255. Construction of Highly Substituted Nitroaromatic Systems by Cyclocondensation

Part II

Conversion of 4-Nitro-3-oxobutyrate to 3-Nitrosalicylates [1])

by **Rudolf O. Duthaler**

Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule, CH-8092 Zürich

(4.X.83)

Summary

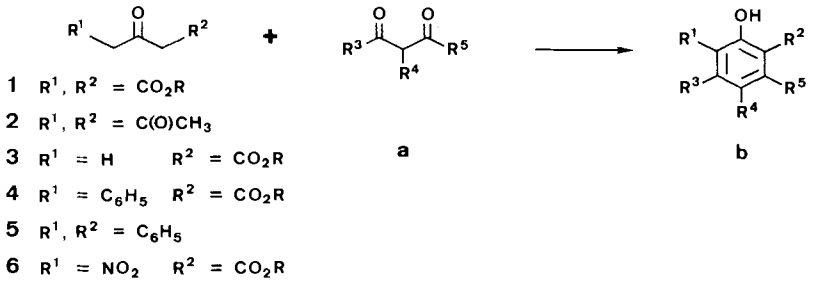
The base-catalyzed reaction of 4-nitro-3-oxobutyrate (**6**) with acetylacetone (**8**, *Scheme 3*), formylacetone (**13**, *Scheme 4*), formylcyclohexanone (**31**, *Scheme 5*), 2,4-dioxopentanoates **39** and **40** *(Scheme 6)*, and 2,4,6-heptanetrione (**2**, *Scheme 7*) affords substituted 3-nitrosalicylates, products of a double aldol condensation. With unsymmetrical dicarbonyl compounds both regioisomers are formed. High selectivity was found in the case of β-keto-aldehydes **13** and **31** with preferred addition of the NO_2-substituted carbon to the aldehyde carbonyl. The major products of these cyclocondensations, which are isolated in yields ranging from 20% to 80%, are all new compounds. Less successful are the conversions with β-alkoxy- and β-chloro-vinyl ketones (**23**, **25**, and **26**), and with alkinone **24**, where the condensation products are formed in very low yield *(Scheme 4)*.

1. Introduction. – A large and important group of natural products is biogenetically derived from polyacetate chains. The cyclocondensations of these polyketides, which lead to phenolic compounds often with high selectivity, can be reproduced in laboratory experiments [2]. Besides the scientific value of such biomimetic processes, these transformations are often welcome synthetic alternatives to the classical electrophilic or radical substitutions on the aromatic nucleus. The construction of phenols **b** by a double aldol condensation between a β-dicarbonyl compound **a** and a ketone with activated α- and α'-methylene-C-atoms is an example of this methodology [3] *(Scheme 1)*.

In the well-established *Prelog* condensation 3-oxoglutarate **1** is used as keto component [3] [4]. This reaction scheme has then been extended to other activated ketones like 2,4,6-heptanetrione (**2**) [5], acetoacetate (**3**) and its derivatives [6], 4-phenyl-3-oxobutyrate (**4**), and 1,3-diphenyl-2-propanone (**5**) [7]. In connection with a natural product synthesis we decided to test the same concept for the synthesis of substituted

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

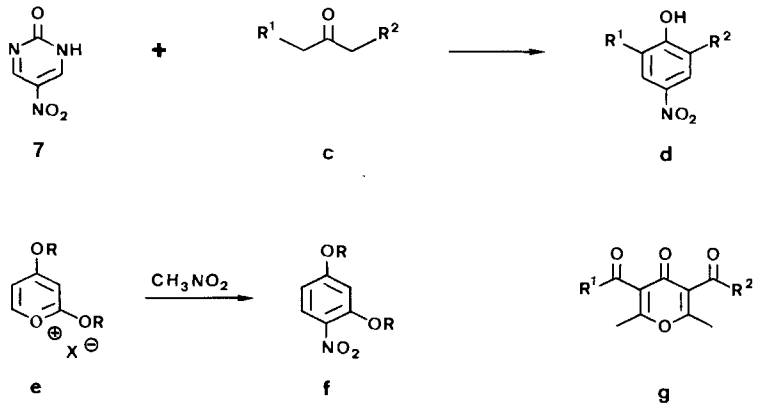
Scheme 1



3-nitrosalicylates (**b**, $R^1 = NO_2$, $R^2 = CO_2R'$), introducing 4-nitro-3-oxobutyrate (**6**) as doubly activated keto component of the cyclocondensation reaction [1]. The scope and limitations of the condensation of **6** with β-diketones and β-keto-aldehydes **a** is the subject of this communication. Although the number of nitro-compounds among natural products is small[2]), this approach is justified by the great synthetic potential of this function and the rather harsh non-selective nature of the electrophilic or radical aromatic nitration [9].

Previous examples for the construction of nitro aromatics by cyclocondensation, leading to *p*-nitrophenols and 3-nitroresorcinols, are depicted in *Scheme 2*.

Scheme 2



A very reactive dicarbonyl component for the *Prelog* condensation with no need for activation of the keto counterpart is nitromalondialdehyde (**a**, R^3, R^5 = H, $R^4 = NO_2$) [3] [7]. Closely related is the transformation of nitropyrimidinone **7** with ketones **c** to nitrophenols **d** *(Scheme 2)* [10]. Reaction of pyrylium salts **e** with CH_3NO_2 leads to nitroresorcinols **f** [11]. An analogous conversion can also be achieved with γ-pyrones **g** [12] *(Scheme 2)*. In addition to these examples nitro aromatics have also been isolated from reactions of nitro-enamines [13].

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[2]) The only known example of a natural 3-nitrosalicylate is methyl 5-methoxy-3-nitrosalicylate (**b**, $R^1 = NO_2$, $R^2 = CO_2CH_3$, $R^4 = OCH_3$, R^3, R^5 = H) found in the roots of *Primula acaulis* [8].

2. Condensation of 6 with Acetylacetone (8) *(Scheme 3).* – The elaboration of nitrobutyrate **6** into 4,6-dimethyl-3-nitrosalicylate **9** has been forestalled in the previous publication [1]. Acetate **10** and methyl ether **11** are obtainable from phenol **9** by acetylation and treatment with dimethyl sulfate/K_2CO_3 in acetone, respectively. The structure of **9** was unequivocally proved by saponification of the methyl ester followed by decarboxylation at 210° in quinoline affording the known 2-nitrophenol **12** [14] *(Scheme 3).*

The *Table* lists the experiments carried out to evaluate optimal reaction parameters. As the strong base in hydroxylic solvents usually employed for such cyclocondensations [3] [4] [5] was found to lead to cleavage of the α-nitroketone group of **6** [1], THF,

Scheme 3

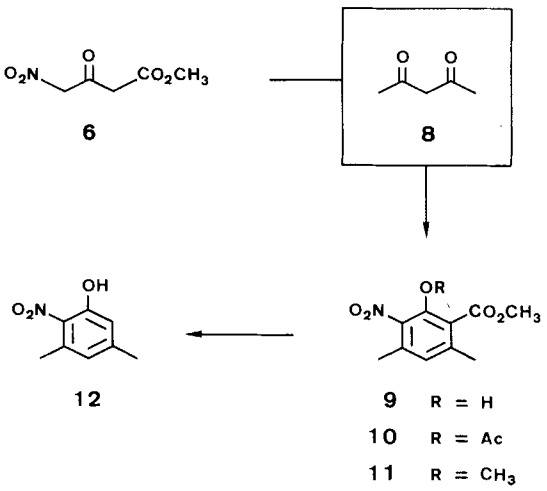


Table. *Conditions and Results of the Reaction of* **6** *with* **8**[a])

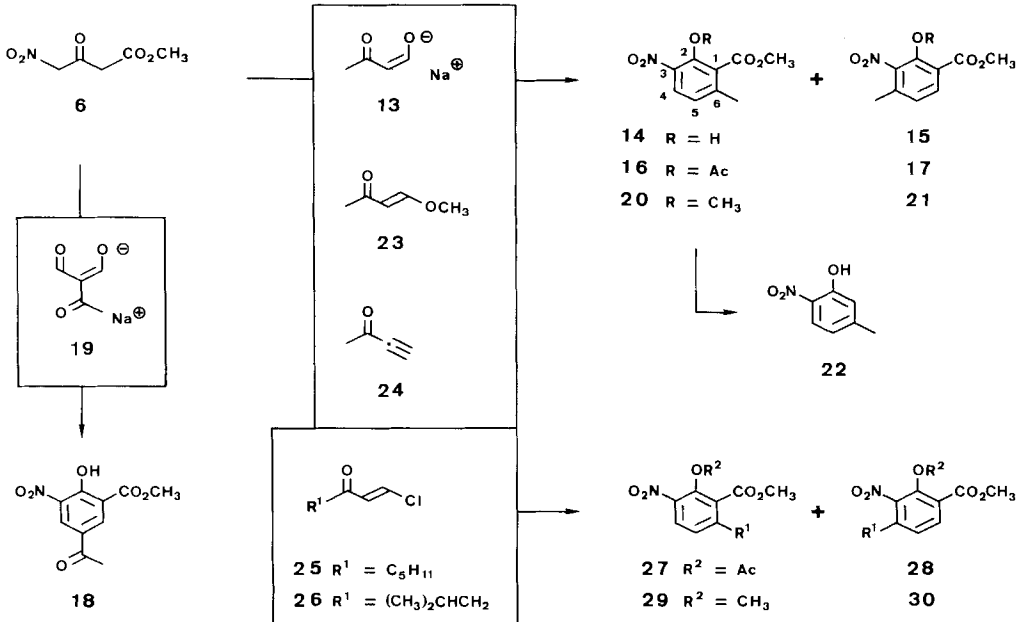
Entry	Base/equiv.	Solvent	Time (days)	Yield/ compound	Recovered **6**
1[b])	*t*-BuOK/1.0	THF	4	trace/**9**	73%
2[b])	*t*-BuOK/1.0	THF/*t*.BuOH	7	trace/**9**	78%
3[b])	*t*-BuOK/1.0	THF/DMF	7	3%/**9**	77%
4[b])	*t*-BuOK/1.0	THF/crown[c])	7	3%/**10**	58%
5[b])	*t*-BuOK/0.2	THF/DMF	7	34%/**9**	36%
6[b])	$(Me_2CH)_2NEt$/1.0	THF	1	23%/**10**	not determ.
7	$(Me_2CH)_2NEt$/1.0	THF	7	66%/**10**	not determ.
8[d])	DBU[e])/1.0	THF	7	71%/**9**	5%
9[b])	DBU[e])/1.5	THF[f])	8	48%/**9**	24%

[a]) 1.0–1.5 equiv. of **8**, molecular sieves 4 Å.
[b]) No description of these transformations will be given in the *Exper. Part.*
[c]) Dicyclohexyl-18-crown-6 (0.25 equiv.).
[d]) See [1].
[e]) 1,8-Diazabicyclo[5.4.0]undec-7-ene.
[f]) Without molecular sieves.

containing molecular sieves as water absorbent, was chosen as solvent. With 1 equiv. of *t*-BuOK in either THF or THF/*t*-BuOH the product **9** was formed only in trace amounts (*Table*, entries 1 and 2). This is partly due to the insolubility of the potassium nitronate of **6** in these media, since a small amount of product (**9** and **10**) can be isolated, when this salt is solubilized by adding either a crown ether or DMF (*Table*, entries 3 and 4). In analogy to the *Prelog* condensation, which was found to be strongly influenced by the pH of the reaction solution [4b], a drastic improvement of the yield of **9** or **10** was observed, when the amount of *t*-BuOK was lowered (*Table*, entry 5), or when an amine was used as catalyst (*Table*, entries 6–9)[3]). It is further evident that the reaction is not terminated after 1 day (*Table*, entry 6), while most of **6** is consumed after 1 week (*Table*, entries 7 and 8). Lower conversion with somewhat lower yield (63% based on consumed **6**) results with more than 1 equiv. of base (*Table*, entry 9).

3. Condensation of 6 with Formylacetone 13 and Related Substrates *(Scheme 4)*. – Due to the unstable nature of formylacetone its Na-salt **13** [16] is usually used for condensations with glutarate **1**, in this case without the necessity of base [4a]. To obtain the optimal pH for the condensation with **6**, a slight excess of ethyldiisopropylammonium chloride was added to the reaction of **6** and **13**. With 1.5 equiv. of **13** the cyclocondensation products are isolated in 44–48% yield either as phenols **14** and **15**, or as acetates **16** and **17**. Favored with a preference of about 9:1 is the formation of the

Scheme 4



[3]) Piperidine in boiling CH_3OH has been used by *Walker* [15] for the condensation with glutarate **1**, and *Barton et al.* [6a] used Et_3N in THF for the reaction of **1** with a malondialdehyde derivative.

6-methyl-substituted salicylates **14** and **16**, respectively *(Scheme 4)* [4]). When the amine hydrochloride is omitted from the reaction, the yield of **16** and **17**, obtained in a 53:47 ratio, drops to 7% [5]). The fact that in DMF 40% of a 94:6 mixture of **16** and **17** is obtained, independent of the presence of hydrochloride, contrasts the results with acetylacetone **8** *(Table,* entry 3) [5]). The presence of small amounts (3%) of 4-acetyl-3-nitrosalicylate **18** in the reaction mixture implies, that the crude Na-salt **13** used for these reactions contained α,α-bis-formylated acetone **19** as an impurity *(Scheme 4)*.

Treatment of the acetates **16** and **17** with Na_2CO_3 in CH_3OH afforded the phenols **14** (from **16**) and **15** (from **17**) in high yield. The *O*-methyl derivatives **20** and **21** are best prepared by the action of CH_2N_2 according to [17]. The structure of **15**, and therefore also of **17** and **21**, was proven by comparison with a sample of **15** prepared from 4-methylsalicylic acid according to [18]. Decarboxylation of the crude acid obtained by saponification of methyl ester **14** gave the nitrophenol **22**, thus corroborating the structures of **14**, **16**, and **20** *(Scheme 4)* [6]). As mentioned above, α-formyl ketones without any further substituent at the α-C-atom are unstable substrates. It has been found, that β-alkoxyvinyl ketones, alkinones, and β-chlorovinyl ketones give also rise to cyclocondensation products, when reacted with activated ketones [3] [19]. The yields of 3-nitrosalicylates from the reactions of **6** with the α-formyl-ketone equivalents **23**, **24**, **25**, and **26** were however low. Condensation of nitrobutyrate **6** with 1-methoxy-1-buten-3-one (**23**) followed by acetylation gave 18% of a mixture of **16** and **17**, while 7% of **20** and **21** resulted from the reaction of **6** and 1-butin-3-one (**24**) followed by treatment with CH_2N_2. In the case of the β-chlorovinyl ketones **25** and **26** [20] the yield of cyclocondensation products, **27**/**28** from **25** and **29**/**30** from **26**, was about 8% in both cases [7]).

4. Condensation of 6 with 2-Formylcyclohexanone (31) *(Scheme 5)*. – Condensation of nitrobutyrate **6** with 2-formylcyclohexanone (**31**) [21] catalyzed by 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) followed by acetylation or direct chromatographic separation of the reaction mixture affords the tetrahydronaphthoates **32** and **33** or **34** and **35** in yields close to 50%. In analogy to the regioselectivity observed in the case of formylacetone *(Scheme 4)*, the 5,6,7,8-tetrahydro-1-naphthoate derivative **32** (or **34**) is formed in great excess (> 90%) [8]). The structure of **34** was determined by saponification of its ester function and decarboxylation of the crude acid **36** leading to the known 3-nitro-5,6,7,8-tetrahydro-2-naphthol (**37**) [22] *(Scheme 5)*.

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[4]) While the phenols **14** and **15** can easily be separated by column chromatography (CC), HPLC is needed for the separation of the acetates **16** and **17**. Pure **16** is however easily obtainable by crystallization.

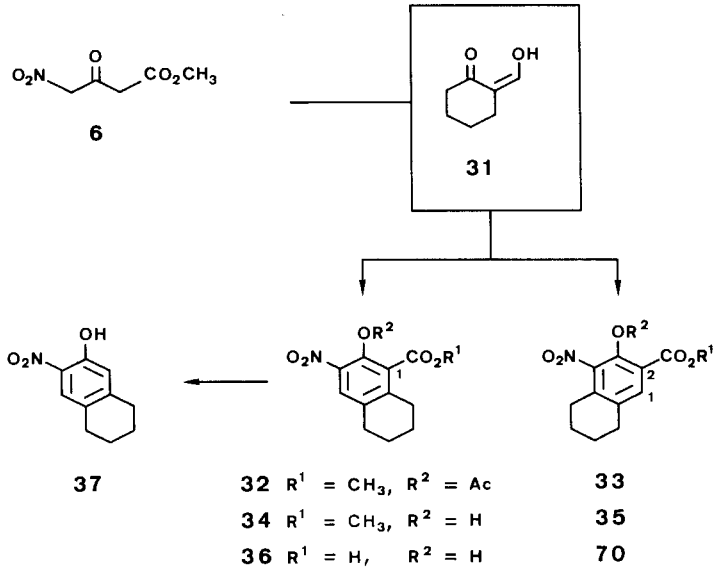
[5]) No description of these transformations will be given in the *Exper. Part*.

[6]) The signals corresponding to H–C(4) and H–C(5) in the ^{1}H-NMR spectra of **14**, **16**, and **20** are coupled with a constant J of 8.5 Hz proving the *ortho*-relationship of the two aromatic H-atoms. This eliminates any ambiguity about the position of the methoxycarbonyl group in **14**, **16**, and **20**.

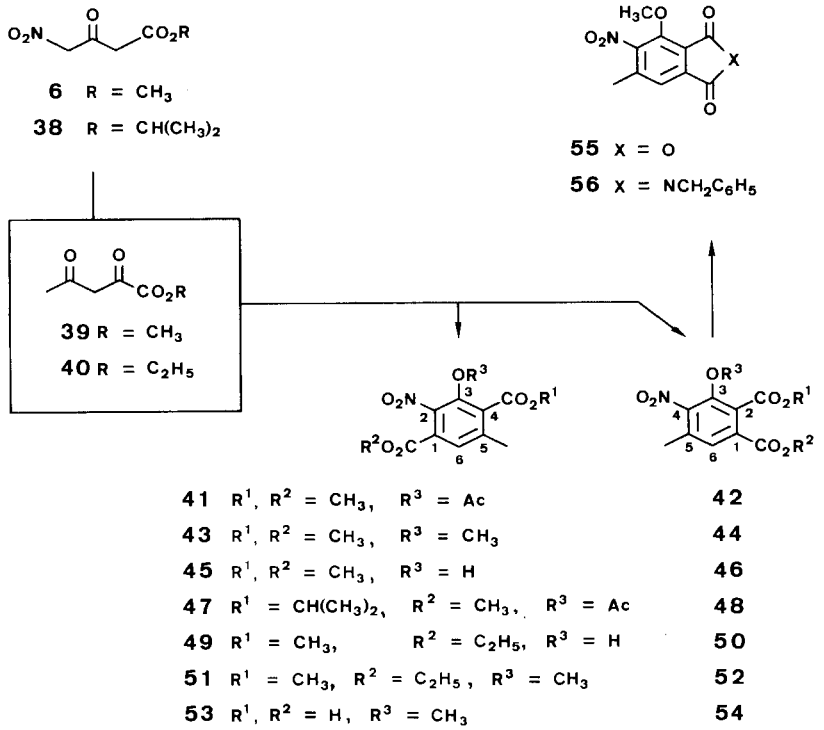
[7]) The ^{1}H-NMR spectra of the crude reaction mixtures before acetylation or etherification implied, that the formation of the 6-alkyl-substituted salicylates **16**, **20**, **27**, and **29** was also the preferred pathway of the reactions with **23**, **24**, **25**, and **26** (see *Exper. Part*). Contrary to the ^{1}H-NMR spectra of the isomeric acetates **16** and **17** or the ethers **20** and **21**, which exhibit only minor differences, the signals of the aromatic protons of the two phenols **14** and **15** appear at significantly different field, 8.04 ppm (H–C(4) of **14**) and 7.86 ppm (H–C(6) of **15**).

[8]) The phenols **34** and **35** are separable by CC. Pure acetate **32** is easily obtainable by crystallization of the mixture of **32** and **33**. HPLC separation of the mother liquor gives pure **33**.

Scheme 5



Scheme 6



5. Condensation of Nitrobutyrates 6 and 38 with Pentanoates 39 and 40 *(Scheme 6)*. – The cyclocondensations with 4-nitro-3-oxobutyrates **6** and **38** proceed under such mild conditions, that no transesterification was observed in the case of 2,4-dioxopentanoates **39** and **40** *(Scheme 6)*. Reaction of **6** with methyl ester **39** [9]) gives a 80% yield of dimethyl terephthalate and dimethyl phthalate derivatives, which have been isolated as acetates **41** and **42** or as methyl ethers **43** and **44**. The terephthalate regioisomers **41** and **43** are thereby formed in slight excess (57:43 ratio) [10]). Acid-catalyzed methanolysis of the acetates **41** and **42** gives the phenols **45** (from **41**) and **46** (from **42**). The etherification of the strongly acidic phenols **45** and **46** with CH_2N_2 is almost instantaneous giving **43** from **45** and **44** from **46** *(Scheme 6)*.

Condensation of the isopropyl ester **38** with methyl pentanoate **39** followed by acetylation allowed the isolation of 1-methyl 4-isopropyl therephthalate **47** and 1-methyl 2-isopropyl phthalate **48** in 48% yield and in a ratio of 53:47 in favor of **47** *(Scheme 6)* [11]). A 76% yield of 1-ethyl 4-methyl terephthalate **49** and 1-ethyl 2-methyl phthalate **50** with a 55:45 ratio in favor of **49** resulted from the condensation of **6** with ethyl pentanoate **40** [23]. The methyl ethers, **51** from **49**, and **52** from **50**, are obtainable by treatment with CH_2N_2. Saponification of the ester functions gives the diacid **53** from **43** [5]) or the phthalic acid **54** from either **44** [5]) or **52** *(Scheme 6)*.

The structural assignment of the regioisomeric condensation products was possible by treating the diacids **53** and **54** with Ac_2O at 160° [12]). While the IR spectrum of the crude material obtained from the terephthalic acid **53** showed a strong band at 1820 cm^{-1} [5]), the nicely crystalline phthalic anhydride **55** formed from diacid **54** exhibited the characteristic IR absorptions at 1850 and 1780 cm^{-1} [25] [13]). Treatment of **55** with benzylamine followed by esterification of the resulting mixture of phthalic monoamides with CH_2N_2 lead to spontaneous formation of phthalimide **56** *(Scheme 6)*.

6. Condensation of 6 with Trione 2 *(Scheme 7)*. – The reaction of nitrobutyrate **6** with 2,4,6-heptanetrione (**2**) [26] is complicated by the autocondensation of **2**. Trione **2** can function at the same time as β-diketone and bis-activated keto component in *Prelog* condensations [5] [26 b]. To suppress this autocondensation as well as possible, a 1.2-fold excess of **2** was added in portions to **6** and base [14]). Because of the sensitivity of the

[9]) Pentanoate **39** was prepared analogously to **40** [23].

[10]) The separation of the regioisomers, achievable by CC, is easier in the case of the acetates **41** and **42** than in the case of the ethers **43** and **44**.

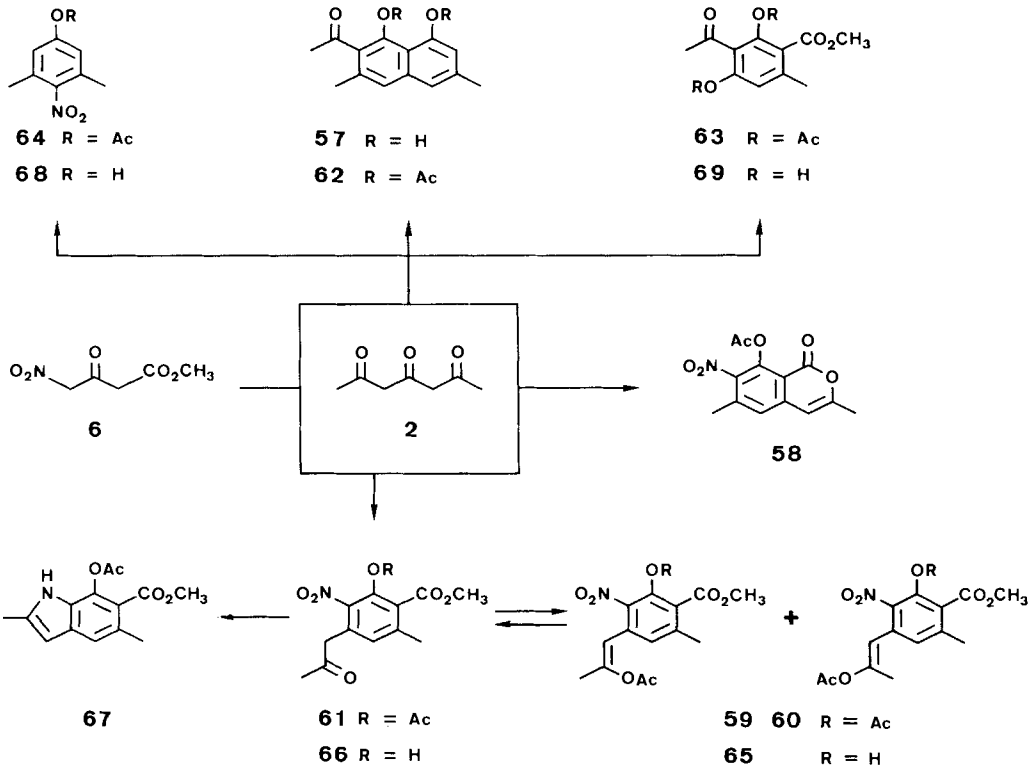
[11]) The lower yield of this condensation is in part due to the lower purity of the sample of **38** used for this experiment. The assignment of the regioisomeric structures of **47** and **48** was achieved by comparison of their spectra (IR, ^{1}H-NMR, and MS) with the data of the dimethyl esters **41** and **42**. For the structure determination of **41** and **42** see below.

[12]) The spectral data (IR, ^{1}H-NMR, and MS) did not allow an assignment of the substitution patterns. A characteristic *ortho*-benzylic coupling of 0.6–0.7 Hz [24] was exhibited in the ^{1}H-NMR spectra of **41** and **42** at 300 MHz, thus confirming the position of the C(5)-CH_3-groups relative to the aromatic proton. The mass spectra on the other hand were rather misleading, since the loss of the mass 17 (OH) from the M^+ of **43** and **51**, much less important in the case of isomers **44** and **52**, most probably involves the carbonyl-O-atom of the C(4)-carboxylate and not an O-atom of the NO_2-function. A similar mass-spectral fragmentation was observed in the case of the methyl ether **20** *(Scheme 4)*.

[13]) The anhydride **55** was characterized by ^{1}H-NMR and MS as well.

[14]) Normally a 1.5–2-fold excess of β-dicarbonyl-component is employed.

Scheme 7



1,8-naphthalenediol **57** still formed, the crude reaction mixture was acetylated before separation. By a series of column chromatographies, HPLC separations, and crystallizations it was possible to isolate the isocoumarin **58** (19%)[15], the enolacetates **59** (3.3%)[15] and **60** (0.5%)[15][16], the methyl ketone **61** (1%)[15], the naphthalene derivative **62** (32%, based on trione **2**), the orsellinic-acid derivative **63** (10.5%)[15], and the nitrophenyl acetate **64** (1.3%)[15][17].

Another experiment with a 1.5-fold excess of trione **2** added in one portion gave 21.5% (based on consumed **6**) of isocoumarin **58** and 30% of naphthalene **62**. The conversion of **6** was 85%; detected but not isolated were **59**, **60**, and **63** *(Scheme 7)* [5].

While the structural assignment of isocoumarin **58** followed from spectral evidence, the relation between **59**, **60** and **61** was established by partial methanolysis of **59**,

[15] These yields are based on consumed nitrobutyrate **6**, 31% of which were recovered from the reaction.

[16] The (*E*)/(*Z*)-assignment of the enolacetate double-bond of **59** and **60** is not possible with the aid of IR, ^{1}H-NMR, and MS data.

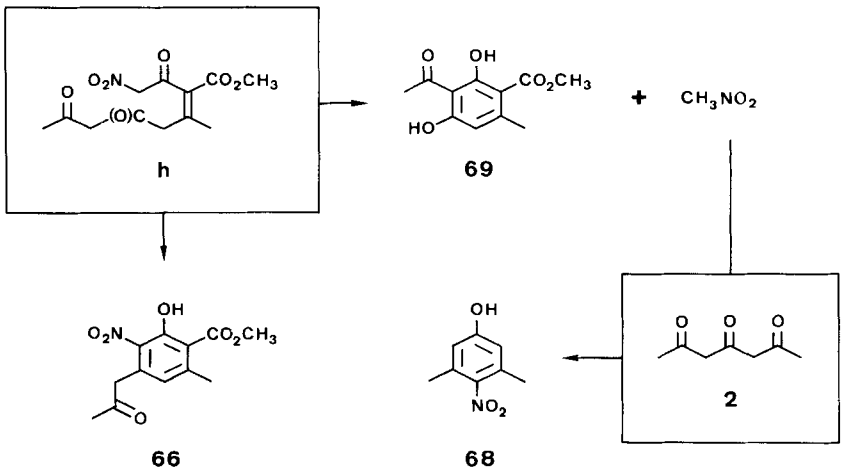
[17] A considerable amount of the main products **58**, **62**, and **63** could be isolated in an early stage of the separation by crystallization of enriched fractions (see *Exper. Part*). In addition to compounds **58**–**64** several other products were found in the reaction mixture, but could not be purified, characterized, or identified with an effort justifiable by their low yield of 1% and less.

affording the phenols **65** (9%)[18]) and **66** (47%)[18]), as well as acetate **61** (30%)[18]). The isomeric enolacetate **60** could be converted to the same ketone **66**. Reduction of the NO_2-group of **66** with aqueous $TiCl_3$ [27] and acetylation gave the indole **67**, thus confirming the structures of **59**, **60**, and **61** *(Scheme 7)*. The identities of the autocondensation product **62** and of **64** were proven by acetylation of authentic samples of the known phenolic compounds **57** [5] [26b] and **68** [14][5]). Methanolysis of the diacetate **63** gave 3-acetylorsellinate **69**, which could be identified by comparison of physical and spectral data with the published values [28][5]) *(Scheme 7)*.

While the isocoumarin **58** and the ketone **66**, the precursor of **59**, **60**, and **61**, are the expected products of the condensation of **6** with trione **2**, the formation of **63** and **64** deserves further comment.

Involvement of an intermediate **h**, formed by a first aldol condensation between **6** and **2**, gives a possible rationalization for the formation of **66** by a second aldol condensation, and of **69** by a *Claisen*-type condensation with CH_3NO_2 as leaving group *(Scheme 8)*[19]). The *p*-nitrophenol **68** on the other hand results from condensation of trione **2** and CH_3NO_2 *(Scheme 8)*, in close analogy to the reaction of γ-pyrones with CH_3NO_2 *(Scheme 2)* [12].

Scheme 8



7. Conclusions. – The literature covering the field of 3-nitrosalicylates and related substrates was searched by the aid of the *Chemical Abstracts Service* data files using the substructural unit **i** (R^1, R^3, R^4, and R^5 = H or any other atom, R^2 = H, or any other atom except N)[20]).

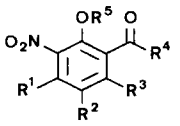
The number of answers, 699, obtained by this search may give a relation to the quantity of work done on such compounds. From the 11 differently C-substituted

[18]) Due to the small scale of this transformation, the inaccuracy of these yields, due to the weighing error of ± 0.5 mg, is greater than usual.

[19]) Cleavage of **6** to malonic-acid derivatives and CH_3NO_2 is a well-documented process [1].

[20]) This search was carried out on March 30 and April 15, 1983.

3-nitrosalicylic-acid derivatives described in this communication, quite surprisingly only two have so far appeared in the literature: the 4-methylsalicylate **15** [18], the minor regioisomer of the condensation with formylacetone **13** *(Scheme 4)*, and **70** [29], the parent acid of the minor isomer **35** isolated from the reaction with formylcyclohexanone *(Scheme 5)*. The aldehyde corresponding to salicylate **9**, **i** (R^1, $R^3 = CH_3$, R^2, R^4, and $R^5 = H$), has been described recently [30].



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The cyclocondensation of 4-nitro-3-oxobutyrate (**6**), successful with a variety of β-dicarbonyl compounds, gives thus an expedient access to new 3-nitrosalicylic-acid derivatives. The influence of the substituents R^3, R^4, and R^5 of the β-dicarbonyl compound **a** *(Scheme 1)* appears to be similar in the case of nitrobutyrate **6** as the effects observed for 3-oxoglutarate **1** [3] [4] [7] and heptanetrione **2** [5]: enhanced reactivity results with electron-withdrawing substituents, while the condensation is thwarted by too many and especially with bulky alkyl groups. Contrarily to the symmetrical ketones **1** and **2**, regioisomer formation is possible in condensations with butyrate **6**. High regioselectivity was observed with β-keto-aldehydes, in the sense that C(4) of butyrate **6**, the NO_2-substituted C-atom, adds preferably to the aldehyde-carbonyl *(Schemes 4* and *5)*. The degree of differentiation between the two modes of cyclocondensation is, however, much lower for unsymmetrically substituted β-diketones. In the case of 2,4-dioxopentanoates **39** and **40**, the isomer ratio is not influenced by the bulk of the ester groups of the two condensation partners *(Scheme 6)*. The result of the condensation with heptanetrione **2**, were an excess of isocoumarin **58** is isolated *(Scheme 7)*, cannot be rationalized by preferred formation of **58**, since the regioisomeric mode of addition giving the ketone **66** might be in concurrence with side reactions from common intermediates *(Scheme 8)*.

The problems encountered in condensations of nitrobutyrate **6** with unfavorably substituted dicarbonyl compounds (*e.g.* trione **2**) can possibly be circumvented by elaboration of a 3-nitrosalicylate obtained from a simpler substrate into the target molecule, making advantage of the activated benzylic protons in *ortho-* and *para*-position of the NO_2-substituent. Examples of such possibilities are outlined by reactions related to the indole syntheses of *Reissert* [31] and *Leimgruber* [32] [27b].

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Experimental Part

General Remarks. See [33] and [1] (HPLC separations).

1. Standard Procedure for the Cyclocondensation with 4-Nitrobutyrate 6. – To a solution of 4-nitro-3-oxobutyrate **6** [1] and 1.5–2.0 equiv. of a 1,3-diketone or an 1,3-keto-aldehyde in dry THF (*ca.* 1 ml/mmol of **6**) freshly activated molecular sieves (m.s.) 4 Å (0.5–1.0 g/ml of THF) and 1.0 equiv. of ethyldiisopropylamine or 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) are added. In case the dicarbonyl compound is added in the form of its Na- or K-salt, the amine base is replaced by an excess of ethyldiisopropylamine hydrochloride. This mixture is stirred for approx. 1 week at r.t. under Ar and exclusion of light, and quenched afterwards by the addition to an excess of 15% H_2SO_4 and ice. Extraction with AcOEt (3x) is followed by separation of the molecular sieves contained in the first extract by filtration. The org. layers are washed twice with half-sat. NaCl-sol., 3x with an excess of 50% K_2HPO_4 sol., once with 15% H_2SO_4 or 0.5M citric acid, and twice with sat. NaCl-solution, dried ($MgSO_4$) and evaporated. The residue of these extracts contains the 3-nitrosalicylates, which are isolated either as phenols or as acetates by chromatography on silica gel. The yields are calculated without taking into account the purity of the nitrobutyrates **6** and **38** [1][11]). The K_2HPO_4-washings are immediately acidified by the addition to an excess of icecold 15% H_2SO_4 containing some urea, saturated with NaCl, and extracted twice with CH_2Cl_2. The org. phases are washed with sat. NaCl-solution, dried ($MgSO_4$), the solvent evaporated. Bulb-to-bulb distillation of the residue, h.v./*ca.* 90°, gives recovered starting material, nitrobutyrate **6**.

2. Condensation of 6 with 2,4-Pentanedione (8). – 2.1. *Methyl 2-Acetoxy-4,6-dimethyl-3-nitrobenzoate* (**10**). Nitrobutyrate **6** (183 mg, 1.132 mmol) was reacted with 170 mg (1.7 mmol, 1.5 equiv.) of dione **8** and 147 mg (1.14 mmol) of ethyldiisopropylamine in 1 ml of THF containing *ca.* 1 g of m.s. 4 Å for 1 week. After workup according to the standard procedure, the residue of the AcOEt-extracts was dried at h.v. to remove unreacted dione **8**. The crude product, phenol **9**, was treated over night with 1 ml of each, pyridine and Ac_2O. The reagents were removed azeotropically with hexane, and the residue subjected to flash-chromatography using hexane/CH_2Cl_2/Et_2O 10:9:1 as eluent. Yield: 200 mg (66%) of **10**, m.p. 110.5–111.5° (subl., h.v./95°). IR ($CHCl_3$): 3030*w*, 2950*w*, 2840*w*, 1780*s*, 1725*s*, 1615*m*, 1562*w*, 1527*s*, 1505*w*, 1437*m*, 1362*s*, 1270*s*, 1176*s*, 1120*m*, 1060*m*, 1025*w*, 1004*w*, 963*w*, 885*w*, 863*m*. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.25 (*s*, $CH_3COO-C(2)$); 2.36 and 2.43 (2*s*, $CH_3-C(4)$, $CH_3-C(6)$); 3.87 (*s*, $COOCH_3$); 7.05 (*M*, $w_{1/2}$ *ca.* 3, H–C(5)). MS: 267 (2, M^+), 236 (2), 225 (43), 207 (10), *193* (100), 176 (9), 163 (4), 147 (5), 135 (20), 119 (7), 91 (15), 79 (6), 77 (9), 65 (18), 51 (7), 43 (99), 39 (10).

$C_{12}H_{13}NO_6$ (267.23) Calc. C 53.93 H 4.90 N 5.24% Found C 53.84 H 4.92 N 5.24%

2.2. *Methyl 4,6-Dimethyl-3-nitro-salicylate* (**9**). – 2.2.1. *By Cyclocondensation.* See [1].

2.2.2. *From Acetate* **10**. A solution of acetate **10** (52 mg, 0.231 mmol) in 2 ml of CH_3OH containing 3 drops of CH_3SO_3H was boiled under reflux for 15 h (Ar). Workup with AcOEt followed by bulb-to-bulb distillation (h.v./140°) gave 39 mg (89%) of **9**.

2.3. *Methyl 4,6-Dimethyl-2-methoxy-3-nitrobenzoate* (**11**). A solution of phenol **9** (161 mg, 0.715 mmol) and 0.2 ml of $(CH_3)_2SO_4$ in 9 ml of acetone containing 0.5 g of K_2CO_3 was boiled under reflux for 1 h under Ar. After workup with AcOEt the excess of reagent was removed at h.v. (50°, bulb-to-bulb dist.). Chromatography (25 g of silica gel) of the residue (175 mg) using hexane/CH_2Cl_2/Et_2O 13:6:1 as eluent gave, after bulb-to-bulb distillation (h.v./100°), 162 mg (94%) of **11**. IR ($CHCl_3$): 3035*w*, 2990*w*, 2950*m*, 2863*w*, 2840*w*, 1725*s*, 1610*m*, 1570*w*, 1527*s*, 1505*w*, 1457*m*, 1437*m*, 1367*s*, 1313*m*, 1276*s*, 1123*s*, 1083*m*, 1035*w*, 1021*w*, 991*w*, 956*w*, 920*w*, 876*w*, 866*m*, 817*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.29 and 2.32 (2*s*, $CH_3-C(4)$, $-C(6)$); 3.85 and 3.93 (2*s*, $CH_3O-C(2)$, $COOCH_3$); 6.89 (*m*, $w_{1/2}$ *ca.* 3, H–C(5)). MS: 239 (56, M^+), *222* (100), 208 (57), 207 (44), 191 (59), 177 (52), 163 (27), 160 (25), 147 (25), 133 (48), 119 (15), 104 (29), 91 (34), 79 (20), 77 (34), 65 (36), 63 (18), 51 (22), 45 (20), 39 (26), 30 (9).

$C_{11}H_{13}NO_5$ (239.22) Calc. C 55.23 H 5.48 N 5.86% Found C 55.25 H 5.58 N 5.78%

2.4. *Decarboxylation of Methyl 4,6-Dimethyl-3-nitrosalicylate* (**9**). A solution of **9** (19.5 mg, 0.086 mmol) in 3 ml of 10% aq. NaOH was stirred for 1 h at 80° under Ar. After workup with AcOEt, the crystalline residue (20 mg) was dissolved in 0.9 ml of freshly distilled quinoline by warming. This solution was stirred for 15 min in an oil bath of 200–210° (Ar). After cooling (ice) the mixture was quenched by the addition to 5 ml 15% H_2SO_4. Workup with CH_2Cl_2, washing with 15% H_2SO_4 and sat. NaCl-solution, purification of the residue of the dried org. phases by chromatography (2 g of silica gel, hexane/CH_2Cl_2/Et_2O 13:6:1 + 2 ppt of AcOH), and sublima-

tion (h.v./50°) gave 13 mg (90%) of *3,5-dimethyl-2-nitrophenol* (**12**), m.p.: 64–65.5°, no depression by admixing material prepared according to [14].

3. Condensation of 6 with Sodium 1,3-Dioxo-2-butanide (**13**). – 3.1. *Isolation of Phenols* **14** *and* **15**. To a solution of **6** (389 mg, 2.416 mmol) in 7.5 ml of dry THF 677 mg (4.09 mmol) of ethyldiisopropylamine hydrochloride and 390 mg of **13** were added. After stirring for 10 days the suspension was worked up according to the general procedure. The residue of the AcOEt-extracts (465 mg) was separated by chromatography (50 g of silica gel, hexane/CH_2Cl_2/Et_2O 13:6:1 + 2 ppt of AcOH) into salicylate **15**, 19 mg (13 mg, 2.5%, after crystallization from hexane/CH_2Cl_2), salicylate **14** (210 mg, 41%), and **18** (17 mg, 3%). From the K_2HPO_4-extracts 35 mg (9%) of impure nitrobutyrate **6** were recovered.

Methyl 6-Methyl-3-nitrosalicylate (**14**). M.p. 46.5–47.5° (Et_2O/toluene/hexane). IR ($CHCl_3$): 3350–2900*w*, 3020*w*, 2950*w*, 2840*w*, 1730*s*, 1670*w*, 1610*m*, 1597*s*, 1540*w*, 1532*m*, 1505*w*, 1467*m*, 1436*m*, 1380*w*, 1326*m*, 1312*w*, 1275*s*, 1160*w*, 1120*s*, 1058*m*, 975*w*, 955*w*, 890*m*, 819*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.41 (*m*, $w_{1/2}$ *ca.* 1.5, CH_3–C(6)); 3.98 (*s*, $COOCH_3$); 6.85 (*dq*, *J* = 8.7 and *ca.* 0.5 (not well resolved), H–C(5)); 8.04 (*d*, *J* = 8.7, H–C(4)); 11.05 (br. *s*, $w_{1/2}$ *ca.* 4, HO–C(2)). MS (di): 211 (18, M^+), 193 (18), 180 (35), *179* (100), 163 (21), 151 (6), 133 (15), 121 (52), 111 (20), 109 (16), 105 (30), 97 (24), 77 (29), 65 (17), 57 (19), 55 (12), 51 (38), 43 (17), 39 (24), 30 (10).

Methyl 4-Methyl-3-nitrosalicylate (**15**). M.p. 88–89° (not depressed by authentic material [18]). IR ($CHCl_3$): 3500–2800*m*, 3030*w*, 2958*m*, 2930*w*, 2900*w*, 2855*w*, 1680*s*, 1626*m*, 1573*m*, 1530*s*, 1492*w*, 1457*w*, 1440*s*, 1367*m*, 1326*s*, 1290*m*, 1265*s*, 1159*m*, 1138*m*, 1060*m*, 1035*w*, 990*w*, 957*m*, 890*m*, 821*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.36 (*s*, CH_3–C(4)); 3.97 (*s*, $COOCH_3$); 6.82 (*d*, *J* = *8*, H–C(5)); 7.86 (*d*, *J* = 8, H–C(6)), 10.9–11.8 (HO–C(2)). MS: 211 (50, M^+), 194 (30), 180 (22), *179* (100), 162 (34), 151 (5), 134 (14), 121 (43), 105 (33), 93 (10), 77 (38), 65 (19), 51 (28), 39 (15).

Methyl 5-Acetyl-3-nitrosalicylate (**18**). M.p. 129.5–131° (CH_2Cl_2/hexane). IR ($CHCl_3$): 3500–2700*m*, 3030*w*, 2955*w*, 1682*s*, 1595*m*, 1533*s*, 1465*m*, 1442*s*, 1422*m*, 1357*s*, 1343*s*, 1297*m*, 1274*s*, 1240*s*, 1175*m*, 1136*m*, 1090*m*, 1020*w*, 984*m*, 968*m*, 912*m*, 902*w*, 886*w*, 880*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.65 (*s*, CH_3CO–C(5)); 4.10 (*s*, $COOCH_3$); 8.76 (*s*, H–C(4), H–C(6)); 11.9–13.0 (HO–C(2)). MS (di): 239 (54, M^+), 224 (94), 208 (18), 207 (26), 192 *(100)*, 178 (3), 161 (6), 134 (3), 118 (29), 91 (12), 77 (5), 62 (14), 53 (7), 43 (32), 39 (3).

$C_{10}H_9NO_6$ (239.18) Calc. C 50.21 H 3.79 N 5.86% Found C 50.24 H 3.80 N 5.76%

3.2. *Isolation of Acetates* **16** *and* **17**. A mixture of **6** (314 mg, 1.95 mmol) ethyldiisopropylammonium chloride (547 mg, 3.316 mmol), Na-salt **13** (315 mg, 2.926 mmol) and 2 g of m.s. 4 Å in 6 ml of dry THF was stirred for 1 week. After the usual workup the residue of the AcOEt extracts (378 mg) was treated with Ac_2O/pyridine, 1 ml of each, over night. These reagents were removed by azeotropical distillation (hexane), the residue (450 mg) was chromatographed on 30 g of silica gel eluting with hexane/CH_2Cl_2/Et_2O 10:9:1 + 2 ppt of AcOH. Reacetylation of the first fraction, which contained some phenols **14** and **15** and rechromatography (35 g of silica gel, hexane/CH_2Cl_2/Et_2O 13:6:1 + 2 ppt of AcOH) gave 8 mg (1.6%) of acetate **17** and 230 mg (46.5%) of a mixture of **16** and **17**, from which 167 mg (34%) of pure **16** were isolated by crystallization (CH_2Cl_2/hexane). The mother liquor was separated by preparative HPLC (hexane/CH_2Cl_2/Et_2O 13:6:1 + 1 ppt of AcOH, 50 Bar, detection at 240 nm) into 16 mg of **17** ($vol._{ret}$ = 240 ml) and 43 mg of **16** ($vol._{ret}$ = 265 ml).

Methyl 2-Acetoxy-6-methyl-3-nitrobenzoate (**16**). Yield: 210 mg (42.5%), m.p. 88–89° (CH_2Cl_2/hexane). IR ($CHCl_3$): 3030*w*, 2950*m*, 2855*w*, 1781*s*, 1732*s*, 1602*s*, 1590*m*, 1525*s*, 1468*w*, 1435*m*, 1367*m*, 1348*s*, 1272*s*, 1175*s*, 1155*m*, 1120*s*, 1052*m*, 1006*m*, 977*w*, 962*w*, 897*w*, 860*w*, 830*m*, 822*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.33 (*s*, CH_3COO–C(2)); 2.43 (*s*, CH_3–C(6)); 3.93 (*s*, $COOCH_3$); 7.25 (*d*, *J* = 8.5, H–C(5)); 8.09 (*d*, *J* = 8.5, H–C(4)). MS (di): 253 (2, M^+), 222 (2), 211 (44), 193 (30), *179* (100), 163 (15), 133 (6), 121 (16), 105 (8), 77 (9), 69 (14), 57 (12), 43 (64).

$C_{11}H_{11}NO_6$ (253.21) Calc. C 52.17 H 4.38 N 5.53% Found C 52.29 H 4.52 N 5.64%

Methyl 2-Acetoxy-4-methyl-3-nitrobenzoate (**17**). Yield: 24 mg (*ca.* 5%), m.p. 106.5–107° (CH_2Cl_2/hexane). IR ($CHCl_3$): 3030*w*, 2955*w*, 2845*w*, 1785*s*, 1725*s*, 1620*m*, 1535*s*, 1487*w*, 1436*m*, 1368*s*, 1282*s*, 1252*m*, 1177*s*, 1156*w*, 1128*s*, 1056*m*, 1007*m*, 995*w*, 963*m*, 908*w*, 895*w*, 863*m*, 838*m*, 818*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.33 (*s*, CH_3COO–C(2)); 2.42 (*m*, $w_{1/2}$ *ca.* 2, CH_3–C(4)); 3.88 (*s*, $COOCH_3$); 7.25 (*dq*, *J* = 8.2 and *ca.* 0.5 (not well resolved), H–C(5)); 8.05 (*d*, *J* = 8.2, H–C(6)). MS (di): 253 (0.1, M^+), 222 (0.1), 211 (39), 194 (17), 179 (35), 162 (13), 133 (4), 121 (10), 105 (9), 77 (11), 65 (6), 51 (11), *43* (100), 39 (5).

$C_{11}H_{11}NO_6$ (253.21) Calc. C 52.17 H 4.38 N 5.53% Found C 52.11 H 4.42 N 5.50%

3.3. *Methanolysis of* **16**. To a solution of **16** (223.4 mg, 0.882 mmol) in 20 ml of CH_3OH, 400 mg of Na_2CO_3 were added. After stirring for 4 h at r.t. under Ar the mixture was poured to 15% H_2SO_4 and ice, and extracted with AcOEt (3x). The residue of the org. layers (193 mg) was purified by bulb-to-bulb distillation (h.v./90°) yielding 187 mg (quant.) of phenol **14**.

3.4. *Methanolysis of* **17**. Isomer **17** (30.6 mg, 0.121 mmol) was treated as above with Na_2CO_3 (75 mg) in CH_3OH (3 ml) for 5 h. Workup as above and bulb-to-bulb distillation (h.v./90°) gave 25 mg (98%) of phenol **15**.

3.5. *Methyl 2-Methoxy-6-methyl-3-nitrobenzoate* (**20**). An ethereal solution of CH_2N_2 (3 ml, *ca.* 0.5M) was added to 115.5 mg (0.548 mmol) of phenol **14** dissolved in 3 ml of Et_2O. After standing for 3 h at r.t., solvent and excess CH_2N_2 were evaporated, and the residue subjected to CC (6 g of silica gel, hexane/CH_2Cl_2/Et_2O 13:6:1 + 2 ppt of AcOH) yielding 116 mg (94%) of **20**. M.p. 66–66.5° (Et_2O/hexane). IR ($CHCl_3$): 3020*w*, 2955*m*, 2850*w*, 1730*s*, 1593*s*, 1520*s*, 1467*m*, 1455*w*, 1432*w*, 1405*w*, 1382*w*, 1350*s*, 1278*s*, 1188*w*, 1159*w*, 1122*s*, 1065*m*, 996*m*, 975*m*, 925*w*, 882*w*, 830*w*, 821*m*. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.37 (*s*, CH_3–C(6)); 3.92 and 3.95 (2*s*, CH_3O–C(2), $COOCH_3$); 7.08 (*d*, *J* = 8.5, H–C(5)); 7.86 (*d*, *J* = 8.5, H–C(4)). MS: 225 (32 M^+), *208* (100), 194 (41), 193 (19), 177 (43), 163 (71), 146 (26), 133 (26), 119 (43), 105 (20), 91 (32), 77 (24), 65 (18), 51 (27), 45 (17), 39 (14), 30 (5).

3.6. *Methyl 2-Methoxy-4-methyl-3-nitrobenzoate* (**21**). A solution of phenol **15** (7.5 mg, 0.036 mmol) in 5 ml of AcOEt was treated with 1.5 ml of 0.5M ethereal CH_2N_2 for 1 h. Evaporation of solvent and excess reagent followed by bulb-to-bulb distillation (h.v./100°) of the crystalline residue gave 7.5 mg (94%) of **21**, m.p. 68.5–69.5° (Et_2O/hexane). IR ($CHCl_3$): 3030*w*, 2950*w*, 2840*w*, 1726*s*, 1611*m*, 1565*w*, 1532*s*, 1505*w*, 1486*w*, 1455*m*, 1434*m*, 1398*w*, 1370*m*, 1295*s*, 1282*s*, 1247*m*, 1154*w*, 1125*m*, 1070*m*, 995*m*, 972*w*, 922*w*, 892*w*, 837*w*. ^{1}H-NMR (300 MHz, $CDCl_3$); 2.35 (*d*, *J ca.* 0.5, CH_3–C(4)); 3.94 (*s*, 6 H, CH_3O–C(2), $COOCH_3$); 7.08 (*dq*, *J* = 8.2 and 0.5 (not well resolved), H–C(5)); 7.89 (*d*, *J* = 8.2, broadened, $w_{1/2}$ *ca.* 1, H–C(6)); *double resonance experiment:* RF[2] at 703 Hz (CH_3–C(4)), observed 7.08 (*d*, *J* = 8.2); 7.89 (*d*, *J* = 8.2, $w_{1/2}$ *ca.* 0.5). MS: 225 (8, M^+), 208 (2), 195 (16), 194 (21), 177 (5), 176 (5), *163* (100), 133 (24), 119 (22), 105 (14), 91 (22), 79 (15), 77 (16), 65 (13), 51 (18), 45 (17), 39 (9).

3.7. *Decarboxylation of* **14**. A solution of **14** (45 mg, 0.213 mmol) in 10% NaOH (5 ml) and dioxane (1 ml) was heated in an oil bath of 80° for 2 h under Ar. After acidification with 15% H_2SO_4 and workup with AcOEt, the crude acid (49 mg) was dissolved in freshly distilled quinoline (2 ml), and the mixture was heated for 15 min in an oil bath of 200–210° under Ar. Cooling with ice, acidification (15% H_2SO_4), and workup with CH_2Cl_2 gave 30 mg (92%) of *5-methyl-2-nitrophenol* (**22**), purified by chromatography (4 g of silica gel, hexane/CH_2Cl_2/Et_2O 16:3:1 + 2 ppt of AcOH) and sublimation (h.v./40°). M.p. 54.5–55°, not depressed upon the addition of authentic commercially available material.

4. Condensation of 6 with 1-Methoxy-1-buten-3-one (23). – A solution of **6** (136 mg, 0.845 mmol), **23** (128 mg, 1.28 mmol) and ethyldiisopropylamine (109 mg, 0.845 mmol) in 1.3 ml of THF containing 1 g of m.s. 4 Å was stirred at r.t. for 7.5 days. Workup according to the general procedure gave 100 mg crude **14** and **15** from the AcOEt-extracts. ^{1}H-NMR (80 MHz, $CDCl_3$): 8.05 (*d*, *J* = 8.5, corresponds to H–C(4) of **14**); 7.83 (*d*, *J* = 8.5, much weaker signal, corresponds to H–C(6) of **15**). This material was acetylated (Ac_2O/pyridine), distilled (bulb-to-bulb, h.v./130°), and chromatographed (3.5 g of silica gel, hexane/CH_2Cl_2/Et_2O 10:9:1 + 2 ppt of AcOH) affording 39 mg (18%) of acetate **16** containing some isomer **17**.

5. Condensation of 6 with 1-Butin-3-one (24). – To a solution of **6** (149 mg, 0.922 mmol) and butinone **24** (95 mg, 1.4 mmol) in 1.5 ml of THF 1 g of m.s. 4 Å and after cooling in an ice bath 118 mg (0.92 mmol) of ethyldiisopropylamine were added. After stirring for 4 days at r.t. the mixture was worked up according to the general procedure. ^{1}H-NMR (80 MHz, $CDCl_3$) of the residue of the AcOEt-extracts showed the presence of phenol **14** (8.05, *d*, *J* = 8.5, H–C(4)) and only minor amounts of isomer **15** (7.85, *d*, *J* = 8.5, H–C(6)). Treatment with ethereal CH_2N_2, distillation (bulb-to-bulb, h.v./150°), and chromatography (3.5 g of silica gel, hexane/CH_2Cl_2/Et_2O 13:6:1 + 2 ppt of AcOH) afforded 15 mg (7%) of **20** containing some **21**.

6. Condensation of 6 with β-Chloro-vinyl Ketones 25 and 26. – 6.1. *With 1-Chloro-1-octen-3-one* (**25**). To a solution of **6** (80 mg, 0.497 mmol) and **25** (78 mg, 0.486 mmol), in 0.8 ml of THF, containing 0.6 g of m.s. 4 Å, 64 mg (0.498 mmol) of ethyldiisopropylamine were added. The mixture was stirred for 4 days at r.t. and worked up according to the general procedure. ^{1}H-NMR (80 MHz, $CDCl_3$) of the crude product showed a signal at 8.09 ppm (*d*, *J* = 8.5) corresponding to H–C(4) of the 6-pentyl-isomer. The signal corresponding to H–C(6) of the

4-pentyl-isomer, 7.88 ppm (*d*, $J = 8.5$), was much weaker. Acetylation and chromatography (4 g of silica gel, hexane/CH_2Cl_2/Et_2O 13:6:1 + 2 ppt of AcOH) gave 12 mg (*ca.* 8%) of *methyl 2-acetoxy-3-nitro-6-pentylbenzoate* (**27**) containing some *methyl 2-acetoxy-3-nitro-4-pentylbenzoate* (**28**). IR ($CHCl_3$): 3030*w*, 2958*m*, 2930*m*, 2860*m*, 1785*s*, 1736*s*, 1603*m*, 1589*m*, 1526*s*, 1505*w*, 1468*w*, 1458*w*, 1439*m*, 1370*m*, 1350*s*, 1281*m*, 1265*m*, 1179*s*, 1121*m*, 1016*m*, 975*w*, 898*w*, 860*w*, 835*w*, 821*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 0.7–1.1 (*m*, 3H–C(5')); 1.0–2.0 (*m*, 2H–C(2'), 2H–C(3'), 2H–C(4')); 2.33 (*s*, CH_3COO–C(2)); 2.5–2.9 (*m*, 2H–C(1')); 3,93 (*s*, $COOCH_3$); 7.28 (*d*, $J = 8.5$, H–C(5)); 8.13 (*d*, $J = 8.5$, H–C(4)). MS: 278 (0.5, M^+), 267 (6), 249 (62), 236 (9), 235 (7), 217 (28), 192 (7), 179 (13), 133 (5), 105 (6), 91 (4), 77 (7), 55 (5), *43* (100), 41 (10).

6.2. *With 1-Chloro-5-methyl-1-hexene-3-one* (**26**). To a solution of **6** (73 mg, 0.453 mmol) and **26** (66 mg, 0,45 mmol) in 1.3 ml of THF containing 0.8 g of m.s. 4 Å 50 mg (0.45 mmol) of ethyldiisopropylamine were added at 0°. The mixture was stirred for 4.5 days at r.t. and worked up according to the general procedure. Chloride **26** contained in the residue of the AcOEt-extracts was removed by bulb-to-bulb distillation (0.1 mm/80°). ^{1}H-NMR (80 MHz, $CDCl_3$) of the residue (82 mg) exhibited a *d* ($J = 8.5$) at 8.10 ppm, corresponding to H–C(4) of 6-alkyl-salicylate, and a much weaker *d* ($J = 8.5$) at 7.88 ppm, corresponding to H–C(6) of the 4-alkyl-isomer. The crude material was treated with ethereal CH_2N_2 and chromatographed (7 g of silica gel, hexane/CH_2Cl_2/Et_2O 13:6:1 + 2 ppt of AcOH). Re-chromatography (3.5 g of silica gel, hexane/CH_2Cl_2/Et_2O 14:5:1 + 2 ppt of AcOH) of the product containing fraction (16 mg) afforded 10 mg (8%) of *methyl 2-methoxy-3-nitro-6-(2'-methylpropyl)benzoate* (**29**) containing some *methyl 2-methoxy-3-nitro-4-(2'-methylpropyl)benzoate* (**30**). IR ($CHCl_3$): 2960*m*, 2870*w*, 1732*s*, 1595*s*, 1523*s*, 1468*m*, 1460*m*, 1435*w*, 1409*w*, 1370*m*, 1350*s*, 1280*s*, 1125*s*, 1105*m*, 1039*m*, 980*w*, 955*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 0.91 (*d*, $J = 7$, 3H–C(3'), CH_3–C(2')); 1.91 (*nonet*, $J = 7$, H–C(2')); 2.51 (*d*, $J = 7$, 2H–C(1')); 3.91 and 3.93 (2*s*, CH_3O–C(2), $COOCH_3$); 7.06 (*d*, $J = 8$, H–C(5)); 7.88 (*d*, $J = 8$, H–C(4)). MS: 267 (4, M^+), 250 (94), 236 (18), *218* (100), 208 (46), 205 (14), 193 (16), 187 (15), 177 (58), 173 (18), 163 (27), 160 (18), 146 (36), 133 (16), 118 (48), 115 (27), 105 (25), 91 (42), 77 (40), 65 (20), 63 (20), 57 (20), 51 (20), 43 (81), 39 (27).

7. Condensation of 6 with 2-(Hydroxymethylene)cyclohexanone (31). – 7.1. *Isolation of Acetates* **32** *and* **33**. A solution of **6** (187 mg, 1.162 mmol) **31** (230 mg, 1.825 mmol) and 177 mg (1.164 mmol) of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in 1 ml of THF containing 1 g of m.s. 4 Å was stirred at r.t. for 6.5 days and worked up according to the general procedure. After removal of **31** by bulb-to-bulb distillation (h.v./50°), the residue (214 mg) was acetylated with 0.7 ml of each, Ac_2O and pyridine. The reagents were removed azeotropically with hexane, the crude product mixture purified by CC (25 g of silica gel, hexane/CH_2Cl_2/Et_2O 13:6:1 + 1 ppt of AcOH) yielding 160 mg of a mixture of **32** and **33** containing some of the phenols **34** and **35**. By crystallization from CH_2Cl_2/hexane 114 mg (33%) of pure **32** were collected. The mother liquor was reacetylated and separated by prep. HPLC (hexane/CH_2Cl_2/Et_2O 30:9:1 ppt of AcOH, 60 Bar, det. at 240 nm) into 29 mg of **32** ($vol._{ret} = 470$ ml) and 6 mg of **33** ($vol._{ret} = 440$ ml).

Methyl 2-Acetoxy-3-nitro-5,6,7,8-tetrahydro-1-naphthoate (**32**). Yield: 143 mg (42%), m.p. 107–108° (changes beginning at 92°, CH_2Cl_2/hexane). IR ($CHCl_3$): 3020*w*, 2945*m*, 2860*w*, 2835*w*, 1780*s*, 1732*s*, 1595*w*, 1585*m*, 1525*s*, 1456*m*, 1447*w*, 1435*m*, 1366*m*, 1344*s*, 1326*m*, 1277*m*, 1256*m*, 1178*s*, 1156*m*, 1070*m*, 1064*m*, 1008*m*, 990*w*, 958*w*, 917*w*, 904*w*, 883*w*, 877*w*, 835*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 1.6–2.0 (*m*, 2H–C(6), 2H–C(7)); 2.31 (*s*, CH_3COO–C(2)); 2.5–3.0 (*m*, 2H–C(5), 2H–C(8)); 3.91 (*s*, $COOCH_3$); 7.91 (*m*, $w_{1/2}$ *ca.* 3, H–C(4)). MS (di.): 262 (1, $M^+ - 31$), 251 (14), 233 (97), 219 (74), 201 (33), 191 (7), 173 (44), 161 (19), 144 (13), 115 (38), 105 (10), 91 (18), 89 (14), 77 (13), 65 (8), 63 (11), 55 (6), 51 (7), *43* (100), 39 (10).

$C_{14}H_{15}NO_6$ (293.27) Calc. C 57.33 H 5.16 N 4.78% Found C 57.18 H 5.17 N 4.87%

Methyl 3-Acetoxy-4-nitro-5,6,7,8-tetrahydro-2-naphthoate (**33**). Yield: 6 mg (1.7%), m.p. 124–125° (changes beginning at *ca.* 114°, CH_2Cl_2/hexane). IR ($CHCl_3$): 3020*w*, 2950*m*, 2885*w*, 2865*w*, 2840*w*, 1780*s*, 1723*s*, 1616*m*, 1562*m*, 1532*s*, 1505*w*, 1480*w*, 1457*w*, 1450*w*, 1435*m*, 1416*w*, 1368*m*, 1340*w*, 1320*m*, 1285*s*, 1180*s*, 1172*s*, 1163*s*, 1140*w*, 1075*m*, 1008*m*, 993*m*, 970*w*, 955*m*, 928*w*, 913*w*, 895*w*, 870*m*, 836*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.75–1.90 (*m*, 2H–C(6), 2H–C(7)); 2.31 (*s*, CH_3COO–C(3)); 2.7–2.8 and 2.8–2.9 (2*m*, 2H–C(5), 2H–C(8)); 3.87 (*s*, $COOCH_3$); 7.88 (*m*, $w_{1/2}$ *ca.* 2, H–C(1)). MS (di.): 293 (1, M^+), 262 (3), 251 (86), 234 (29), 219 (100), 206 (14), 201 (20), 191 (12), 173 (21), 163 (12), 145 (18), 115 (32), 105 (12), 91 (25), 89 (13), 77 (16), 63 (11), 55 (13), 43 (92), 41 (12), 39 (10).

7.2. *Isolation of Phenols* **34** *and* **35**. To a solution of **6** (331 mg, 2.06 mmol) and keto-aldehyde **31** (435 mg, 3.45 mmol) in 2 ml of THF, containing 1.6 g of m.s. 4 Å, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (306 mg, 2.02 mmol) was added. After stirring at r.t. for 8.5 days and workup according to the general procedure, the residue

of the AcOEt-extracts (505 mg) was subjected to bulb-to-bulb distillation (h.v./50°) to remove excess **31**. CC (50 g of silica gel, hexane/CH_2Cl_2/Et_2O 14:5:1 + 2 ppt of AcOH) gave 15 mg of impure **35** and 253 mg of almost pure **34**. Crystallization of these fractions from CH_2Cl_2/hexane yielded 214 mg (41%) of pure **34** and 10 mg (2%) of pure **35**. HPLC (hexane/CH_2Cl_2/Et_2O 14:5:1 + 2 ppt of AcOH) of the mother liquors gave another 30 mg (6%) of **34** (vol.$_{ret}$ = 160 ml) and 3 mg (0.5%) of **35** (vol.$_{ret}$ = 125 ml). Minor impurities (vol.$_{ret}$ = 115, 135, and 145 ml) were discarded.

Methyl 2-Hydroxy-3-nitro-5,6,7,8-tetrahydro-1-naphthoate (**34**). M.p. 92–93° (CH_2Cl_2/hexane). IR ($CHCl_3$): 3230*m*, 3030*w*, 2950*m*, 2863*w*, 2820*w*, 1728*s*, 1617*m*, 1589*m*, 1527*m*, 1505*w*, 1450*s*, 1435*m*, 1370*w*, 1325*s*, 1313*s*, 1295*m*, 1270*s*, 1250*s*, 1163*s*, 1075*m*, 1069*m*, 996*m*, 960*w*, 950*w*, 918*w*, 898*m*, 883*w*, 875*w*, 847*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 1.6–2.0 (*m*, 2H–C(6), 2H–C(7)); 2.5–3.0 (*m*, 2H–C(5), 2H–C(8)); 3.98 (*s*, $COOCH_3$); 7.88 (*m*, $w_{1/2}$ *ca.* 3, H–C(4)); 10.58 (br. *s*, $w_{1/2}$ *ca.* 5, HO–C(2)). MS (di.): 251 (14, M^+), 233 (65), 220 (38), *219* (100), 201 (29), 191 (11), 173 (47), 161 (23), 144 (20), 129 (4), 115 (45), 103 (8), 91 (22), 89 (19), 77 (15), 65 (11), 63 (17), 51 (12), 39 (16), 30 (8).

$C_{12}H_{13}NO_5$ (251.23) Calc. C 57.37 H 5.22 N 5.58% Found C 57.44 H 5.25 N 5.49%

Methyl 3-Hydroxy-4-nitro-5,6,7,8-tetrahydro-2-naphthoate (**35**). M.p. 107–109° (CH_2Cl_2/hexane). IR ($CHCl_3$): 3150*m*, 3030*w*, 3010*w*, 2945*m*, 2885*w*, 2863*w*, 2840*w*, 1680*s*, 1622*m*, 1575*m*, 1528*s*, 1505*w*, 1475*m*, 1439*s*, 1378*m*, 1361*m*, 1343*m*, 1317*s*, 1288*m*, 1272*s*, 1175*w*, 1117*m*, 1085*m*, 991*w*, 970*w*, 951*m*, 925*w*, 900*w*, 890*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 1.6–2.0 (*m*, 2H–C(6), 2H–C(7)); 2.5–3.0 (*m*, 2H–C(5), 2H–C(8)); 3.99 (*s*, $COOCH_3$); 7.68 (*m*, $w_{1/2}$ *ca.* 3, H–C(1)); 10.91 (*s*, HO–C(3)). MS (di.): 251 (61, M^+), 234 (21), 220 (22), 219 (94), 206 (19), 202 (20), 201 (18), 191 (13), 173 (29), 161 (24), 145 (39), 133 (21), 117 (53), *115* (100), 105 (34), 91 (68), 89 (41), 77 (40), 65 (21), 63 (29), 55 (28), 51 (23), 43 (19), 41 (24), 39 (28), 30 (9).

$C_{12}H_{13}NO_5$ (251.23) Calc. C 57.37 H 5.22 N 5.58% Found C 57.38 H 5.15 N 5.69%

7.3. *Decarboxylation of* **34**. A solution of **34** (46 mg, 0.183 mmol) in dioxane (1 ml) and 10% NaOH-solution (5 ml) was stirred for 2 h in an oil bath of 80° under Ar. After quenching with ice and 15% H_2SO_4, the product was isolated by extraction with AcOEt (3x). The crude acid **36**, which contained some starting material **34**, was dissolved in 2 ml of freshly distilled quinoline, and the solution was heated for 15 min in an oil bath of 205° under Ar. After cooling with ice, the mixture was poured to 15% H_2SO_4 and worked up by extraction with CH_2Cl_2 (3x). The residue of the org. phases (40 mg) was purified by chromatography (3 g of silica gel, hexane/CH_2Cl_2/Et_2O 16:3:1 + 2 ppt of AcOH) and bulb-to-bulb distillation (h.v./90°) yielding 21 mg (59%) of *3-nitro-5,6,7,8-tetrahydro-2-naphthol* (**37**). M.p. 88–89° (Et_2O/hexane, [22 b]: 88.5°). IR ($CHCl_3$): 3260*m*, 3020*w*, 2935*m*, 2880*w*, 2860*w*, 2840*w*, 1628*s*, 1578*s*, 1520*s*, 1505*w*, 1478*m*, 1428*s*, 1372*m*, 1313*s*, 1295*s*, 1265*s*, 1257*s*, 1163*m*, 1146*m*, 1070*m*, 1061*w*, 957*w*, 945*w*, 920*m*, 878*m*, 865*m*, 840*m*, 815*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 1.6–2.0 (*m*, 2H–C(6), 2H–C(7)); 2.5–3.0 (*m*, 2H–C(5), 2H–C(8)); 6.83 (*m*, $w_{1/2}$ *ca.* 2, H–C(1)); 7.78 (*m*, $w_{1/2}$ *ca.* 3, H–C(4)); 10.33 (br. *s*, $w_{1/2}$ *ca.* 3, HO–C(2)). MS (di.): *193* (100, M^+), 177 (2), 176 (2), 175 (1), 165 (55), 147 (29), 130 (7), 117 (26), 115 (15), 103 (7), 91 (23), 77 (12), 65 (9), 63 (7), 51 (9), 39 (10).

8. Condensations with 2,4-Dioxo-pentanoates 39 and 40. – 8.1. *Condensation of* **6** *with Methyl Ester* **39**. – 8.1.1. *Isolation of Acetates* **41** *and* **42**. A solution of **6** (111 mg, 0.67 mmol), diketone **39** (153 mg, 1.062 mmol) and DBU (105 mg, 0.69 mmol) in THF (2 ml), containing 0.8 g of m.s. 4 Å, was stirred for 3 days at r.t. under Ar. The residue of the AcOEt-extracts (169 mg), obtained by workup according to the general procedure, was treated over night with Ac_2O/pyridine (1 ml of each). The reagents were removed azeotropically with hexane, and the residue (201 mg) was separated by chromatography (30 g of silica gel, hexane/CH_2Cl_2/Et_2O 19:19:2 + 2 ppt of AcOH) into 95 mg (44%) of terephthalate **41** (R_f 0.17) and 71 mg (33%) of phthalate **42** (R_f 0.14).

Dimethyl 3-Acetoxy-5-methyl-2-nitroterephthalate (**41**). M.p. 108–110° (CH_2Cl_2/hexane). IR ($CHCl_3$): 3030*w*, 2955*m*, 2925*w*, 2850*w*, 1785*s*, 1732*s*, 1610*w*, 1545*s*, 1505*w*, 1435*m*, 1400*w*, 1368*s*, 1318*m*, 1290*m*, 1272*s*, 1173*s*, 1121*m*, 1052*m*, 1010*w*, 970*w*, 915*w*, 857*m*, 820*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.28 (*s*, CH_3COO–C(3)); 2.50 (*d*, J = 0.6, CH_3–C(5)); 3.91 and 3.93 (2*s*, $2COOCH_3$); 7.73 (*m*, $w_{1/2}$ *ca.* 2, H–C(6)); *double resonance experiment:* RF^2 at 750.4 Hz (CH_3–C(5)); observed: 7.73 (*s*, $w_{1/2}$ *ca.* 0.5, H–C(6)). MS (di.): 311 (1, M^+), 280 (1), 269 (30), 251 (15), 238 (20), 237 (44), 221 (5), 206 (3), 179 (15), 162 (5), 151 (4), 133 (3), 120 (2), 105 (3), 91 (5), 84 (7), 77 (6), 67 (7), 55 (8), *43* (100), 39 (8).

$C_{13}H_{13}NO_8$ (311.24) Calc. C 50.16 H 4.21 N 4.50% Found C 50.18 H 4.22 N 4.51%

Dimethyl 3-Acetoxy-5-methyl-4-nitrophthalate (**42**). M.p. 136–138° (CH_2Cl_2/hexane). IR ($CHCl_3$): 3030*w*, 2950*m*, 2840*w*, 1790*s*, 1735*s*, 1617*m*, 1560*w*, 1539*s*, 1505*w*, 1465*w*, 1460*w*, 1432*m*, 1367*m*, 1319*s*, 1275*s*, 1174*s*,

1126*m*, 1056*m*, 1020*m*, 969*m*, 920*w*, 870*m*, 855*m*, 818*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.27 (*s*, $CH_3COO-C(3)$); 2.45 (*d*, $J = 0.7$, $CH_3-C(5)$); 3.90 and 3.92 (2*s*, $2\,COOCH_3$); 7.77 (*q*, not well resolved, $w_{1/2}$ *ca.* 2, H–C(6)); *double resonance experiment:* RF^2 at 734 Hz ($CH_3-C(5)$); observed: 7.77 (*s*, $w_{1/2}$ *ca.* 0.3, H–C(6)). MS (di.): 311 (1, M^+), 280 (1), 269 (27), 238 (30), 237 (61), 221 (3), 207 (6), 192 (4), 179 (39), 161 (4), 151 (4), 133 (3), 105 (4), 92 (4), 77 (8), 59 (7), 51 (6), *43* (100), 39 (4). –

$C_{13}H_{13}NO_8$ (311.24) Calc. C 50.16 H 4.21 N 4.50% Found C 50.21 H 4.21 N 4.53%

8.1.2. *Isolation of Methyl Ethers* **43** *and* **44**. To a solution of **6** (86 mg, 0.535 mmol) and diketone **39** (158 mg, 1.098 mmol) in THF (1.5 ml), containing 0.7 g of m.s. 4 Å, DBU (81 mg, 0.533 mmol) was added at 0°. After stirring at r.t. for 3 days, workup according to the general procedure gave 138 mg product mixture, which was dissolved in AcOEt and treated with 0.5M ethereal CH_2N_2-solution (*ca.* 5 ml) for 30 min. Evaporation of solvent and CH_2N_2 followed by chromatographic separation (28 g of silica gel, hexane/CH_2Cl_2/Et_2O 13:6:1) of the residue (148 mg) gave 74 mg (49%) of **43** (R_f 0.125) and 53 mg (35%) of **44** (R_f 0.094).

Dimethyl 3-Methoxy-5-methyl-2-nitroterephthalate (**43**). M.p. 41.5–42° (Et_2O/hexane). IR ($CHCl_3$): 3030*w*, 2950*m*, 2840*w*, 1732*s*, 1600*w*, 1575*w*, 1570*w*, 1560*w*, 1545*s*, 1505*w*, 1451*m*, 1435*m*, 1395*w*, 1370*m*, 1320*s*, 1280*s*, 1125*s*, 1070*m*, 1010*w*, 967*m*, 935*w*, 893*w*, 870*m*, 818*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.39 (*s*, $CH_3-C(5)$); 3.90 (6 H) and 3.98 (3 H) (2*s*, $CH_3O-C(3)$, $2\,COOCH_3$); 7.63 (*m*, $w_{1/2}$ *ca.* 2, H–C(6)). MS: 283 (45, M^+), *266* (100), 252 (74), 251 (39), 235 (56), 222 (15), 221 (98), 207 (27), 204 (26), 191 (16), 190 (20), 178 (77), 177 (99), 176 (39), 175 (24), 162 (24), 161 (24), 148 (58), 147 (56), 133 (25), 132 (16), 119 (25), 117 (25), 105 (18), 104 (18), 91 (43), 89 (56), 77 (40), 67 (33), 65 (26), 63 (32), 59 (32), 51 (23), 45 (68), 43 (23), 41 (13), 39 (28), 30 (11).

Dimethyl 3-Methoxy-5-methyl-4-nitrophthalate (**44**). M.p. 65–66° (Et_2O/hexane). IR ($CHCl_3$): 3030*w*, 2950*m*, 2900*w*, 2870*w*, 2845*w*, 1730*s*, 1610*m*, 1533*s*, 1455*m*, 1433*m*, 1395*w*, 1368*m*, 1320*s*, 1275*s*, 1170*m*, 1126*s*, 1070*s*, 1020*m*, 973*m*, 942*w*, 907*w*, 893*w*, 867*m*, 818*w*. ^{1}H-NMR (90 MHz, $CDCl_3$): 2.35 (*s*, $CH_3-C(5)$); 3.93, 3.94, and 3.97 (3*s*, $CH_3O-C(3)$, $2\,COOCH_3$); 7.70 (*m*, $w_{1/2}$ *ca.* 2, H–C(6)). MS: 283 (16, M^+), 266 (3), 252 (67), 235 (11), 234 (8), *221* (100), 205 (5), 191 (8), 177 (14), 175 (33), 161 (13), 148 (28), 133 (9), 119 (23), 118 (26), 117 (12), 91 (15), 90 (20), 89 (18), 77 (16), 63 (12), 59 (15), 45 (18), 39 (10).

8.1.3. *Dimethyl 3-Hydroxy-5-methyl-2-nitroterephthalate* (**45**). A solution of **41** (56 mg, 0.18 mmol) and CH_3SO_3H (50 µl) in CH_3OH (5 ml) was boiled under reflux for 4 h under Ar. Workup with AcOEt gave 46 mg (95%) of **45**, m.p. 148–150° (CH_2Cl_2/hexane). IR ($CHCl_3$): 3500 – 2700*m*, 3020*w*, 2950*m*, 2845*w*, 1732*s*, 1673*s*, 1610*m*, 1593*w*, 1562*m*, 1544*s*, 1470*m*, 1437*s*, 1400*m*, 1380*m*, 1349*s*, 1298*w*, 1177*s*, 1136*s*, 1064*m*, 1022*w*, 1004*w*, 971*m*, 913*w*, 863*m*, 827*w*, 812*w*, 650*w*. ^{1}H-NMR (90 MHz, $CDCl_3$): 2.60 (*s*, $CH_3-C(5)$); 3.92 and 4.05 (2*s*, $2\,COOCH_3$); 7.32 (*m*, $w_{1/2}$ *ca.* 3, H–C(6)); 10.1–12.3 (br. *s*, HO–C(3)). MS: 269 (23, M^+), 251 (34), 238 (32), *237* (100), 221 (10), 207 (18), 179 (73), 175 (10), 162 (19), 161 (14), 151 (25), 147 (10), 133 (14), 105 (13), 95 (17), 92 (12), 91 (10), 85 (34), 77 (21), 67 (30), 55 (18), 51 (21), 41 (24), 39 (19).

8.1.4. *Dimethyl 3-Hydroxy-5-methyl-4-nitrophthalate* (**46**). To a solution of **42** (47 mg, 0.151 mmol) in CH_3OH (5 ml) Na_2CO_3 (100 mg) was added. After stirring for 1 h at r.t. under Ar, the mixture was poured to 15% H_2SO_4 and ice and worked up with AcOEt yielding 36 mg (88%) of **46**, m.p. 100–103° (CH_2Cl_2/hexane). IR ($CHCl_3$): 3600 – 2700*m*, 3030*w*, 2950*m*, 2840*w*, 1732*s*, 1680*s*, 1613*m*, 1590*w*, 1570*m*, 1532*s*, 1495*w*, 1436*s*, 1400*w*, 1370*m*, 1355*m*, 1329*s*, 1270*s*, 1189*w*, 1173*m*, 1140*m*, 1120*w*, 1072*m*, 1015*m*, 970*m*, 921*w*, 866*m*, 857*m*, 825*m*, 810*w*. ^{1}H-NMR (90 MHz, $CDCl_3$): 2.38 (*s*, $CH_3-C(5)$); 3.90 and 3.95 (2*s*, $2\,COOCH_3$); 6.92 (*m*, $w_{1/2}$ *ca.* 3, H–C(6)); 10.6–11.6 (br. *s*, HO–C(3)). MS: 269 (20, M^+), 252 (0.1), 238 (33), 237 (85), 221 (6), 207 (15), 192 (10), *179* (100), 161 (11), 151 (15), 133 (9), 121 (6), 105 (11), 95 (10), 92 (10), 91 (7), 77 (22), 67 (14), 65 (11), 59 (14), 51 (20), 41 (15), 39 (16).

8.1.5. *Methylation of* **45**. A solution of **45** (14 mg, 0.052 mmol) in AcOEt (3 ml) was treated with a 0.5M ethereal CH_2N_2-solution (*ca.* 1.5 ml). After 10 min. at r.t., solvents and CH_2N_2 were removed by evaporation. The residue, 15 mg (quant.) was identified as **43** by IR and R_f-value.

8.1.6. *Methylation of* **46**. A solution of **46** (12 mg, 0.0446 mmol) in 3 ml of AcOEt was treated with 0.5M ethereal CH_2N_2 (*ca.* 1.5 ml) at r.t. Evaporation of solvents and excess CH_2N_2 after 15 min gave 14 mg (quant.) of **44**, identified by IR and R_f-value.

8.2. *Condensation of* **38** *with Methyl Ester* **39**. A solution of nitrobutyrate **38** (92 mg, 0.487 mmol) diketone **39** (140 mg, 0.973 mmol) and DBU (72 mg, 0.474 mmol) in THF (1 ml) containing m.s. 4 Å (0.5 g) was stirred for 3.5 days at r.t. under Ar. Workup according to the general procedure followed by treatment with Ac_2O/pyridine, 1 ml of each (over night), gave 134 mg of crude products, which were separated by chromatography (27 g of silica gel, hexane/CH_3Cl_2/Et_2O 19:19:2 + 2 ppt of AcOH). Yield: 37 mg (22%) of acetate **47** (R_f 0.206), 9 mg (5%) of a 1:1 mixture of **47** and **48**, and 33 mg (20%) of acetate **48** (R_f 0.185).

1-Methyl 4-(2-Propyl) 3-Acetoxy-5-methyl-2-nitroterephthalate (**47**). IR ($CHCl_3$): 3030*w*, 2975*m*, 2950*w*, 1787*s*, 1730*s*, 1610*w*, 1545*s*, 1466*w*, 1450*w*, 1436*m*, 1405*w*, 1367*m*, 1318*m*, 1290*m*, 1275*s*, 1176*s*, 1136*m*, 1099*s*, 1053*m*, 1015*m*, 942*w*, 908*w*, 878*w*, 862*m*, 839*w*, 818*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 1.36 (*d*, $J = 6.5$, $COOCH(CH_3)_2$); 2.28 (*s*, $CH_3COO-C(3)$); 2.49 (*s*, $CH_3-C(5)$); 3.90 (*s*, $COOCH_3$); 5.28 (*hept.*, $J = 6.5$, $COOCH(CH_3)_2$); 7.73 (*m*, $w_{1/2}$ *ca.* 2, H–C(6)). MS (di.): 339 (0.5, M^+), 297 (30), 280 (8), 266 (5), 255 (48), 238 (42), *237* (100), 221 (9), 206 (5), 179 (28), 162 (10), 133 (2), 105 (1), 91 (1), 77 (3), 51 (2), 43 (40), 39 (2).

1-Methyl 2-(2-Propyl) 3-Acetoxy-5-methyl-4-nitrophthalate (**48**). IR ($CHCl_3$): 2975*w*, 2950*w*, 1787*s*, 1728*s*, 1613*m*, 1569*w*, 1535*s*, 1505*w*, 1465*w*, 1450*w*, 1435*m*, 1385*w*, 1366*m*, 1347*w*, 1320*s*, 1280*s*, 1175*s*, 1135*w*, 1100*m*, 1056*m*, 1019*m*, 940*w*, 910*w*, 876*w*, 862*m*, 839*w*, 820*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 1.32 (*d*, $J = 6.5$, $COOCH(CH_3)_2$); 2.28 (*s*, $CH_3COO-C(3)$); 2.44 (*s*, $CH_3-C(5)$); 3.90 (*s*, $COOCH_3$); 5.25 (*hept.*, $J = 6.5$, $COOCH(CH_3)_2$); 7.78 (*m*, $w_{1/2}$ *ca.* 3, H–C(6)). MS (di.): 339 (0.2, M^+), 297 (9), 280 (2), 266 (1), 255 (23), 237 (64), 207 (9), 192 (3), 179 (36), 161 (3), 148 (2), 133 (3), 120 (2), 77 (7), 51 (6), *43* (100).

8.3. *Condensation of* **6** *with Ethyl Ester* **40**. A solution of **6** (480 mg, 2.985 mmol), diketone **40** (1.071 g, 6.779 mmol), and DBU (307 mg, 2.02 mmol) in THF (7 ml) was stirred for 3 days at r.t. under Ar. Workup according to the general procedure, using more 50% K_2HPO_4 (90 ml in 8 portions) than usual, to remove a dimer of dione **40**, gave 1.054 g of crude mixture from the AcOEt-extracts. Flash chromatography (100 g of silica gel, hexane/CH_2Cl_2/Et_2O 6:13:1 + 2 ppt of AcOH) followed by re-chromatography (50 g of silica gel, same solvent) of the mixed fractions (580 mg) gave 340 mg (40%) of terephthalate **49** (R_f 0.26), 52 mg (6%) of a 1:2 mixture of **49** and **50**, and 253 mg (30%) of phthalate **50** (R_f 0.20).

1-Ethyl 4-Methyl 3-Hydroxy-5-methyl-2-nitroterephthalate (**49**). M.p. 100–103° (CH_2Cl_2/hexane). IR ($CHCl_3$): 3600 – 2600*m*, 3020*w*, 2985*m*, 2975*w*, 2940*w*, 2905*w*, 1727*s*, 1673*s*, 1611*m*, 1593*w*, 1563*m*, 1543*s*, 1470*m*, 1441*m*, 1400*m*, 1380*m*, 1369*s*, 1342*s*, 1298*w*, 1260*s*, 1185*s*, 1133*m*, 1095*w*, 1063*m*, 1025*m*, 1003*w*, 996*w*, 955*w*, 870*m*, 825*m*, 810*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 1.36 (*t*, $J = 7.5$, $COOCH_2CH_3$); 2.61 (*s*, $CH_3-C(5)$); 4.05 (*s*, $COOCH_3$); 4.38 (*q*, $J = 7.5$, $COOCH_2CH_3$); 7.28 (*m*, $w_{1/2}$ *ca.* 3, H–C(6)); 11.64 (br. *s*, $w_{1/2}$ *ca.* 7, HO–C(3)). MS (di.): 283 (27, M^+), 265 (17), 252 (24), *251* (100), 238 (11), 235 (7), 223 (5), 221 (5), 206 (9), 193 (42), 177 (9), 162 (20), 133 (14), 121 (16), 104 (11), 77 (15), 67 (23), 65 (13), 51 (19), 39 (14).

1-Ethyl 2-Methyl 3-Hydroxy-5-methyl-4-nitrophthalate (**50**). M.p. 110–112° (CH_2Cl_2/hexane). IR ($CHCl_3$): 3600 – 2700*m*, 3020*w*, 2985*m*, 2955*w*, 2940*w*, 2900*w*, 1730*s*, 1680*s*, 1650*w*, 1616*m*, 1590*w*, 1572*m*, 1532*s*, 1495*w*, 1440*m*, 1390*w*, 1370*m*, 1349*m*, 1326*s*, 1270*s*, 1182*s*, 1140*m*, 1120*w*, 1093*w*, 1072*m*, 1023*m*, 1001*w*, 987*w*, 960*w*, 875*w*, 866*m*, 853*m*, 824*m*. ^{1}H-NMR (80 MHz, $CDCl_3$): 1.38 (*t*, $J = 7.5$, $COOCH_2CH_3$); 2.40 (*s*, $CH_3-C(5)$); 3.96 (*s*, $COOCH_3$); 4.36 (*q*, $J = 7.5$, $COOCH_2CH_3$); 6.91 (*m*, $w_{1/2}$ *ca.* 2, H–C(6)); 10.8–11.5 (br. *s*, HO–C(3)). MS (di.): 283 (27, M^+), 252 (12), 251 (56), 238 (30), 224 (14), 223 (32), 207 (15), 206 (31), 192 (8), *179* (100), 161 (8), 133 (19), 121 (8), 117 (7), 105 (12), 93 (10), 77 (16), 67 (10), 65 (10), 51 (17), 43 (10), 39 (10).

8.4. *1-Ethyl 4-Methyl 3-Methoxy-5-methyl-2-nitroterephthalate* (**51**). A solution of **49** (153 mg, 0.541 mmol) in AcOEt (10 ml) was treated with an excess of 0.5M ethereal CH_2N_2-solution. Evaporation after 30 min and CC (15 g of silica gel, hexane/CH_2Cl_2/Et_2O 13:6:1) of the residue (181 mg) gave 141 mg (88%) of **51**. IR ($CHCl_3$): 3020*w*, 2980*w*, 2955*m*, 2905*w*, 2865*w*, 1728*s*, 1600*w*, 1575*w*, 1545*s*, 1505*w*, 1451*m*, 1400*m*, 1370*s*, 1316*s*, 1280*s*, 1125*s*, 1071*m*, 1026*m*, 995*w*, 950*w*, 925*w*, 895*w*, 880*w*, 862*w*, 820*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 1.35 (*t*, $J = 7.5$, $COOCH_2CH_3$); 2.40 (*s*, $CH_3-C(5)$); 3.90 and 3.98 (2*s*, $CH_3O-C(3)$, $COOCH_3$); 4.38 (*q*, $J = 7.5$, $COOCH_2CH_3$); 7.63 (*m*, $w_{1/2}$ *ca.* 2, H–C(6)). MS: 297 (46, M^+), 280 (57), 266 (41), 265 (28), 252 (28), 249 (19), 235 (49), 221 (25), 207 (12), 206 (8), 191 (16), 190 (17), 178 (76), *177* (100), 162 (15), 148 (35), 137 (32), 134 (12), 133 (11), 119 (13), 105 (10), 91 (24), 89 (33), 77 (20), 67 (22), 65 (18), 63 (17), 51 (13), 45 (42), 39 (16).

8.5. *1-Ethyl 2-Methyl 3-Methoxy-5-methyl-4-nitrophthalate* (**52**). A solution of **50** (106 mg, 0.374 mmol) in AcOEt (10 ml) was treated with 0.5M ethereal CH_2N_2 (*ca.* 5 ml). Excess solvent and CH_2N_2 were removed after 30 min by evaporation, and the residue (114 mg) was purified by chromatography (15 g of silica gel, hexane/CH_2Cl_2/Et_2O 13:6:1) yielding 111 mg (99%) of **52**, m.p. 53.5–54° (Et_2O/hexane). IR ($CHCl_3$): 3020*w*, 2985*w*, 2950*w*, 2905*w*, 2870*w*, 2840*w*, 1725*s*, 1610*m*, 1573*w*, 1534*s*, 1505*w*, 1459*m*, 1445*w*, 1430*w*, 1400*w*, 1366*s*, 1318*s*, 1275*s*, 1180*m*, 1127*m*, 1071*m*, 1028*m*, 995*w*, 953*w*, 923*w*, 895*w*, 882*w*, 860*w*, 818*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 1.39 (*t*, $J = 7.5$, $COOCH_2CH_3$); 2.38 (*s*, $CH_3-C(5)$); 3.95 and 3.98 (2*s*, $CH_3O-C(3)$, $COOCH_3$); 4.39 (*q*, $J = 7.5$, $COOCH_2CH_3$); 7.73 (*m*, $w_{1/2}$ *ca.* 2, H–C(6)). MS: 297 (44, M^+), 280 (5), 266 (30), 265 (2), 252 (48), *238* (100), 235 (55), 221 (15), 220 (18), 207 (84), 191 (11), 177 (11), 175 (21), 161 (16), 148 (41), 134 (12), 118 (28), 106 (11), 91 (20), 90 (22), 89 (22), 77 (18), 63 (14), 51 (14), 39 (12).

8.6. *3-Methoxy-5-methyl-4-nitrophthalic Acid* (**54**). A solution of diester **52** (125 mg, 0.421 mmol) in dioxane (5 ml) and 10% NaOH-solution (5 ml) was stirred for 4 days at r.t. under Ar. The mixture was poured to ice-water

and extracted twice with AcOEt. The org. phases were washed with 10% NaOH-solution and H_2O. The aq. phases were acidified with 15% H_2SO_4, saturated with NaCl, and extracted with AcOEt (3x). The residue of the org. layers was dissolved in Et_2O, filtered *(Celite)*, and the solvent was evaporated affording 102 mg (95%) of crude diacid **54**, m.p. 169–176° (CH_2Cl_2/Et_2O/toluene). IR (KBr): 1710*s*, 1609*m*, 1553*s*, 1458*m*, 1460*w*, 1426*m*, 1393*w*, 1370*s*, 1325*s*, 1283*m*, 1260*m*, 1206*w*, 1185*w*, 1146*m*, 1073*s*, 1033*w*, 1012*m*, 993*w*, 920*m*, 890*m*, 877*m*, 803*m*, 772*w*, 729*m*, 635*m*, 473*m*, 442*w*, 426*w*. ^{1}H-NMR (80 MHz, $(CD_3)_2CO$): 2.39 (*s*, $CH_3-C(5)$); 3.97 (*s*, CH_3O); 7.85 (*m*, $w_{1/2}$ *ca.* 2, H–C(6)); 7.5–10.5 (br., 2 COOH). MS (di.): 237 (11, $M^+ - 18$), 220 (2), *207* (100), 193 (12), 189 (23), 179 (12), 177 (10), 161 (47), 159 (14), 147 (12), 133 (24), 117 (62), 107 (50), 104 (22), 91 (26), 89 (75), 77 (38), 62 (25), 50 (39), 39 (25).

8.7. *3-Methoxy-5-methyl-4-nitrophthalic Anhydride* (**55**). A mixture of **54** (33 mg, 0.129 mmol) and 1.5 ml of Ac_2O was heated within 20 min to 160° and held at this temp. for 5 min, distilling off some reagent and AcOH at the same time. Evaporation of reagent (h.v.) and bulb-to-bulb distillation (h.v./140°) of the residue gave 25 mg (81%) of **55**, m.p. 118–119.5°. IR ($CHCl_3$): 3020*w*, 2950*w*, 1850*m*, 1830*w*, 1811*w*, 1780*s*, 1622*m*, 1580*m*, 1543*s*, 1473*m*, 1436*w*, 1403*m*, 1365*m*, 1298*m*, 1236*s*, 1167*w*, 1140*w*, 1099*m*, 1017*m*, 934*m*, 913*s*, 884*w*, 863*m*, 656*m*, 630*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.49 (*s*, $CH_3-C(5)$); 4.36 (*s*, CH_3O); 7.65 (*m*, $w_{1/2}$ *ca.* 2, H–C(6)). MS (di.): 237 (12, M^+), 220 (3), *207* (100), 193 (12), 189 (25), 179 (13), 177 (10), 161 (46), 159 (13), 147 (10), 133 (22), 117 (52), 107 (42), 104 (19), 91 (17), 89 (63), 77 (30), 76 (31), 67 (16), 65 (15), 63 (31), 62 (20), 57 (13), 51 (21), 50 (30), 43 (56), 39 (20).

8.8. *N-Benzyl-3-methoxy-5-methyl-4-nitrophthalimide* (**56**). To a solution of **55** (24 mg, 0.101 mmol) in CH_2Cl_2 (1.5 ml), a solution of benzylamine (21 mg, 0.2 mmol) and Et_3N (22 mg, 0.22 mmol) in CH_2Cl_2 (0.5 ml) was added. After stirring for 17 h at r.t., the mixture was diluted with AcOEt (100 ml) and washed with 2N HCl (3x) and sat. NaCl-solution (2x). The aq. phases were re-extracted twice with AcOEt. The residue of the org. phases (34 mg) was dissolved in CH_3OH and treated with an excess of 0.5M ethereal CH_2N_2-solution. Evaporation after 15 min and chromatography (3.5 g of silica gel, hexane/CH_2Cl_2/Et_2O 13:6:1 + 2 ppt of AcOH) gave 28 mg of **56** containing some dimethyl ester **44**. Purification by crystallization (CH_2Cl_2/hexane) gave 25 mg (75%) of **56**, m.p. 132–133°. IR ($CHCl_3$): 3030*w*, 2955*w*, 2930*w*, 2860*w*, 1772*m*, 1712*s*, 1625*m*, 1589*w*, 1540*s*, 1505*w*, 1496*w*, 1470*m*, 1432*m*, 1408*m*, 1395*m*, 1370*s*, 1300*m*, 1293*m*, 1190*w*, 1165*w*, 1121*m*, 1100*m*, 1075*m*, 1031*w*, 996*m*, 920*w*, 910*w*, 889*w*, 842*w*, 699*w*, 626*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.39 (*s*, $CH_3-C(5)$); 4.29 (*s*, CH_3O); 4.84 (*s*, $C_6H_5CH_2N$); 7.2–7.6 (*m*, $C_6H_5CH_2N$); 7.61 (*m*, $w_{1/2}$ *ca.* 2, H–C(6)). MS (di.): 326 (42, M^+), 309 (15), 296 (16), 279 (15), 278 (14), 250 (12), 222 (7), 194 (5), 175 (19), 148 (12), 132 (13), 119 (13), 104 (18), *91* (100), 89 (20), 77 (16), 65 (16), 63 (10), 51 (10), 39 (8).

$C_{17}H_{14}N_2O_5$ (326.30) Calc. C 62.57 H 4.32 N 8.59% Found C 62.59 H 4.34 N 8.52%

9. Condensation of 6 with 2,4,6-Heptanetrione (2). – 9.1. *Addition of Trione* **2** *in Portions.* To a solution of **6** (1.359 g, 8.44 mmol), **2** (356 mg, 2.50 mmol, 0.3 equiv.), and DBU (1.278 g, 8.4 mmol) in THF (15 ml), containing 8 g of m.s. 4 Å, additional **2** (1.071 g, 7.55 mmol, 0.9 equiv.) was added in 5 portions of 1.4–2.0 mmol over a period of 9 days. The mixture was stirred for another 3 days at r.t. and worked up according to the general procedure. Bulb-to-bulb distillation (h.v./95°) of the material extracted with 50% K_2HPO_4 (510 mg) gave 420 mg (31%) of recovered **6**. The residue of the AcOEt-extracts (1.644 g) was treated over night with Ac_2O/pyridine (5 ml of each). After evaporation of the reagents with hexane, the mixture (2.241 g) was separated by flash chromatography (200 g of silica gel, hexane/CH_2Cl_2/Et_2O 9:10:1 + 2 ppt of AcOH), re-chromatography (150 g of silica gel, hexane/CH_2Cl_2/Et_2O 19:19:2 + 2 ppt of AcOH) of the nonpolar components, and re-chromatography (50 g of silica gel, hexane/CH_2Cl_2/Et_2O 6:13:1 + 2 ppt of AcOH) of the polar products. Crystallization (CH_2Cl_2/Et_2O/hexane) of enriched fractions gave 264 mg (11%) of isocoumarin **58**, 514 mg (32% based on **2**) of naphtalin **62**, and 160 mg (6%) of orsellinate **63**. Additional **58** and **63**, as well as the other products, **59**, **60**, **61**, and **64**, listed below in the order of elution, were obtained from mother liquors and mixed fractions by CC, HPLC, and crystallizations.

3,5-Dimethyl-4-nitrophenyl Acetate (**64**). Isolated by re-chromatography (10 g of silica gel, hexane/CH_2Cl_2/Et_2O 13:6:1 + 2 ppt of AcOH). Yield: 16 mg (0.9%, 1.3% based on consumed **6**), R_f 0.415 (hexane/CH_2Cl_2/Et_2O 19:19:2), 0.272 (hexane/CH_2Cl_2/Et_2O 13:6:1), m.p. 58–58.5° (Et_2O/hexane). IR ($CHCl_3$): 3020*w*, 2990*w*, 2970*w*, 2930*w*, 2875*w*, 1770*s*, 1750*s*, 1613*m*, 1587*m*, 1520*s*, 1463*w*, 1363*s*, 1298*m*, 1183*m*, 1148*s*, 1097*w*, 1032*s*, 1005*w*, 969*m*, 901*m*, 855*w*, 825*m*. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.30 and 2.32 (2*s*, $CH_3-C(3')$, $CH_3-C(5')$, 3 H–C(2)); 6.90 (*m*, $w_{1/2}$ *ca.* 3, H–C(2'), H–C(6')). MS (di.): 209 (37, M^+), 167 (96), *150* (100), 137 (23), 122 (22), 94 (17), 91 (29), 77 (19), 51 (10), 43 (76), 39 (10).

3,6-Dimethyl-7-nitro-8-isocoumaryl Acetate (**58**). HPLC and crystallization gave additional 45 mg of **58**. Yield: 309 mg (13%, 19% based on consumed **6**), R_f 0.21 (hexane/CH_2Cl_2/Et_2O 19:19:2), $vol._{ret}$ = 215 ml (hexane/CH_2Cl_2/Et_2O 19:19:2 + 2 ppt of AcOH), m.p. 192–193° (CH_2Cl_2/hexane). IR ($CHCl_3$): 3030*w*, 1788*s*, 1753*s*, 1660*s*, 1615*m*, 1563*m*, 1556*m*, 1532*s*, 1467*w*, 1450*w*, 1429*w*, 1383*m*, 1370*s*, 1360*m*, 1325*w*, 1293*m*, 1176*s*, 1167*s*, 1095*m*, 1051*m*, 1015*w*, 1002*w*, 992*w*, 976*m*, 881*m*, 859*m*. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.25, 2.39 and 2.41 (3*s*, 3 H–C(2), CH_3–C(3'), CH_3–C(6')); 6.20 (*m*, $w_{1/2}$ *ca.* 4, H–C(4')); 7.10 (*m*, $w_{1/2}$ *ca.* 3, H–C(5')). MS (di.): 277 (10, M^+), *235* (100), 218 (42), 205 (18), 177 (21), 161 (7), 133 (4), 117 (5), 115 (5), 105 (6), 89 (10), 77 (10), 63 (10), 57 (14), 43 (83).

$C_{13}H_{11}NO_6$ (277.23) Calc. C 56.32 H 4.00 N 5.05% Found C 56.27 H 3.94 N 5.11%

Methyl 2-Acetoxy-4-(2'-acetoxy-1'-propenyl)-6-methyl-3-nitro-1-benzoate (major isomer (**59**))[16]. Isolated by HPLC and crystallization. According to ^{1}H-NMR, the mother liquor (24 mg) contained considerable amounts of a non-identified compound not separated by HPLC. Yield of pure **59**: 67 mg (2.3%, 3.3% based on consumed **6**). R_f 0.175 (hexane/CH_2Cl_2/Et_2O 19:19:2), $vol._{ret}$ = 265 ml (hexane/CH_2Cl_2/Et_2O 19:19:2 + 2 ppt of AcOH), m.p. 93.5–94.5° (CH_2Cl_2/Et_2O/hexane). IR ($CHCl_3$): 3020*w*, 2950*w*, 1782*s*, 1750*s*, 1727*s*, 1678*m*, 1665*w*, 1608*m*, 1559*m*, 1529*s*, 1505*w*, 1434*m*, 1360*s*, 1280*m*, 1270*s*, 1177*s*, 1156*s*, 1121*m*, 1070*w*, 1048*m*, 1013*m*, 965*w*, 938*w*, 882*w*, 863*m*. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.08 (6H), 2.25 and 2.93 (3*s*, 3 H–C(3'), CH_3–C(6), CH_3COO–C(2), CH_3COO–C(2')); 3.90 (*s*, $COOCH_3$); 5.98 (*m*, $w_{1/2}$ *ca.* 4, H–C(1')); 7.23 (*m*, $w_{1/2}$ *ca.* 2, H–C(5)). MS (di.): 352 (1, M^+ + 1), 320 (2), 309 (17), 277 (9), 268 (4), 249 (3), 235 (7), 225 (7), 217 (10), 207 (11), 193 (37), 192 (15), 175 (33), 147 (29), 134 (3), 119 (10), 91 (5), 77 (3), *43* (100).

$C_{16}H_{17}NO_8$ (351.30) Calc. C 54.70 H 4.88 N 3.99% Found C 54.88 H 5.07 N 3.99%

Methyl 2-Acetoxy-4-(2'-acetoxy-1'-propenyl)-6-methyl-3-nitro-benzoate (minor isomer (**60**))[16]. Isolated by HPLC. Yield: 10 mg (0.3%, 0.5% based on consumed **6**), R_f 0.16 (hexane/CH_2Cl_2/Et_2O 19:19:2), $vol._{ret}$ = 310 ml (hexane/CH_2Cl_2/Et_2O 19:19:2 + 2 ppt of AcOH), m.p. 85–85.5° (CH_2Cl_2/Et_2O/hexane). IR ($CHCl_3$): 3030*w*, 2950*w*, 1780*s*, 1750*s*, 1729*s*, 1673*m*, 1610*m*, 1555*m*, 1529*s*, 1505*w*, 1432*m*, 1380*m*, 1366*s*, 1280*s*, 1270*s*, 1176*s*, 1144*s*, 1120*m*, 1065*m*, 1045*m*, 1021*m*, 1010*w*, 972*w*, 912*m*, 891*w*, 866*m*. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.01, 2.18, 2.26, and 2.49 (4*s*, 3 H–C(3'), CH_3–C(6), CH_3COO–C(2), CH_3COO–C(2')); 3.90 (*s*, $COOCH_3$); 6.23 (*m*, $w_{1/2}$ *ca.* 4, H–C(1')); 7.20 (*m*, $w_{1/2}$ *ca.* 2, H–C(5)). MS (di.): 352 (0.2, M^+ + *1*), 320 (1), 309 (17), 278 (9), 277 (14), 268 (3), 249 (5), 235 (13), 225 (12), 224 (11), 217 (20), 207 (21), 193 (77), 192 (30), 176 (33), 175 (71), 147 (59), 134 (5), 119 (22), 91 (9), 77 (6), 65 (7), *43* (100).

2-Acetyl-3,6-dimethyl-1,8-naphthalenediyl Diacetate (**62**). Yield: 514 mg (32% based on trione **2**), R_f 0.125 (hexane/CH_2Cl_2/Et_2O 19:19:2), 0.226 (hexane/CH_2Cl_2/Et_2O 6:13:1), m.p. 164–166° (dec., changes observable from *ca.* 158°). IR ($CHCl_3$): 3030*w*, 2920*w*, 2850*w*, 1770*s*, 1700*s*, 1640*m*, 1612*w*, 1565*w*, 1557*w*, 1430*m*, 1368*s*, 1352*m*, 1331*s*, 1257*m*, 1185*s*, 1160*m*, 1072*s*, 1045*w*, 1021*m*, 973*w*, 960*w*, 908*w*, 890*s*, 860*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.30, 2.34, 2.36, 2.45, and 2.50 (5*s*, CH_3COO–C(1), CH_3COO–C(8), CH_3–C(3), CH_3–C(6), CH_3CO–C(2)); 6.9–7.5 (1 H) and 7.4–7.6 (2 H) (2*m*, H–C(4), H–C(5), H–C(7)). MS (di.): 314 (3, M^+), 272 (8), *230* (100), 215 (51), 212 (18), 201 (6), 169 (5), 141 (7), 128 (2), 115 (10), 77 (3), 57 (5), 43 (31).

Methyl 2-Acetoxy-6-methyl-3-nitro-4-(2'-oxopropyl)benzoate (**61**). Isolated by re-chromatography (hexane/CH_2Cl_2/Et_2O 6:13:1) and HPLC. Yield: 16 mg (0.6%, 0.9% based on consumed **6**), R_f 0.075 (hexane/CH_2Cl_2/Et_2O 19:19:2), 0.176 (hexane/CH_2Cl_2/Et_2O 6:13:1), $vol._{ret}$ = 280 ml (hexane/CH_2Cl_2/Et_2O 6:13:1 + 2 ppt of AcOH), m.p. 96–97° (CH_2Cl_2/Et_2O/hexane). IR ($CHCl_3$): 3030*w*, 2950*w*, 1780*s*, 1726*s*, 1612*m*, 1565*w*, 1555*w*, 1527*s*, 1505*w*, 1432*m*, 1356*s*, 1285*m*, 1275*s*, 1176*s*, 1160*s*, 1121*m*, 1061*m*, 1040*w*, 1007*w*, 980*w*, 882*w*, 865*m*. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.24, 2.26, and 2.45 (3*s*, 3 H–C(3'), CH_3–C(6), CH_3COO–C(2)); 3.84 (*s*, 2 H–C(1')); 3.91 (*s*, $COOCH_3$); 7.06 (*m*, $w_{1/2}$ *ca.* 2, H–C(5)). MS (di.): 310 (0.2, M^+ + *1*), 278 (1), 267 (7), 236 (8), 235 (9), 225 (4), 221 (4), 208 (25), 193 (15), 176 (30), 147 (6), 120 (5), 119 (5), 91 (4), 77 (3), 65 (5), *43* (100).

Methyl 3-Acetyl-2,4-diacetoxy-6-methylbenzoate (**63**). Further **63**, 30 mg, was isolated by re-chromatography, HPLC, and crystallization. Yield: 190 mg (7.3%, 10.5% based on consumed **6**), R_f 0.075 (hexane/CH_2Cl_2/Et_2O 19:19:2), 0.122 (hexane/CH_2Cl_2/Et_2O 6:13:1), $vol._{ret}$ = 360 ml (hexane/CH_2Cl_2/Et_2O 6:13:1 + 2 ppt of AcOH), m.p. 99–100.5° (CH_2Cl_2/Et_2O/hexane). IR ($CHCl_3$): 3020*w*, 2950*w*, 1773*s*, 1725*s*, 1699*s*, 1612*m*, 1565*w*, 1555*w*, 1435*m*, 1405*w*, 1368*s*, 1355*m*, 1290*s*, 1180*s*, 1170*s*, 1098*m*, 1059*s*, 1045*w*, 1004*m*, 955*m*, 900*m*, 876*m*, 855*w*, 830*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.24, 2.27, 2.41, and 2.42 (4*s*, CH_3–C(6), CH_3CO–C(3), CH_3COO–C(2), CH_3COO–C(4)); 3.89 (*s*, $COOCH_3$); 6.98 (*m*, $w_{1/2}$ *ca.* 2, H–C(5)). ^{13}C-NMR (25.2 MHz, $CDCl_3$): 20.3, 20.5, and 20.8 (CH_3CO–C(3), CH_3COO–C(2), CH_3COO–C(4)); 30.9 (CH_3–C(6)); 52.3 ($COOCH_3$); 122.7 (C(5)); 124.9 and 126.5 (C(1), C(3)); 141.0 (C(6)); 146.1 (C(2)); 148.6 (C(4)); 165.8 ($COOCH_3$); 168.4 (CH_3COO–C(2), CH_3COO–C(4)); 197.3 (CH_3CO–C(3)). MS (di.): 308 (3, M^+), 277 (3), 267 (13), 266 (34), 235 (10), *224* (100),

209 (6), 193 (29), 192 (91), 177 (29), 164 (80), 147 (2), 135 (3), 121 (2), 93 (3), 91 (2), 77 (2), 67 (3), 65 (3), 43 (65), 39 (2).

$C_{15}H_{16}O_7$ (308.28) Calc. C 58.44 H 5.23% Found M.Wt. 318 C 58.52 H 5.19%

9.2. *Addition of Trione* **2** *in One Batch.* A solution of **6** (142 mg, 0.883 mmol), **2** (188 mg, 1.32 mmol, 1.5 equiv.) and DBU (134 mg, 0.833 mmol) in THF (1.5 ml) containing 1 g of m.s. 4 Å was stirred for 1 week at r.t. under Ar. Workup according to the general procedure gave 22 mg (15%) of recovered **6** from the K_2HPO_4-extracts. The residue of the AcOEt-extracts was treated with Ac_2O/pyridine over night. Chromatography and crystallization of the resulting product mixture as above afforded 44.5 mg (18%, 21.5% based on consumed **6**) of isocoumarin **58** and 75 mg (36% based on trione **2**) of naphthalene derivative **62**. Detected but not isolated pure were **59**, **60**, and **63**.

9.3. *Partial Methynolysis of* **59**. To a solution of **59** (12 mg, 0.034 mmol) in CH_3OH (3 ml) cooled to 0° Na_2CO_3 (45 mg) was added. The suspension was stirred at 0° for 1 h under Ar, then poured to 15% H_2SO_4 and ice, and extracted twice with AcOEt. The extracts were washed with sat. NaCl-solution (4x), dried ($MgSO_4$), and evaporated. Chromatography (4 g of silica gel, hexane/CH_2Cl_2/Et_2O 6:13:1 + 2 ppt of AcOH) of the residue (11 mg) gave 1 mg (9%) of phenol **65**, 4.3 mg (47%) of keto phenol **66**, and 3.2 mg (30%) of acetate **61**.

4-(2'-Acetoxy-1'-propenyl)-6-methyl-3-nitrosalicylate (**65**). IR ($CHCl_3$): 3500 – 2500*m*, 3030*w*, 2955*w*, 2925*w*, 2850*w*, 1752*s*, 1663*s*, 1611*m*, 1582*w*, 1560*w*, 1550*m*, 1528*s*, 1505*w*, 1440*m*, 1400*w*, 1370*s*, 1355*m*, 1296*w*, 1264*s*, 1190*w*, 1159*s*, 1135*m*, 1079*w*, 1051*w*, 1018*w*, 995*w*, 970*w*, 940*w*, 872*m*. MS (di.): 309 (1, M^+), 277 (5), 267 (1), 235 (5), 224 (4), 217 (7), 207 (7), 193 (43), 175 (32), 162 (2), 147 (36), 134 (4), 119 (17), 107 (4), 91 (8), 77 (5), 65 (6), *43* (100).

Methyl 6-Methyl-3-nitro-4-(2'-oxopropyl)salicylate (**66**). M.p. 122–123° (CH_2Cl_2/hexane). IR ($CHCl_3$): 3500 – 2500*m*, 3030*w*, 2955*w*, 1725*s*, 1668*s*, 1650*w*, 1615*m*, 1586*m*, 1564*m*, 1555*w*, 1528*s*, 1505*w*, 1440*m*, 1405*m*, 1360*m*, 1352*s*, 1305*m*, 1263*s*, 1160*m*, 1133*m*, 1122*m*, 1076*m*, 1030*w*, 980*w*, 967*w*, 869*m*. ^{1}H-NMR (80 MHz, $CDCl_3$): 2.29 (*s*, 3 H–C(3')); 2.53 (*s*, CH_3–C(6)); 3.80 (*s*, 2 H–C(1')); 4.00 (*s*, $COOCH_3$); 6.64 (*m*, $w_{1/2}$ *ca.* 2, H–C(5)); 11.81 (br. *s*, $w_{1/2}$ *ca.* 5, HO–C(2)). MS (di.): 267 (4, M^+), 236 (7), 235 (4), 225 (4), 221 (11), 208 (33), 193 (22), 189 (5), 177 (10), 176 (66), 148 (7), 134 (5), 120 (11), 91 (9), 77 (8), 65 (11), *43* (100).

9.4. *Methanolysis of* **60**. A solution of **60** (3.5 mg, 0.01 mmol), in 0.5 ml of CH_3OH was treated at 0° with Na_2CO_3 (35 mg) for 2.75 h under Ar. The mixture was then acidified, 15% H_2SO_4 (4 ml)/ice, and worked up with AcOEt. Chromatography (4 g of silica gel, hexane/CH_2Cl_2/Et_2O 6:13:1 + 2 ppt of AcOH) gave 2.2 mg (83%) of **66**.

9.5. *Methyl 7-Acetoxy-2,5-dimethyl-6-indolecarboxylate* (**67**). To a solution of **66** (3.3 mg, 0.0124 mmol) in a 5:1 (v/v) mixture of AcOH and H_2O (0.75 ml) 15% aq. $TiCl_3$-solution (0.15 ml, *ca.* 0.2 mmol) was added at 0°. After stirring at r.t. for 80 min, the mixture was poured to ice and CH_2Cl_2 and neutralized carefully, first with 10% NaOH (3 ml), then with sat. $NaHCO_3$. Workup with CH_2Cl_2, treatment with Ac_2O/pyridine of the residue of the org. phases (2.6 mg) over night, and chromatography (1 g of silica gel, hexane/CH_2Cl_2/Et_2O 2:2:1) of the crude product (3.4 mg) gave 2 mg (62%) of indole **67**, m.p. 148–150° (CH_2Cl_2/hexane). IR ($CHCl_3$): 3465*m*, 3380 br. *w*, 3030*w*, 3000*w*, 2950*w*, 2925*w*, 2850*w*, 1768*s*, 1745*s*, 1715*s*, 1636*w*, 1600*w*, 1576*m*, 1550*m*, 1482*m*, 1440*m*, 1392*w*, 1367*m*, 1329*s*, 1299*s*, 1260*s*, 1186*s*, 1175*m*, 1147*m*, 1076*m*, 1052*m*, 1010*w*, 994*w*, 955*w*, 895*w*, 869*m*, 623*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.37 (*s*, CH_3COO–C(7)); 2.42 (*d*, $J = 0.9$) and 2.47 (*d*, J *ca.* 0.7) (CH_3–C(2), CH_3–C(5)); 3.89 (*s*, $COOCH_3$); 6.15 (*m*, $w_{1/2}$ *ca.* 5, H–C(3)); 7.20 (*m*, $w_{1/2}$ *ca.* 2, H–C(4)); 7.8–7.9 (br., NH). MS (di.): 261 (15, M^+), 230 (3), 219 (20), 202 (0.4), *187* (100), 159 (5), 130 (9), 103 (3), 77 (2), 57 (5), 43 (4).

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