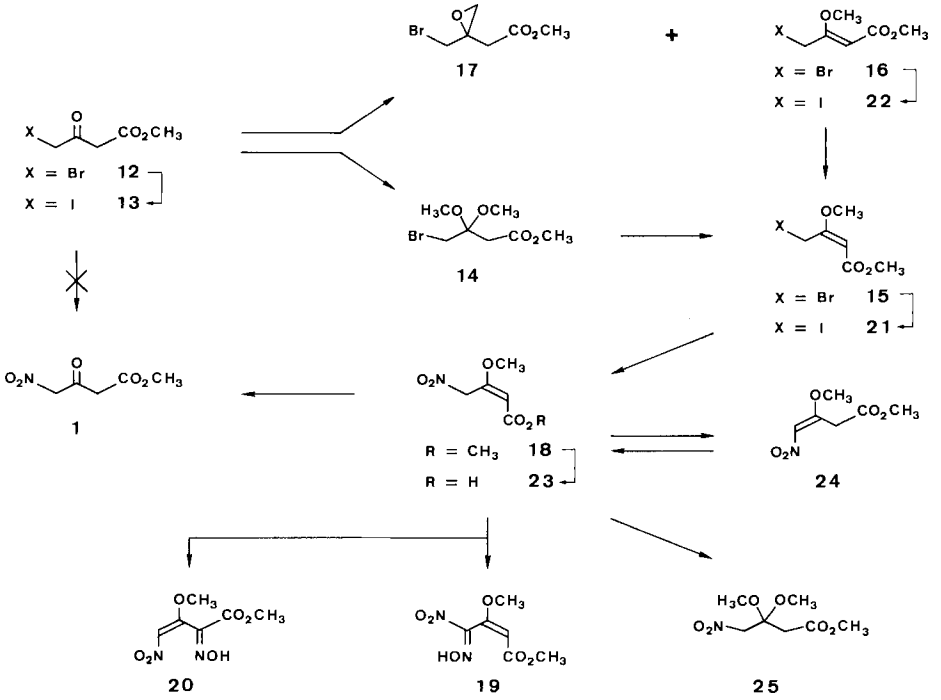
[2]) A CAS on-line literature search has been done on March 28, 1983.

[3]) It was later found, that the instability of **13** is due to impurities, most probably dihalogenides, in the starting bromide **12** [13c]. An alternative approach (see below, *Scheme 3*) gives purer and stable **13**, which afforded a 5% yield of nitro compound **1** upon treatment with $AgNO_2$ in the presence of phloroglucinol.

[4]) The product **15** obtained by distillation (91% based on ketone **12**) contained as main impurity *ca.* 5% of acetal **14**. This material is suited for most synthetic purposes.

Treatment of the bromo ketone **12** with diazomethane in ether gave the crystalline (*Z*)-enol ether **16** (46%) [18d][5]) together with some (*E*)-isomer **15** (3–4%) and epoxide **17** (14%). Enol ether **16** slowly isomerized to the more stable (*E*)-isomer **15** on standing [18d]; a high-yield conversion of **16** to **15** (91%) was obtained by short heating to 125° *(Scheme 2)*[6]).

Scheme 2



Reaction of bromide **15** with $NaNO_2$ in DMF using phloroglucinol as alkyl nitrite scavenger [12c] afforded the crystalline nitrobutenoate **18**[7]) in 46% yield together with the stable hydroxyimino(nitro)butenoate **19** (8%) and its isomer **20** (1%)[8]). A much better yield of **18** was obtained, when the bromide **15** was first transformed to the iodide **21** [18 l] [22] by substitution with NaI [15] (96%), followed by treatment with $AgNO_2$ in ether [12 b] (87%, *Scheme 2*).

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[5]) The configuration of the double bond in **15** is neglected or erroneously assumed to be *Z* by most authors [18] [19]. Comparison of the ^{1}H-NMR spectra of both isomers **15** and **16** allows an unambiguous assignment [18d], which could be confirmed by ^{13}C-NMR (this work) and difference nuclear-*Overhauser*-effect (NOE) measurements [18i].

[6]) The thermodynamic preference of the (*E*)-isomer of 3-alkoxy-2-butenoates has first been recognized by *Arndt* and by *Smissman* [20].

[7]) The configuration of the double bond of **18** is implied by the precursor **15**, the observation, that the primary products from (*Z*)-enol ether **16** isomerize to **18** during workup (see below), and by the finding, that enol ether derivatives of the related 3-oxoglutarate **2** prefer the (*E*)-configuration [21].

[8]) When crystalline **19** is heated beyond 80°, a violent decomposition is observed, but only minor disintegration occurs upon heating a dioxane solution of **19** to 100°.

The structures of **19** and **20** follow from their analytical and spectroscopic data, including molecular-weight determination. Furthermore **19** and **20** are secondary products arising from the action of alkyl nitrites in the reaction mixture [23], since treatment of **18** with *t*-butyl nitrite and $NaNO_2$ in DMF gave 29% of **19** and **20** at 70% conversion[9]).

Lower yields of **18** were achieved by substituting the bromide **15** directly with $AgNO_2$ (40% of **18**), or by using *Amberlite-IRA 900* (NO_2^-) [24] for the introduction of the NO_2-group (40 and 18% of **18** from **15** and **21**, resp.)[9]).

Treatment of the polar enol ether **16** with NaI in acetone [15] resulted in fast precipitation of NaBr. TLC analysis of the reaction mixture showed a polar product with similar R_f value as the bromide **16**, most probably the (*Z*)-iodide **22**. During workup and chromatography, **22** was, however, completely isomerized to the less polar (*E*)-iodide **21**[9]). Aiming at the (*Z*)-isomer of nitro compound **18**, the bromide **16** was reacted with $AgNO_2$. Attempts to isolate the polar products (observed in the reaction mixture by TLC) by chromatography resulted again in isomerization to the (*E*)-isomer **18**, which was isolated in 39% yield[9]).

The 4-nitro-2-butenoate **18** is a strong acid, which can be extracted from organic solvents with weak bases (K_2CO_3) in water. The free acid **23** was readily obtained by saponification with 2 N NaOH. Deprotonation of **18** with $KOCH_3$ in CH_3OH resulted in partial precipitation of the storable 'nitronate'. Reprotonation gave a 4:1 mixture of **18** and 3-butenoate **24**[10]). Silica gel was found to catalyze the equilibration of **18** and **24**. An attempted chromatographic separation of **18** and **24** resulted in almost complete isomerization of **24** to the less polar isomer **18** *(Scheme 2)*. Addition of CH_3OH to the double bond of **18**, catalyzed by either K_2CO_3 or CsF, gave the dimethyl acetal **25**. Separation of the 85:15 mixture of **25** and starting material **18**, preferably by HPLC, gave 75% of **25** from the reaction with CsF.

The final conversion of enol ether **18** or acetal **25**[11]) to the desired 4-nitro-3-oxobutyrate **1** was rather delicate. Neither treatment with aqueous acid nor mercuric-acetate-assisted cleavage of the enol ether [27] were successful. A low yield (28%) low conversion (44%) of **18** to **1** was achieved using 15% H_2SO_4 on silica gel [28] in 1,2-dichloroethane at 50° (2.5 days)[9]). It was then found that **18** is very slowly cleaved to **1** by CF_3CO_2H in THF [18j]. After 16.5 days at r.t. 49% of **1** was separated from 44% of starting material by extraction with sat. $NaHCO_3$ solution. The nitro ketone **1**, obtained in 40% overall yield (72% based on consumed **18**) from the readily available bromide **15** [18], is a stable distillable liquid[12]).

Treatment of **1** with 1 equiv. of CH_2N_2 gave a complex mixture, from which 22% of enol ether **18** was separated by chromatography. The other more polar and complex products were due to concomitant *O*-alkylation of the NO_2-group [29][9]).

3. Synthesis of *1* from *12 via* enol acetates *32* and *33* *(Scheme 3)*. – The slow rates of the last step (**18** → **1**) of the sequence described in *Scheme 2* render this otherwise acceptable synthesis of **1** impracticable. Therefore the same synthetic strategy was

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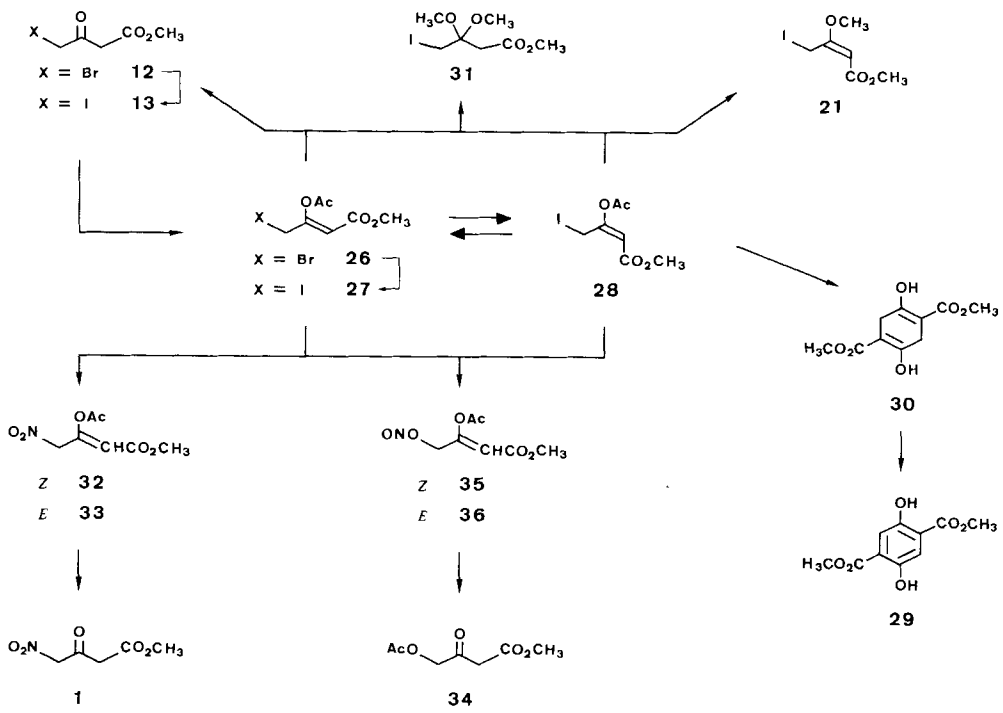
[9]) No description for these transformations will be given in the *Exper. Part.*

[10]) This ratio corresponds not necessarily to the thermodynamic equilibrium of **18** and **24**. According to recent studies of such equilibria [25], configuration with NO_2- and alkoxycarbonyl groups has a similar effect on the stability of double bonds.

[11]) The formation of the same carbenium ion, destabilized by polar substituents, is the rate-determining step in the hydrolysis of either **18** or **25** [26].

[12]) For a more extensive discussion of the spectroscopic and chemical properties of **1** see below *(Scheme 5)*.

Scheme 3



tested using another, more readily removable protecting group for the keto function of **12**. Rejected were the methoxymethyl enol ether [30] because of the toxicity of chloromethyl methyl ether, the trimethylsilyl enol ether because of its instability, and the (*t*-butyl)dimethylsilyl enol ether because of the high cost of the corresponding chloride.

Treatment of 4-bromo-3-oxobutyrate **12** [13] with 2-propenyl acetate/acid [31] gave the known (*Z*)-enol acetate **26** [32] in 72% yield, purified by distillation *(Scheme 3)*. This method of preparing **26** is a welcome alternative to the existing method using *N*-bromosuccinimide [32]. NaI in acetone [15] converted **26** in 60–90% yield to the (*Z*)-iodide **27** and variable amounts (4–10%) of the (*E*)-isomer **28**[13]).

The iodides **27** and **28** are crystalline compounds, quite stable and storable in the pure state. Their solutions are however light-sensitive, and light should be excluded during workup, if a maximal yield of **27** is desired. Exposure of solutions of either pure **27** or **28** to daylight resulted in equilibration to 2:3 mixtures of **27** and **28** and concomitant decomposition (68% recovery)[14]). The main secondary product was the fluorescent 2,5-dihydroxyterephthalate **29** formed by dehydrogenation of the cyclodimer **30** [14] *(Scheme 3)*. Deprotection of either **27** or **28**, best achieved by treatment with $KOCH_3$

[13]) The ^{1}H-NMR data of **27** and **28** are almost identical with those of the corresponding bromides [32].

[14]) No reaction is observed with iodine in the dark at r.t. Interestingly the (*Z*)-bromide **26** seems to be unaffected by exposure to light and iodine.

in CH_3OH[15]), gave the pure stable iodide **13** in 87–95% yield[3]). Methanol/methanesulfonic acid converted the enol acetate **27** into a separable mixture of dimethyl acetal **31** (70%)[16]), enol ether **21** (10%), and keto ester **13** (9%) *(Scheme 3)*.

The transformation of iodides **27** and **28** with $AgNO_2$ was less clean than in the case of enol ether **21**. Exclusion of air, light, and moisture proved to be crucial. The ^{1}H-NMR spectra of the crude mixtures showed as main components the signals of the expected nitroenol acetates: **32** from **27** and **33** from **28**[17]). Always present in such preparations was 4-acetoxy-3-oxobutyrate **34** [9e] [14][18]), a secondary product arising from the nitrites **35** and **36**, which could however not be detected. Purification of the nitroenol acetates **32** and **33** was difficult, since they decompose on silica gel, and attempts of distillation, in some cases successful, were discontinued, when one sample decomposed violently. The crude product mixtures containing **32** or **33** were therefore directly deprotected either under acidic (CH_3SO_3H/CH_3OH) or strongly basic (CH_3OK/CH_3OH) conditions to yield 30–40% of 4-nitro-3-oxobutyrate **1** based on the iodides **27** or **28**[19]) (overall yield from **12**: 20–25%). The enol-ester function of **32** was not affected by CF_3CO_2H in THF, and the cleavage using weak aqueous bases or 15% H_2SO_4 on silica gel [28] gave inferior results[20]).

4. Synthesis of *1* from *38* by nitration of a dianion *37* *(Scheme 4)*. – The four-step conversion of bromide **12** to **1** depicted in *Scheme 3* is much faster and more convenient than the enol-ether variant *(Scheme 2)*. The overall yield is however low (20–25%) due to the unpredictable nature of the heterogeneous substitution with $AgNO_2$; a scale-up is therefore questionable.

A much better access to 4-nitro-3-oxobutyrate **1** is shown in *Scheme 4*. When the sodium-lithium salt **37**, prepared from methyl acetoacetate (**38**) [33], was treated with 0.5 equiv. of propyl nitrate at -37 to $-32°$, or with 0.5 equiv. of 2-propyl nitrate at -11 to $-5°$ [34][21]), a voluminous yellow precipitate, the dianion **39** of 4-nitro-3-oxobutyrate, was formed during warming up to 0°. Product **1** was isolated by acidification and extraction, and separated from starting material **38**

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[15]) Dimer **30** would be the product of the reaction of a weak base with **27** or **28** [9a] [14].

[16]) The α-halogenated dimethyl acetals **14** *(Scheme 2)* and **31** are inert towards substitution reactions, *e.g.* NaI/acetone, $NaNO_2$/DMF, and *Amberlite-IRA 900* (NO_2^-).

[17]) In analogy to the isomeric iodides **27** and **28**, as well as for the enol ethers **15** and **16** *(Scheme 2)*[5]), the configuration of the double bond of **32** and **33** is assignable by the ^{1}H-NMR chemical shift of the CH_2NO_2-group, which is at lower field for the (*E*)-isomer **33** (5.77 ppm) than for the (*Z*)-isomer **32** (5.08 ppm).

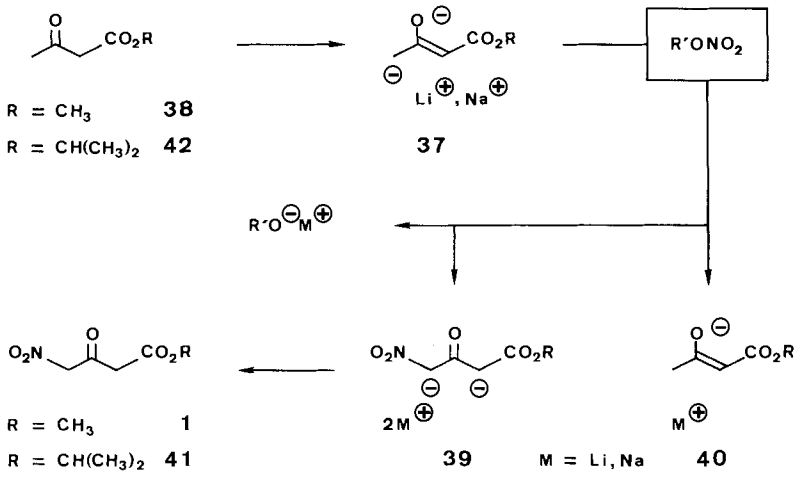
[18]) The structural assignment of **34** was made by comparison with an authentic sample prepared from bromide **12** [9e].

[19]) The yield of these transformations could probably be improved by using an efficient nitrite scavenger like phloroglucinol [12c] in the reaction with $AgNO_2$.

[20]) Deprotonation of **32** and **33** is faster than the enol-acetate cleavage, since **32** was extractable with sat. $NaHCO_3$- or 10% K_2CO_3-solution, and was partially recovered upon careful acidification at 0°[9]). Under weak basic conditions the acetate cleavage of the deprotonated species is slow, and concomitant decomposition of the product **1** occurs (see below, *Scheme 5*).

[21]) The higher temperature chosen in the case of 2-propyl nitrate is justified by its lower reactivity. Substitution of pentyl nitrate by 2-propyl nitrate in the nitration of acetone [11] had the effect, that the reaction did not start at $-35°$ and went out of control during warming up in an ice-bath.

Scheme 4



by extraction with sat. $NaHCO_3$- or preferably 50% K_2HPO_4-solution. After purification by bulb-to-bulb distillation, the yield of **1** was 55–65% (based on propyl nitrate) or *ca.* 58% (based on consumed **38**).

A better way of isolating **1** from the reaction mixture, especially for large scale preparations, would be the separation of the precipitated salt **39** from the THF solution. Due to clogging of normal fritted funnels, filtration was met with problems. A non-optimal separation of **39** was achieved by centrifuging; acidification, extraction, and distillation gave a purer product than the material obtained by K_2HPO_4-extraction. Only about 10% of the total amount of **1** remained in the THF solution after separation of precipitated **39**.

The drawback, that only half of the acetoacetate dianion **37** is transformable to product, is also a problem in acylations with alkyl carboxylates. There, a better conversion is obtained, if the monoanion **40** is deprotonated *in situ* with BuLi before more acylating agent is added [33b]. In the case of nitrations with alkyl nitrate, the precipitated product **39** is dissolved upon addition of BuLi and destroyed by propyl nitrate.

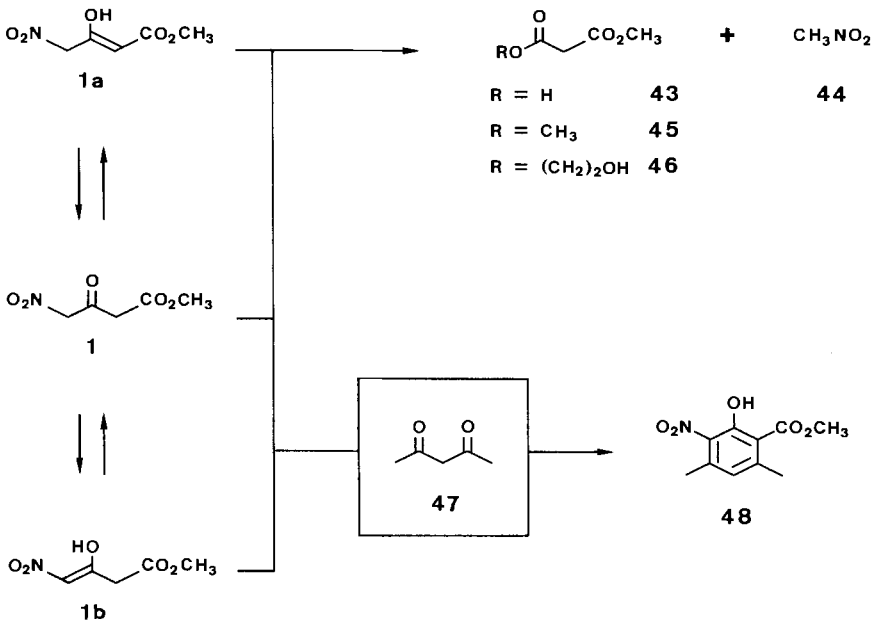
The nitration with alkyl nitrate is also successful with the dilithium salt of acetoacetates generated with 2 equiv. of lithium diisopropylamide [33]. In this case, however, most of the product salt remains in solution[9]). The procedure depicted in *Scheme 4* is also applicable to other esters of acetoacetic acid; *e.g.* 2-propyl 4-nitro-3-oxobutyrate (**41**) is obtained analogously from acetoacetate **42**[9]).

5. Properties and reactions of *1*. – The 4-nitro-3-oxobutyrates **1** and **41** obtained according to *Schemes 2–4* are sufficiently pure after bulb-to-bulb distillation for further reactions. Judging from the ^{1}H-NMR data the main impurities are nitroacetone, and monoesters of malonic acid. In the case of samples prepared by nitration with alkyl nitrate, the NMR spectra also exhibit signals corresponding to the alkoxy group of the reagent, which might be due to transesterification[22]).

[22]) *Methyl nitrate*, an ideal nitrating agent for the preparation of **1**, was rejected for safety reasons [35].

Analytically pure **1** was obtained in 70–80% yield from distilled samples by preparative HPLC on silica gel (reverse phase). It is a stable, storable, pale-yellow liquid, which can be handled safely[23]). The structure of **1** is unambiguously confirmed by its analytical and spectroscopic data. The ^{1}H- and ^{13}C-NMR spectra show, that **1** is a mixture of the keto form **1** and the enol tautomers **1a** and **1b** *(Scheme 5)*. Since the NO_2-group is a poor H-bond acceptor [36], the enolization of **1** favors the methoxycarbonyl group, with 30% of **1a** in $CHCl_3$, and 10% of **1a** in acetonitrile.

Scheme 5



A typical reaction of *α*-nitro ketones is a *Claisen*-type cleavage to nitroalkanes and carboxylic acids [8b]. Treatment of **1** with sat. $NaHCO_3$-solution for 17 h at r.t. resulted in a 87% conversion to methyl hydrogen malonate (**43**) and nitromethane (**44**)[9]). Nitro ketone **1** is also cleaved to dimethyl malonate (**45**) and **44** by CH_3SO_3H (60% conversion in 4 days) or by 1 equiv. of Na-salt of acetylacetone (**47**) in CH_3OH. Attempted acetalization of **1** with ethylene glycol using *p*-toluenesulfonic acid as catalyst led to malonate **46**, isolated in 77% yield *(Scheme 5)*[9]).

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[23]) Redistillation of a brown sample, that had been stored for 2 years in the refrigerator, gave more than 90% recovery. Fast decomposition of **1** begins at about 180° with darkening and the formation of nitrous-oxide fumes. Compound **1** and its salt **39** are inert to hammer-blows, and when heated in a flame, only carbonization is observed, however accompanied with a sudden and considerable increase of volume in case of the salt **39**. The 4-nitro-3-oxobutyrate **1** is unaffected by acylation agents like acetanhydride or acetyl chloride alone. However, an extremely violent exothermic decomposition occurs with such reagents in the presence of tertiary amines.

With the possibility of preparing multigram quantities of 4-nitro-3-oxobutyrate **1** in one step, experiments for the target cyclocondensation *(Scheme 1)* became feasible. Because of the facile cleavage of **1** to malonates and nitromethane, the usual conditions for the *Prelog* condensation, base in alcoholic solvents [2], are not applicable. Reaction of **1** with 1.5 equiv. of acetylacetone (**47**) in THF using 1,8-diazabicyclo[5.4.0]undec-7-ene as base gave 70% of 4,6-dimethyl-3-nitrosalicylate **48** *(Scheme 5)*. The scope of this promising condensation reaction is under investigation. The results will be published in due course.

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Experimental Part

General Remarks. See [37]. *High Performance Liquid Chromatographic* separations (HPLC) were carried out on a *DuPont Instruments* HPLC system using *DuPont* preparative columns, 25 cm/21.2 mm outer diameter, 7 μm silica gel (normal or reverse phase).

Nitration of acetoacetate dianion **37** *with alkyl nitrate. a) Using propyl nitrate.* A solution of 9.29 g (80 mmol) of methyl acetoacetate (**38**) in a few ml of dry THF was added within 70 min to an ice-cooled suspension of 3.54 g (80–90 mmol) of NaH (55–60% suspension in nujol) in 200 ml of dry THF (temp. 4–5°). The temp. was then lowered to −10° (ice/NaCl) and 47 ml (80–83 mmol) of 1.7–1.76M BuLi in hexane were added by syringe within 15 min at −8 to −5°. After stirring for 10 min at 0°, the mixture was cooled to −44° (dry ice/2-propanol), and 4 ml (4.22 g, 40 mmol) of freshly distilled propyl nitrate were added by syringe within 5 min at −37 to −32° (exothermic). By successive cooling with ice/NaCl and ice/H_2O the temp. was brought to 0° within 50 min and held at 0° for 15 min. Beginning at *ca.* −13° (after 30 min), a heavy yellow precipitate was formed. After careful quenching of excess NaH by CH_3OH, the mixture was poured to 160 ml of precooled 15% H_2SO_4, 2 g of urea, and ice. The 2 AcOEt-extracts (500 and 300 ml) were washed twice with sat. NaCl-solution, the product was separated by extraction with 4 portions of 50% (w/v) K_2HPO_4-solution (2×50 ml and 2×30 ml). The K_2HPO_4 extracts were immediately added to 200 ml of precooled 15% H_2SO_4 and 2 g of urea, and extracted with CH_2Cl_2 (400 ml, 2×250 ml, after sat. with NaCl). The CH_2Cl_2-phases were washed with NaCl-solution (2×50 ml), dried ($MgSO_4$), and evaporated. Two bulb-to-bulb distillations (85–100°/h.v.) of the residue (4.832 g) gave 4.295 g (32% based on **38**, 58% based on consumed **38**, 65% based on 2-propyl nitrate) crude *methyl 4-nitro-3-oxobutyrate* (**1**)[23]). Extraction of the AcOEt-phases (see above) with 10% NaOH-solution, acidification with 15% H_2SO_4, and extraction with CH_2Cl_2 gave, after bulb-to-bulb distillation (100°/12 Torr) of the residue, 4.042 g (43%) of starting material **38**.

b) Using 2-propyl nitrate. A solution of **37** in 200 ml of THF, prepared as described above from 9.29 g (80 mmol) of **38**, was cooled with ice/NaCl to −11°. The 2-propyl nitrate (4.2 g, 40 mmol) was then added at a rate, that the temp. did not exceed −5°[21]). After stirring for 30 min in an ice bath, the mixture was worked up as described above: 3.471 g (27% based on **38**, 54% based on 2-propyl nitrate) of **1**.

c) Workup by separation of salt **39**. A solution of **37** in 150 ml of THF, prepared from 5.817 g (50 mmol) of **38**, was treated as described above with 2.6 ml (26 mmol) of propyl nitrate at −45 to −31°. The heavy yellow precipitate, which had been formed during warming up to 0° (16 min) and stirring at this temp. (40 min), was separated by centrifuging the mixture in portions (15 min at 1500 rpm) and decantation of the yellow solution. The gummy residue was washed with THF. A small sample was washed more extensively with THF and Et_2O. Drying under h.v. gave yellow to brown amorphous **39**,

which is stable and storable in a refrigerator. The remaining bulk of **39** was transfered with H_2O to 100 ml of precooled 15% H_2SO_4 and extracted with 250 ml of AcOEt. The aq. phase was extracted twice more in portions. The org. phases were then washed with sat. NaCl-solution, dried ($MgSO_4$) and evaporated. The residue (4.232 g) was freed from some nujol by extraction with pentane and subjected to bulb-to-bulb distillation. After distillation of some **38** at 12 Torr, two distillations at 85–100° (under h.v.) yielded 2.313 g (28% based on **38**, 55% based on propyl nitrate) of **1**, which was according to ^{1}H-NMR slightly purer than the material obtained above. Workup of the THF-solution, separated by centrifuging, as described above, yielded another 228 mg (2.5% based on **38**, 5% based on propyl nitrate) of impure **1**, separated by K_2HPO_4-extraction.

d) Purification and data of methyl 4-nitro-3-oxobutyrate (**1**). Distilled **1** (162 mg) from the reaction with 2-propyl nitrate was purified by prep. HPLC (reverse-phase silica gel, CH_2Cl_2+AcOH (2 ppt), 30 bar (12 ml/min), detection at 235 nm). The chromatogram showed essentially one peak with t_{ret} = 4 min 50 sec, which was collected discarding minor impurities contained in the forerun (5 mg) and in the tailing (17 mg). Bulb-to-bulb distillation (85–100°/h.v.) of the main fraction gave 133 mg (82%) of analytically pure **1**, which was further purified by extraction with 50% K_2HPO_4-solution and distillation to afford 117 mg (72%) of **1**. Comparison of the ^{1}H-NMR spectra before and after purification shows the disappearance of peaks due to $(CH_3)_2CHO$ groups (from 2-propyl nitrate), nitroacetone (2.31 and 5.27 ppm), and methyl hydrogen malonate (3.43 ppm), and of an unidentified peak (5.16 ppm). – IR ($CHCl_3$): 3200–2800*w*, 2955*m*, 2930*w*, 2845*w*, 1735*s*, 1667*m*, 1630*w*, 1565*s*, 1449*m*, 1437*m*, 1400*w*, 1375*w*, 1366*m*, 1330*m*, 1240*s*, 1170*m*, 1015*w*, 905*w*. – ^{1}H-NMR (300 MHz, $CDCl_3$): *Keto form* **1**: 3.65 (*s*, 2 H–C(2)); 3.79 (*s*, CH_3O); 5.48 (*s*, 2 H–C(4)). *Methyl 4-nitro-3-hydroxy-2-butenoate* (**1a**): 3.81 (*s*, CH_3O); 5.00 (*s*, 2 H–C(4)); 5.34 (*s*, H–C(2)); 11.9 (br. *s*, HO–C(3)). *Methyl 4-nitro-3-hydroxy-3-butenoate* (**1b**): 3.34 (*s*, 2 H–C(2)); 3.78 (*s*, CH_3O); 6.90 (*s*, H–C(4)); 12.9 (br. *s*, HO–C(3)). Integration: **1**/**1a**/**1b** = 63:31:6. – ^{13}C-NMR (75 MHz, C_6D_6): **1**: 46.3 (C(2)); 52.6 (CH_3O); 83.5 (C(4)); 166.8 (C(1)); 191.0 (C(3)). **1a**: 51.8 (CH_3O); 77.4 (C(4)); 95.8 (C(2)); 163.6, 172.4 (C(1), C(3)). **1b**: 38.7 (C(2)); 118.1 (C(4)); 167.3, 167.5 (weak signals, possibly C(1), C(3)). – MS: 161 (1, M^+), 130 (5), 115 (7), 114 (10), 101 (50), 87 (16), 84 (7), 74 (5), 69 (19), 62 (12), 59 (37), 57 (22), 55 (13), 44 (68), *43* (100), 42 (54).

$C_5H_7NO_5$ (161.11) Calc. C 37.27 H 4.38 N 8.69% Found C 37.10 H 4.40 N 8.65%

Methyl 4,6-dimethyl-3-nitrosalicylate (**48**). A solution of 161 mg (1.0 mmol) of **1**, 160 µl (155 mg, 1.55 mmol) of acetylacetone (**47**), and 150 µl (153 mg, 1.0 mmol) of 1,8-diazabicyclo[5.4.0]undec-7-en in 1.5 ml of dry THF containing 1 g of freshly activated molecular sieves (4Å) was stirred for 6.5 days at r.t. under Ar and exclusion of light. The mixture was then poured to 15 ml of 15% H_2SO_4 and ice and extracted with AcOEt. After removal of the molecular sieves by filtration, the aq. phase was extracted twice more with AcOEt. The org. layers were washed with NaCl-solution (once), 50% K_2HPO_4 solution (4×) to remove unreacted **1**, and NaCl-solution (2×), dried ($MgSO_4$), and evaporated. Bulb-to-bulb distillation (130°/h.v.) of the residue (184 mg) gave 161 mg (71%) of **48**, m.p. 113–115°/120–121° (CH_2Cl_2/hexane, sublimed (98°/h.v.)). – UV (EtOH): 244 (8800), 313 (3260). – IR ($CHCl_3$): 3500–2600*m*, 3035*w*, 2980*w*, 2955*m*, 2935*w*, 2850*w*, 1730*m*, 1663*s*, 1628*m*, 1563*m*, 1535*s*, 1440*s*, 1395*w*, 1372*m*, 1355*s*, 1300*m*, 1263*s*, 1133*m*, 1081*m*, 1021*w*, 963*m*, 865*m*, 855*w*, 824*m*. – ^{1}H-NMR (90 MHz, $CDCl_3$): 2.31, 2.51 (2 *s*, H_3C–C(4), H_3C–C(6)); 3.98 (*s*, CH_3O); 6.63 (*s*, $w_{1/2}$ *ca.* 3, H–C(5)); 11.90 (br. *s*, $w_{1/2}$ *ca.* 12, HO–C(2)). – MS (di.): 225 (47, M^+), 207 (8), 194 (37), *193* (100), 176 (11), 163 (5), 148 (8), 147 (7), 135 (41), 119 (10), 91 (21), 77 (11), 67 (12), 65 (21), 51 (11), 39 (14).

$C_{10}H_{11}NO_5$ (225.20) Calc. C 53.33 H 4.92 N 6.22% Found C 53.32 H 4.90 N 6.15%

Methyl 4-bromo-3-oxobutyrate (**12**). Br_2 (160 g, 1.0 mol) was added within 1.5 h to a stirred solution of methyl acetoacetate (**38**; 116 g, 1.0 mol) in CH_2Cl_2 (900 ml) at −10°. After standing for 1 h at r.t., O_2 was passed for 2 h through the mixture. The solvent was removed at normal pressure. The residue, which had been dried for a short time at an aspirator, was immediately subjected to distillation under h.v. The fraction boiling at 80°/0.3 Torr (167.5 g) was redistilled over a *Vigreux* column (17 cm). A third distillation of the material boiling at 57°/0.1 Torr (145.1 g) gave 133.2 g (68%) of **12**, b.p. 41°/0.01 Torr. Further purification was possible by distillation using spinning-band or concentric-tube columns, followed by redistillation or chromatography in order to remove some 1,3-dibromo-2-propanone [38] formed by decomposition of polybrominated impurities at the high temp. associated with the use of more efficient columns. **12**: IR (CCl_4): 3030*w*, 3000*w*, 2955*m*, 2845*w*, 1745*s*, 1720*s*, 1657*m*, 1630*m*,

1447*m*, 1437*s*, 1401*m*, 1365*w*, 1325*s*, 1240*s*, 1170*m*, 1155*m*, 1075*w*, 1009*m*, 948*w*, 913*w*, 860*w*. – ^{1}H-NMR (90 MHz, CCl_4): *Keto form* **12**: 3.62 (*s*, 2 H–C(2)); 3.73 (*s*, CH_3O); 3.99 (*s*, 2 H–C(4)). *Methyl 4-bromo-3-hydroxy-2-butenoate (enol form, ca.* 30% according to integration): 3.74 (*s*, CH_3O); 3.82 (*s*, 2 H–C(4)); 5.25 (*s*, H–C(2)); 11.88 (*s*, $w_{1/2}$ *ca.* 4, HO–C(3)). – MS: 196/194 (each 2, M^+), 165 (10), 164 (6), 163 (10), 162 (6), 138 (6), 136 (6), 123 (16), 121 (16), 115 (27), *101* (100), 95 (10), 93 (10), 74 (2), 69 (26), 59 (32), 57 (11), 55 (4), 43 (82), 42 (30).

Treatment of **12** *with orthoformate.* A solution of 54.4 g (0.279 mol) of **12**, 58.2 g (0.549 mol) of trimethyl orthoformate, and 1 ml of CH_3SO_3H in 150 ml of CH_3OH was boiled under reflux under Ar for 60 h. The cooled mixture was quenched with 5 g of $NaHCO_3$ in 200 ml of H_2O, and worked up by extraction with Et_2O. A small portion (753 mg) of the crude material (63.8 g) was subjected to chromatography (45 g of silica gel). Elution with pentane/CH_2Cl_2/Et_2O 12:6:1 gave 82 mg (12%) of **15** and 567 mg (71%) of **14**. To the remaining bulk of material, 1.5 g (4.98 mmol) of ethyldiisopropylammonium *p*-toluenesulfonate were added, and, by heating to 150° for 45 min under Ar, CH_3OH was distilled off over a *Vigreux* column (15 cm). The distillation of volatile material was continued under reduced pressure (120°/12 Torr). Distillation under h.v. gave 53.0 g (91% based on **12**) of crude **15**, b.p. 48–53°/0.07 Torr. Purification of 506 mg by chromatography (50 g of silica gel) eluting with pentane/CH_2Cl_2/Et_2O 12:6:1 gave 435 mg (78% based on **12**) of **15** and 30 mg (4.5%) of *methyl 4-bromo-3,3-dimethoxybutyrate* (**14**). – IR (CCl_4): 3000*w*, 2955*m*, 2905*w*, 2835*w*, 1745*s*, 1455*w*, 1445*m*, 1438*m*, 1425*m*, 1360–1330*m*, 1317*m*, 1270*m*, 1255*m*, 1220*m*, 1206*m*, 1192*m*, 1170*s*, 1155*m*, 1112*m*, 1090*s*, 1062*s*, 1028*m*, 1002*w*, 980*m*, 900*w*, 865*w*, 830*m*, 690*m*. – ^{1}H-NMR (90 MHz, CCl_4): 2.85 (*s*, 2 H–C(2)); 3.26 (*s*, $(CH_3O)_2C(3)$); 3.65 (*s*, 2 H–C(4)); 3.71 (*s*, CH_3O). – MS (di., 30°): 211/209 (30 each, $M^+ - 31$), 179 (6), 177 (7), 169 (33), 167 (31), 151 (11), 149 (12), *147* (100), 129 (6), 123 (2), 121 (4), 114 (4), 105 (32), 101 (5), 95 (2), 93 (2), 73 (14), 71 (11), 59 (18), 57 (8), 55 (4), 47 (5), 45 (9), 43 (12), 41 (20), 39 (8).

$C_7H_{13}BrO_4$ (241.08) Calc. C 34.87 H 5.44 Br 33.15% Found C 34.78 H 5.64 Br 32.88%

*Methyl (*E*)-4-bromo-3-methoxy-2-butenoate* (**15**): IR (CCl_4): 3070*w*, 3020*w*, 2970*w*, 2950*m*, 2910*w*, 2845*w*, 1720*s*, 1632*s*, 1455*w*, 1442*m*, 1435*m*, 1422*m*, 1362*s*, 1298*s*, 1240*w*, 1222*w*, 1195*s*, 1155*s*, 1132*s*, 1053*s*, 1020*m*, 932*m*, 830*m*, 702*w*. – ^{1}H-NMR (100 MHz, CCl_4): 3.64, 3.68 (2 *s*, CH_3O–C(1), CH_3O–C(3)); 4.45 (*s*, 2 H–C(4)); 5.01 (*s*, H–C(2)). – ^{13}C-NMR (25.2 MHz, CCl_4/C_6D_6): 25.2 (C(4)); 50.8, 55.7 (2 CH_3O); 92.8 (C(2)); 166.0, 169.1 (C(1), C(3)). – MS: 210/208 (70 each, M^+), 179 (97), 178 (73), *177* (100), 176 (81), 151 (3), 149 (5), 129 (13), 128 (15), 101 (15), 99 (13), 98 (46), 97 (22), 96 (17), 85 (12), 83 (17), 69 (41), 68 (66), 67 (25), 59 (34), 55 (36), 53 (8), 45 (15), 43 (10), 42 (12), 41 (20), 40 (36), 39 (51).

Treatment of **12** *with diazomethane.* To a solution of 5.374 g (27.6 mmol) of **12** in 50 ml of Et_2O at 0°, 70 ml of 0.5 M CH_2N_2 in Et_2O (*ca.* 35 mmol) were added. After 2 h at 0°, the solution was kept for 40 h at 8°. Solvent and reagent were removed by distillation at normal pressure; the residue was subjected to flash chromatography (210 g of silica gel) eluting with pentane/Et_2O 3:2. Rechromatography (30 g of silica gel) of the first fraction with pentane/Et_2O 9:1 gave 212 mg (3.5%) of **15**. Then 1.087 g of **17** (822 mg (14%) after rechromatography with pentane/Et_2O 4:1) followed by 2.645 g (46%) of **16**, m.p. 55–59°, were eluted.

*Methyl (*Z*)-4-bromo-3-methoxy-2-butenoate* (**16**): m.p. 59–60.5° (pentane/Et_2O; [18d]: 59.5–60°). – IR (CCl_4): 3000*w*, 2950*m*, 2905*w*, 2865*w*, 2822*w*, 1725*s*, 1632*s*, 1460*s*, 1435*s*, 1370*m*, 1290*m*, 1237*s*, 1207*s*, 1182*s*, 1167*s*, 1135*w*, 1121*w*, 1078*s*, 1055*s*, 1035*w*, 1015*m*, 930*m*, 886*w*, 702*m*.. – ^{1}H-NMR (100 MHz, CCl_4): 3.59, 3.97 (2 *s*, CH_3O–C(1), CH_3O–C(3)); 3.81 (*s*, 2 H–C(4)); 5.17 (*s*, H–C(2)). – ^{13}C-NMR (25.2 MHz, CCl_4/C_6D_6): 29.9 (C(4)); 50.6, 58.6 (2 CH_3O); 98.8 (C(4)); 163.9, 164.1 (C(1), C(3)). – MS: 210/208 (40 each, M^+), 179 (93), 178 (86), 177 (93), *176* (100), 151 (2), 129 (21), 101 (19), 99 (14), 98 (43), 97 (29), 96 (17), 83 (17), 69 (36), 68 (52), 67 (19), 59 (29), 55 (33), 45 (17), 43 (7), 41 (19), 40 (26), 39 (40).

Methyl 2-bromomethyl-2-oxiranylacetate (**17**): IR (CCl_4): 3050*m*, 3030*w*, 3002*m*, 2975*m*, 2930*w*, 2850*w*, 1745*s*, 1483*w*, 1439*s*, 1418*m*, 1395*w*, 1380*m*, 1348*m*, 1339*m*, 1300*w*, 1260*w*, 1225*s*, 1205*s*, 1175*s*, 1140*m*, 1105*w*, 1012*m*, 985*w*, 965*w*, 952*w*, 936*w*, 925*w*, 911*w*, 882*w*, 713*m*, 663*m*. – ^{1}H-NMR (100 MHz, CCl_4): 2.50, 2.92 (2 *d*, $J = 17$, CH_2COO); 2.75 (*d*, $J = 5$, further splitted) and 2.83 (*d*, $J = 5$) (2 H–C(3)); 3.50 (*s*, splits into an *AB* pattern upon the addition of 10 mol-% $Eu(dpm)_3$, $BrCH_2$–C(2)); 3.66 (*s*, CH_3O). – ^{13}C-NMR (25.2 MHz, CCl_4/C_6D_6): 36.6, 37.3 (CH_2COO, $BrCH_2$); 51.5 (CH_3O); 53.6

(C(3)); 55.3 (C(2)); 169.4 (CH_2COO). – MS: 179/177 (1 each, $M^+ - 31$), 137 (2), 135 (4), 133 (2), 129 (38), 121 (11), 119 (5), 109 (2), 107 (2), 99 (8), 97 (89), 87 (61), 71 (28), 59 (53), 53 (17), *45* (100), 41 (67), 39 (62).

$C_6H_9BrO_3$ (209.04) Calc. C 34.47 H 4.34 Br 38.23% Found C 34.30 H 4.51 Br 38.53%

Isomerization of **16**. Without solvent, 305 mg (1.458 mmol) of **16** and 34 mg (0.113 mmol) of ethyl-diisopropylammonium *p*-toluenesulfonate were heated for 30 min to 125°. Bulb-to-bulb distillation (80°/h.v.) and flash chromatography (20 g of silica gel) with pentane/Et_2O 9:1 gave 279 mg (91%) of **15**.

*Methyl (*E*)-4-iodo-3-methoxy-2-butenoate* (**21**). A solution of 5.177 g (24.7 mmol) of **15** in 5 ml of acetone was added to an ice-cooled solution of 6 g (40 mmol) of NaI in 30 ml of acetone. After stirring under Ar and exclusion of light for 45 min at 0° and 45 min at r.t., the precipitated NaBr was removed by filtration, the acetone evaporated, the residue dissolved in Et_2O, and filtered again to remove excess NaI. Flash chromatography (200 g of silica gel) of the crude product (6.274 g) with pentane/Et_2O 4:1 gave 6.108 g (96%) of **21**. – IR (CCl_4): 3070*w*, 3020*w*, 2975*w*, 2955*m*, 2910*w*, 2845*w*, 1717*s*, 1625*s*, 1453*m*, 1442*m*, 1433*m*, 1414*m*, 1359*s*, 1292*s*, 1239*w*, 1196*s*, 1172*m*, 1150*s*, 1120*s*, 1053*m*, 1012*m*, 932*m*, 975*w*, 825*m*, 676*w*. – ^{1}H-NMR (90 MHz, CCl_4): 3.68, 3.72 (2 *s*, CH_3O–C(1), CH_3O–C(3)); 4.45 (*s*, 2 H–C(4)); 5.01 (*s*, H–C(2)). – MS: *256* (100, M^+), 225 (31), 224 (3), 197 (1), 165 (2), 141 (2), 129 (81), 114 (4), 101 (56), 98 (19), 85 (2), 69 (15), 68 (22), 67 (5), 59 (11), 55 (18), 45 (6), 41 (8), 40 (15), 39 (18).

$C_6H_9IO_3$ (256.04) Calc. C 28.14 H 3.54 I 49.57% Found C 28.17 H 3.60 I 49.75%

*Methyl (*E*)-3-methoxy-4-nitro-2-butenoate* (**18**). *a) From iodide* **21**. A solution of 6.066 g (23.7 mmol) **21** in a few ml of dry Et_2O was added within 15 min to a magnetically stirred suspension of 7.7 g (50 mmol) of $AgNO_2$ in 100 ml of dry Et_2O (0°, Ar, exclusion of light). After stirring for 4 days at r.t. in the dark, the mixture was filtered through *Celite*, the filtrate evaporated, and the residue (4.025 g) dissolved in 5 ml of CH_3OH to hydrolyze any alkyl nitrites. After standing for 2 days at r.t., the CH_3OH-solution was worked up with Et_2O. The org. phases were washed with H_2O (2×) and sat. NaCl-solution (once), dried ($MgSO_4$), and evaporated. Crystallization of the oily residue (3.873 g) from pentane/Et_2O using seeding crystals gave 3.041 g (73%) of **18**. Flash chromatography (40 g of silica gel) with pentane/Et_2O 3:2 yielded another 611 mg (14%) of **18** from the mother liquor, m.p. 49–50° (pentane/Et_2O). – UV (EtOH): 231 (12300). – IR (CCl_4): 3030*w*, 3000*w*, 2980*w*, 2957*m*, 2940*w*, 2910*w*, 2845*w*, 1720*s*, 1650*s*, 1645*s*, 1566*s*, 1457*w*, 1445*m*, 1438*m*, 1427*w*, 1390*s*, 1355*m*, 1293*m*, 1253*w*, 1199*s*, 1152*s*, 1051*s*, 1042*m*, 965*w*, 938*m*, 908*w*, 837*m*. – ^{1}H-NMR (90 MHz, CCl_4): 3.68, 3.79 (2 *s*, CH_3O–C(1), CH_3O–C(3)); 5.30 (*s*, H–C(2)); 5.59 (*s*, 2 H–C(4)). – MS: 175 (2, M^+), 158 (1), 145 (9), 144 (36), 129 (95), 116 (8), 114 (6), *101* (100), 98 (41), 85 (8), 75 (7), 69 (28), 68 (38), 59 (32), 55 (47), 45 (16), 41 (17), 40 (19), 39 (22).

$C_6H_9NO_5$ (175.14) Calc. C 41.14 H 5.18 N 8.00% Found C 41.16 H 5.17 N 7.92%

b) From bromide **15**. A solution of 1.874 g (8.96 mmol) of **15** in 4 ml of DMF was added under Ar within 8 min to a mixture of 1.2 g (17.4 mmol) of $NaNO_2$ and 1.5 g (11.9 mmol) of phloroglucinol in 30 ml of DMF cooled with ice/NaCl. After stirring for 7 h, the temp. had reached –10°. The mixture was kept at 0° over night, poured to ice/H_2O, and extracted with Et_2O (3×). The org. phases were washed with H_2O (2×) and sat. NaCl-solution (once), dried, and evaporated. The residue (1.247 g) was separated by flash chromatography (60 g of silica gel, pentane/CH_2Cl_2/Et_2O 3:3:2) into 863.3 mg containing **18** and 232.5 mg containing the polar **19** and **20**. Several chromatographic separations with pentane/Et_2O 3:2 for **18** and pentane/CH_2Cl_2/Et_2O 3:3:2 for **19**/**20** gave 726 mg (46%) of **18**, purified by bulb-to-bulb distillation (90°/h.v.), 142 mg (7.7%) of **19**, purified by recrystallization (hexane/CH_2Cl_2) from 188 mg of chromatographically pure material, and 18 mg (1%) of **20**, obtained by recrystallization (hexane/CH_2Cl_2) from 34 mg of chromatographically pure material.

*Methyl (*E*)-4-hydroxyimino-3-methoxy-4-nitro-2-butenoate* (**19**): m.p. 80° (dec.). – IR ($CHCl_3$): 3700–3200*m*, 3530*m*, 3200*m*, 3030*m*, 2980*w*, 2950*m*, 2940*m*, 2900*m*, 2840*m*, 1710*s*, 1670*m*, 1622*s*, 1561*s*, 1552*s*, 1500*w*, 1453*m*, 1439*s*, 1408*w*, 1383*m*, 1358*s*, 1346*s*, 1305*s*, 1256*w*, 1190*m*, 1153*s*, 1113*s*, 1037*s*, 1030*s*, 987*w*, 925*m*, 875*w*, 832*s*. – ^{1}H-NMR (90 MHz, $(CD_3)_2CO$): 3.63, 3.90 (2 *s*, CH_3O–C(1), CH_3O–C(3)); 5.70 (*s*, H–C(2)); 12.47 (*s*, $w_{1/2}$ *ca.* 8, HON=C(4)). –MS (di., <100°): 204 (2, M^+), 187 (1), 173 (15), 158 (62), 157 (38), 140 (6), 129 (5), 128 (10), 127 (10), 126 (92), 115 (4), 110 (67),

100 (17), 99 (35), 96 (25), 85 (6), 84 (6), 83 (8), *69* (100), 66 (17), 59 (37), 53 (17), 43 (10), 41 (17), 30 (50).

$C_6H_8N_2O_6$ Calc. 204.14 C 35.30 H 3.95 N 13.72% Found 206.66 C 35.24 H 3.98 N 13.35%

Methyl (E)-2-hydroxyimino-3-methoxy-4-nitro-3-butenoate (**20**): m.p. 99–102° (hexane/CH_2Cl_2). – IR ($CHCl_3$): 3750–2500*m*, 3540*m*, 3130*w*, 3030*w*, 2980*w*, 2950*m*, 2840*w*, 1727*s*, 1640*m*, 1612*s*, 1560*w*, 1502*s*, 1455*m*, 1440*m*, 1370*m*, 1353*s*, 1276*m*, 1238*s*, 1150*m*, 1112*s*, 1030*m*, 978*w*. – ^{1}H-NMR (90 MHz, $(CD_3)_2CO$); 3.83, 3.96 (2 *s*, CH_3O–C(1), CH_3O–C(3)); 7.33 (*s*, H–C(4)); 12.15 (*s*, $w_{1/2}$ *ca.* 3, HON=C(2)). – MS (di., < 120°): 168 (17), 167 (27), 166 (3), 159 (3), 155 (2), 139 (5), 136 (20), 123 (7), 108 (4), 93 (5), 81 (12), 80 (10), *59* (100), 54 (30), 45 (15), 44 (32), 43 (15), 42 (44), 31 (15), 30 (29).

$C_6H_8N_2O_6$ (204.14) Calc. C 35.30 H 3.95 N 13.72% Found C 35.36 H 4.00 N 13.54%

Deprotonation and reprotonation of **18**. To a solution of 200 mg (2.85 mmol) of CH_3OK in 5 ml of CH_3OH, 465 mg (2.66 mmol) of **18** were added. A pale yellow precipitate formed soon after the addition was collected, after cooling to −20°, by filtration, and washed with a minimum of cold CH_3OH. Drying under h.v. gave 230 mg (*ca.* 40%) of storable 'potassium nitronate'.

A similar mixture, obtained from 710 mg (4.06 mmol) of **18** and 300 mg (4.28 mmol) of CH_3OK in 10 ml of CH_3OH was quenched, after stirring for 30 min at r.t., by the addition to 50 ml of 15% H_2SO_4 and some urea. Extraction with Et_2O gave 717 mg of a 82:18 mixture (NMR) of **18** and **24**. Two recrystallizations from pentane/Et_2O gave 310 mg of pure **18** and 408 mg residue of the mother liquor consisting of *ca.* 65% of **18** and 35% of **24**. Several chromatographies of **18**/**24** with pentane/CH_2Cl_2/Et_2O 6:3:1 gave another 352 mg of pure **18** and 13 mg of **24** still containing *ca.* 12% of **18**.

Methyl (E)-3-methoxy-4-nitro-3-butenoate (**24**): IR (CCl_4): 3138*w*, 3020*w*, 2978*w*, 2955*m*, 2940*w*, 2842*w*, 1751*s*, 1628*s*, 1509*s*, 1459*w*, 1442*w*, 1437*m*, 1409*m*, 1388*w*, 1355*m*, 1350*s*, 1321*m*, 1290*w*, 1259*s*, 1207*s*, 1170*s*, 1150*m*, 1050*m*, 1012*w*, 935*w*, 901*w*, 858*w*, 835*w*. – ^{1}H-NMR (90 MHz, CCl_4, only the signals of **24**): 3.64, 3.71 (2 *s*, CH_3O–C(3), CH_3O–C(1)); 3.69 (*s*, 2 H–C(2)); 6.85 (*s*, H–C(4)). – MS: 175 (1, M^+), 145 (11), 144 (35), 129 (90), 113 (9), 111 (7), *101* (100), 98 (39), 85 (7), 75 (7), 69 (30), 68 (33), 59 (30), 55 (47), 45 (18), 41 (19), 40 (21), 39 (23).

(E)-3-Methoxy-4-nitro-2-butenoic acid (**23**). A solution of 229 mg (1.34 mmol) of **18** in 10 ml of 2N NaOH was stirred for 43 h at r.t. The mixture was then poured to 10 ml of 15% H_2SO_4 and extracted with Et_2O. The acid was isolated by extraction with sat. $NaHCO_3$-solution (3×), careful acidification with 15% H_2SO_4 containing urea, and reextraction with Et_2O. Purification of the crude acid (179 mg, 85%) by 4 recrystallizations from benzene/cyclohexane gave 84 mg (40%) of pure **23**, m.p. 101–103°. – IR ($CHCl_3$): 3600–2400*m*, 2980*w*, 2940*m*, 2925*m*, 2855*w*, 1800*w*, 1780*w*, 1695*s*, 1630*s*, 1567*s*, 1503*w*, 1458*w*, 1444*w*, 1412*m*, 1393*m*, 1350*m*, 1317*w*, 1297*w*, 1257*w*, 1193*m*, 1169*s*, 1115*m*, 1054*m*, 1012*w*, 952*w*, 908*w*, 840*m*. – ^{1}H-NMR (90 MHz, $CDCl_3$): 3.78 (*s*, CH_3O–C(3)); 5.41 (*s*, H–C(2)); 5.64 (*s*, 2 H–C(4)); 9.8–10.8 (br., HO–C(1)). – MS (di., 130°): 161 (2, M^+), 144 (5), 143 (13), 131 (12), 127 (8), 116 (27), 115 (85), 114 (11), 113 (12), 110 (6), 100 (10), 87 (10), 85 (19), 84 (15), *83* (100), 69 (58), 59 (24), 55 (62), 45 (16), 44 (13), 43 (10), 42 (10), 41 (19), 40 (12), 39 (24).

$C_5H_7NO_5$ (161.11) Calc. C 37.27 H 4.38 N 8.69% Found C 37.80 H 4.35 N 8.56%

Methyl 3,3-dimethoxy-4-nitrobutyrate (**25**). *a) CsF as catalyst.* A solution of 130 mg (0.743 mmol) of **18** and 194 mg (1.277 mmol) of CsF in 16 ml of CH_3OH was sealed under Ar in an ampule and heated for 19 days in an oil bath of 50°. The cooled mixture was then poured to H_2O and extracted with Et_2O. The org. phases were washed with sat. $NaHCO_3$-solution (2×) and NaCl-solution (2×), dried ($MgSO_4$), and evaporated. Bulb-to-bulb distillation (100°/h.v.) of the residue (166 mg) gave 156 mg of **25** containing according to ^{1}H-NMR *ca.* 15% of **18**. Separation of 147 mg of this mixture by HPLC (silica gel, hexane/CH_2Cl_2/Et_2O 13:6:1 + AcOH (1 ppt), 47 bar, detection at 240 nm) gave 18 mg (14%) of **18** (t_{ret} = 16 min 55 sec) and 109 mg (75%) of **25** (t_{ret} = 20 min 30 sec).

b) Na_2CO_3 as catalyst. A solution of 114 mg (0.651 mmol) of **18** and 7 mg (0.07 mmol) of Na_2CO_3 in 15 ml of CH_3OH was stirred for 13 days at r.t. under Ar. Workup with Et_2O gave, after washing with H_2O, sat. $NaHCO_3$- (2×), and NaCl-solution (2×), 102 mg of distilled **25** containing according to NMR *ca.* 6% of **18**. Acidification of the basic aq. phases and extraction with Et_2O gave another 14 mg of a 1:1 mixture of **18** and **25**. **25**: IR ($CHCl_3$): 3030*w*, 2990*w*, 2950*m*, 2839*w*, 1735*s*, 1559*s*, 1552*s*, 1457*w*, 1436*m*, 1424*w*, 1418*w*, 1380*m*, 1360*m*, 1317*m*, 1283*w*, 1175*m*, 1152*w*, 1108*s*, 1069*m*,

1037*m*, 1000*w*, 892*w*, 845*w*. – ^{1}H-NMR (90 MHz, $CDCl_3$): 2.98 (*s*, 2 H–C(2)); 3.30 (*s*, $(CH_3O)_2C(3)$); 3.70 (*s*, CH_3O–C(1)); 4.95 (*s*, 2 H–C(4)). – MS: 176 (65, $M^+ - 31$), 158 (70), 147 (81), 144 (57), 134 (75), 130 (33), 129 (33), 128 (24), 126 (20), 115 (17), 105 (54), 101 (61), 99 (15), 98 (17), *88* (100), 72 (44), 71 (28), 69 (16), 59 (65), 58 (28), 57 (23), 55 (19), 45 (46), 43 (66), 42 (26), 41 (66), 40 (14), 39 (23).

$C_7H_{13}NO_6$ (207.18) Calc. C 40.58 H 6.32 N 6.76% Found C 40.70 H 6.38 N 6.69%

4-Nitro-3-oxobutyrate **1** *by treatment of* **18** *with* CF_3CO_2H. To a solution of 1.0 g (5.72 mmol) of **18** in 8 ml of dry THF, 10 ml of CF_3CO_2H were added at 0° under Ar. After standing at r.t. for 16.5 days, the bulk of solvent and reagent was removed under h.v. The residue was dissolved in Et_2O and extracted with sat. $NaHCO_3$-solution (1 × 15 ml, 2 × 5 ml). The $NaHCO_3$ extracts were shaken twice with Et_2O, cooled in ice, and, after the addition of some urea, carefully acidified with 15% H_2SO_4. Saturation with NaCl and extraction with Et_2O (3 × 200 ml) gave, after washing with NaCl-solution, drying, and evaporation of the solvent, 498 mg of **1**, 458 mg (49%) after bulb-to-bulb distillation (85–100°/h.v.). From the first Et_2O extracts, 439 mg (44%) of **18** were reisolated.

Methyl (Z)-3-acetoxy-4-bromo-2-butenoate (**26**). A mixture of 25.64 g (0.132 mol) of **12**, 135 g (1.35 mol) of 2-propenyl acetate, and 1.5 g (7.9 mmol) of *p*-toluenesulfonic acid was boiled for 4 h under reflux and Ar. Acetone and reagent were then removed by slow distillation at normal pressure (120–140° bath temp., 3 h). The brown residue was purified by repeated distillation under h.v. The third distillation using a 10-cm-*Vigreux* column yielded 22.6 g (72%) of **26**, b.p. 64–70°/0.05 Torr. – IR (CCl_4): 3030*w*, 3000*w*, 2955*m*, 2845*w*, 1776*s*, 1732*s*, 1665*s*, 1436*m*, 1405*w*, 1372*m*, 1355*m*, 1285*m*, 1242*s*, 1219*m*, 1192*s*, 1165*s*, 1150*s*, 1127*m*, 1029*m*, 1010*m*, 946*w*, 923*m*, 893*w*, 845*w*, 706*w*, 688*w*. – ^{1}H-NMR (90 MHz, CCl_4): 2.23 (*s*, CH_3CO_2–C(3)); 3.67 (*s*, CH_3O); 3.93 (*s*, 2 H–C(4)); 5.85 (*s*, H–C(2)). – MS: 238/236 (0.1 each, M^+), 207 (3), 205 (3), 165 (8), 163 (9), 157 (8), 115 (2), 101 (22), 93 (2), 87 (2), 84 (3), 69 (14), 59 (3), 55 (3), *43* (100), 39 (2).

$C_7H_9BrO_4$ (237.05) Calc. C 35.46 H 3.83 Br 33.71% Found C 35.46 H 4.00 Br 33.70%

Treatment of **26** *with NaI. a) Large scale.* Enol acetate **26** (21.605 g, 91.2 mmol) was added within 40 min to an ice-cooled and filtered solution of 23 g (0.153 mmol) of NaI in 100 ml of dry acetone (Ar, exclusion of light). After stirring for 2.5 h at r.t. in the dark, the mixture was filtered, the filtrate evaporated, the residue dissolved in Et_2O/CH_2Cl_2 and filtered again. The residue of the filtrate (26.2 g) was subjected to flash chromatography (200 g of silica gel). Elution with pentane/CH_2Cl_2/Et_2O 6:3:1 gave 1.95 g of impure **28** followed by 22 g, from which 15.07 g (58%) of pure **27** were obtained by crystallization (pentane/Et_2O). From a second crop (1.06 g) and material obtained by chromatography of the mother liquor (1.874 g), an additional 1.407 g (5%) of **27** were obtained by recrystallization. Several crystallizations (pentane/Et_2O) of impure **28** (4.089 g) obtained by the chromatographic separations, gave 2.697 g (10%) of **28**. In the course of handling the light sensitive solutions of **27** and **28**, *ca.* 120 mg of a less soluble strongly fluorescent compound, which was found to be *dimethyl 2,5-dihydroxyterephthalate* (**29**), were collected.

b) Small scale (better exclusion of light). Treatment of 1.995 g (8.42 mmol) of **26** with 2 g (13.3 mmol) of NaI in 10 ml of acetone as described above gave 97 mg (4%) of **28** and 2.241 g (93%) of **27** separated by flash chromatography (80 g of silica gel, pentane/CH_2Cl_2/Et_2O 12:6:1). Recrystallization from pentane/Et_2O gave 1.887 g (79%) of *methyl (Z)-3-acetoxy-4-iodo-2-butenoate* (**27**), m.p. 66–67.5°. – IR ($CHCl_3$): 3030*w*, 3000*w*, 2950*w*, 2840*w*, 1768*s*, 1720*s*, 1652*m*, 1432*m*, 1420*w*, 1368*m*, 1350*m*, 1286*w*, 1245*s*, 1174*s*, 1157*s*, 1135*s*, 1107*w*, 1021*m*, 1005*m*, 945*w*, 918*m*, 842*m*. – ^{1}H-NMR (90 MHz, CCl_4): 2.25 (*s*, CH_3CO_2–C(3)); 3.67 (*s*, CH_3O); 3.92 (*s*, 2 H–C(4)); 5.87 (*s*, H–C(2)). – MS (di.): 284 (1, M^+), 253 (4), *242* (100), 211 (11), 169 (1), 157 (10), 141 (3), 127 (4), 115 (12), 101 (14), 87 (11), 84 (6), 69 (8), 59 (3), 55 (6), 43 (76), 39 (2).

$C_7H_9IO_4$ (284.05) Calc. C 29.60 H 3.19 I 44.68% Found C 29.77 H 3.19 I 44.62%

Methyl (E)-3-acetoxy-4-iodo-2-butenoate (**28**): m.p. 38–38.5°. – IR (CCl_4): 3065*w*, 3030*w*, 2990*w*, 2950*m*, 2840*w*, 1770*s*, 1725*s*, 1653*s*, 1455*w*, 1433*m*, 1415*m*, 1368*m*, 1344*s*, 1275*w*, 1243*s*, 1200*s*, 1190*s*, 1162*m*, 1136*s*, 1082*s*, 1031*s*, 1002*w*, 945*w*, 900*m*, 870*m*, 670*w*. – ^{1}H-NMR (90 MHz, CCl_4): 2.22 (*s*, CH_3CO_2–C(3)); 3.71 (*s*, CH_3O); 4.62 (*s*, 2 H–C(4)); 5.75 (*s*, H–C(2)). – MS: 284 (2, M^+), 253 (3), 242 (78), 211 (10), 157 (8), 141 (2), 127 (3), 115 (12), 101 (9), 97 (10), 94 (7), 69 (9), 59 (4), 55 (9), *43* (100), 39 (4).

$C_7H_9IO_4$ (284.05) Calc. C 29.60 H 3.19 I 44.68% Found C 29.51 H 3.17 I 44.68%

Isomerization of **27** *and* **28**. *a) From* **27**. A solution of 305 mg (1.073 mmol) of **27** in 10 ml of dry Et_2O was stored in the dark at 6°. A small portion of this solution was kept in the dark for 3 days at r.t. TLC analysis showed no isomerization. Brought to daylight, this solution became coloured by I_2 in short time, and TLC analysis after 2.5 h showed the formation of considerable amounts of (*E*)-isomer **28**. A second portion of the above solution, which was kept in the dark at r.t. after the addition of a catalytic amount of I_2, showed no isomerization. The remaining bulk of the Et_2O solution of **27** was then exposed to daylight for *ca.* 15 h. ^{1}H-NMR analysis of the residue, after evaporation of the solvent, showed **27**/**28** in a 43:57 ratio.

b) From **28**. A solution of 258 mg (0.908 mmol) of **28** in 10 ml of Et_2O was exposed to daylight for 15 h. Flash chromatography (20 g of silica gel) of the resulting 38:62 mixture **27**/**28** with pentane/CH_2Cl_2/Et_2O 12:6:1 gave 84 mg (32.5%) of **28**, 52 mg (20.2%) of a 1:1 mixture **27**/**28**, and 40 mg (15.5%) of **27**.

Methyl 4-iodo-3-oxobutyrate (**13**). *a) From* **27**. A solution of 1.387 g (4.88 mmol) of **27** in 10 ml of CH_3OH was added slowly to 770 mg (11 mmol) of $KOCH_3$ in 10 ml of CH_3OH at 0°. After stirring for 10 min at 0°, the mixture was poured to 10 ml of 15% H_2SO_4 and ice. The product **13** was extracted with Et_2O and purified by bulb-to-bulb distillation (60°/0.03 Torr). Yield: 1.127 g (95%) of slightly tan **13**.

b) From **28**. Treatment of 724 mg (2.55 mmol) of **28** with 467 mg (6.5 mmol) of $KOCH_3$ in CH_3OH as described above gave 539 mg (87%) of distilled **13**.

c) From **12**. A solution of 2.156 g (11.07 mmol) of **12**, purified by distillation using a concentric-tube column, in a few ml of acetone was added within 15 min to a filtered solution of 3 g (20 mmol) of dry NaI in 20 ml of acetone (Ar, exclusion of light, 0°). After stirring for 20 min at 0°, the mixture was allowed to warm up to r.t. (10 min). The precipitated NaBr was removed by filtration, and the residue of the filtrate was worked up by extraction with Et_2O. The org. phases were washed with H_2O, sat. $NaHCO_3$- and NaCl-solution, dried, and evaporated. Bulb-to-bulb distillation (60°/0.03 Torr) of the residue (2.555 g) gave 2.176 g (81%) of tan **13**. – IR (CCl_4): 3030*w*, 3000*w*, 2950*m*, 2840*w*, 1755*s*, 1742*s*, 1719*s*, 1660*m*, 1625*s*, 1448*m*, 1438*m*, 1402*m*, 1321*m*, 1236*s*, 1199*m*, 1170*m*, 1143*m*, 1100*w*, 1029*w*, 1005*w*, 950*w*, 913*w*. – ^{1}H-NMR (90 MHz, CCl_4): *keto form:* 3.64 (*s*, 2 H–C(2)); 3.72 (*s*, CH_3O); 3.94 (*s*, 2 H–C(4)). *Methyl 3-hydroxy-4-iodo-2-butenoate* (*enol form*, 38% according to integration): 3.72 (*s*, CH_3O); 3.76 (*s*, 2 H–C(4)); 5.25 (*s*, H–C(2)); 11.95 (*s*, $w_{1/2}$ *ca.* 4, HO–C(3)). – MS: 242 (24, M^+), 211 (15), 210 (17), 184 (35), 183 (9), 169 (48), 168 (7), 141 (35), 127 (22), *115* (100), 101 (46), 87 (9), 85 (7), 84 (7), 83 (9), 73 (9), 69 (22), 59 (43), 57 (15), 55 (11), 44 (22), 43 (83), 42 (52).

$C_5H_7IO_3$ (242.01) Calc. C 24.81 H 2.92 I 52.44% Found C 24.71 H 3.01 I 52.18%

Treatment of **27** *with* CH_3OH/CH_3SO_3H. A solution of 568 mg (2 mmol) of **27** and 0.25 ml of CH_3SO_3H in 10 ml of CH_3OH was stirred for 20 h at r.t. After quenching with $NaHCO_3$ solution, the products were isolated by extraction with Et_2O. The residue of the org. phases (559 mg) was separated by chromatography (60 g of silica gel). Elution with hexane/CH_2Cl_2/Et_2O 12:6:1 gave 54 mg (10%) of **21**, 405 mg (70%) of **31** and 46 mg (9%) of **13**. *Methyl 3,3-dimethoxy-4-iodobutyrate* (**31**): IR (CCl_4): 3000*m*, 2955*m*, 2900*w*, 2835*m*, 1745*s*, 1455*m*, 1438*m*, 1417*m*, 1332*m*, 1315*m*, 1264*m*, 1240*m*, 1212*m*, 1190*m*, 1167*s*, 1155*m*, 1105*m*, 1080*s*, 1056*s*, 1022*m*, 982*w*, 965*m*, 889*w*, 850*w*, 840*w*, 655*w*, 630*w*. – ^{1}H-NMR (90 MHz, CCl_4): 2.82 (*s*, 2 H–C(2)); 3.20 (*s*, $(CH_3O)_2C(3)$); 3.50 (*s*, 2 H–C(4)); 3.69 (*s*, CH_3O–C(1)). – MS: 257 (43, $M^+ - 31$), 256 (17), 225 (15), 215 (43), 197 (18), 184 (4), 169 (2), 167 (3), 161 (3), *147* (100), 141 (4), 129 (19), 115 (4), 105 (29), 101 (12), 98 (4), 88 (23), 71 (12), 59 (16), 57 (7), 55 (5), 45 (7), 43 (15), 41 (17), 39 (6).

Conversion of **27** *and* **28** *to* **1**. *a) Substitution of* **27** *using* $AgNO_2$. A solution of 4.444 g (15.63 mmol) of **27** in 50 ml of dry Et_2O was added within 80 min to a stirred suspension of 5 g (32.4 mmol) of $AgNO_2$ and 5 g of quartz sand in 100 ml of Et_2O (Ar, exclusion of light). After stirring for 4.5 days in the dark, the silver salts were separated by filtration. Evaporation of the filtrate gave 2.522 g of crude **32** containing according to ^{1}H-NMR *ca.* 20 mol-% of *methyl 4-acetoxy-3-oxobutyrate* (**34**). *Methyl (Z)-3-acetoxy-4-nitro-2-butenoate* (**32**): IR ($CHCl_3$): 3023*w*, 2950*m*, 2842*w*, 1773*s*, 1730*s*, 1678*m*, 1567*s*, 1437*m*, 1420*w*, 1370*m*, 1355*m*, 1311*w*, 1281*w*, 1235*m*, 1165*s*, 1148*m*, 1060*w*, 1032*m*, 1013*m*, 946*w*, 920*w*, 904*w*, 836*w*. – ^{1}H-NMR (90 MHz, $CDCl_3$, only signals of **32**): 2.27 (*s*, CH_3CO_2–C(3)); 3.74 (*s*, CH_3O–C(1)); 5.08 (*s*, 2 H–C(4)); 5.98 (*s*, H–C(2)). – MS (peaks arising

from **34** excluded): 203 (0.5, M^+), 172 (3), 143 (2), 130 (2), 115 (3), 100 (6), 87 (7), 84 (3), 69 (21), 60 (14), 59 (12), 55 (5), 44 (19), *43* (100), 42 (16), 41 (5), 39 (12).

b) Treatment of **32** *with* CH_3SO_3H/CH_3OH. A solution of 2.023 g (9.95 mmol) of crude **32** and 0.5 ml of CH_3SO_3H in 20 ml of CH_3OH was stirred for 31 h at r.t. under Ar. The mixture was worked up with Et_2O. The org. layers were washed with H_2O (2×) and sat. $NaHCO_3$ solution (20 ml, 2× 10 ml). Immmediate acidification of the basic extracts with 15% H_2SO_4 in the presence of urea, extraction with Et_2O (3×), washing of the org. phases with sat. NaCl-solution (2×), drying, evaporation of the solvent, and bulb-to-bulb distillation (85–100°/h.v.) gave 620 mg (38%, 30% based on **27**) of **1**.

c) Treatment of **32** *with* $KOCH_3/CH_3OH$. A solution of 1.735 g (8.55 mmol) of crude **32**, obtained from 2.79 g (9.83 mmol) of **27** as described above, in 7 ml of CH_3OH was added within 15 min to an ice-cold solution of 1.949 g (27.8 mmol) of $KOCH_3$ and 2.5 g of urea in 25 ml of CH_3OH. After stirring for 5 min at 0°, the reaction was quenched by the addition to 20 ml of 15% H_2SO_4 and ice and extracted with Et_2O (3× 150 ml). The product **1** was extracted with sat. $NaHCO_3$ solution (25 ml, 10 ml, 5 ml) from the org. phases, which had been washed first with NaCl-solution. Acidification of the basic extracts, extraction with Et_2O, and distillation of the residue of the org. phases (778 mg) as described above gave 476 mg (34%, 30% based on **27**) of **1**. Chromatography of the material obtained by evaporation of the first Et_2O extracts with pentane/CH_2Cl_2/Et_2O 6:3:1 gave 42 mg of *methyl 4-acetoxy-3-oxobutyrate* (**34**). – IR (CCl_4): 3025*w*, 3000*w*, 2955*m*, 2840*w*, 1753*s*, 1735*s*, 1662*m*, 1650*w*, 1636*m*, 1496*m*, 1483*m*, 1411*w*, 1370*m*, 1363*m*, 1320*m*, 1260*m*, 1225*s*, 1166*m*, 1060*m*, 1035*m*, 996*w*. – ^{1}H-NMR (90 MHz, $CDCl_3$): 2.15 (*s*, CH_3CO_2–C(4)); 3.50 (*s*, 2 H–C(2)); 3.75 (*s*, CH_3O); 4.76 (*s*, 2 H–C(4). *Enol tautomer:* 4.63 (*s*, 2 H–C(4)); 5.22 (*s*, H–C(2)). – MS: 174 (0.5, M^+), 132 (9), 116 (15), 101 (22), 88 (1), 86 (5), 74 (7), 73 (6), 69 (5), 58 (7), 57 (4), 55 (1), 44 (9), *43* (100), 42 (7), 41 (1).

$C_7H_{10}O_5$ (174.15) Calc. C 48.27 H 5.79% Found C 48.21 H 5.80%

d) Substitution of **28** *using* $AgNO_2$. A solution of 690 mg (2.43 mmol) of **28** in 15 ml of dry Et_2O was added within 40 min to a suspension of 0.8 g (5.2 mmol) of $AgNO_2$ in 30 ml of Et_2O (0°, Ar, protection from light). Stirring for 4.5 days at r.t. in the dark, filtration, and evaporation of the solvent gave 501 mg of crude **33**, containing according to ^{1}H-NMR, 14 mol-% of starting material **28** and 10 mol-% of **34**. *Methyl (E)-3-acetoxy-4-nitro-2-butenoate* (**33**): IR ($CHCl_3$): 3020*w*, 2950*m*, 2840*w*, 1770*s*, 1720*s*, 1670*m*, 1655*m*, 1562*s*, 1433*m*, 1412*w*, 1370*m*, 1345*m*, 1298*w*, 1180*s*, 1118*s*, 1084*w*, 1030*m*, 1010*w*, 940*w*, 900*w*, 880*w*. – ^{1}H-NMR (90 MHz, $CDCl_3$, only signals of **33**): 2.23 (*s*, CH_3CO_2–C(3)); 3.78 (*s*, CH_3O); 5.77 (*s*, 2 H–C(4)); 6.23 (*s*, H–C(2)). – MS (peaks arising from **28** and **34** excluded): 203 (0.3, M^+), 172 (2), 143 (1), 115 (4), 87 (5), 84 (3), 69 (15), 60 (7), 59 (5), 55 (5), 45 (11), 44 (13), *43* (100), 42 (9), 41 (3), 39 (2).

e) Treatment of **33** *with* $KOCH_3/CH_3OH$. Crude **33** (501 mg) was added with a few ml of CH_3OH to an ice-cooled solution of 625 mg (8.9 mmol) of $KOCH_3$ and 1 g urea in 10 ml of CH_3OH. After stirring for 10 min at r.t., the mixture was worked up as described above by extraction with Et_2O. The nitro ketone **1** was separated by extraction with $NaHCO_3$ solution, acidification, and reextraction with Et_2O. Purification by bulb-to-bulb distillation (h.v.) gave 161 mg (41% based on **28**) **1**.

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