From 3,4-Dinitrothiophene to Nitrocyclopropanes and 1,1′-Dinitro-1,1′-bi(cyclopropyl) Compounds[‡]

Tiziana Armaroli,[a] Carlo Dell'Erba,[a] Antonella Gabellini,[a] Francesco Gasparrini,[b] Angelo Mugnoli,[a] Marino Novi,[a] Giovanni Petrillo,*[a] and Cinzia Tavani[a]

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Treatment of (*E*,*E*)-1,4-diaryl-2,3-dinitro-1,3-butadienes **1a**–**f** with diazomethane in Et_2O or THF represents a facile and high-yielding route to 2,2′-diaryl-1,1′-dinitro-1,1′-bi(cyclopropyl)s **2**. The process exclusively produces diastereomeric mixtures of a chiral *d,l* pair and a *meso* form, the relative percentages of which depend on the aryl moiety, consistently with a concerted *syn*-stereoselective cyclopropanation of each double bond. With 1 mol-equiv. of CH_2N_2, the cyclopropanation can effectively be limited to one double bond of the starting dinitrobutadiene, thus allowing a synthetically useful differentiation between the two originally conjugated nitrovinyl moieties. As verified with model derivatives, the resulting vinylcyclopropanes **3** can be cyclopropanated with excess diazomethane to give the same diastereomeric mixtures as obtained by direct bis(cyclopropanation) of **1**.

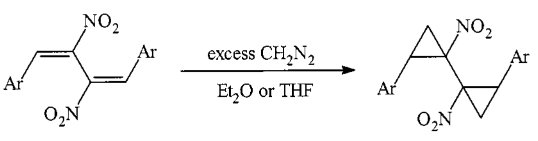
The cyclopropane ring represents a carbocyclic moiety of varied and undeniably well-established relevance both in synthesis and in the vast field of biologically active molecules.[1] Thus, recent reports deal with, for instance, the participation of such small ring systems in drugs endowed with anti-cancer activity,[2] in antagonists of glutamate receptors[3] and in amino acids of natural or synthetic origin,[4] to which the conformationally constrained three-carbon structure imparts interesting biological properties. Nitrocyclopropyl moieties, in particular, represent the essential feature of active molecules such as, for example, nitropyrethroids[5a] and the naturally occurring peptido lactone hormaomycin.[5b] Moreover, the recent identification of polycyclopropane arrays in a protein inhibitor[6a] and in an antifungal antibiotic[6b] has in turn fostered considerable efforts in search of suitable stereoselective approaches to such structural units in the last decade.[6]

In the light of this interest in cyclopropane moieties and in the context of a longstanding project on the synthetic exploitation of the ring-opening of 3,4-dinitrothiophene,[7] we have undertaken a chemical and stereochemical study of both mono- and bis(cyclopropanation) of 1,4-diaryl-2,3-dinitro-1,3-butadienes **1** (easily available by a standardised two-step procedure from 3,4-dinitrothiophene[8]) with diazomethane. As a matter of fact, it is well known that alkenes in general and 1-nitroalkenes in particular undergo cyclopropanation with carbenes or carbenoid species:[9] a reaction that continues to be the subject of numerous investigations and of extensive mechanistic discussions concerning, for example, the stereochemical outcome and its dependence on the experimental conditions (thermal, photochemical or metal catalysis) employed.[9]

Results and Discussion

Treatment of 1,4-Bis(4-methylphenyl)-2,3-dinitro-1,3-butadiene (1a) with Excess Diazomethane: Identification of Products and Mechanistic Aspects

Treatment of the (*E*,*E*)-1,4-bis(4-methylphenyl)-2,3-dinitro-1,3-butadiene (**1a**) with excess diazomethane (5 mol-equiv.) in anhydrous Et_2O smoothly afforded a final mixture essentially constituted (TLC) of two products (Scheme 1).



(*E*,*E*)-**1** **a**: Ar = *p*-tolyl **2**

Scheme 1

[‡] Synthetic Exploitation of the Ring-Opening of 3,4-Dinitrothiophene, XI. – Part X: Ref.[7a]

[a] Dipartimento di Chimica e Chimica Industriale, Università di Genova,
Via Dodecaneso 31, 16146 Genova, Italy
Fax: (internat.) + 39-010/353-6118
E-mail: petrillo@chimica.unige.it
[b] Dipartimento di Studi di Chimica e Tecnologia delle Sostanze Biologicamente Attive, Università "La Sapienza",
Piazzale Aldo Moro 5, 00185 Roma, Italy

^1H NMR analysis of the crude reaction mixture showed the presence of multiplet systems reasonably attributable to the cyclopropane rings of two isomeric bi(cyclopropyl) derivatives. From the stereochemical point of view, as a matter of fact, the reaction shown in Scheme 1 is characterized by the generation of two pairs of chemically equivalent stereocentres, giving rise in principle to six pairs of enantiomers and two *meso* forms. Actually, stereoselective HPLC analysis of the crude residue on chiral columns with UV and CD detectors found the presence of one optically inactive compound (*meso*-**2a**) and of a racemic mixture (*d,l*-**2a**) (Figure 1) as the only significant components, thus confirming a high degree of stereoselectivity.

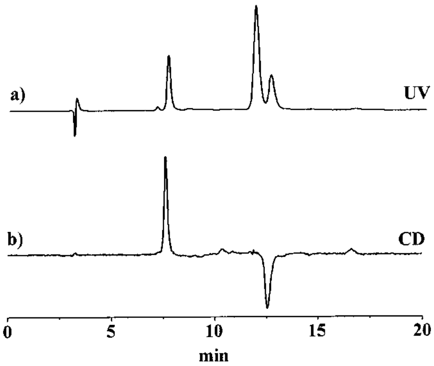
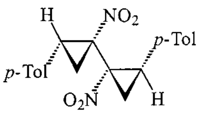


Figure 1. Stereoselective (enantio- and diastereoselective) chromatography of the final mixture from the bis(cyclopropanation) of **1a**: column (*S,S*)-Whelk O-1 (250×4.6 mm I.D.); eluent *n*-hexane/CH_2Cl_2 (80:20, v/v) + 0.5% *i*PrOH; flow rate 1.0 mL/min; *T* = 25 °C; UV (a) and CD (b) detections at 254 nm; CD trace vertically expanded by a factor of 10

In agreement with the above analytical results, two $C_{20}H_{20}N_2O_4$ products could be isolated by chromatography, in 54 and 24% yield, and were identified (HPLC on chiral columns) as *meso*-**2a** and *d,l*-**2a**, respectively; their spectroscopic data (both ^1H and ^{13}C NMR) were consistent with the bi(cyclopropyl) structure **2a**. An X-ray structure determination of *d,l*-**2a** (Figure 2), easily obtainable in a pure monocrystalline form, allowed the configurations of the four stereocentres to be assigned and the compound to be identified as a racemic mixture of (1*S*,1′*S*,2*R*,2′*R*)- and (1*R*,1′*R*,2*S*,2′*S*)-**2a**.

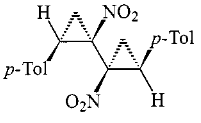
From a mechanistic point of view, the stereochemistry of *d,l*-**2a** provides evidence of a concerted *syn*-stereoselective cyclopropanation[9a] of both double bonds in the starting (*E,E*)-dinitrobutadiene, an outcome in excellent agreement with the isolation of only two diastereomeric bi(cyclopropyl)s. Accordingly, the (1*R*,1′*S*,2*S*,2′*R*)-**2a** configuration can confidently be assigned to *meso*-**2a**.

In our opinion, the stereochemical outcome itself in turn provides sound evidence for the participation, as the actual reactive species, of singlet carbene, originating from diazomethane under the experimental conditions employed.[10] The system would otherwise proceed, as generally believed for uncatalysed reactions of diazo compounds with alkenes,[9a][9d] through an intermediate pyrazoline, thermal evolution of which into the cyclopropane ring by nitrogen extrusion should reportedly result in scrambling of stereochemistry.[9a,10] In this regard, it is worth pointing out that no evidence whatsoever of the intermediacy of pyrazolines was observed throughout the experiments described in this section, nor in those below.

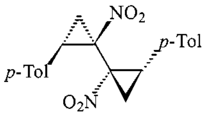


1*S*,1′*S*,2*R*,2′*R*

(*d,l*)-**2a**



1*R*,1′*R*,2*S*,2′*S*



meso-**2a**

Extension of the Reaction with Excess Diazomethane to 1,4-Diaryl-2,3-dinitro-1,3-butadienes 1b−f

The results obtained from the treatment of **1b−f** with excess diazomethane in anhydrous Et_2O or THF are reported in Table 1, together with those for the model reaction of **1a** under similar conditions. The configurations of the bi(cyclopropyl)s **2b**, **2d** and **2e** were assigned essentially on the grounds of physical (higher melting point for the *d,l* isomer), chromatographic (lower R_f parameter for the *d,l* isomer) and spectroscopic similarities with *meso*- and *d,l*-**2a**. In particular, one proton in each cyclopropane ring of *meso*-**2a** gave a very flat and broad signal at $\delta \approx 2.0$, the only exception to this peculiar behaviour being represented, throughout the **2a−f** series, by the naphthalene derivative **2e**, in which both *meso*-**2e** and *d,l*-**2e** displayed well-resolved multiplets for the three protons of each cyclopropane ring. The diastereomeric mixtures of both **2c** and **2f** revealed instability during chromatography on silica gel, and it was only possible to isolate a pure sample of *d,l*-**2c**. Nonetheless, the presence of *d,l* and *meso* derivatives was also assumed from the ^1H NMR spectra of the crude reaction mixtures in these cases, by analogy with the corresponding *d,l*- and *meso*-**2a**, -**2b**, -**2d** and -**2e**. In most cases the stereochemistry of the isolated products was confirmed by the HPLC/CD analysis; *meso* configurations were thus definitely assigned, particularly to the minor isomer of **2d**. It was noteworthy that the nature of the aryl substituent strongly affected the *d,l*/*meso* ratio.

Monocyclopropanation of 1,4-Diaryl-2,3-dinitro-1,3-butadienes

The nature of the products isolated from treatment with excess diazomethane strongly suggests consecutive cyclopropanations of the two double bonds of the dinitrobutadienes **1**. Thus, the possibility of achieving selective monocyclopropanation (Scheme 2) was evaluated, and the results

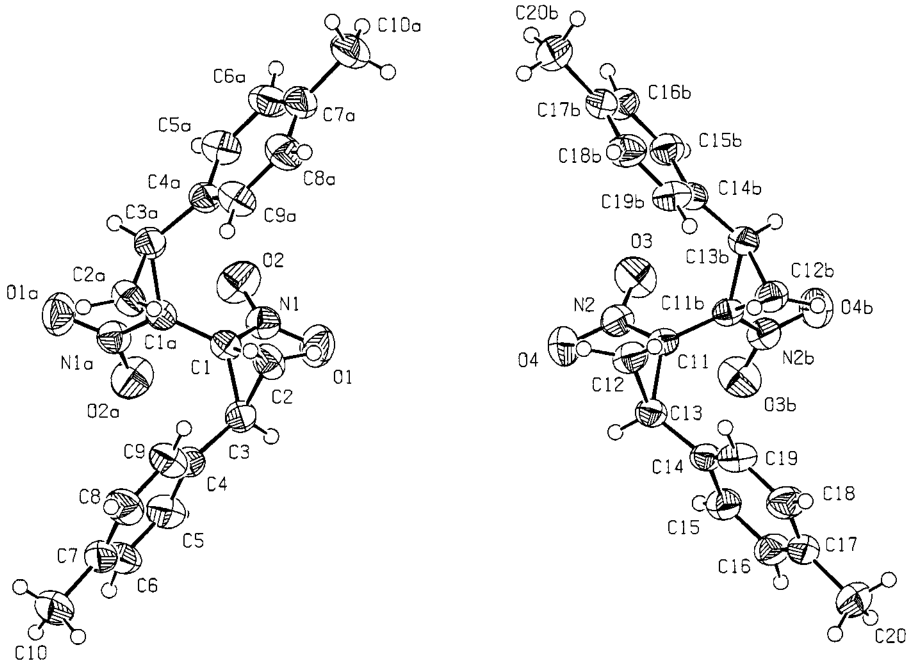


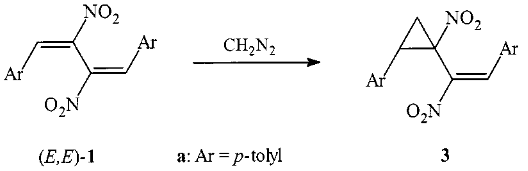
Figure 2. Crystal structure of compound **2a**, with numbering of atoms; the asymmetric unit is one whole molecule (see text); the central bond in each molecule is normal to a twofold crystallographic axis; thermal ellipsoids are drawn at the 50% probability level; hydrogen atoms, treated as isotropic, are on an arbitrary scale

Table 1. Reactions of (*E*,*E*)-1,4-diaryl-2,3-dinitro-1,3-butadienes **1a**−**f** with excess diazomethane

Entry[a]	**1**, Ar	Yield of **2** (%)[b] *d,l*; *meso*	*d,l*/*meso* molar ratio[c]
1	**1a**, 4-MeC_6H_4	24; 54	31:69
2	**1b**, C_6H_5	23; 54	30:70
3	**1c**, 4-$MeOC_6H_4$	92[d]	38:62
4	**1d**, 3-ClC_6H_4	52; 40	57:43
5	**1e**, 1-naphthyl	21; 70	23:77
6	**1f**, 2-thienyl[e]	90[f]	62:38

[a] Reactions performed in Et_2O at room temperature with a diazomethane/**1** molar ratio of 5, if not otherwise stated. [b] Yields of isolated products. [c] Relative yields determined by ^1H NMR of crude reaction mixtures. [d] Crude mixture, from which only a pure sample of the *d,l* isomer could be isolated by chromatography. [e] Performed in THF owing to the higher solubility of **1f** in this solvent. [f] Crude mixture; no efficient separation of the diastereomers could be attained (see Exp. Sect.).

for the model dinitrobutadiene **1a** are reported in Table 2. Indeed, a threefold molar excess of substrate exclusively afforded the monocyclopropanation product **3a** (Entry 1), while traces of **2a** were, as expected, observed on reducing the substrate to diazomethane molar ratio (Entries 1−4). Optimization of the absolute yield of the desired **3a** could most conveniently be achieved by starting with 1 mol of substrate and successively adding fractional (0.2−0.4) molar amounts of CH_2N_2 up to a final slight excess of the latter (Entry 5); monitoring of the progress of the reaction by ^1H NMR allowed addition to be stopped at a point corresponding to practically complete conversion of the substrate. In comparison, the employment of a slight excess of diazomethane added all at once at the very beginning of the reaction resulted (Entry 4) in incomplete substrate conversion, possibly due to time-dependent competitive CH_2N_2 decomposition.



Scheme 2

On the grounds of the results in Table 2, the monocyclopropanation was extended to the diaryldinitrobutadienes **1b**−**f** by the methodology involving progressive addition of an overall slight excess (1.2−1.4 mol) of diazomethane until disappearance of substrate (Table 3). This procedure simplified the recovery of **3** from the final mixture, thanks to its generally easier chromatographic separation from **2** than from unchanged substrate.

A peculiar aspect of the chromatographically isolated compounds **3** was that their ^1H NMR spectra (both in $CDCl_3$ and in $[D_6]DMSO$) always showed [with the single exception of the bis(1-naphthyl) derivative] minor peak systems attributable to an isomeric product. As the isolated products displayed reasonably sharp melting points, it was plausible to infer the occurrence in solution of conformational isomerism visible on the NMR timescale.[11] This view was supported by stereoselective HPLC analysis of **3b** on chiral columns at 25 °C (Figure 3), which showed the presence of a single racemic mixture, this in turn reinforcing

Table 2. Reactions between **1a** and diazomethane in different molar ratios

Entry[a]	[**1a**]/[CH_2N_2]	**3a** (%)[b]	**2a** (%)[c]	Recovered **1a** (%)	Material balance (%)
1	3:1	28 (84)	–	68	96
2	2.5:1	30 (75)	trace	66	96
3	2:1	32 (64)	trace	61	93
4	1:1.2	56	14	14	84
5	1:1.3[d]	67	20	trace	87

[a] Reactions performed in anhydrous THF at 0 °C; [**1a**] = 0.015 M. Yields are of chromatographed products. [b] The yield in parentheses refers to the insufficient reactant (diazomethane). [c] Cumulative yields of the *meso* and *d,l* diastereomers. [d] Successive additions of fractional molar equivalents of diazomethane (see text).

Table 3. Results of the monocyclopropanation of 1,4-diaryl-2,3-dinitro-1,3-butadienes **1a**−**f**

1, Ar[a]	**3** (%)[b]	**2** (%)[c]
1a, 4-MeC_6H_4	67 (90:10)	20
1b, C_6H_5	77 (83:17)	14
1c, 4-$MeOC_6H_4$	65[d] (88:12)	10[d]
1d, 3-ClC_6H_4	70 (74:26)	9
1e, 1-naphthyl	71	15
1f, 2-thienyl	42[d] (83:17)	22[d]

[a] Reactions performed in anhydrous THF at 0 °C, with successive additions of aliquots of diazomethane (see text). Yields are of isolated products, if not otherwise stated. [b] Figures in parentheses are the relative percentages of the two conformers found by ^1H NMR (see text). [c] Cumulative yields of the *meso* and D,L diastereomers. [d] Yield as determined by ^1H NMR on the crude final residue, due to instability on silica gel.

the above hypothesis of a stereoselective *syn* addition of singlet carbene to the nitrovinyl moieties in **1**. Consistently with such observations, treatment of isolated **3a** and **3d** with excess diazomethane under the usual conditions almost quantitatively afforded the same diastereomeric mixtures of bi(cyclopropyl) derivatives as obtained by the single-step treatment of the parent dinitrobutadienes with excess diazomethane.

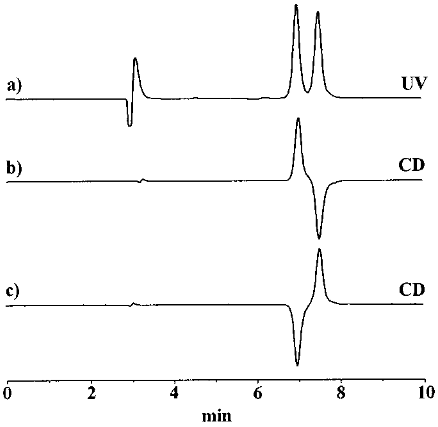


Figure 3. Enantioselective chromatography of compound **3b**: column (*S*,*S*)-Whelk O-1 (250×4.6 mm I.D.) (a and b) and (*R*,*R*)-Whelk O-1 (250×4.6 mm I.D.) (c); eluent *n*-hexane/CH_2Cl_2/*i*PrOH (70:29:1); flow rate 1.0 mL/min; *T* = 25 °C; UV (a) and CD (b and c) detection at 254 nm; CD traces vertically expanded by a factor of 10

The above results clearly identified **3** as a single racemic [(1*R*,2*S*) and (1*S*,2*R*)] mixture, intermediate in the overall bis(cyclopropanation) process, and thus allowed the assignment of the (1*R*,1′*S*,2*S*,2′*R*) stereochemistry to *meso*-**2** to be definitely confirmed.

It should be underlined that the monocyclopropanation results described here are unquestionably of synthetic interest because of the remarkable potentials generally acknowledged for vinylcyclopropanes, substrates in, for example, well-known rearrangements to larger cyclic compounds.[12]

X-ray Crystal Structural Determination of D,L-2a

In crystals of the examined compound, each of the eight molecules in the unit cell possesses a crystallographic twofold axis of symmetry; the asymmetric unit consists of one half of a molecule and one half of another, the two half molecules not being related by symmetry operations. A historical example of an analogous case is offered by the crystal structure of *trans*-stilbene,[13] in which each molecule contains a crystallographic centre of symmetry and the asymmetric unit encompasses one whole molecule. In the current case, the symmetry operations that generate the second half within each molecule are $2 - x$, y, $1/2 - z$ and $-x$, y, $1/2 - z$, respectively. The complete (relative) stereochemistry of the examined compound and the thermal ellipsoids of two whole molecules are shown in Figure 2,[14] in which the asymmetric unit includes C(1) to C(20), N(1), N(2), and O(1) to O(4). The configurations of the independent chiral centres C(1), C(3), C(11) and C(13) are (*R*), (*S*), (*S*) and (*R*), respectively. As in 1,1′-dinitro-1,1′-bi(cyclopropyl),[11] the molecular conformation is gauche, the N(1)−C(1)−C(1a)−N(1a) and N(2)−C(11)−C(11b)−N(2b) torsion angles being 69.4(2) and −67.1(2)°, respectively. The central bond lengths C(1)−C(1a) [1.470(3) Å] and C(11)−C(11b) [1.471(3) Å] are both very similar to the corresponding bond length found in 1,1′-dinitro-1,1′-bi(cyclopropyl) [1.476(2) Å without libration correction].[11] Selected bond lengths, bond angles and torsion angles between heavier atoms are given in Table 4. As far as the geometrical parameters (not involving H atoms) for the whole molecule are concerned, the corresponding standard deviations are in the ranges 0.002−0.003 Å, 0.1°−0.2° and 0.2°−0.3°, respectively. In the crystal structure there are no intermolecular contacts shorter than 0.16 Å with respect to the sum of the van der Waals radii involved.

Table 4. Selected bond lengths [Å], bond angles [°] and torsion angles [°] for *d,l*-**2a**

Bond or bond angle[a]	[Å] or [°]	Bond angle or bond torsion[a]	[°]
C(1)−C(1a)	1.470(3)	C(2)−C(3)−C(1)	59.78(11)
C(1)−N(1)	1.489(2)	C(11b)−C(11)−N(2)	113.03(11)
C(1)−C(2)	1.506(2)	N(2)−C(11)−C(12)	113.85(14)
C(1)−C(3)	1.542(2)	N(2)−C(11)−C(13)	113.54(13)
C(2)−C(3)	1.478(3)	C(12)−C(11)−C(13)	58.19(11)
C(3)−C(4)	1.493(2)	C(13)−C(12)−C(11)	61.70(11)
C(11)−C(11b)	1.471(3)	C(12)−C(13)−C(11)	60.10(11)
C(11)−N(2)	1.484(2)	O(2)−N(1)−O(1)	123.21(15)
C(11)−C(12)	1.512(2)	O(2)−N(1)−C(1)	118.23(15)
C(11)−C(13)	1.536(2)	O(1)−N(1)−C(1)	118.56(14)
C(12)−C(13)	1.482(2)	O(3)−N(2)−O(4)	123.13(16)
C(13)−C(14)	1.487(2)	O(3)−N(2)−C(11)	117.91(14)
N(1)−O(2)	1.2149(19)	O(4)−N(2)−C(11)	118.95(15)
N(1)−O(1)	1.2223(19)		
N(2)−O(3)	1.2174(19)	C(1a)−C(1)−N(1)−O(2)	1.3(2)
N(2)−O(4)	1.2193(19)	C(2)−C(1)−N(1)−O(1)	32.9(2)
		C(3)−C(1)−N(1)−O(1)	−30.7(2)
C(1a)−C(1)−N(1)	113.47(12)	C(11b)−C(11)−N(2)−O(3)	−6.4(2)
N(1)−C(1)−C(2)	113.14(14)	C(12)−C(11)−N(2)−O(4)	−37.9(2)
N(1)−C(1)−C(3)	113.08(14)	C(13)−C(11)−N(2)−O(4)	26.2(2)
C(2)−C(1)−C(3)	57.99(11)	N(1)−C(1)−C(1a)−N(1a)	69.4(2)
C(3)−C(2)−C(1)	62.22(11)	N(2)−C(11)−C(11b)−N(2b)	−67.1(2)

[a] Symmetry transformations used to generate equivalent atoms: a: $-x + 2, y, -z + 1/2$; b: $-x, y, -z + 1/2$.

Geometry calculations were performed with PLATON[14] and PARST.[15] Atomic coordinates, thermal parameters, bond lengths, bond angles and torsion angles have been deposited at the Cambridge Crystallographic Data Centre.[16]

Experimental Section

General Remarks: Melting points were determined with a Büchi 535 apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ solution (unless otherwise stated) at 200 and 50 MHz, respectively, with a Varian Gemini 200 spectrometer; TMS was used as internal standard, and chemical shifts are reported as δ values (ppm). Analytical chromatography was performed on an HPLC system comprising a Waters model 510 pump, a Rheodyne model 7725i 20 µL injector, and a Jasco model CD 995 UV/CD detector. Chromatographic data were collected and processed with Millennium 2010 Chromatography Manager software (Waters Chromatography).

Materials: "Petroleum ether" refers to the fraction with b.p. 40−60 °C, unless otherwise statet. Tetrahydrofuran (THF) was purified by standard methods and distilled from potassium benzophenone ketyl radical before use. (*E*,*E*)-1,4-Diaryl-2,3-dinitro-1,3-butadienes **1a/c/e/f**,[8b] **1b**[8a] and **1d**[8c] were synthesized as previously reported. Diazomethane (in diethyl ether) was prepared and titrated according to a reported procedure.[17] Column or preparative plate chromatography was performed on silica gel, with petroleum ether and gradients (or appropriate mixtures) with CH_2Cl_2, Et_2O or EtOAc as eluents, the solvents being distilled before use.

Bis(cyclopropanation) of 1,4-Diaryl-2,3-dinitro-1,3-butadienes 1a−f with Excess Diazomethane: The substrate (0.6 mmol) was dissolved in anhydrous diethyl ether (40 mL) in a flask equipped with a rubber septum and a magnetic stirring bar, and 3 mmol of diazomethane in ether were added at room temperature, with magnetic stirring. The reaction was practically complete, as judged by TLC, within a few hours, although the reaction time was routinely prolonged overnight in order to ensure complete disposal of the excess diazomethane. In the case of compound **1f**, sparingly soluble in diethyl ether, THF was used as solvent and the reaction was complete within 5 h at 0 °C. Rotoevaporation of the solvent under reduced pressure yielded a crude residue, which was generally chromatographed on silica gel. In some instances the less soluble stereomeric bi(cyclopropyl) derivative precipitated from the final ethereal solution and could be recovered almost quantitatively in a pure form by filtration.

2,2′-Bis(4-methylphenyl)-1,1′-dinitro-1,1′-bi(cyclopropyl) (2a): The less soluble *d,l* stereoisomer precipitated in essentially pure form from the ethereal reaction solution and could be collected by filtration. The *meso* form and the remaining traces of the *d,l* isomer could easily be separated by column chromatography. Racemic mixture (1*S*,1′*S*,2*R*,2′*R*)- and (1*R*,1′*R*,2*S*,2′*S*)-**2a** (*d,l*-**2a**): M.p. 240.0−240.5 °C (dec.) (taken up with diethyl ether) ^{1}H NMR: δ = 1.66 (dd, *J* = 7.2, 8.7 Hz, 2 H), 2.09 (dd, *J* = 7.2, 10.7 Hz, 2 H), 2.32 (s, 6 H), 3.62 (dd, *J* = 8.7, 10.7 Hz, 2 H), 7.11 (app. s, 8 H). ^{13}C NMR: δ = 21.13, 22.71, 35.30, 67.90, 128.58, 128.87, 129.22, 138.32. $C_{20}H_{20}N_2O_4$ (352.41): calcd. C 68.17, H 5.72, N 7.95; found C 67.84, H 5.71, N 7.90. *meso* form (1*R*,1′*S*,2*S*,2′*R*)-**2a** (*meso*-**2a**): M.p. 152.2−153.3 °C (petroleum ether, b. p. 80−100 °C). ^{1}H NMR: δ = 2.38 (8 H in all, s and m partly overlapped), 3.65 (app. t, *J* = 10.6 Hz, 2 H), 6.88 (m, 4 H), 7.14 (m, 4 H); the signal of one methylenic hydrogen atom for each cyclopropyl ring was not clearly detectable; probably a very br. signal at δ ≈ 1.7−2.0. ^{13}C NMR: δ = 21.20, 23 (br.), 36.94, 67 (br.), 128.38, 128.95, 129.17, 138.66. $C_{20}H_{20}N_2O_4$ (352.41): calcd. C 68.17, H 5.72, N 7.95; found C 67.80, H 5.69, N 7.78.

1,1′-Dinitro-2,2′-diphenyl-1,1′-bi(cyclopropyl) (2b): The less soluble *d,l* stereoisomer precipitated from the ethereal reaction solution in essentially pure form and could be collected by filtration. The *meso* form and the remaining traces of the *d,l* isomer could easily be separated by column chromatography. Racemic mixture (1*S*,1′*S*,2*R*,2′*R*)- and (1*R*,1′*R*,2*S*,2′*S*)-**2b** (*d,l*-**2b**): M.p. 240.0−240.8 °C (dec.) (taken up with diethyl ether). ^{1}H NMR: δ = 1.67 (dd, *J* = 7.2, 8.6 Hz, 2 H), 2.08 (dd, *J* = 7.2, 10.7 Hz, 2 H), 3.68 (dd, *J* = 8.6, 10.7 Hz, 2 H), 7.30 (m, 10 H). ^{13}C NMR: δ = 22.49, 35.24, 67.77, 128.47, 128.52, 129.00, 131.57. $C_{18}H_{16}N_2O_4$ (324.36): calcd. C 66.66, H 4.97, N 8.64; found C 66.55, H 5.12, N 8.61. *meso* form (1*R*,1′*S*,2*S*,2′*R*)-**2b** (*meso*-**2b**): M.p. 144.0−145.0 °C (taken up with diethyl ether). ^{1}H NMR: δ = 2.30 (m, 2 H), 3.69 (app. t, *J* = 10.3 Hz, 2 H), 6.97 (m, 4 H), 7.34 (m, 6 H); the signal of one methylenic hydrogen atom for each cyclopropyl ring was not clearly detectable; probably a very br. signal at δ ≈ 1.7−2.0. ^{13}C NMR: δ = 22.57 (br.), 36.85, 68.69 (br.), 126.05, 128.50, 128.73, 131.36. $C_{18}H_{16}N_2O_4$ (324.36): calcd. C 66.66, H 4.97, N 8.64; found C 66.51, H 5.30, N 8.64.

2,2′-Bis(4-methoxyphenyl)-1,1′-dinitro-1,1′-bi(cyclopropyl) (2c): Because of its instability on silica gel, only a pure sample of the *d,l* isomer could be isolated by chromatography. Racemic mixture (1*S*,1′*S*,2*R*,2′*R*)- and (1*R*,1′*R*,2*S*,2′*S*)-**2c** (*d,l*-**2c**): M.p. 164.2−165.3 °C (dec.) (taken up with petroleum ether). ^{1}H NMR: δ = 1.61 (dd, *J* = 7.0, 8.6 Hz, 2 H), 2.09 (dd, *J* = 7.0, 10.6 Hz, 2 H), 3.62 (dd, *J* = 8.6, 10.6 Hz, 2 H), 3.79 (s, 6 H), 6.82 and 7.16 (4 H each, AA′BB′ system, *J* = 8.6 Hz). ^{13}C NMR: δ = 22.78, 35.03, 55.25, 67.86, 113.88, 123.49, 130.19, 159.54. $C_{20}H_{20}N_2O_6$ (384.41): calcd. C 62.50, H 5.24, N 7.29; found C 62.80, H 5.21, N 7.14. *meso* form (1*R*,1′*S*,2*S*,2′*R*)-**2c** (*meso*-**2c**): Only the following characteristic signals could be observed in the ^{1}H NMR spectrum of the crude diastereomeric mixture: δ = 3.64 (app. t, *J* = 10.3 Hz, 2 H), 3.84 (s, 6 H), 6.90 (8 H, br. signal); the signals of two methylenic hydrogen atoms for each cyclopropyl group were not clearly detectable; probably very br. signals at δ ≈ 1.5−2.5.

2,2′-Bis(3-chlorophenyl)-1,1′-dinitro-1,1′-bi(cyclopropyl) (2d): The two diastereomers could be isolated by chromatography. Racemic mixture (1*S*,1′*S*,2*R*,2′*R*)- and (1*R*,1′*R*,2*S*,2′*S*)-**2d** (*d,l*-**2d**): M.p. 270.9−271.5 °C (ethyl acetate). ^{1}H NMR: δ = 1.64 (dd, *J* = 7.3, 8.7 Hz, 2 H), 2.14 (dd, *J* = 7.3, 10.7 Hz, 2 H), 3.68 (dd, *J* = 8.7, 10.7 Hz, 2 H), 7.25 (m, 8 H). ^{13}C NMR: δ = 22.28, 34.38, 127.78, 128.69, 128.85, 129.94; the signals of one aliphatic and two aromatic carbon atoms were not clearly detectable. $C_{18}H_{14}Cl_2N_2O_4$ (393.25): calcd. C 54.98, H 3.59, N 7.12; found C 55.21, H 3.62, N 7.03. *meso* form (1*R*,1′*S*,2*S*,2′*R*)-**2d** (*meso*-**2d**): M.p. 186.7−188.1 °C (toluene/petroleum ether). ^{1}H NMR: δ = ca. 1.0−2.0 (very br. signal, 2 H), ca. 2.4 (app. br. s, 2 H), 3.68 (app. t, *J* = 10.3 Hz, 2 H), 6.94 (app. br. s, 4 H), 7.36 (m, 4 H). ^{13}C NMR: δ = 22.48 (br.), 35.98, 68.46 (br.), 129 (br., overlapping with the two following signals), 129.14, 129.99, 133.29, 134.73. $C_{18}H_{14}Cl_2N_2O_4$ (393.25): calcd. C 54.98, H 3.59, N 7.12; found C 54.85, H 3.63, N 6.88.

2,2′-Bis(1-naphthyl)-1,1′-dinitro-1,1′-bi(cyclopropyl) (2e): The two diastereomers could be isolated by chromatography. Racemic mixture (1*S*,1′*S*,2*R*,2′*R*)- and (1*R*,1′*R*,2*S*,2′*S*)-**2e** (*d,l*-**2e**): M.p. 235.5−236.2 °C (toluene/petroleum ether). ^{1}H NMR: δ = 2.10 (dd, *J* = 7.3, 8.9 Hz, 2 H), 2.30 (dd, *J* = 7.3, 10.8 Hz, 2 H), 4.25 (dd, *J* = 8.9, 10.8 Hz, 2 H), 7.24 (d, *J* = 8.4 Hz, 2 H), 7.44 (app. t, *J* = 7.7 Hz, 2 H), 7.57 (m, 4 H), 7.85 (m, 4 H), 8.25 (d, *J* = 8.4 Hz, 2 H). ^{13}C NMR: δ = 22.80, 32.50, 68.26, 123.93, 124.22, 124.79, 126.53, 126.73, 127.81, 128.41, 129.66, 133.30, 133.85. $C_{26}H_{20}N_2O_4$ (424.49): calcd. C 73.57, H 4.75, N 6.60; found C 73.42, H 4.64, N 6.61. *meso* form (1*R*,1′*S*,2*S*,2′*R*)-**2e** (*meso*-**2e**): M.p. 193.8−194.5 °C (toluene/petroleum ether). ^{1}H NMR: δ = 1.85 (dd, *J* = 7.0, 10.0 Hz, 2 H), 2.43 (dd, *J* = 7.0, 10.8 Hz, 2 H), 4.34 (app. t, 2 H, *J* = 10.0, 10.8 Hz), 6.53 (d, *J* = 7.0 Hz, 2 H), 7.10 (app. t, *J* = 7.7 Hz, 2 H), 7.56 (m, 4 H), 7.86 (m, 6 H). ^{13}C NMR: δ = 22.52, 34.37, 69.76, 124.58, 124.61, 124.94, 126.56, 126.94, 127.47, 128.84, 129.65, 133.13, 133.84. $C_{26}H_{20}N_2O_4$ (424.49): calcd. C 73.57, H 4.75, N 6.60; found C 73.57, H 4.64, N 6.45.

1,1′-Dinitro-2,2′-bis(2-thienyl)-1,1′-bi(cyclopropyl) (2f): Because of its instability on silica gel, only a pure sample of the *d,l* stereoisomer, which precipitated from the reaction solution, could be isolated. Racemic mixture (1*S*,1′*S*,2*R*,2′*R*)- and (1*R*,1′*R*,2*S*,2′*S*)-**2f** (*d,l*-**2f**): M.p. 158.6−159.9 °C (dec.) (taken up with diethyl ether). ^{1}H NMR: δ = 1.67 (dd, *J* = 7.2, 8.3 Hz, 2 H), 2.33 (dd, *J* = 7.2, 10.6 Hz, 2 H), 3.83 (dd, *J* = 8.3, 10.6 Hz, 2 H), 6.93 (m, 4 H), 7.23 (dd, *J* = 1.6, 4.7 Hz, 2 H). ^{13}C NMR: δ = 25.68, 30.58, 69.15, 125.98, 127.44, 128.84, 135.45. $C_{14}H_{12}N_2O_4S_2$ (336.41): calcd. C 49.99, H 3.60, N 8.33; found C 50.12, H 3.70, N 8.26. *meso* form (1*R*,1′*S*,2*S*,2′*R*)-**2f** (*meso*-**2f**): Only the following characteristic signals could be identified in the ^{1}H NMR spectrum of the crude diastereomeric mixture: δ = 6.80 (app. br. d, *J* = 3.6 Hz, 2 H) and 7.29 (app. br. d, *J* = 5.5 Hz, 2 H).

Monocyclopropanation of (1*E*,3*E*)-1,4-Diaryl-2,3-dinitro-1,3-butadienes 1a−f: The reactions, the results of which are collected in Table 3, were carried out in THF at 0 °C, starting with a solution of 1 mmol of substrate in THF (40 mL) and successively adding fractional (0.2−0.4) mmolar amounts of CH_2N_2 in diethyl ether to reach a practically complete conversion of substrate with an overall slight excess of CH_2N_2. Progress of the reaction was monitored by ^{1}H NMR spectroscopy. The workup procedure was that already described for the bis(cyclopropanation). Thus, after rotoevaporation of the solvent under reduced pressure, products and unchanged substrate (if any) were recovered by column chromatography in all cases except for that of the 2-thienyl derivative, for which extensive transformation on silica gel occurred for both the mono- and the bis(cyclopropanation) products. As outlined above in the discussion, with the sole exception of the naphthyl derivative **3e**, pure, crystallised **3a−d** and **3f** appeared in solution (^{1}H NMR) as mixtures of two conformers in a ratio that varied as a function of the aryl substituent [from 9:1 (**3a**) to 3:1 (**3d**) in $CDCl_3$ at 22 °C]. For the minor conformer, some ^{1}H NMR signals were in all cases covered by those of the major one, while the ^{13}C NMR signals were most often practically undetectable. In one case (**3d**) it was not even possible to attribute the ^{13}C NMR signals to the major conformer unequivocally.

1-Methyl-4-{(*E*)-2-[2-(4-methylphenyl)-1-nitrocyclopropyl]-2-nitrovinyl}benzene (3a): M.p. 153.5−154.4 °C (ethanol). In solution, the NMR showed the presence of two conformers (see Table 3). Major conformer: ^{1}H NMR: δ = 1.58 (dd, *J* = 7.0, 9.2 Hz, 1 H), 2.28 (s, 3 H), 2.46 (s, 3 H), 2.49 (dd, *J* = 7.0, 10.5 Hz, 1 H), 3.94 (app. t, *J* = 9.9 Hz, 1 H), 6.80 and 7.03 (2 H each, AA′BB′, *J* = 7.8 Hz), 7.33 (s, 4 H), 8.40 (s, 1 H). ^{13}C NMR: δ = 21.09, 21.71, 24.62, 39.32, 67.67, 127.01, 127.81, 128.12, 129.24, 129.98, 130.53, 138.26, 140.40, 142.33, 142.98. Minor conformer: ^{1}H NMR: δ = 2.00 (dd, *J* = 7.4, 9.0 Hz, 1 H), 2.17 (s, 3 H), 2.35 (s, 3 H), 2.88 (dd, *J* = 7.4, 10.6 Hz, 1 H), 3.59 (app. t, *J* = 9.2, 10.6 Hz, 1 H), 6.37 and 6.65 (2 H each, AA′BB′ system, *J* = 7.8 Hz), 8.24 (s, 1 H); the signals of four aromatic protons are covered by those of the major conformer. $C_{19}H_{18}N_2O_4$ (338.39): calcd. C 67.45, H 5.36, N 8.28; found C 67.41, H 5.53, N 8.36.

[(*E*)-2-Nitro-2-(1-nitro-2-phenylcyclopropyl)vinyl]benzene (3b): M.p. 166.0−166.8 °C (ethanol). In solution, the NMR showed the presence of two conformers (see Table 3). Major conformer: ^{1}H NMR: δ = 1.56 (dd, *J* = 7.2, 9.2 Hz, 1 H), 2.48 (dd, *J* = 7.2, 10.3 Hz, 1 H), 3.97 (app. t, *J* = 9.4, 10.1 Hz, 1 H), 6.93 (m, 2 H), 7.26 (m, 3

H), 7.50 (m, 5 H), 8.44 (s, 1 H). ^{13}C NMR: δ = 24.42, 39.09, 67.61, 127.96, 128.45, 128.56, 129.28, 129.90, 130.23, 131.10, 131.94, 141.15, 142.32. Minor conformer: ^{1}H NMR: δ = 2.03 (dd, J = 7.4, 9.2 Hz, 1 H), 2.91 (dd, J = 7.4, 10.8 Hz, 1 H), 3.60 (app. t, J = 9.2, 10.6 Hz, 1 H), 6.47 (m, 2 H), 6.83 (m, 3 H), 8.28 (s, 1 H); the signals of the protons of one phenyl ring are covered by those of the major conformer. $C_{17}H_{14}N_2O_4$ (310.33): calcd. C 65.80, H 4.55, N 9.03; found C 65.60, H 4.48, N 9.00.

1-Methoxy-4-{(*E*)-2-[2-(4-methoxyphenyl)-1-nitrocyclopropyl]-2-nitrovinyl}benzene (3c): M.p. 144.4−145.5 °C (toluene). In solution, the NMR showed the presence of two conformers (see Table 3). Major conformer: ^{1}H NMR: δ = 1.62 (dd, J = 7.0, 9.1 Hz, 1 H), 2.55 (dd, J = 7.0, 10.5 Hz, 1 H), 3.76 (s, 3 H), 3.91 and 3.95 [4 H in all, s and app. t (J = 9.5 Hz) partly overlapping], 6.75 and 6.86 (2 H each, AA′BB′ system, J = 8.9 Hz), 7.02 and 7.42 (2 H each, AA′BB′ system, J = 8.8 Hz), 8.38 (s, 1 H). ^{13}C NMR: δ = 24.80, 39.33, 55.26, 55.62, 67.75, 114.06, 114.88, 122.22, 123.23, 129.22, 132.88, 139.42, 141.98, 159.71, 162.92. Minor conformer: ^{1}H NMR: δ = 1.98 (dd, J = 7.7, 9.2 Hz, 1 H), 2.91 (dd, J = 7.7, 11.0 Hz, 1 H), 3.62 (app. t, 1 H, partly overlapping with the following singlet), 3.68 (s, 3 H), 3.83 (s, 3 H), 6.46 and 6.49 (2 H each, AA′BB′ system, J = 9.0 Hz), 8.22 (s, 1 H); the signals of four aromatic protons are covered by those of the major conformer. $C_{19}H_{18}N_2O_6$ (370.39): calcd. C 61.62, H 4.90, N 7.56; found C 61.71, H 4.78, N 7.50.

1-Chloro-3-{(*E*)-2-[2-(3-chlorophenyl)-1-nitrocyclopropyl]-2-nitrovinyl}benzene (3d): M.p. 190.8−192.3 °C (ethanol). In solution, the NMR showed the presence of two conformers (see Table 3). Major conformer: ^{1}H NMR: δ = 1.51 (dd, J = 7.3, 9.1 Hz, 1 H), 2.49 (dd, J = 7.3, 10.5 Hz, 1 H), 3.96 (app. t, J = 10.0 Hz, 1 H), 6.88 (m, 2 H), 7.26 (m, 3 H), 7.50 (m, 3 H), 8.40 (s, 1 H). ^{13}C NMR: it was not possible to attribute the signals unequivocally, even to the major conformer. Minor conformer: ^{1}H NMR: δ = 1.99 (app. t, J = 7.6, 9.2 Hz, 1 H), 2.93 (dd, J = 7.6, 10.8 Hz, 1 H), 3.50 (app. t, J = 9.4, 10.6 Hz, 1 H), 6.37 (m, 1 H), 6.47 (br. s, 1 H), 6.66 (br. s, 1 H), 8.28 (s, 1 H); the remaining aromatic signals could not be unequivocally assigned due to partial overlapping with those of the major conformer. $C_{17}H_{12}Cl_2N_2O_4$ (379.22): calcd. C 53.85, H 3.19, N 7.39; found C 54.0, H 3.38, N 7.22.

1-{(*E*)-2-[2-(1-Naphthyl)-1-nitrocyclopropyl]-2-nitrovinyl}naphthalene (3e): M.p. 185.6−186.8 °C (toluene). ^{1}H NMR: δ = 1.56 (m, 1 H), 2.30 (m, 1 H), 4.64 (app. t, J = 9.7 Hz, 1 H), 6.45 (d, J = 7.0 Hz, 1 H), 7.60 (m, 12 H), 8.24 (m, 1 H), 8.94 (s, 1 H). ^{13}C NMR: δ = 23.60, 34.72, 69.04, 122.73, 123.62, 124.06, 124.22, 125.48, 126.44, 126.86, 127.24, 127.62, 127.84, 128.53, 129.03, 129.23, 129.50, 130.88, 132.03, 132.99 (br.), 133.56 (br.), 140.64, 142.26. $C_{25}H_{18}N_2O_4$ (410.46): calcd. C 73.16, H 4.42, N 6.83; found C 72.90, H 4.26, N 6.81.

2-{(*E*)-2-[1-Nitro-2-(2-thienyl)cyclopropyl]-2-nitrovinyl}thiophene (3f): Because of its instability on silica gel, this compound could not be purified by chromatography. The NMR spectrum of the crude reaction mixture showed the presence of two conformers (see Table 3). Major conformer: ^{1}H NMR: δ = 2.01 (dd, J = 6.9, 8.8 Hz, 1 H), 2.98 (dd, J = 6.9, 10.5 Hz, 1 H), 4.18 (app. t, J = 9.0, 10.2 Hz, 1 H,), 6.82 (app. d, J = 3.6 Hz, 1 H), 6.91 (dd, J = 3.6, 5.1 Hz, 1 H), 7.18 (dd, J = 1.1, 5.1 Hz, 1 H), 7.26 (m, 1 H, partly overlapping with the $CHCl_3$ signal), 7.54 (app. d, J = 3.6 Hz, 1 H), 7.81 (app. d, J = 5.1 Hz, 1 H), 8.61 (m, 1 H). ^{13}C NMR: it was not possible to attribute the signals unequivocally, even to the major conformer. Except for the nitrovinylic protons (δ = 8.49), the ^{1}H NMR signals of the minor conformer were not clearly distinguishable in the spectrum of the final crude residue.

Enantioselective HPLC: Enantioselective HPLC was performed on "brush-type" chiral columns: (*S*,*S*)-Whelk O-1 (250×4.6 mm I.D.) and/or (*R*,*R*)-Whelk O-1 (250×4.6 mm I.D.) from Regis Chemical Co. (Morton Groove, IL) using multiple detection: UV and CD (see Figures 1 and 3).

X-Ray Crystallographic Study of d,l-2a: Transparent, colourless single crystals were grown from chloroform. After preliminary Laue photographs, X-ray data were recorded with an Enraf−Nonius CAD4 diffractometer with graphite-monochromated MoK_α (λ = 0.7107 Å) radiation. Cell constants were determined by least-squares refinement of diffractometer angles for 25 automatically centred reflections. During the data collection, the centreing of seven reflections was repeated periodically to test the crystal orientation, and two reflections were monitored every 1.5 h to check the crystal stability. No significant crystal decay was observed. Crystal data: Compound **2a**, $C_{20}H_{20}N_2O_4$, M = 352.4, m.p. 240 °C (dec). Monoclinic, observed Laue symmetry $2/m$, a = 9.807(2), b = 24.018(5), c = 15.892(4) Å, β = 107.87(2)°, V = 3563(1) Å^3, space group $C2/c$, Z = 8, D_c = 1.314 g cm^{-3}, $F(000)$ = 1488. Rounded crystal, $0.20 \leq r \leq 0.24$ mm, μ = 0.092 mm^{-1}; ω/θ scan mode, scan width 1.35°, scan speed 0.9−16.5° min^{-1}; 4098 unique reflections measured ($2.5° \leq \theta \leq 27.5°$). Structure solution and refinement: The structure was solved by direct methods with the NRCVAX system of programs[18] and refined by full-matrix, least-squares techniques,[19] including the whole data set of 4098 F_o^2 in the calculations. In the final refinement all heavier atoms were treated as anisotropic. For most hydrogen atoms the positional parameters (obtained from difference Fourier syntheses) and also the isotropic displacement parameters could be refined. The hydrogen atoms bound to the methyl carbon atoms C(10) and C(20) were localised by circular difference syntheses and refined as belonging to idealised rigid groups. Convergence was reached within a maximum shift-to-e.s.d. ratio of 0.003. The largest correlation factor was 0.52, between $U_{1,3}$ and $U_{3,3}$ of atom C(2). Final reliability factors are: R_1 = 0.0506 on 2964 $F_o \geq 4\sigma(F_o)$, wR_2 = 0.1368 for all 4098 F_o^2 and 293 parameters, with a goodness of fit S = 1.070. At the end of the refinement the difference Fourier map was essentially flat, the electron density ranging between 0.18 and −0.20 eÅ^{-3}.

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