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Asymmetric Catalysis, CIII [1]: Enantioselective *Michael* Addition of 1,3-Dicarbonyl Compounds to Conjugated Nitroalkenes

H. Brunner* and **B. Kimel**

Institut für Anorganische Chemie, Universität Regensburg, D-93040 Regensburg, Deutschland

Summary. Optically active *Michael* adducts were synthesized by addition of 1,3-dicarbonyl compounds to conjugated nitroalkenes. Good chemical yields were obtained for nitroalkenes stabilized by an aromatic substituent without any further substituents at the double bond. Acetylacetone and methyl-2,3-dihydro-1-oxo-1*H*-indene-2-carboxylate were used as *Michael* donors and four cinchona alkaloids as chiral base catalysts. Enantiomeric excess determinations were performed by ^{1}H NMR spectroscopy in the presence of the *Pirkle* alcohol and by HPLC on chiral stationary phases. A correlation between the relative configuration of the prevailing isomer of the *Michael* adduct and the catalysts was established.

Keywords. Enantioselective catalysis; Enantioselective *Michael* addition; Nitroalkenes; Chiral HPLC.

Asymmetrische Katalyse, 103. Mitt. [1]: Enantioselektive *Michael*-Addition von 1,3-Dicarbonylverbindungen an konjugierte Nitroalkene

Zusammenfassung. Optisch aktive *Michael*-Addukte werden durch die Addition von 1,3-Dicarbonylverbindungen an konjugierte Nitroalkene synthetisiert. Gute chemische Ausbeuten werden für durch aromatische Substituenten stabilisierte Nitroalkene ohne weitere Substituenten an der Doppelbindung erreicht. Acetylaceton und 2,3-Dihydro-1-oxo-1*H*-inden-2-carbonsäuremethylester werden als *Michael*-Donoren und vier Cinchona-Alkaloide als chirale basische Katalysatoren verwendet. Die Bestimmung des Enantiomerenüberschusses wird mittels ^{1}H-NMR-Spektroskopie in Gegenwart von *Pirkle*-Alkohol und HPLC an chiralen stationären Phasen durchgeführt. Eine Korrelation zwischen der relativen Konfiguration der Vorzugsisomeren der *Michael*-Addukte und den Katalysatoren wurde hergestellt.

Introduction

Two catalytic approaches are used in *Michael* addition reactions: base catalysis and transition metal catalysis. The first enantioselective base catalyzed *Michael* additions were reported in 1973 by *Langström* and *Bergson* [2]. Later *Hermann* and *Wynberg* [3] carried out a series of experiments with various *Michael* donors and acceptors involving cinchona alkaloids and their derivatives as chiral catalysts.

(−)-Quinine catalyzed addition of methyl 2,3-dihydro-1-oxo-1*H*-indene-2-carboxylate to methyl vinyl ketone proceeded with 99% chemical yield and 76% enantiomeric excess (*ee*).

Catalysis involving transition metal complexes [4] has the following advantages compared with traditional base catalysis: (*i*) higher yields, since the reaction proceeds under non-equilibrium conditions; (*ii*) reduction of unwanted side reactions, such as rearrangements, secondary condensations, and polymerizations as reported for base catalysis; (*iii*) simplification of the work-up procedures.

Some enantioselective *Michael* additions catalyzed by chiral transition metal complexes have been reported. Complexes formed *in situ* from Co(*acac*)$_2$ and (+)- or (−)-1,2-diphenyl-1,2-diaminoethane together with a series of 1,3-dicarbonyl compounds as *Michael* donors and α,β-unsaturated carbonyl compounds as *Michael* acceptors were used. In the addition of methyl 2,3-dihydro-1-oxo-1*H*-indene-2-carboxylate to methyl vinyl ketone, enantioselectivities up to 66% *ee* were achieved, chemical yields amounting to 75–85% [5, 6]. *Desimoni* and co-workers [7] applied chiral Cu(II) complexes with nitrogen ligands to the *Michael* donor/acceptor pair methyl 2,3-dihydro-1-oxo-1*H*-indene-2-carboxylate/methyl vinyl ketone to provide enantiomeric excesses up to 70%. *Botteghi* and co-workers [8] studied enantioselective *Michael* additions of nitromethane to α,β-unsaturated ketones catalyzed by Ni(II) and Co(II) complexes with chiral nitrogen ligands. The catalytic system derived from Ni(*acac*)$_2$ and (+)-(*S*)-2-(anilinomethyl)pyrrolidine gave up to 24% *ee*.

Michael additions to conjugated nitroalkenes were investigated by *Perekalin* and co-workers [9]. Triethylamine and alkali metal alkoxides catalyze these reactions providing high chemical yields. Thus, *Michael* adducts of β-nitrostyrene with acetylacetone and ethyl acetoacetate were formed after 10 hours at room temperature with 98% and 78% yields, respectively, using catalytic amounts of triethylamine. In a series of publications, *Boberg* and co-workers [10] developed an approach to the synthesis of heterocyclic compounds, including furans, dihydrofurans, and pyrroles based on subsequent *in situ* transformations of *Michael* adducts obtained from conjugated nitroalkenes.

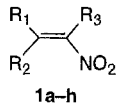
Metal complex catalysis was applied to *Michael* additions involving conjugated nitroalkenes as *Michael* acceptors by *Nelson* [4] and *Fei* and *Chan* [11]. Ni(*acac*)$_2$ catalyzed the addition of acetylacetone to β-nitrostyrene upon heating with good chemical yields. However, such conditions do not seem mild enough to provide reasonable enantioselectivity.

In this paper, we present results obtained from *Michael* additions of acetylacetone and methyl 2,3-dihydro-1-oxo-1*H*-indene-2-carboxylate to various conjugated nitroalkenes using cinchona alkaloids as chiral catalysts.

Results and Discussion

Screening experiments

Eight conjugated nitroalkenes (**1a–h**, Scheme 1) were synthesized according to previously described procedures.



1a–h

Nitroalkene	R_1	R_2	R_3	Ref.
1a	Ph	H	H	[12][1]
1b	2-thienyl	H	H	[13]
1c	1-naphthyl	H	H	[2]
1d	Ph	H	Me	[14]
1e	Ph	H	Et	[14]
1f	Ph	Me	H	[15]
1g	Me	H	H	[16]
1h	Me	H	Me	[16]

[1] Commercially available product (Merck) was used with the same efficiency; [2] the same technique as described in Ref. [12] was used

Scheme 1

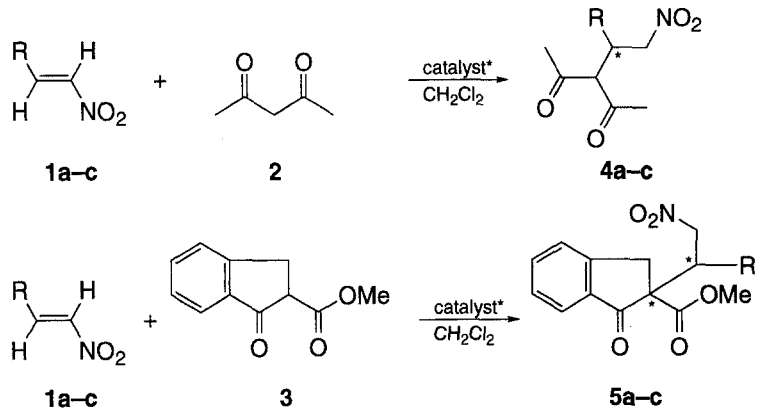
First of all, the applicability of Ni(*acac*)$_2$ and Co(*acac*)$_2$ as catalysts in *Michael* additions of acetylacetone to the conjugated nitroalkenes **1a–h** was investigated. No reasonable reaction rate was observed at room temperature. Additions carried out in chloroform at 60 °C gave the desired products for nitroalkenes with aromatic substituents as previously described by *Nelson* and co-workers [4]. However, significant amounts of polymerization products were formed in these reactions. In a recent publication of *Deutsch* and co-workers [17], Ni(*acac*)$_2$ catalyzed additions of methyl cyclopentanone-2-carboxylate and analogous compounds to β-nitrostyrene are reported, chemical yields being 45% after 70 days of reaction time.

Therefore, it was decided to study enantioselective *Michael* additions of conjugated nitroalkenes catalyzed by chiral bases. As chiral bases, four cinchona alkaloids (−)-quinine, (+)-quinidine, (+)-cinchonine, and (−)-cinchonidine were used.

However, even in these experiments only three of the nitroalkenes **1a–h** turned out to be suitable *Michael* acceptors. These were (*E*)-1-nitro-2-phenylethene (**1a**), (*E*)-1-nitro-2-(2-thienyl)ethene (**1b**), and (*E*)-1-nitro-2-(1-naphthyl)ethene (**1c**). The common features of these substances which we consider to be essential for their success in Michael reaction are (*i*) the presence of a 2-nitroethenyl moiety, *i.e.* hydrogen atoms in both α- and β-positions to the nitro group, and (*ii*) the presence of an aromatic substituent conjugated with the nitroalkene system.

(*E*)-2-Nitro-1-phenylpropene-1 (**1d**) and (*E*)-2-nitro-1-phenylbutene-1 (**1e**) which bear an alkyl group at the NO_2-bonded carbon atom did not undergo *Michael* additions with acetylacetone upon catalysis with organic bases such as alkaloids or triethylamine. (*E*)-1-Nitro-2-phenylpropene-1 (**1f**), possessing a methyl group at the β-position to the nitro group, also did not participate in the *Michael* reaction.

In 1-nitropropene (**1g**) and (*E*)-2-nitro-butene-2 (**1h**), the *Michael* acceptor system of which is not stabilized by a conjugated aromatic substituent, the polymerization under basic conditions predominated the *Michael* addition to such an extent that the *Michael* adduct could not be detected in the reaction mixtures.



1a, 4a, 5a: R = C_6H_5: **1b, 4b, 5b:** R = 2-C_4H_3S; **1c, 4c, 5c:** R = 1-$C_{10}H_7$

Scheme 2

According to these screening experiments, the scope of *Michael* acceptors to be investigated in chiral base catalyzed additions was reduced to the three nitroalkenes **1a–c** satisfying the conditions stated above.

Michael additions

The reaction schemes of the *Michael* additions performed are shown in Scheme 2.

Base catalyzed *Michael* addition of **2** and **3** to the conjugated nitroalkenes **1a–c** in methylene chloride solution at room temperature affords **4a–c** and **5a–c**, respectively, in high chemical yields. *Michael* adducts **4a, b** and **5a, b** are colourless crystalline solids, **4c** and **5c** are yellow oils.

The reaction time depends on the nature of the aromatic substituent, being longer (about 36 hours) for **1c** compared to 18 hours for **1a** as determined by ^1H NMR spectroscopy. Observable amounts of side products are formed in these reactions, especially in the case of **1b**. These side products were separated during work-up and were not investigated further.

Adducts **4a–c** were obtained as mixtures of enantiomers. Neither polarimetry nor absolute configuration data have been published previously. Attempts were made to prepare enantiomerically pure **4a** by means of repeated fractional crystallization using a sample obtained from the (−)-cinchonidine catalyzed addition with about 25% *ee*. Adduct **4a** turned out to be configurationally unstable. Complete racemization was observed at the melting point temperature. Nevertheless, successive enantiomeric enrichment on crystallization was established by polarimetry and by ^1H NMR spectroscopy (400 MHz) in the presence of (*S*)-(+)-1-(9-anthryl)-2,2,2-trifluoroethanol (*Pirkle* alcohol). Good peak resolution was observed for the methyl groups of **4a** ($\Delta\delta$ = 2.8–3.3 Hz, 0.02 mmol of **4a** and 0.12 mmol of the *Pirkle* alcohol in $CDCl_3$). A sample of **4a**, obtained after 5 crystallizations from absolute toluene, exhibited an enantiomeric ratio of 84.5:15.5. Thus, the optical rotation of enantiomerically pure **4a** can be calculated: $[\alpha]_D^{RT} = \pm 147.5°$. Using this value, con-

Table 1. Data for *Michael* adducts **4a–c**

Adduct	Catalyst	Yield (%)	$[\alpha]_D^{RT}$ (deg)	Enantiomeric Excess (%) polarimetric	HPLC
4a	Et_3N	87.6	–	–	–
4a	(−)-quinine	88.9	−23.9	16.2	16.3
4a	(+)-quinidine	89.4	+15.3	10.4	11.0
4a	(+)-cinchonine	90.3	+24.5	16.6	15.6
4a	(−)-cinchonidine	89.7	−37.3	25.3	26.7
4b	Et_3N	72.1	–	–	–
4b	(−)-quinine	74.0	−22.1	–	17.9
4b	(+)-quinidine	75.3	+15.4	–	16.8
4b	(+)-cinchonine	76.9	+26.2	–	24.8
4b	(−)-cinchonidine	74.5	−32.7	–	29.1
4c	Et_3N	85.4	–	–	–
4c	(−)-quinine	89.8	−17.6	–	18.0
4c	(+)-quinidine	93.8	+11.6	–	9.2
4c	(+)-cinchonine	93.7	+18.5	–	20.8
4c	(−)-cinchonidine	90.7	−31.9	–	29.9

clusions concerning the enantiomeric excess of the adducts obtained in different experiments could be drawn.

Adduct **4a** was also analyzed by gas chromatography using several chiral stationary phases. However, no separation was achieved due to the configurational instability of the compound upon heating.

HPLC enantiomeric excess determinations for **4a** were carried out using a Chiracel OD-H column (250 × 4.6 mm, Daicel Chemical Industries Ltd.) and a mixture of 95% hexane and 5% ethanol as the eluent. The results agree satisfactorily with those obtained by ^{1}H NMR and polarimetric measurements for **4a**. Analyses of adducts **4b, c** were performed using a Chiracel AD column (50 × 4.6 mm, Daicel Chemical Industries Ltd.) since no reasonable peak separation was observed on the Chiracel OD-H column applied for the analysis of **4a**. A mixture of 90% hexane and 10% ethanol was used as the eluent for the analysis of **4b** and a mixture of 97% hexane and 3% ethanol for **4c**. All results obtained for the *Michael* adducts **4a–c** are given in Table 1.

The data in Table 1 show that the configuration of the prevailing enantiomer strongly depends on the configuration of the catalyst. (−)-Cinchonidine exhibits the highest enantioselectivity for all three acetylacetone derivatives **4a–c**. The highest enantioselectivity is reached for **4c** with 29.9% *ee*.

The *Michael* adducts **5a–c** were obtained as mixtures of two diastereomeric pairs of enantiomers which differ in their ^{1}H NMR spectra. The determination of the diastereomeric ratio for **5a** and **5c** was based upon integration of the methine protons adjacent to the aromatic substituents, the former appearing as double

doublets (4.21 and 4.48 ppm for **5a**, 5.03 and 5.63 ppm for **5c**). For **5b**, the diastereomeric ratio was established by integration of the double doublet at 5.39 ppm (one of the diastereotopic methylene protons of the minor diastereomer) and two overlapping double doublets at 4.89 and 4.92 ppm (both methylene protons of the major diastereomer). The diastereomeric ratios determined by ^{1}H NMR measurements were in accordance with those obtained by the HPLC analyses.

All individual diastereomers of **5a–c** were isolated by column chromatography on silica gel, using appropriate mixtures of diethyl ether and petroleum ether as eluents, and characterized by their ^{1}H NMR spectra.

The relative configurations of analogous diastereomeric *Michael* adducts have been determined recently by *Deutsch et al.* [17] using X-ray structure analysis. However, we failed to establish a correlation with those data. Nevertheless, analysis of the ^{1}H NMR spectroscopic parameters demonstrates that the major diastereomers of **5a–c** have the same relative configuration. This conclusion is based on the chemical shifts of the two diastereotopic protons at the carbon atoms adjacent to the nitro group and their coupling constants with the methine proton at the chiral carbon atoms. In all three cases, the methylene proton exhibiting stronger coupling (*transoid* conformation with respect to the methine proton) appears at lower field for the major diastereomers and at higher field for the minor diastereomers relative to the proton exhibiting weaker coupling (*cisoid* conformation with respect to the methine proton). The major diastereomers were always eluted first in column chromatographic separations, whereas the minor diastereomers were eluted first in HPLC analyses.

HPLC analyses of the adducts **5a–c** using a column with a chiral stationary phase (Chiracel OD, 50 × 4.6 mm, Daicel Chemical Industries Ltd.) were performed to determine the enantiomeric excess. An unusual elution sequence was observed for **5a** and **5b** with two enantiomers belonging to different diastereomeric pairs eluting first with short retention times and with a short interval between each other, whereas the other two enantiomers were eluted with long retention times and a long interval between each other in reversed order (Table 2). This assignment was proven by measurements involving racemic diastereomers obtained by the triethylamine catalyzed reaction and individual diastereomers separated by column chromatography.

For the adduct **5c**, no peak separation was observed for the two isomers eluted first. Therefore, preparative HPLC was applied to isolate the two respective

Table 2. Chromatographic behaviour of **5a–c**

Adduct	Retention time (min)			
	minor 1	major 1	major 2	minor 2
5a[1]	7.14	8.70	28.59	52.00
5b[1]	4.39	6.07	21.10	31.45
5c[2]	5.23	5.25	11.61	16.93

[1] Eluent: 99.3% hexane, 0.7% ethanol (1 ml/min); [2] eluent: 97.0% hexane, 3.0% ethanol (1 ml/min)

Table 3. Data for *Michael* adducts **5a–c**

Adduct	Catalyst	Yield (%)	Diastereomeric Excess (%) HPLC (NMR)	Enantiomeric Excess (%)[1] pair 1[2]	pair 2[3]
5a	Et_3N	74.8	(22.8)	–	–
5a	(−)-quinine	80.2	4.8	8.0	26.5
5a	(+)-quinidine	88.2	1.6	(10.6)	(15.8)
5a	(+)-cinchonine	84.7	6.5	(19.4)	(23.9)
5a	(−)-cinchonidine	81.5	30.2	7.6	10.3
5b	Et_3N	86.2	(30.0)	–	–
5b	(−)-quinine	91.5	0.3	2.1	24.8
5b	(+)-quinidine	88.6	1.1	(3.8)	(10.9)
5b	(+)-cinchonine	89.2	7.7	(5.5)	(43.2)
5b	(−)-cinchonidine	86.2	12.2	5.0	46.2
5c	Et_3N	98.1	(40.7)	–	–
5c	(−)-quinine	91.7	35.8	1.7	11.1
5c	(+)-quinidine	93.6	49.2	(0.4)	(6.3)
5c	(+)-cinchonine	95.6	36.9	(6.4)	(11.0)
5c	(−)-cinchonidine	88.7	46.0	3.5	18.0

[1] Values in parentheses mean that the opposite enantiomer prevails (compared with the (−)-quinine catalyzed addition); [2] Minor diastereomer; [3] Major diastereomer

diastereomers using a silica gel column Spherisorb Si 5 μm (250 × 4.0 mm, Bischoff Chromatography) and a mixture of 70% methylene chloride and 30% hexane as the eluent. The analytical HPLC measurements were performed similar to **5a** and **5b** with increased ethanol content in the eluent in order to decrease the retention times.

The data obtained for the *Michael* adducts **5a–c** are summarized in Table 3. The results of the (−)-quinine catalyzed addition were taken as reference to assign the relative configurations of the adducts **5a–c**, *i.e.* enantiomeric excess values given in parentheses mean favoured formation of the opposite enantiomer. The data given in Table 3 show that the configuration of the prevailing product enantiomer is strongly controlled by the catalyst. (−)-Cinchonidine and (+)-cinchonine exhibit the highest enantioselectivity, and the enantioselectivity for pair 2 (major diastereomer) is universally higher than for pair 1 (minor diastereomer). The highest enantioselectivity is attained for the major diastereomer of **5b** with 46.2% *ee*. Considerably lower enantioselectivity and weaker influence of the catalysts are observed for **5c**.

Experimental

General procedure for Michael additions

The following general procedure for *Michael* additions is based on the solvent methylene chloride since the adducts are only sparingly soluble in toluene, the solvent used for analogous reactions involving α,β-unsaturated carbonyl compounds as *Michael* acceptors.

5 mmol of the nitroalkene were dissolved in 2 ml of absolute methylene chloride. First, 0.05 mmol (1 mol%) of the catalyst and then 10 mmol (1.03 ml) of acetylacetone without solvent or a solution of 5 mmol (951 mg) of methyl 2,3-dihydro-1-oxo-1*H*-indene-2-carboxylate in 2 ml of absolute methylene chloride were added. The volume of the reaction mixture was increased to 5 ml by addition of absolute methylene chloride.

The progress of the reaction was monitored by thin layer chromatography on silica gel precoated plates (Merck Kieselgel 60) using methylene chloride as the eluent, by polarimetry, and by ^{1}H NMR spectroscopy (Varian EM 360L, 60 MHz) using deuterochloroform as the solvent.

Several techniques were used for product isolation. For chemical yield determination, polarimetric, and NMR measurements, the reaction mixture was chromatographed on a silica gel column (25 × 2.5 cm Merck Kieselgel 60) using dry methylene chloride as the eluent which was removed under reduced pressure at about 30 °C. This technique removed the catalyst and polymerization products and separated the unreacted nitroalkene which eluted before the *Michael* addition product. For HPLC determinations, the reaction mixture was filtered through 15 g of silica gel which was then washed with 200 ml of dry methylene chloride, removing the catalyst and polymerization products only.

Diastereomeric products formed by *Michael* addition of methyl 2,3-dihydro-1-oxo-1*H*-indene-2-carboxylate to nitroalkenes were separated by column chromatography on silica gel using diethyl ether/petroleum ether mixtures to characterize the isomers by their NMR spectra.

Racemic products were needed to serve as standards in NMR and HPLC experiments. Catalyzed with 3 mol% of triethylamine, these syntheses were carried out according to the general procedure.

Analytical measurements

^{1}H NMR spectra were recorded in $CDCl_3$ solutions using *TMS* as internal standard on Bruker AC 250 (250 MHz) and Bruker ARX 400 (400 MHz) spectrometers. Optical rotation values were measured on a Perkin-Elmer 241 polarimeter at 589 nm in acetone ($c = 1.0 - 1.10$). IR spectra were recorded on a Beckman AccuLab 2 spectrometer. HPLC purity determinations were performed on a Hewlett-Packard 1084B chromatograph equipped with a Lichrospher Si100 RP18 column (250 × 4.0 mm) using an eluent of 70% methanol and 30% water (1.0 ml/min, 240 bar, UV detection at 254 nm). The Hewlett-Packard 1084B chromatograph was also used for preparative HPLC separations (parameters given in the text). HPLC determinations of enantiomeric purity were performed on a Merck L-6200A chromatograph with UV detection at 200 nm using different chiral columns and eluents (data for each procedure given in the text). Melting points were determined on a Büchi SMP-20 apparatus and are uncorrected.

3-Nitro-1,1-diacetyl-2-phenylpropane (**4a**)

Crystallization of the racemic product from absolute methanol; white crystalline solid; m.p.: 114–115 °C; IR (KBr, cm^{-1}): 1350 (NO_2 sym.), 1535 (NO_2 asym.), 1725 (C=O); ^{1}H NMR (250 MHz, $CDCl_3$, *TMS*): $\delta = 1.94$ (s, 3H, $COCH_3$), 2.29 (s, 3H, $COCH'_3$), 4.25 (ddd, 1H, Ph-CH, ^3J(C(O)-CH-C(O)) = 10.8 Hz, ^3J(C*H*H'-NO_2) = 8.9 Hz, ^3J(CH*H'*-NO_2) = 3.7 Hz), 4.38 (d, 1H, C(O)-CH-C(O), ^3J(Ph-CH) = 10.8 Hz), 4.62 (dd, 1H, C*H*H'-NO_2, ^2J(CHH'-NO_2) = 12.3 Hz, ^3J(Ph-CH) = 3.7 Hz), 4.64 (dd, 1H, CH*H'*-NO_2), ^2J(CHH'-NO_2) = 12.3 Hz, ^3J(Ph-CH) = 8.9 Hz), 7.17–7.37 (m, 5H, C_6H_5) ppm.

3-Nitro-1,1-diacetyl-2-(2-thienyl)pyropane (**4b**)

Crystallization of racemic product from absolute methanol; white crystalline solid; m.p.: 88–89 °C; IR (KBr, cm^{-1}): 1355 (NO_2 sym.), 1540 (NO_2 asym.), 1720 (C=O); ^{1}H NMR (250 MHz, $CDCl_3$, *TMS*): $\delta = 2.08$ (s, 3H, $COCH_3$), 2.30 (s, 3H, $COCH'_3$), 4.40 (d, 1H, C(O)-CH-C(O), ^3J(Ph-CH) = 9.9 Hz), 4.55 (ddd, 1H, C*H*-CHH'-NO_2, ^3J(C(O)-CH-C(O)) = 9.9 Hz, ^3J(C*H*H'-NO_2) = 5.6 Hz, ^3J(CH*H'*-NO_2) = 6.4 Hz), 4.65 (dd, 1H, C*H*H'-NO_2, ^2J(CHH'-NO_2) = 12.4 Hz, ^3J(Ph-CH) = 5.6 Hz), 4.67 (dd,

1H, CH*H'*-NO_2, ^2J(CHH'-NO_2) = 12.4 Hz, ^3J(Ph-CH) = 6.4 Hz), 6.89 (dd, 1H, 2-thienyl 3-H, ^3J(2-thienyl 4-H) = 3.6 Hz, ^4J(2-thienyl 5-H) = 1.3 Hz), 6.94 (dd, 1H, 2-thienyl 4-H, ^3J(2-thienyl 3-H) = 3.6 Hz, ^3J(2-thienyl 5-H) = 5.0 Hz), 7.24 (dd, 1H, 2-thienyl 5-H, ^3J(2-thienyl 4-H) = 5.0 Hz, ^4J(2-thienyl 3-H) = 1.3 Hz) ppm.

3-Nitro-1,1-diacetyl-2-(1-naphthyl)propane (**4c**)

Column chromatography of racemic product (silica gel, eluent: dry methylene chloride); yellow oil; IR (neat, cm^{-1}): 1330 (NO_2 sym.), 1535 (NO_2 asym.), 1700 (C=O); ^{1}H NMR (250 MHz, $CDCl_3$, *TMS*): δ = 1.87 (s, 3H, $COCH_3$), 2.32 (s, 3H, $COCH_3$), 4.71 (d, 1H, C(O)-CH-C(O), ^3J(C*H*-CH_2NO_2) = 10.4 Hz), 4.73 (dd, 1H, C*H*H'-NO_2, ^2J(CHH'-NO_2) = 12.2 Hz, ^3J(C*H*-CH_2NO_2) = 4.8 Hz), 4.82 (dd, 1H, CH*H'*-NO_2, ^2J(CHH'-NO_2) = 12.2 Hz, ^3J(CH-CH_2NO_2) = 6.2 Hz), 5.21 (m, 1H, C*H*-CH_2NO_2); 7.29–8.20 (m, 7H, $C_{10}H_7$) ppm.

Methyl 2,3-dihydro-1-oxo-2-(2-nitro-1-phenylethyl)-1H-indene-2-carboxylate (**5a**)

Separation of the diastereomers by column chromatography on silica gel (Merck Silica Gel 60) using a mixture of diethyl ether and petroleum ether (1:1.5) as eluent; ^{1}H NMR (first eluted diastereomer, 250 MHz, $CDCl_3$, *TMS*): δ = 3.16 (d, 1H, C*H*H' cyclic, ^2J(CHH' cyclic) = 17.6 Hz), 3.49 (d, 1H, CH*H'* cyclic, ^2J(CHH' cyclic) = 17.6 Hz), 3.70 (s, 3H, $COOCH_3$), 4.48 (dd, 1H, Ph-C*H*-CHH'-NO_2, ^3J(C*H*H'-NO_2) = 3.7 Hz, ^3J(CH*H'*-NO_2) = 10.9 Hz), 5.06 (dd, 1H, C*H*H'-NO_2, ^2J(CHH'-NO_2) = 13.4 Hz, ^3J(Ph-CH) = 3.7 Hz), 5.20 (dd, 1H, CH*H'*-NO_2, ^2J(CHH'-NO_2) = 13.4 Hz, ^3J(Ph-CH) = 10.9 Hz), 7.13–7.78 (m, 9H, C_6H_5 and C_6H_4) ppm; ^{1}H NMR (second eluted diastereomer, 250 MHz, $CDCl_3$, *TMS*): δ = 3.21 (d, 1H, C*H*H' cyclic, ^2J(CHH' cyclic) = 17.6 Hz), 3.65 (d, 1H, CH*H'* cyclic, ^2J(CHH' cyclic) = 17.6 Hz), 3.75 (s, 3H, $COOCH_3$), 4.21 (dd, 1H, Ph-C*H*-CHH'-NO_2, ^3J(C*H*H'-NO_2) = 10.8 Hz, ^3J(CH*H'*-NO_2) = 3.7 Hz), 5.20 (dd, 1H, C*H*H'-NO_2, ^2J(CHH'-NO_2) = 13.6 Hz, ^3J(Ph-CH) = 10.8 Hz), 5.44 (dd, 1H, CH*H'*-NO_2, ^2J(CHH'-NO_2) = 13.6 Hz, ^3J(Ph-CH) = 3.7 Hz), 7.13–7.70 (m, 9H, C_6H_5 and C_6H_4) ppm.

Methyl 2,3-dihydro-1-oxo-2-(2-nitro-1-(2-thienyl)ethyl)-1H-indene-2-carboxylate (**5b**)

Separation of the diastereomers by column chromatography on silica gel (Merck Silica Gel 60) using a mixture of diethyl ether and petroleum ether (1:1.5) as eluent; ^{1}H NMR (first eluted diasteromer, 250 MHz, $CDCl_3$, *TMS*): δ = 3.28 (d, 1H, C*H*H' cyclic, ^2J(CHH' cyclic) = 17.5 Hz), 3.59 (d, 1H, CH*H'* cyclic, ^2J(CHH' cyclic) = 17.5 Hz), 3.71 (s, 3H, $COOCH_3$), 4.89 (dd, 1H, C*H*-CHH'-NO_2, ^3J(C*H*H'-NO_2) = 3.2 Hz, ^3J(CH*H'*-NO_2) = 11.4 Hz), 4.92 (dd, 1H, C*H*H'-NO_2, ^2J(CHH'-NO_2) = 13.3 Hz, ^3J(Ph-CH) = 3.2 Hz), 5.06 (dd, 1H, CH*H'*-NO_2, ^2J(CHH'-NO_2) = 13.3 Hz, ^3J(Ph-CH) = 11.4 Hz), 6.80–8.20 (m, 7H, C_6H_4 and C_4H_3S) ppm; ^{1}H NMR (second eluted diastereomer, 250 MHz, $CDCl_3$, *TMS*): δ = 3.30 (d, 1H, C*H*H' cyclic, ^2J(CHH' cyclic) = 17.7 Hz), 3.70 (d, 1H, CH*H'* cyclic, ^2J(CHH' cyclic) = 17.7 Hz), 3.75 (s, 3H, $COOCH_3$), 4.57 (dd, 1H, C*H*-CHH'-NO_2, ^3J(C*H*H'-NO_2) = 10.3 Hz, ^3J(CH*H'*-NO_2) = 3.5 Hz), 5.10 (dd, 1H, C*H*H'-NO_2, ^2J(CHH'-NO_2) = 13.6 Hz, ^3J(Ph-CH) = 10.3 Hz), 5.39 (dd, 1H, CH*H'*-NO_2, ^2J(CHH'-NO_2) = 13.6 Hz, ^3J(Ph-CH) = 3.5 Hz); 7.13–7.70 (m, 7H, C_6H_4 and C_4H_3S) ppm.

Methyl 2,3-dihydro-1-oxo-2-(2-nitro-1-(1-naphthyl)ethyl)-1H-indene-2-carboxylate (**5c**)

Separation of the diastereomers by column chromatography on silica gel (Merck Silica Gel 60) using a mixture of diethyl ether and petroleum ether (1:2) as eluent; ^{1}H NMR (first eluted diastereomer, 250 MHz, $CDCl_3$, *TMS*): δ = 2.96 (d, 1H, C*H*H' cyclic, ^2J(CHH' cyclic) = 17.5 Hz), 3.40 (d, 1H, CH*H'* cyclic, ^2J(CHH' cyclic) = 17.5 Hz), 3.67 (s, 3H, $COOCH_3$), 5.30 (dd, 1H, C*H*H'-NO_2, ^2J(CHH'-NO_2) = 13.6 Hz, ^3J(Ph-CH) = 4.0 Hz), 5.42 (dd, 1H, CH*H'*-NO_2, ^2J(CHH'-NO_2) = 13.6 Hz, ^3J(Ph-CH) = 10.3 Hz), 5.63 (dd, 1H, C*H*-CHH'-NO_2, ^3J(C*H*H'-NO_2) = 4.0 Hz, ^3J(CH*H'*-NO_2) = 10.3 Hz),

7.00–8.40 (m, 11H, C_6H_4 and $C_{10}H_7$) ppm; ^{1}H NMR (second eluted diastereomer, 250 MHz, $CDCl_3$, *TMS*): $\delta = 3.07$ (d, 1H, C*H*H′ cyclic, ^2J(CHH′ cyclic) = 17.8 Hz), 3.55 (d, 1H, CH*H*′ cyclic, ^2J(CHH′ cyclic) = 17.8 Hz), 3.77 (s, 3H, $COOCH_3$), 5.03 (dd, 1H, C*H*-CHH′-NO_2, ^{3}J(C*H*H′-NO_2) = 10.1 Hz, ^3J(CH*H*′-NO_2) = 3.6 Hz), 5.20 (dd, 1H, C*H*H′-NO_2, ^2J(CHH′-NO_2) = 14.0 Hz, ^3J(Ph-CH) = 10.1 Hz), 5.44 (dd, 1H, CH*H*′-NO_2, ^2J(CHH′-NO_2) = 14.0 Hz, ^3J(Ph-CH) = 3.6 Hz), 7.00–8.40 (m, 11H, C_6H_4 and $C_{10}H_7$) ppm.

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