A General Synthesis of 1-Nitro-2-phenyl-4-oxospiro[2.5]octanes

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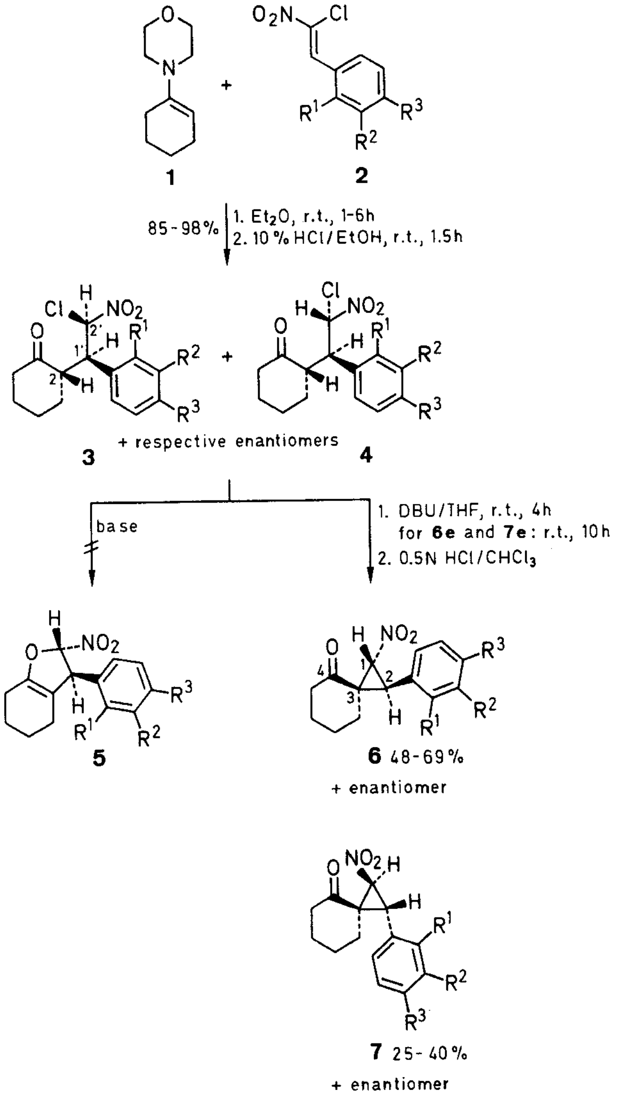
The novel title compounds **6** and **7** were conveniently synthesized by a facile two-step route starting from (2-chloro-2-nitroethenyl)benzenes **2** via the base-induced cyclopropanations of the intermediate 2-(2-chloro-2-nitro-1-phenylethyl)cyclohexanones **3** and **4**.

The condensation of conjugated nitroalkenes with enamines has attracted considerable interest during the past thirty years, and numerous results relevant to this subject have been reported.[1–33] In this context, and in continuation of our investigations devoted to the use of (2-chloro-2-nitroethenyl)benzenes **2** as building blocks to prepare heterocyclic systems,[34–37] we became interested in examining the behavior of these β-chloro-β-nitrostyrenes **2** towards 1-morpholino-1-cyclohexene (**1**).

The present study was undertaken with the aim of exploring an approach to the not easily accessible 3-phenyl-4,5,6,7-tetrahydrobenzofurans. The conceived pathway, involving the preliminary preparation of the novel 2-(2-chloro-2-nitro-1-phenylethyl)cyclohexanones **3** and **4**, supposed the subsequent formation of 2,3,4,5,6,7-hexahydro-2-nitro-3-phenylbenzofurans **5** followed by the loss of a molecule of nitrous acid. Surprisingly, however, the attempted base-promoted cyclizations of the precursors **3** and **4** did not give the expected heterocyclic derivatives **5**, but resulted exclusively in the formation of the hitherto unknown 1-nitro-2-phenyl-4-oxospiro[2.5] octanes as a mixture of the two diastereoisomers **6** and **7** with the relative configurations 1*R**, 2*S**, 3*R** and 1*R**, 2S*, 3*S**, respectively. In this connection, it is worth recalling that, following the earliest work of Kohler,[38] a number of nitrocyclopropane derivatives were prepared using different methods.[39–68] However, to our knowledge, only one report dealt with spiro compounds and described the synthesis of a few products belonging to the series of the 2-aryl-3-nitrospiro[cyclopropane-1,9′-fluorene] starting from 9-diazofluorene and β-nitrostyrenes.[50] The reaction conditions have been optimized, and the 2-(2-chloro-2-nitro-1-phenylethyl)cyclohexanones were readily synthesized in good to excellent yields as a mixture of the two diastereoisomers **3** and **4** by the reaction between 1-morpholino-1-cyclohexene (**1**) and (2-chloro-2-nitroethenyl)benzenes **2** in dry diethyl ether at room temperature, followed by alcoholic hydrolysis of the intrmediate enamine adduct (Table 1). The chromatographed cyclohexanone derivatives **3** and **4** were further treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in anhydrous tetrahydrofuran at 20 °C to provide the title compounds **6** and **7** which were efficiently separated from each other by flash-chromatography (Table 2). The presence of solely two diastereoisomers (among the four possible) in the products of the reaction between 1-morpholino-1-cyclohexene (**1**) and (2-chloro-2-nitroethenyl)benzenes **2** has been inferred from the analysis of the ^{1}H NMR spectra in which each proton 1′-H and 2′-H appears as a group of two, and only two, distinct signals of different intensity. In each case, in spite of the complexity of the rest of the spectrum, the abovementioned signals were sufficiently separated to allow a measurement of the integrations, which permitted evaluation of the relative proportions of the diastereoisomers **3** and **4** (Table 1). In this context, it is noteworthy that several attempted epimerizations at the C-2 carbon of **3** and **4** carried out in the presence of *p*-toluenesulfonic acid in benzene led to complex mixtures, the ^{1}H NMR spectra of which exhibited undistinguishable signals in the resonance area of 1′H and 2′-H, due to the formation of the two other diastereoisomers.



2–7	R^1	R^2	R^3	2–7	R^1	R^2	R^3
a	H	H	H	**f**	H	NO$_2$	H
b	Cl	H	H	**g**	H	H	NO$_2$
c	H	Cl	H	**h**	OMe	H	H
d	H	H	Cl	**i**	H	OMe	H
e	NO$_2$	H	H	**j**	H	H	OMe

Table 1. 2-(2-Chloro-2-nitro-1-phenylethyl)cyclohexanones **3** and **4** Prepared

Products	Time[a] (h)	Yield[b] (%)	Molecular Formula[c]	3/4[d]
3a + **4a**	2	97	$C_{14}H_{16}ClNO_3$ (281.7)	62 : 38
3b + **4b**	1.5	96	$C_{14}H_{15}Cl_2NO_3$ (316.2)	56 : 44
3c + **4c**	3	93	$C_{14}H_{15}Cl_2NO_3$ (316.2)	72 : 28
3d + **4d**	1	98	$C_{14}H_{15}Cl_2NO_3$ (316.2)	60 : 40
3e + **4e**	6	85	$C_{14}H_{15}ClN_2O_5$ (326.7)	81 : 19
3f + **4f**	5	95	$C_{14}H_{15}ClN_2O_5$ (326.7)	76 : 24
3g + **4g**	1.5	90	$C_{14}H_{15}ClN_2O_5$ (326.7)	67 : 33
3h + **4h**	3	98	$C_{15}H_{18}ClNO_4$ (311.8)	64 : 36
3i + **4i**	1.5	95	$C_{15}H_{18}ClNO_4$ (311.8)	69 : 31
3j + **4j**	4	93	$C_{15}H_{18}ClNO_4$ (311.8)	79 : 21

[a] The reactions were monitored by TLC (eluent $CHCl_3$).
[b] Yield of chromatographed product obtained as a mixture of diastereoisomers.
[c] Satisfactory microanalyses obtained: C ±0.25, H ±0.09, N ±0.10.
[d] Determined by ^1H NMR analyses of the chromatographed products.

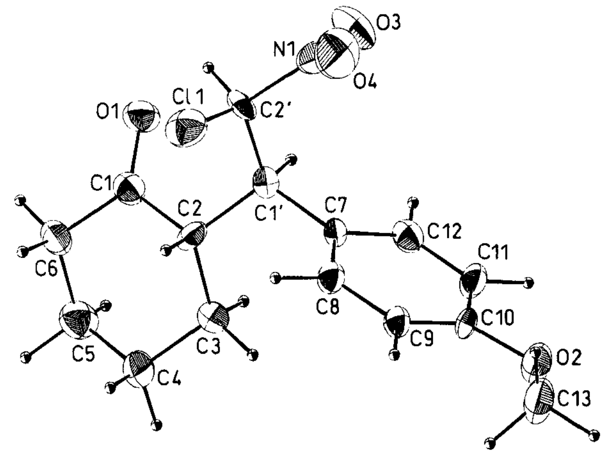


Figure 1. X-ray Crystal Structure of **3j** with Atomic Labeling

This route to the spiro derivatives **6** and **7** has been investigated starting from a large range of β-chloro-β-nitrostyrenes **2** bearing either electron-donating groups or electron-withdrawing substituents, and proved quite general.

As an example, in order to examine the possible influence of the stereochemistry of the intermediates **3** or **4** on the relative proportions of the end products **6** and **7**, we have selectively prepared the 2-[2-chloro-1-(4-methoxyphenyl)-2-nitroethyl]cyclohexanone (**3j**) with the relative configuration [2*R**(1*R**,2*S**)] to the exclusion of its epimer having the relative configuration [2*R**(1R*,2*R**)] (**4j**). This product has been conveniently obtained pure by performing the condensation between 1-morpholino-1-cyclohexene (**1**) and 1-(2-chloro-2-nitroethenyl)-4-methoxybenzene (**2j**) in diethyl ether at −20 °C instead of +20 °C. The subsequent treatment of the above described diastereoisomer **3j** with DBU in tetrahydrofuran at room temperature provided the two isomers **6j** and **7j** in 50% and 37% yields, respectively. The comparison of these yields with those obtained starting from the mixture of diastereoisomers reported in Table 2 (52% and 39%, respectively) obviously shows that the stereochemistry of the precursors **3** or **4** has practically no effect on the ratio observed for the isomers **6** and **7**.

The relative configuration [2*R**(1*R**,2*S**)] for the stereoselectively synthesized compound **3j** has been ascertained using X-ray diffraction analysis (Figure 1). The relative configuration of the two chiral carbons C-2 and C-1′ is a consequence of the (*Re** *Re**)-approach of the reactants, which is quite consistent with the previously reported results dealing with the Michael-additions of enamines derived from cyclic ketones to nitroolefins.[5,8,12–14,20,21,23,24,26,28,31,32] Taking into consideration this (*Re** *Re**)-approach, it becomes evident that the minor diastereoisomers **4j**, and therefore all the products **4a–j** have the relative configuration [2*R**(1*R**,2*R**)].

The structures of the spiro derivatives **6** and **7** have also been unambiguously evidenced by X-ray crystallography, as depicted in Figures 2 and 3, relative to the isomeric 2-(2-chlorophenyl)-1-nitro-4-oxo-spiro[2.5]octanes (**6b**) and (**7b**), respectively selected as representatives of their classes of compounds. Furthermore, the *trans* configura-

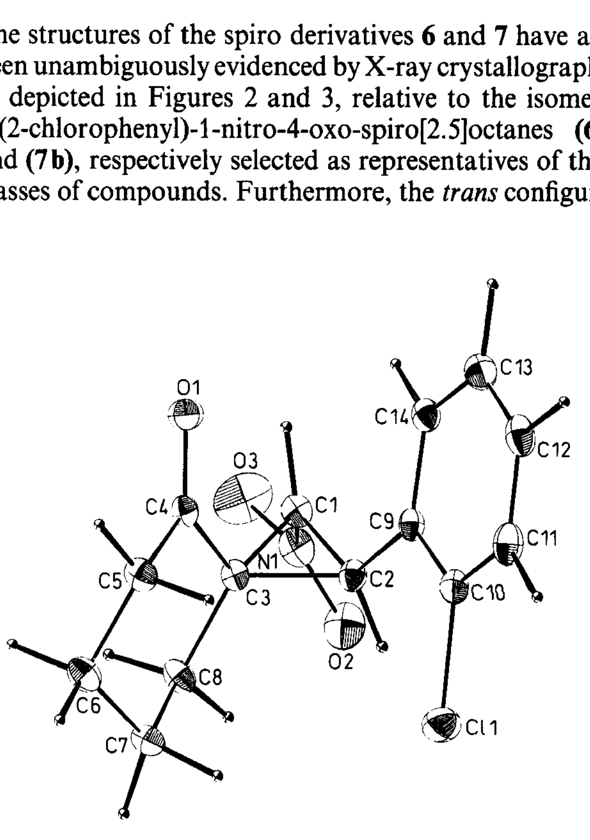


Figure 2. X-ray Crystal Structure of **6b** with Atomic Labeling

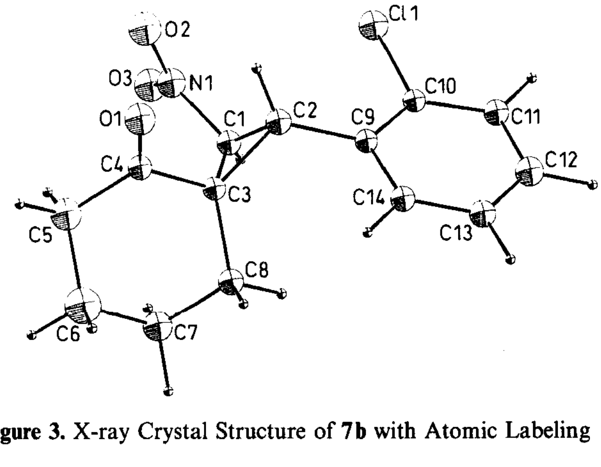


Figure 3. X-ray Crystal Structure of **7b** with Atomic Labeling

Table 2. 1-Nitro-2-phenyl-4-oxospiro[2.5]octanes **6** and **7** Prepared

Product	Yield[a] (%)	mp (°C) (solvent)	Molecular Formula[b]	IR ($CHCl_3$) $\nu_{C=0}$ (cm^{-1})	^1H NMR ($CDCl_3$/TMS) δ, J (Hz)
6a	53	81–82.5 (hexane)	$C_{14}H_{15}NO_3$ (245.3)	1705	1.45–2.58 (m, 8H), 3.55 (d, 1H, $J = 5.6$), 5.60 (d, 1H, $J = 5.6$), 6.98–7.42 (m, 5H)
7a	40	89–90 (heptane)	$C_{14}H_{15}NO_3$ (245.3)	1719	1.08–2.82 (m, 8H), 4.10 (d, 1H, $J = 5.2$), 4.60 (d, 1H, $J = 5.2$), 7.10–7.48 (m, 5H)
6b	69	126–127 (cyclohexane)	$C_{14}H_{14}ClNO_3$ (279.7)	1704	1.46–2.57 (m, 8H), 3.72 (d, 1H, $J = 5.6$), 5.61 (d, 1H, $J = 5.6$), 6.94–7.50 (m, 4H)
7b	25	98–99 (hexane/cyclohexane)	$C_{14}H_{14}ClNO_3$ (279.7)	1722	1.08–2.87 (m, 8H), 4.10 (d, 1H, $J = 5.4$), 4.55 (d, 1H, $J = 5.4$), 7.07–7.52 (m, 4H)
6c	50	91.5–92.5 (hexane/cyclohexane)	$C_{14}H_{14}ClNO_3$ (279.7)	1706	1.11–2.57 (m, 8H), 3.52 (d, 1H, $J = 5.4$), 5.57 (d, 1H, $J = 5.4$), 6.85–7.32 (m, 4H)
7c	29	68–69 (hexane)	$C_{14}H_{14}ClNO_3$ (279.7)	1721	1.07–2.82 (m, 8H), 4.08 (d, 1H, $J = 5.1$), 4.59 (d, 1H, $J = 5.1$), 6.98–7.40 (m, 4H)
6d	56	119–120 (cyclohexane)	$C_{14}H_{14}ClNO_3$ (279.7)	1704	1.45–2.57 (m, 8H), 3.52 (d, 1H, $J = 5.4$), 5.56 (d, 1H, $J = 5.4$), 7.02 and 7.26 (AA'BB' system, 4H)
7d	32	93–94 (hexane/cyclohexane)	$C_{14}H_{14}ClNO_3$ (279.7)	1719	1.02–2.80 (m, 8H), 4.05 (d, 1H, $J = 5.1$), 4.56 (d, 1H, $J = 5.1$), 7.12 and 7.30 (AA'BB' system, 4H)
6e	53	113.5–115 (hexane)	$C_{14}H_{14}N_2O_5$ (290.3)	1701	1.23–2.57 (m, 8H), 4.01 (d, 1H, $J = 5.7$), 5.54 (d, 1H, $J = 5.7$), 7.20–7.73 (m, 3H), 7.92–8.08 (m, 1H)
7e	31	102–103.5 (hexane)	$C_{14}H_{14}N_2O_5$ (290.3)	1721	1.01–2.90 (m, 8H), 4.45 (d, 1H, $J = 5.4$), 4.55 (d, 1H, $J = 5.4$), 7.35–7.92 (m, 3H), 8.00–8.20 (m, 1H)
6f	66	152–153 (benzene/heptane)	$C_{14}H_{14}N_2O_5$ (290.3)	1706	1.18–2.67 (m, 8H), 3.65 (d, 1H, $J = 5.4$), 5.65 (d, 1H, $J = 5.4$), 7.32–7.68 (m, 2H), 7.98–8.28 (m, 2H)
7f	26	98.5–100 (benzene/hexane)	$C_{14}H_{14}N_2O_5$ (290.3)	1723	1.10–2.87 (m, 8H), 4.21 (d, 1H, $J = 5.1$), 4.71 (d, 1H, $J = 5.1$), 7.45–7.73 (m, 2H), 8.00–8.32 (m, 2H)
6g	59	138.5–139.5 (benzene/hexane)	$C_{14}H_{14}N_2O_5$ (290.3)	1709	1.20–2.63 (m, 8H), 3.61 (d, 1H, $J = 5.5$), 5.63 (d, 1H, $J = 5.5$), 7.28 and 8.13 (AA'BB' system, 4H)
7g	32	152–153 (benzene/hexane)	$C_{14}H_{14}N_2O_5$ (290.3)	1722	1.10–2.83 (m, 8H), 4.19 (d, 1H, $J = 5.0$), 4.67 (d, 1H, $J = 5.0$), 7.40 and 8.21 (AA'BB' system, 4H)
6h	67	116–117 (cyclohexane)	$C_{15}H_{17}NO_4$ (275.3)	1703	1.50–2.45 (m, 8H), 3.61 (d, 1H, $J = 5.5$), 3.88 (s, 3H), 5.56 (d, 1H, $J = 5.5$), 6.73–7.07 (m, 3H), 7.10–7.38 (m, 1H)
7h	28	oil	$C_{15}H_{17}NO_4$ (275.3)	1719	1.15–2.82 (m, 8H), 3.83 (s, 3H), 3.95 (d, 1H, $J = 5.4$), 4.50 (d, 1H, $J = 5.4$), 6.77–7.42 (m, 4H)
6i	48	77–78.5 (hexane)	$C_{15}H_{17}NO_4$ (275.3)	1707	1.50–2.55 (m, 8H), 3.53 (d, 1H, $J = 5.3$), 3.78 (s, 3H), 5.58 (d, 1H, $J = 5.3$), 6.52–6.88 (m, 3H), 7.07–7.36 (m, 1H)
7i	38	oil	$C_{15}H_{17}NO_4$ (275.3)	1720	1.10–1.82 (m, 8H), 3.79 (s, 3H), 4.08 (d, 1H, $J = 5.2$), 4.58 (d, 1H, $J = 5.2$), 6.66–6.92 (m, 3H), 7.10–7.37 (m, 1H)
6j	52	86.5–88 (hexane)	$C_{15}H_{17}NO_4$ (275.3)	1704	1.43–2.57 (m, 8H), 3.50 (d, 1H, $J = 5.4$), 3.75 (s, 3H), 5.55 (d, 1H, $J = 5.4$), 6.76 and 7.01 (AA'BB' system, 4H)
7j	39	99–100 (benzene/hexane)	$C_{15}H_{17}NO_4$ (275.3)	1719	1.10–2.85 (m, 8H), 3.78 (s, 3H), 4.02 (d, 1H, $J = 5.0$), 4.53 (d, 1H, $J = 5.0$), 6.82 and 7.11 (AA'BB' system, 4H)

[a] Yield of pure chromatographed product.

[b] Satisfactory microanalyses obtained: C ±0.21, H ±0.11, N ±0.10.

tion at C-1 and C-2 in the cyclopropane ring is consistent with the rather weak ^3J coupling constants (5.0–5.7 Hz[69] observed between 1-H and 2-H in the ^1H NMR spectra. It is worth pointing out that, in the cases of compounds **3b**, **4b**, **6b** and **7b**, the CIP assignment of the chiral center bearing the 2-chlorophenyl residue requires a formal inversion due to the chlorine being higher in priority than oxygen.

Starting (2-chloro-2-nitroethenyl)benzenes **2a–j** were prepared according to a previously described procedure.[35] DBU and 1-morpholino-1-cyclohexane (**1**) were purchased from Aldrich Chemical Company and were used without further purification. Et_2O and THF were dried before use by distillation from benzophenone/sodium. Melting points were measured on a Kofler hot-stage apparatus and are uncorrected. IR spectra were obtained using a Perkin-Elmer 1710 spectrophotometer as $CHCl_3$ solutions. ^1H NMR spectra were recorded at 90 MHz using a Varian EM 390 spectrometer or at 200 MHz with a Bruker AC200 apparatus. The mass spectrum of **3j** was obtained using a Nermag Ribermag R10-10C spectrometer. Microanalysis were performed by the "Service d'Analyse du CNRS", Vernaison. TLC was performed with Merck silica gel $60F_{254}$, TLC plates (200 μ).

Table 3. Bond Lengths (Å) and Angles (deg) for **3j**

Atoms, Molecule 1		Atoms, Molecule 2	
Cl(1)–C(2)′	1.755(9)	Cl(1)–C(2)′	1.763(9)
O(1)–C(1)	1.21(1)	O(1)–C(1)	1.20(1)
O(2)–C(10)	1.388(9)	O(2)–C(10)	1.36(1)
O(2)–C(13)	1.42(1)	O(2)–C(13)	1.40(1)
O(3)–N(1)	1.16(1)	O(3)–N(1)	1.23(1)
O(4)–N(1)	1.23(1)	O(4)–N(1)	1.18(1)
N(1)–C(2)′	1.51(1)	N(1)–C(2)′	1.51(1)
C(1)–C(2)	1.53(1)	C(1)–C(2)	1.52(1)
C(1)–C(6)	1.49(1)	C(1)–C(6)	1.53(1)
C(1)′–C(2)′	1.55(1)	C(1)′–C(2)′	1.55(1)
C(1)′–C(7)	1.52(1)	C(1)′–C(7)	1.52(1)
C(2)–C(3)	1.54(1)	C(2)–C(3)	1.55(1)
C(2)–C(1)′	1.53(1)	C(2)–C(1)′	1.53(1)
C(3)–C(4)	1.52(1)	C(3)–C(4)	1.51(1)
C(4)–C(5)	1.52(1)	C(4)–C(5)	1.54(1)
C(5)–C(6)	1.53(1)	C(5)–C(6)	1.54(1)
C(7)–C(8)	1.40(1)	C(7)–C(8)	1.39(1)
C(7)–C(12)	1.40(1)	C(7)–C(12)	1.39(1)
C(8)–C(9)	1.30(1)	C(8)–C(9)	1.38(1)
C(9)–C(10)	1.37(1)	C(9)–C(10)	1.37(1)
C(10)–C(11)	1.38(1)	C(10)–C(11)	1.39(1)
C(11)–C(12)	1.38(1)	C(11)–C(12)	1.38(1)
C(13)–O(2)–C(10)	117.9(7)	C(13)–O(2)–C(10)	118.0(9)
O(4)–N(1)–O(3)	124.5(12)	O(4)–N(1)–O(3)	124.1(10)
C(2)′–N(1)–O(3)	118.0(10)	C(2)′–N(1)–O(3)	119.5(10)
C(2)′–N(1)–O(4)	117.5(10)	C(2)′–N(1)–O(4)	116.4(10)
C(2)–C(1)–O(1)	120.9(8)	C(2)–C(1)–O(1)	122.3(9)
C(6)–C(1)–O(1)	123.5(9)	C(6)–C(1)–O(1)	121.3(10)
C(6)–C(1)–C(2)	115.5(8)	C(6)–C(1)–C(2)	116.4(9)
C(2)′–C(1)′–C(2)	110.2(6)	C(2)′–C(1)′–C(2)	110.3(7)
C(7)–C(1)′–C(2)	113.7(7)	C(7)–C(1)′–C(2)	113.8(7)
C(7)–C(1)′–C(2)′	113.7(7)	C(7)–C(1)′–C(2)′	113.2(7)
C(3)–C(2)–C(1)	107.3(7)	C(3)–C(2)–C(1)	107.2(7)
C(1)–C(2)–C(1)′	112.8(7)	C(1)–C(2)–C(1)′	112.1(7)
C(1)′–C(2)–C(3)	112.8(7)	C(1)′–C(2)–C(3)	111.3(7)
N(1)–C(2)′–Cl(1)	110.6(7)	N(1)–C(2)′–Cl(1)	109.5(7)
C(1)′–C(2)′–Cl(1)	115.7(6)	C(1)′–C(2)′–Cl(1)	115.3(6)
C(1)′–C(2)′–N(1)	108.4(7)	C(1)′–C(2)′–N(1)	108.6(7)
C(4)–C(3)–C(2)	112.2(7)	C(4)–C(3)–C(2)	111.7(8)
C(5)–C(4)–C(3)	112.1(8)	C(5)–C(4)–C(3)	112.3(8)
C(6)–C(5)–C(4)	110.4(8)	C(6)–C(5)–C(4)	109.3(8)
C(5)–C(6)–C(1)	111.5(8)	C(5)–C(6)–C(1)	110.6(8)
C(8)–C(7)–C(1)	123.4(7)	C(8)–C(7)–C(1)	118.4(8)
C(12)–C(7)–C(1)	119.4(8)	C(12)–C(7)–C(1)	123.5(8)
C(12)–C(7)–C(8)	117.1(8)	C(12)–C(7)–C(8)	118.0(8)
C(9)–C(8)–C(7)	121.2(8)	C(9)–C(8)–C(7)	120.2(9)
C(10)–C(9)–C(8)	119.1(8)	C(10)–C(9)–C(8)	121.2(9)
C(9)–C(10)–O(2)	124.8(8)	C(9)–C(10)–O(2)	115.7(10)
C(11)–C(10)–O(2)	113.6(8)	C(11)–C(10)–O(2)	124.7(10)
C(11)–C(10)–C(9)	121.6(8)	C(11)–C(10)–C(9)	119.6(9)
C(12)–C(11)–C(10)	118.5(8)	C(12)–C(11)–C(10)	118.9(9)
C(11)–C(12)–C(7)	122.4(8)	C(11)–C(12)–C(7)	122.0(9)

Table 4. Bond Lengths (Å) and Angles (deg) for **6b**

Atoms		Atoms	
Cl(1)–C(10)	1.752(4)	O(1)–C(4)	1.217(4)
O(2)–N(1)	1.213(5)	O(3)–N(1)	1.204(5)
N(1)–C(1)	1.475(5)	C(1)–C(2)	1.493(5)
C(1)–C(3)	1.510(5)	C(2)–C(9)	1.495(5)
C(2)–C(3)	1.547(5)	C(3)–C(4)	1.495(5)
C(3)–C(8)	1.527(5)	C(4)–C(5)	1.499(6)
C(5)–C(6)	1.530(6)	C(6)–C(7)	1.511(6)
C(7)–C(8)	1.525(6)	C(9)–C(10)	1.379(5)
C(9)–C(14)	1.397(5)	C(10)–C(11)	1.390(6)
C(11)–C(12)	1.379(6)	C(12)–C(13)	1.372(6)
C(13)–C(14)	1.394(6)		
O(3)–N(1)–O(2)	123.6(5)	C(1)–N(1)–O(2)	120.1(4)
C(1)–N(1)–O(3)	116.1(4)	C(3)–C(2)–C(1)	59.6(2)
C(9)–C(2)–C(1)	122.1(3)	C(9)–C(2)–C(3)	121.8(3)
C(2)–C(1)–N(1)	118.8(4)	C(3)–C(1)–N(1)	117.4(3)
C(3)–C(1)–C(2)	62.0(3)	C(1)–C(3)–C(2)	58.4(2)
C(4)–C(3)–C(2)	115.4(3)	C(4)–C(3)–C(1)	115.1(3)
C(8)–C(3)–C(2)	118.9(3)	C(8)–C(3)–C(1)	121.5(3)
C(8)–C(3)–C(4)	115.6(3)	C(3)–C(4)–O(1)	122.2(4)
C(5)–C(4)–O(1)	122.2(4)	C(5)–C(4)–C(3)	115.5(3)
C(6)–C(5)–C(4)	113.5(4)	C(7)–C(6)–C(5)	111.3(4)
C(8)–C(7)–C(6)	111.2(4)	C(7)–C(8)–C(3)	110.5(3)
C(10)–C(9)–C(2)	120.3(4)	C(14)–C(9)–C(2)	122.4(4)
C(14)–C(9)–C(10)	117.2(4)	C(9)–C(10)–Cl(1)	119.4(3)
C(11)–C(10)–Cl(1)	117.5(4)	C(11)–C(10)–C(9)	123.1(4)
C(12)–C(11)–C(10)	118.3(4)	C(13)–C(12)–C(11)	120.5(4)
C(14)–C(13)–C(12)	120.4(4)	C(13)–C(14)–C(9)	120.5(4)

Table 5. Bond Lengths (Å) and Angles (deg) for **7b**

Atoms		Atoms	
Cl(1)–C(10)	1.75(1)	O(1)–C(4)	1.21(1)
O(2)–N(1)	1.24(1)	O(3)–N(1)	1.24(1)
N(1)–C(1)	1.46(2)	C(1)–C(2)	1.49(2)
C(1)–C(3)	1.49(2)	C(2)–C(9)	1.51(2)
C(2)–C(3)	1.52(2)	C(3)–C(4)	1.51(2)
C(3)–C(8)	1.53(2)	C(4)–C(5)	1.51(2)
C(5)–C(6)	1.51(2)	C(6)–C(7)	1.56(2)
C(7)–C(8)	1.53(2)	C(9)–C(10)	1.38(2)
C(9)–C(14)	1.39(2)	C(10)–C(11)	1.40(2)
C(11)–C(12)	1.38(2)	C(12)–C(13)	1.39(2)
C(13)–C(14)	1.37(2)		
O(3)–N(1)–O(2)	120.6(13)	C(1)–N(1)–O(2)	118.6(12)
C(1)–N(1)–O(3)	120.7(13)	C(3)–C(1)–C(2)	61.5(9)
C(2)–C(1)–N(1)	120.3(12)	C(3)–C(1)–N(1)	121.7(11)
C(9)–C(2)–C(1)	118.1(12)	C(9)–C(2)–C(3)	123.4(12)
C(3)–C(2)–C(1)	59.0(8)	C(1)–C(3)–C(2)	59.5(8)
C(4)–C(3)–C(2)	116.8(11)	C(4)–C(3)–C(1)	117.7(11)
C(8)–C(3)–C(2)	124.2(13)	C(8)–C(3)–C(1)	115.9(12)
C(8)–C(3)–C(4)	112.6(12)	C(3)–C(4)–O(1)	122.9(13)
C(5)–C(4)–O(1)	122.6(14)	C(5)–C(4)–C(3)	114.5(12)
C(6)–C(5)–C(4)	110.7(15)	C(7)–C(6)–C(5)	113.3(17)
C(8)–C(7)–C(6)	109.7(13)	C(7)–C(8)–C(3)	109.6(12)
C(10)–C(9)–C(2)	119.5(11)	C(14)–C(9)–C(2)	122.8(12)
C(14)–C(9)–C(10)	117.6(12)	C(9)–C(10)–Cl(1)	120.4(9)
C(11)–C(10)–Cl(1)	116.1(10)	C(11)–C(10)–C(9)	123.4(12)
C(12)–C(11)–C(10)	117.1(13)	C(13)–C(12)–C(11)	120.6(14)
C(14)–C(13)–C(12)	120.8(14)	C(13)–C(14)–C(9)	120.4(13)

2-(2-Chloro-2-nitro-1-phenylethyl)cyclohexanones 3a–j and 4a–j; General Procedure:

A solution of 1-morpholino-1-cyclohexene (**1**; 4.60 g, 27.5 mmol) in anhydr. Et_2O (100 mL) was prepared in a dried, Ar-filled, 250 mL round-bottomed flask and stirred with a magnetic bar. The appropriate (2-chloro-2-nitroethenyl)benzene **2a–j** (25 mmol) was added portionwise over a period of about 10 min. The mixture was stirred at r. t. for the reported times (Table 1), monitoring the progress of the reaction by TLC (silica gel, eluent $CHCl_3$). The volatiles were then removed in vacuo using a rotary evaporator avoiding excessive heating (below 30 °C). The residue was taken up with EtOH (50 mL), then 1 N HCl (50 mL). The mixture was stirred afterwards at r. t. for 1.5 h. $CHCl_3$ (150 mL) was added, and the lower phase was separated. The upper layer was extracted with $CHCl_3$ (3 × 30 mL).

The combined $CHCl_3$ extracts were washed with H_2O (3 × 20 mL), dried ($MgSO_4$), filtered, then evaporated under reduced pressure and gave a crude product, which was chromatographed on a silica gel column (150 g, 230–400 mesh ASTM, eluent $CHCl_3$). Evaporation of the solvent gave analytically correct mixtures of diastereomers **3a–j** and **4a–j** which could be used directly in the subsequent reactions (Table 1). However, it should be noted that, in most cases, the chromatographed products were solid and could be recrystallized from hexane (**3h** and **4b**), or a hexane/cyclohexane mixture (**3a** and **4a, 3b** and **4b, 3d** and **4d, 3j** and **4j**) or a benzene/cyclohexane mixture (**3e–g** and **4e–g**).

(±)-(2*R**)-2-[(1*R**,2*S**)-2-Chloro-1-(4-methoxyphenyl)-2-nitroethyl]cyclohexanone (3j):

This compound was obtained starting from 1-morpholino-1-cyclohexene (**1**; 4.60 g, 27.5 mmol) and 1-(2-chloro-2-nitroethenyl)-4-methoxybenzene (**2**, 5.34 g, 25 mmol) according to the above described procedure, but maintaining the mixture at – 20 °C instead of r.t. The chromatographed product (7.31 g) was recrystallized to give pure **3j**; yield: 6.01 g (77 %); mp 113–114.5 °C (hexane/cyclohexane).

		C	H	N
$C_{15}H_{18}ClNO_4$	calc.	57.79	5.82	4.49
(311.8)	found	57.63	5.86	4.44

MS (EI, 70 eV): m/z = 311, 313 (M^+).

IR ($CHCl_3$): ν = 1709 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$/TMS): δ = 0.97–2.63 (m, 8 H), 2.77–3.33 (m, 1 H), 3.77 (s, 3 H), 4.03 (dd, 1 H, J = 4.4, 10.5 Hz), 6.91 (d, 1 H, J = 4.4 Hz), 6.82, 7.13 (AA′BB′system, 4 H).

1-Nitro-2-phenyl-4-oxospiro[2.5]octanes 6a–j and 7a–j; General Procedure:

The appropriate couple of diastereoisomeric 2-(2-chloro-2-nitro-1-phenylethyl)cyclohexanone **3a–j** and **4a–j** (5 mmol) were placed in a flame-dried 100-mL round-bottomed flask containing a magnetic stirring bar and fitted with a septum inlet. This material was dissolved in anhydr. THF (25 mL) under inert atmosphere, then DBU (0.837 g, 0.823 mL, 5.5 mmol) was added in one portion with a syringe. The mixture was efficiently stirred at r.t. for 4 h whilst a precipitate appeared. After this time, 0.5 N HCl (20 mL) and $CHCl_3$ (50 mL) were successively poured in the flask. The organic layer was separated and the aqueous phase was extracted with $CHCl_3$ (3 × 20 mL). The combined organic extracts were dried ($MgSO_4$), filtered, then evaporated under reduced pressure to provide a crude product, which was flash-chromatographed over a silica gel column (100 g, 230–400 mesh ASTM, eluent $CHCl_3$/cyclohexane, 2:1). Evaporation of the solvents in vacuo gave pure products **6a–j** and **7a–j** in the reported yields (Table 2).

Starting from the couple of nitro-derivatives **3e** and **4e**, using the above conditions, the medium became pasty and difficult to stir. In this case, it was advisable to carry out the reaction in a 250-mL round-bottomed flask. Starting material (1.62 g, 5 mmol) was then dissolved in THF (50 mL), the time is prolonged to 10 h, and $CHCl_3$ (125 mL) were employed instead of 50 mL in the subsequent work-up.

X-ray Diffraction Studies of 3j, 6b and 7b:

Crystal Data:

3j: monoclinic; space group $P2_1/n$; unit cell a = 19.255, b = 17.094, c = 9.786 Å; β = 103.65 deg.; V = 3130 $Å^3$; μ = 2.6 cm^{-1}; ρ_{calc} = 1.32 g cm^{-3}; Z = 8.

6b: monoclinic; space group $P2_1/a$; unit cell a = 10.022, b = 17.067, c = 8.043 Å; β = 102.14 deg.; V = 1344.9 $Å^3$; μ = 2.8 cm^{-1}; ρ_{calc} = 1.38 g cm^{-3}; Z = 4.

7b: orthorhombic; space group $P2_1ca$; unit cell a = 12.521, b = 11.897, c = 9.009 Å; V = 1342.0 $Å^3$; μ = 2.8 cm^{-1}; ρ_{calc} = 1.38 g cm^{-3}; Z = 4.

Parameters obtained from least squares refinement of twenty-five reflections in the 11–12 deg. Θ range for **3j** and **7b**, in the 15–16 deg. Θ range for **6b**.

Data Collection: The crystal sizes were respectively 0.65 × 0.40 × 0.25 mm for **3j**, 0.65 × 0.50 × 0.25 mm for **6b**, 0.65 × 0.45 × 0.25 mm for **7b**; Philips PW 1100 diffractometer, MoK_α radiation (λ = 0.71073 Å) and graphite monochromator; 2136 independent reflections for **3j**, 1839 for **6b** and 949 for **7b** in the ranges $1 \leq \Theta \leq 20$ deg. for **3j**, or $1 \leq \Theta \leq 25$ deg. for **6b** and **7b** were measured; ω-2Θ scan mode; scan width (1.3 + 0.34 tanΘ) deg. for **3j**, (1.0 + 0.34 tanΘ) deg. for **6b** and (0.90 + 0.34 tanΘ) deg. for **7b**; no absorption correction as suggested by a flat psi-scan.

Structure resolution and refinement: The three structures were solved by direct methods and subsequent Fourier maps. An empiric absorption correction was applied with DIFABS[70] from CRYSTALS.[71] Refinements were carried out by least squares methods in several blocks with 1383 reflections for **3j**, 1206 reflections for **6b** and 512 reflections for **7b** [$I \geq 3\,\sigma(I)$]. With regard to **3j** and **6b**, all non-hydrogen atoms were refined anisotropically, whilst, for **7b**, only isotropic refinement could be carried out because of the few number of reflections collected. For **6b**, the hydrogen atoms positions were found on difference maps but not refined. In the cases of **3j** and **7b** the hydrogen atoms positions were geometrically located. In each study, an overall isotropic parameter was given for hydrogen atoms. Secondary extinction correction was not necessary. The refinements converged respectively at R = 0.063, $R_w = [\Sigma_w (\Delta F)^2/\Sigma_w F_0^2]^{1/2}$ = 0.060 for **3j**, at R = 0.043, R_w = 0.042 for **6b** and at R = 0.061, R_w = 0.060 for **7b**. The final difference maps showed no significant feature. Interatomic bond lengths and bond angles for non-hydrogen atoms are listed in Tables 3, 4 and 5. In the case of **3j**, two molecules exist in the asymetric unit, therefore two sets of parameters are reported.[72]

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