Polynitro-Substituted Strained-Ring Compounds. 2. 1,2-Dinitrospiropentanes

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Abstract: *trans*-1,2-Dinitrospiropentane was prepared in 43% yield from 1,1-bis(nitromethyl)cyclopropane, best obtained by dry-phase ozonolysis of the corresponding diamine. The structure of *trans*-1,2-dinitrospiropentane was assigned on the basis of spectroscopic data, elemental analysis, and X-ray crystallographic data. The first pK_a was determined to be 18.6–21.6 in DMSO solution with decomposition. Reaction of *trans*-1,2-dinitrospiropentane with sodium methoxide and iodine gave a mixture of iodinated spiropentanes, from which, *cis*- and *trans*-1,2-diiodo-1,2-dinitrospiropentane could be isolated in pure form. These diiodides were stable at room temperature but gave off iodine upon melting at 150–160 °C. Treatment with sodium thiosulfate in aqueous DMSO solution gave back the deiodinated dinitro compound. *trans*-1,2-Dinitrospiropentane reacted with lithium diisopropylamide and benzaldehyde in THF to afford a bis(nitroaldol) product in 59% yield.

By the mid 1940s the existence of the strained-ring hydrocarbon spiropentane was firmly established.[1] Since that time a modest number of synthetic routes to spiropentane derivatives have been developed.[2] However, the synthesis of nitro-substituted spiropentanes has not yet been reported.[3] Nitro-substituted spiropentanes would be of interest as compounds with markedly differentiated cyclopropane rings. Presumably one could transform the nitro-substituted ring via nitronate chemistry and the unsubstituted ring by electrophilic reactions. The incorporation of nitro groups on the spiropentane nucleus would also be of theoretical interest. Would the known rearrangement of spiropentane to methylenecyclobutane be enhanced? A recent theoretical study[4] suggests that rearrangement begins with peripheral C,C bond scission to a diradical; presumably the diradical would be stabilized by nitro groups. Would the bending and twisting motions[5] of spiropentane become more or less favorable when nitro groups are present? This has implications on the construction of functionalized bridged spiropentanes (e.g., tricyclo[4.1.0.0^{1,3}]heptanes).

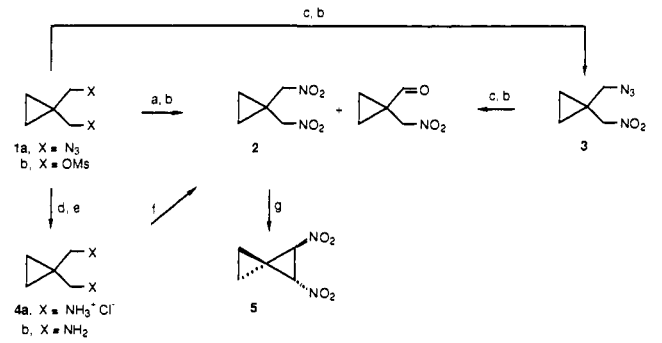
In a continuation of our work on strained-ring polynitro polycycloalkanes,[6] we wish to report the preparation of several dinitrospiropentanes. The key intermediate providing access to these dinitrospiropentanes is 1,1-bis(nitromethyl)cyclopropane (**2**). Oxidative cyclization of this key intermediate then provides 1,2-dinitrospiropentane, which can be further functionalized to give other dinitrospiropentanes.

Results

The dinitro compound **2** was prepared from 1,1-bis(azidomethyl)cyclopropane (**1a**), available from the corresponding dimesylate **1b**[7] (Scheme I). Initially the general procedure of Corey et al.[8] was followed: **1a** was treated with tributylphosphine, and the resulting iminophosphorane was oxidized with ozone. Optimum conditions involved adding the iminophosphorane to a dichloromethane solution kept excess in ozone at dry ice temperature. Even so, only a 12% yield of pure **2** could be obtained. The most significant byproducts were aldehydes: impure 1-(nitromethyl)cyclopropanecarboxaldehyde was obtained in 13% yield. Thus, formation of carbonyl-containing side products was a severe problem here. Attempts to improve the situation by changing the phosphine reactant were unproductive. No dinitro compound **2** was obtained after ozonolysis when triphenylphosphine was employed. Although not optimized, only a 7% yield of **2** was obtained when triethylphosphine was employed.

The major problem with the preparation of compound **2** appears to be in the oxidation of the first iminophosphorane group of the intermediate derived from diazide **1a**. Thus, reaction of **1a** with 1.5 equiv of tributylphosphine followed by ozonolysis gave the nitro azide **3** in 13% yield and **2** in 7% yield. Nitro azide **3** was isolated and characterized; treatment with tributylphosphine followed by ozonolysis afforded **2** in 55% yield.

Scheme I[a]



[a] (a) $(n\text{-Bu})_3P$ (2.2 equiv), CH_2Cl_2. (b) O_3 (excess), CH_2Cl_2, −78 °C. (c) $(n\text{-Bu})_3P$ (1–1.7 equiv), CH_2Cl_2. (d) Ph_3P, wet THF, then aqueous HCl. (e) KOH, distillation. (f) O_3 (excess), silica gel, −78 °C. (g) Dimsyl sodium (excess), I_2 (excess), then aqueous $Na_2S_2O_3$.

A better synthetic route to **2** involves reduction of diazide **1a** to the diamine **4b** by the Staudinger reaction[9] and subsequent dry-phase ozonolysis.[10] Thus, **1a** was reacted with triphenylphosphine and water followed by dilute hydrochloric acid to give the known salt **4a**[7] in 93% yield. One major advantage of this approach is safety: it was possible to use a solution of crude diazide **1a**, a likely explosive, without the need of isolation. The overall yield of the salt **4a** from dimesylate **1b** was 85%. This procedure

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(2) For reviews, see: Krapcho, A. P. *Synthesis* **1978**, 77–126 (cycloaddition routes). Krapcho, A. P. *Synthesis* **1974**, 383–419 (intramolecular substitution).
(3) Spiro[2.4]heptanes containing a nitro group on the cyclopropane ring are known: Berestovitskaya, V. M.; Sopova, A. S.; Perekalin, V. V. *Zh. Org. Khim.* **1967**, *3*, 1703.
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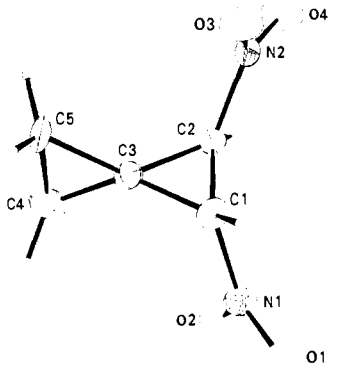


Figure 1. ORTEP drawing for *trans*-1,2-dinitrospiropentane (**5**). Only one enantiomer is shown. For C, N, and O, 30% probability elliposides are shown; hydrogen atoms have been drawn artificially small.

is amenable to scaleup and has been performed on multigram quantities of **1b**.

The free diamine **4b**, containing 15–25% water, was obtained from the hydrochloride salt. The wet diamine was ozonolyzed on silica gel at −78 °C to provide the dinitro compound **2** in 20–28% yield. Some variation in yield was noted depending on the grade and quantity of silica gel. Simple column-grade material was used for preparative runs, and a typical yield of 22% was obtained. Flash-grade silica gel gave dinitro compound **2** in 28% yield when used in a 150:1 w/w ratio to **4b**. Also obtained in 6% yield was 1-(nitromethyl)cyclopropanecarboxaldehyde.

Introduction of the spiro ring juncture via cyclization of dinitro compound **2** was straightforward. The dianion of **2** was generated using a solution of excess dimsyl sodium in DMSO.[6] Treatment of the dianion with iodine followed by workup using aqueous sodium thiosulfate gave a 43% yield of pure crystalline *trans*-1,2-dinitrospiropentane (**5**) in a typical experiment. Yields ranging from 24 to 55% were obtained in other runs. It seems that rapid addition rates and maintained low temperature are crucial conditions for the success of this reaction. The product also decomposes in basic DMSO solution.

The structure of dinitrospiropentane **5** is based on its spectral properties and correct elemental analysis and by analogy to *trans*-1,2-dinitrocyclopropane.[6] The trans stereochemistry of **5** was rigorously established on the basis of X-ray crystallographic data (Figure 1).

There is one interesting structural feature apparent for dinitrospiropentane **5** in the crystalline state. Both of the nitro groups are oriented in a preferred bisected conformation with respect to the ring to which they are attached. This is in keeping with the preferred crystalline-state conformation of *trans*-1,2-dinitrocyclopropane where both nitro groups also assume a bisected conformation.

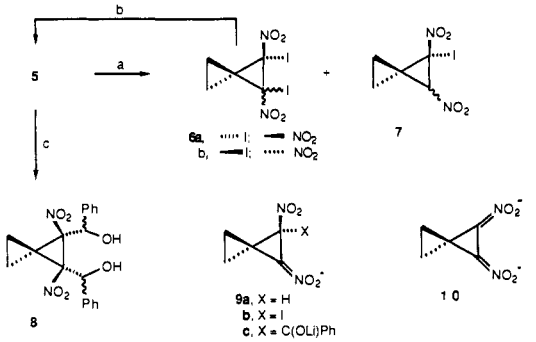
When sodium thiosulfate was not added during workup, additional products besides **5** were obtained in varying amounts. These products consisted of a mixture of 1-iodo-1,2-dinitrospiropentane (**7**, one isomer) and the cis and trans isomers of 1,2-diiodo-1,2-dinitrospiropentane (**6a,b**).

Controlled experiments aimed at synthesizing **6** were then conducted. Treatment of dinitrospiropentane **5** with methanolic sodium methoxide and iodine gave diiodo compound **6** in 72% isolated yield (50:50 **a**/**b** ratio) after 15 min (Scheme II). An inseparable mixture of **7** and **5** was also obtained in this reaction as a byproduct. Running the reaction for a longer time markedly reduced the yield of **6a,b**.

The mixture of **6a** and **6b** was initially difficult to separate until acetic acid was employed as a cosolvent for chromatography. TLC and subsequent recrystallization then afforded pure samples of **6a** and **6b**. Structures were assigned on the basis of spectral data and an elemental analysis performed on the mixture.

Iodination is believed to proceed through the nitronate anions **9a,b**. This hypothesis is supported by the reaction of dinitrospiropentane **5** with excess lithium diisopropylamide in THF at

Scheme II[a]



[a] (a) NaOMe (excess), I_2 (excess), MeOH. (b) $Na_2S_2O_3$, aqueous DMSO. (c) LDA (excess), PhCH=O (excess), THF, −78 → +20 °C.

−78 °C. Here presumably the dianion **10** was generated. Addition of iodine then led to the diiodo compound **6**, although in only 46% yield under these conditions.

Exposure of pure **6a** to catalytic potassium iodide in dry DMSO led to isomerization; a 50:50 mixture of **6a** and **6b** was obtained, which is presumably the equilibrium mixture. Consistent with the intermediacy of **9b** is the observation of **7** and **5** as significant byproducts using wet DMSO. Thus, nucleophilic attack of iodide ion on an iodine atom presumably affords the nitronate **9b**, which then iodinates at either face to regenerate the diiodo product as an **a**/**b** mixture. Alternatively, the nitronates can be intercepted by water.

Complete deiodination of **6** to dinitrospiropentane **5** occurred in aqueous DMSO solution containing sodium thiosulfate. After 5 min the only isolable product was *trans*-1,2-dinitrospiropentane. It is likely that here also the reaction involves formation of nitronates **9a,b** as intermediates.

Nitroaldol functionalization of **5** has been carried out as a demonstration of the feasibility of nitronate chemistry on the spiropentane ring. Thus, reaction of **5** with excess lithium diisopropylamide at −78 °C in THF in the presence of excess benzaldehyde afforded the dinitrospiropentane **8** in 59% yield. The anion, likely the dianion **10**, could also be preformed and benzaldehyde added after 1 h to give **8** in a somewhat reduced yield (49%). Only one diastereomer of **8** was obtained in these reactions, apparently one in which the nitro groupings are cis and the benzylic centers are related as mirror images (either the *R**,*R**,*S**,*S** or *R**,*S**,*R**,*S** diastereomer). The ^{13}C NMR spectrum showed separate signals for the unsubstituted ring methylene carbons, four aryl carbons that were equivalent for both rings, and equivalent benzylic carbons. An isomer with *trans*-nitro groups would require equivalent methylene carbons on the unsubstituted ring or, alternatively, dissimilar aryl and benzylic carbon atoms. The ^1H NMR spectrum showed equivalent benzylic protons coupled to equivalent hydroxylic protons. The coupling pattern for the unsubstituted ring protons was an apparent pair of triplets, similar to the *cis*-diiodo compound **6a**. An attempt to further elaborate the structure of dinitrospiropentane **8** from crystallographic data was unsuccessful; X-ray data were obtained but could not be refined.

Discussion

The synthesis of *trans*-1,2-dinitrospiropentane (**5**) was relatively straightforward after initial difficulties in obtaining the precursor **2** were worked out. One remarkable feature concerning the structure of **5** is the strong preference for a trans arrangement of the nitro groups. This same preference has previously been noted for 1,2-dinitrocyclopropanes.[6] For dinitrospiropentane **5** equilibrium with the cis isomer is clearly possible through the intermediacy of nitronate **9a**. However, no formation of *cis*-dinitrospiropentane has been observed under conditions where the nitronate of **5** has been generated (i.e., during formation of **5** and during deiodination of **6a,b**).

The iodinated dinitrospiropentanes **6a,b** and **7** are without precedence in the literature. Simple α-iodo nitro compounds are

Table I. Effect of Various Bases on Dinitrospiropentane **5** in DMSO Solution

conjugate acid	pK_a[a]	result	time (min)
fluorene	*22.6*	***5 destroyed***	*12*
pyrazole	19.8	**5** destroyed	16
4-chloro-2-nitroaniline	18.9	**5** destroyed	15
imidazole	18.6	25% recovery of **5**[b]	15
$PhCOCH_2Ph$	17.65	**5** remains	15
CH_3NO_2	17.2	92% recovery of **5**[b]	12
$PhSO_2NH_2$	16.1	**5** remains	10
2,3-dihydroxynaphthalene	13.7	**5** remains	12

[a] K^+ salt in DMSO; data from ref 14a. [b] By isolation.

well-known,[11] but α-iodo, 1,2-dinitro compounds would be expected to undergo elimination of hydrogen iodide. Thus, it would be anticipated that **7** and **6a,b** would afford 1,2-dinitrospiropentene or, more likely, products derived from the spiropentene. Indeed, heating either **6a** or **6b** to its melting point (159 and 152 °C, respectively) gave iodine. Photolysis of **6a,b** in solution also produced iodine. The organic products formed by thermal and photochemical deiodination of **6a** and **6b** are currently under study and will be reported separately.

The formation of diiodo compounds **6a,b** requires nitronate intermediates. The formation of a nitronate on a 3-membered ring is difficult owing to dramatically reduced acidity; thus, the pK_a of nitrocyclopropane was determined to be 26.9 ± 0.2 in DMSO solution with concomitant decomposition.[12] When formed at low temperature in THF, cyclopropyl nitronates typically dimerize, although it has recently been shown that 1,1-dialkyl-2-nitrocyclopropanes can form anions sufficiently stable to undergo nitroaldol reactions.[13]

The first pK_a of dinitrospiropentane **5** in DMSO solution has been estimated using the method of Bordwell et al.[14] Using fluorene (pK_a = 22.6) and its anion as indicators, it was determined that the first pK_a is less than 21.6 for dinitrospiropentane **5**; rapid complete monodeprotonation within experimental error was noted. However, dinitrospiropentane is base-sensitive in DMSO. Thus, **5** was totally decomposed within 15 min using the conjugate bases of acids having pK_a's ≥ 18.9 (Table I). Attempts to isolate the products of decomposition were unsuccessful as several materials were present. Dinitrospiropentane **5** can be recovered from less basic DMSO solutions (pK_a ≤ 18.6 for the conjugate acid of the base). Thus, the pK_a of **5** must lie in the range of 18.6–21.6, at least five pK_a units lower than nitrocyclopropane.

Two factors may be responsible for the relatively high acidity of dinitrospiropentane **5**. The inductive effect of a β-nitro group would be expected to increase the acidity of a nitro compound significantly. Such is the case for 1,2-dinitroethane (pK_a's: first, 5.9; second, 7.4) compared to nitroethane (pK_a 9.58) in aqueous alcohol.[15] Indeed, double deprotonation of **5** by excess lithium diispropylamide to give the conjugatively stabilized dinitronate **10** is consistent with the very low second pK_a value for 1,2-dinitroethane.

A second factor that may contribute to stabilization of the nitronates **9** and **10** is interaction with the adjacent spiro cyclopropane ring. The anion of (cyclopropylmethyl)benzene is slightly stabilized compared to the anion of butylbenzene.[16] Semiempirical

Figure 2. Conformations of cyclopropylcarbinyl anions.

INDO calculations are in agreement with such stabilization but suggest a preferred perpendicular conformation for maximum stabilization (Figure 2).[17] Unfortunately, the geometry of the spiropentane ring system requires a bisected conformation for the nitronate. It is therefore concluded that minimal stabilization of the nitronate is provided by the spiro cyclopropane ring.

In conclusion, we note that several spiropentanes containing two vicinal nitro groups can be readily prepared. Such compounds open the door to nitronate chemistry on the spiropentane nucleus. Functionalization of the spiropentane ring via nitronate reactions is clearly feasible. Two routes to nitronate intermediates from dinitrospiropentanes are apparent: simple deprotonation and nucleophilic dehalogenation.

Experimental Section

General. NMR spectra were taken on a Brucker WM-250A instrument in $CDCl_3$ (TMS internal standard), unless noted as CD_2Cl_2 or D_2O (sodium 3-(trimethylsilyl)propionate-*2,2,3,3-d*$_4$ internal standard). Infrared spectra were recorded on Perkin-Elmer 457 and 1610 instruments. Electronic spectra were recorded on a Perkin-Elmer Lambda 2 (version 3.6) UV–vis spectrophotometer. A Welsbach T-408 ozonator fitted with an oxygen cylinder and drying tower (sequential Dry-Rite filled and dry ice cooled traps) was used to generate an ozone/oxygen stream. Elemental analyses were performed by Micro-Analysis, Inc. and Robertson Laboratories. 1,1-Cyclopropanedicarboxylic acid was prepared in 62% yield according to the procedure of Singh and Danishefsky.[18] DMSO was distilled at reduced pressure from CaH_2, and THF was distilled from sodium benzophenone ketyl. Reactions run in DMSO (2–10 mL) were routinely worked up by pouring into water (100 mL), extracting with three 20-mL portions of CH_2Cl_2, combining and washing the CH_2Cl_2 extracts with three 10-mL portions of water, drying the combined extracts with anhydrous Na_2SO_4, and concentrating at reduced pressure.

Preparation of Dimesylate 1b.[7] A 1 M solution of BH_3·THF (84 mL, 84 mmol) was added dropwise over 5 min to a cold (0–5 °C) solution of 1,1-cyclopropanedicarboxylic acid (4.5 g, 34.6 mmol) in THF (90 mL). The resulting solution was stirred for 15 h at ambient temperature and then THF/water (20 mL, 50:50) followed by K_2CO_3 was added. The mixture was stirred for 1 h and was filtered. The filtrate was dried over anhydrous $MgSO_4$. Concentration and Kugelrohr distillation gave 2.7 g (77% yield) of diol as an oil: bp 85–95 °C (0.05 mm); ^1H NMR δ 3.60 (s, 4 H), 3.13 (s, 2 H, OH), 0.51 (s, 4 H).

A cold (0–5 °C) solution of the diol (2.47 g, 24.2 mmol) in pyridine (15 mL) was treated dropwise over 5 min with MsCl (5 mL, 65 mmol), and the mixture was stirred in the cold for 2 h. Water (20 mL) and then concentrated HCl (5 mL) were added. After overnight refrigeration, the mixture was filtered and the solid recrystallized from absolute ethanol. A 4.74-g portion (76% yield) of pure **1b** was obtained as the first crop of crystals: mp 119.5–120 °C (dec, lit.[7] mp 58–60 °C [!]); ^1H NMR δ 4.17 (s, 4 H), 3.06 (s, 6 H), 0.84 (s, 4 H).

Preparation of 1,1-Bis(azidomethyl)cyclopropane (1a). A mixture of **1b** (0.74 g, 2.9 mmol), NaN_3 (0.61 g, 9.4 mmol), and DMSO (12 ml) was heated for 16 h at 58–65 °C under N_2. The reaction mixture was worked up according to the general procedure up to the point where a dried CH_2Cl_2 solution was obtained. In one run the solution was concentrated at room temperature (*caution: potentially explosive product*), giving 0.41 g (93% yield) of **1a**[7] as an oil: IR 2100 cm^{-1} (N_3); ^1H NMR δ 3.29 (s, 4 H), 0.61 (s, 4 H).

The dried CH_2Cl_2 solution of diazide **1a** should be used *without complete concentration* for preparation of the hydrochloride salt **4a**.

Preparation of Hydrochloride Salt 4a. Diazide **1a** was prepared from **1b** (12.93 g, 50 mmol), NaN_3 (8.14 g, 125 mmol), and DMSO (300 mL) by the preceding procedure. The combined washed and dried CH_2Cl_2 layers (250 mL) were concentrated to 20 mL, and THF (200 mL) was added. A solution of Ph_3P (31.47 g, 120 mmol) in THF (100 mL) was added (N_2 evolution), and after 10 min water (3.6 mL) was added. After

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15 h, the reaction mixture was concentrated under reduced pressure, and the residue was taken up in CH_2Cl_2 (200 mL). The amine was extracted as its salt into two 80-mL portions of 10% aqueous HCl. The combined aqueous extracts were washed with CH_2Cl_2 (two 50-mL portions) and concentrated at reduced pressure. The residue was dried under high vacuum over P_2O_5 to give **4a**[7] (7.72 g, 89% yield): ^1H NMR (D_2O) δ 3.09 (s, 4 H), 0.87 (s, 4 H).

Preparation of 1,1-Bis(nitromethyl)cyclopropane (2). Procedure A: From Diamine 4b. Powdered KOH (1.65 g, 29.4 mmol) was added to the cold (0–5 °C) hydrochloride salt **4a** (0.51 g, 2.94 mmol). The resulting mixture was stirred for 1 h at ambient temperature and then Kugelrohr distilled (oven temp 25–55 °C, 0.05 mm) into a dry ice cooled receiver. The wet diamine **4b** (397 mg) was dissolved in MeOH/Et_2O (5 mL, 50:50) and the solution mixed with flash-grade silica gel (20 g, Merck Kieselgel 60, 230–400 mesh). Solvents were removed from the mixture on a rotary evaporator, and the resulting powder was diluted with more silica gel (total weight 240 g) and placed in a jacketed column (5-cm i.d.), which was cooled with dry ice. A 2–3% ozone/oxygen stream was passed through the column for 45 min (blue column contents during the last 10 min). The column was brought to room temperature, purged with N_2, and eluted with Et_2O (500 mL). The eluent was concentrated and the residue purified by preparative TLC (CH_2Cl_2 elution) to give 133 mg (28% yield) of **2**. The analytical sample was Kugelrohr distilled (45–55 °C, 0.05 mm), whereupon it crystallized: mp 27.5–28.5 °C; IR 1555, 1385 cm^{-1} (NO_2); ^1H NMR δ 4.51 (s, 4 H), 1.05 (s, 4 H); ^{13}C NMR δ 79.49 (CH_2NO_2), 17.83 (quat *C*), 12.44 (CH_2CH_2). Anal. Calcd for $C_5H_8N_2O_4$: C, 37.50; H, 5.03. Found: C, 37.81; H, 5.06.

Also isolated as a more polar fraction from the preparative TLC was 1-(nitromethyl)cyclopropanecarboxaldehyde (21 mg, 6% yield). Repeated preparative TLC followed by Kugelrohr distillation (bp 40–55 °C, 0.1 mm) gave an analytical sample: IR (film) 1705 (CH=O), 1555, 1375 cm^{-1} (NO_2); ^1H NMR δ 8.79 (s, 1 H), 4.58 (s, 2 H), 1.54 (m, 2 H), 1.31 (m, 2 H); ^{13}C NMR δ 197.04 (*C*HO), 75.19 (CH_2NO_2), 29.8 (quat *C*), 13.33 (CH_2CH_2). Anal. Calcd for $C_5H_7NO_3$: C, 46.51; H, 5.46. Found: C, 46.33; H, 5.46.

In other runs, column-grade silica gel (Baker, 60–200 mesh) was used, and typical yields of 20–23% were obtained. In some runs a nitrile byproduct and traces of an unidentified aldehyde (likely 1,1-cyclopropanedicarboxaldehyde) contaminating the 1-(nitromethyl)cyclopropanecarboxaldehyde fraction were noted.

Procedure B: From Diazide 1a. To a solution of **1a** (135 mg, 0.9 mmol) in CH_2Cl_2 (4 mL) under N_2 was added Bu_3P (400 mg, 2 mmol) (N_2 evolution). After 45 min the reaction solution was added dropwise over 30 min to a cold (−78 °C) solution of ozone in CH_2Cl_2 (ozone was continuously replenished during addition; a strong blue color was maintained throughout the reaction). At the end of the addition, stirring was continued for 5 min, and then the solution was swept with N_2 to remove excess ozone. The solution was gradually warmed to room temperature, washed with water, and dried over anhydrous Na_2SO_4. Concentration gave crude products that were purified by preparative TLC (CH_2Cl_2). Dinitro compound **2** (17 mg, 12% yield) was obtained as an oil, pure by ^1H NMR. Also obtained was an impure mixture of aldehydes: 1-(nitromethyl)cyclopropane carboxaldehyde and a compound tentatively identified by ^1H NMR as 1,1-cyclopropanedicarboxaldehyde (18 mg, 8:1 ratio, respectively, 13% combined yield). Peaks assigned to the dialdehyde: ^1H NMR δ 9.86 (s, 2 H), 1.76 (s, 4 H). The crude product obtained by PCC oxidation of 1,1-cyclopropanedimethanol gave similar signals but could not be obtained pure by TLC.

When Ph_3P was used rather than Bu_3P, ozonolysis of the crude iminophosphorane gave no nitro product. Using Et_3P gave, after ozonolysis, a 7% yield of **2** accompanied by aldehyde byproducts.

Procedure C: From Nitro Azide 3. A solution of **3** (51 mg, 0.33 mmol) in CH_2Cl_2 (4 mL) under N_2 was treated with Bu_3P (79 mg, 0.39 mmol). After 15 min the solution was added dropwise to a cold (−78 °C) solution of excess ozone in CH_2Cl_2 (15 mL) as in procedure B. Preparative TLC (CH_2Cl_2) of the crude product gave 29 mg (55% yield) of pure **2**.

Preparation of *trans*-1,2-Dinitrospiropentane (5). A solution of dimsyl sodium was prepared under N_2 by reaction of sodium hydride (0.7 g of a 50% w/w mineral oil dispersion, washed with three 5-mL portions of hexanes, 14.7 mmol NaH) with DMSO (200 mL) at 65–75 °C for 20 min. To the cooled (17 °C) solution was added a trace of Ph_3CH followed dropwise over 1 min by a solution of **2** (0.21 g, 1.33 mmol) in DMSO (4 mL). After the red mixture was stirred for 1 additional min at 20 °C, a solution of iodine (6.3 g, 25 mmol) in DMSO (15 mL) was added dropwise over 4 min, slowly at first, more rapidly at the end. After 2 min of additional stirring at 20–25 °C, the reaction mixture was added to cold water (300 mL), and the resultant was treated with $Na_2S_2O_3$ and extracted with three 70-mL portions of CH_2Cl_2. The combined extracts were washed (three 100-mL portions of water), dried (anhydrous Na_2SO_4), and concentrated at reduced pressure, affording a brown oil that was purified by preparative TLC (CCl_4/CH_2Cl_2, 50:50) to give 91 mg (43% yield) of **5** as a white solid. Recrystallization from CCl_4 gave the analytical sample: mp 110–111 °C; IR 1555, 1370 cm^{-1} (NO_2); ^1H NMR δ 5.31 (s, 2 H), 1.72 (m, 2 H), 1.4 (m, 2 H); ^{13}C NMR δ 64.51 ($CHNO_2$), 27.57 (spiro *C*), 9.31 (CH_2). Anal. Calcd for $C_5H_6N_2O_4$: C, 37.98; H, 3.82; N, 17.71. Found: C, 37.96; H, 3.63; N, 17.67.

Preparation of Nitro Azide 3. A cool (15 °C) solution of diazide **1a** (0.31 g, 2.04 mmol) in CH_2Cl_2 (20 mL) was treated with Bu_3P (0.91 g, 3.5 mmol). The resulting solution was stirred for 50 min at 14–17 °C and was then added dropwise to a cold CH_2Cl_2 solution of excess ozone as in the preparation of dinitro compound **2**, procedure B. The crude products were purified by preparative TLC (CCl_4, CH_2Cl_2, 30:70). The least polar fraction (R_f 0.64, 43 mg, 13% yield) was Kugelrohr distilled to furnish an analytical sample of **3**: IR (film) 2095 (N_3), 1555, 1385 cm^{-1} (NO_2); ^1H NMR δ 4.33 (s, 2 H), 3.36 (s, 2 H), 0.77–0.82 (m, 4 H); ^{13}C NMR δ 79.94 (CH_2NO_2), 55.94 (CH_2N_3), 20.03 (quat *C*), 10.92 (CH_2CH_2). Anal. Calcd for $C_5H_8N_4O_2$: C, 37.50; H, 5.03. Found: C, 37.81; H, 5.06.

Also isolated from the preparative TLC was **2** (R_f 0.38, 23.4 mg, 7% yield). 1-(Nitromethyl)cyclopropanecarboxaldehyde was present (R_f 0.16) but was not isolated.

Preparation of 1,2-Diiodo-1,2-dinitrospiropentane (6a,b). To an 0.8 M solution of NaOMe in MeOH (2 mL, 1.6 mmol of NaOMe) was added **5** (13 mg, 0.08 mmol). The resulting solution was stirred for 20 min, and a solution of I_2 (0.58 g, 2.28 mmol) in MeOH (10 mL) was added dropwise over 90 s. The resulting solution was stirred for 10 min. Water and CH_2Cl_2 were added and the layers were separated. The aqueous layer was further extracted with CH_2Cl_2, and the combined CH_2Cl_2 extracts were washed with aqueous $Na_2S_2O_3$ followed by water, dried (anhydrous Na_2SO_4), and concentrated. The residue was purified by preparative TLC (CH_2Cl_2/CCl_4, 50:50) followed by recrystallization from CCl_4 to give 24 mg (72% yield) of **6a,b** (R_f 0.62, 50:50 **a**/**b** mixture). Anal. Calcd for $C_5H_4I_2N_2O_4$: C, 14.65; H, 0.98; N, 6.83. Found: C, 15.02; H, 1.04; N, 6.68.

A mixture of **7** and **5** (5 mg, 75:25 ratio, respectively) was obtained as a more polar fraction (R_f 0.55). The structure of **7** was assigned on the basis of the following spectral data from the mixture: IR (film) 1550, 1355, 1330 cm^{-1} (NO_2); ^1H NMR δ 5.46 (s, 1 H), 1.95–2.05 (m, 1 H), 1.8–1.9 (m, 1 H), 1.6–1.7 (m, 1 H), 1.45–1.55 (m, 1 H); ^{13}C NMR (CD_2Cl_2) δ 69.45 ($CHNO_2$), 43.90 ($CINO_2$), 34.62 (spiro *C*), 15.35 (CH_2), 13.82 (CH_2).

Separation of **6a,b** was effected by preparative TLC (HOAc/EtOAc/hexanes, 2:20:78). A 15-mg sample (50:50 **a**/**b** mixture) afforded 7 mg of *cis*-diiodo compound **6a** as the more polar (R_f 0.74) component: mp 158.5–159.5 °C dec, IR (KBr) 1545, 1340, 1320 cm^{-1} (NO_2); ^1H NMR δ 2.64 (m (apparent t, J = 9.05 Hz), 2 H), 1.35 (m (apparent t, J = 9.05 Hz), 2 H); ^{13}C NMR (CD_2Cl_2) δ 52.16 ($CINO_2$), 41.93 (spiro *C*), 21.9 (CH_2), 19.58 (CH_2).

Also obtained was 7 mg of *trans*-diiodo compound **6b** (R_f 0.81): mp 151–152 °C dec; IR (KBr) 1545, 1315 cm^{-1} (NO_2); ^1H NMR δ 2.29 (m (apparent dd), 2 H), 1.73 (m (apparent dd), 2 H); ^{13}C NMR (CD_2Cl_2) δ 42.96 ($CINO_2$), 40.55 (spiro *C*), 20.11 (2 CH_2).

Isomerization of 6a. A solution containing **6a** (2.6 mg, 0.006 mmol) and KI (0.2 mg, 0.001 mmol) in DMSO (2 mL) was stirred under Ar for 45 min. Workup by the general procedure afforded 2.2 mg (85% recovery) of **6a,b**, which was a 50:50 mixture of cis and trans isomers by ^1H NMR.

Deiodination of 6. A solution of **6a** (6 mg, 0.015 mmol) in DMSO (5 mL) was added to a stirred solution of $Na_2S_2O_3$ (2 g) in water (20 mL). After 5 min the reaction was worked up by the general procedure to give 2 mg of crude product (all **5** by ^1H NMR). Preparative TLC gave 1.5 mg (60% yield) of pure **5**. A sample of **6b** gave similar results.

Nitroaldol Reaction of Dinitrospiropentane 5. Benzaldehyde (0.3 mL, 2.7 mmol) was added to a cold (−78 °C) solution of LDA (0.9 mmol, prepared from 0.37 mL of 2.5 M BuLi and 0.16 mL of iPr_2NH) in THF (10 mL), and the resulting solution was stirred for 2 min. A solution of **5** (22 mg, 0.14 mmol) in THF (3 mL) was then added dropwise over 4 min. The resulting solution was stirred for 2 h at −78 °C and subsequently at room temperature for 2 h. The solution was cooled to −20 °C and was acidified with glacial HOAc (1.5 mL). Volatiles were removed on the rotary evaporator at room temperature, and the residue was taken up in Et_2O (100 mL). The etheral solution was washed (water, 50 mL), dried (anhydrous Na_2SO_4), and concentrated at 0.05 mm. The solid residue was purified by preparative TLC (CH_2Cl_2/HOAc, 99:1) followed by recrystallization from CH_2Cl_2/hexanes to give 30 mg (59% yield) of dinitrospiropentane **8**: mp 134–135 °C; IR (KBr) 3365 (OH), 1555, 1350 cm^{-1} (NO_2); ^1H NMR δ 7.1–7.5 (m, 10 H), 5.29 (d, 2 H, J = 7.1 Hz, C*H*Ph), 4.95 (d, 2 H, J = 7.1 Hz, O*H*), 1.97 (m (apparent t), 2 H), 1.55 (m (apparent t), 2 H); ^{13}C NMR (CD_2Cl_2) δ 136.85, 129.36,

129.25, 125.08 (aryl C), 79.94 (CNO_2), 74.53 (CHPh), 28.95 (spiro C), 9.45 (CH_2), 8.27 (CH_2). Anal. Calcd for $C_{19}H_{18}N_2O_6$: C, 61.62; H, 4.90; N, 7.57. Found: C, 61.22; H, 4.76; N, 7.62.

Dinitrospiropentane **8** was obtained in 49% yield when **5** (11 mg, 0.07 mmol) was added to an LDA (0.5 mmol) solution at -78 °C with stirring for 1 h, followed by addition of PhCHO (0.08 mL, 0.75 mmol) and continuation of the reaction as above.

pK_a of Dinitrospiropentane 5. Spectrophotometric Experiments.[14a] All solutions were weighed directly in the reaction vessels to determine the quantity of added material. Dimsyl potassium solutions (0.1 M) were freshly prepared from KH (35% mineral oil suspension, washed with three portions of hexanes) and distilled, degassed (Ar stream) DMSO. A DMSO solution of fluorene (45.9 mg in 7.88 g of solution) was added in small aliquots (at least six) to the dimsyl potassium solution, with the absorptions at 517 and 455 nm being used to construct a Beer's law plot: the plot was used to determine the concentration of fluorene anion. Excess fluorene was added in all cases prior to the addition of small aliquots of a DMSO solution of **5** (9.5 mg in 11.01 g of solution). The nitronate concentration was determined by the disappearance of fluorene anion, measured spectroscopically.

Isolation Experiments. Dimsyl potassium solution (0.75 mL, 0.11 M, 0.08 mmol of dimsyl potassium) was added to a stirred solution of the conjugate acid (Table I, 0.6 mmol) in DMSO (4 mL). After 4 min, a solution of **5** (2 mg, 0.01 mmol) in DMSO (2 mL) was added. After 10-16 min of additional stirring, the reaction solution was worked up by the general procedure. Results are shown in Table I.

X-ray Structure Determination of Dinitrospiropentane 5. X-ray intensity data were collected on an Enraf-Nonius CAD4 diffractometer employing graphite-monochromated Cu K_α radiation (λ = 1.541 84 Å) and using the ω-2θ scan technique. A total of 673 reflections were measured over the following ranges: $4 \le 2\theta \le 130°$, $0 \le h \le 13$, $0 \le k \le 7$, $-11 \le l \le 11$. Three standard reflections measured every 3500 s of X-ray exposure showed no intensity decay over the course of data collection. The intensity data were corrected for Lorentz and polarization effects but not for absorption. Of the reflections measured, a total of 551 unique reflections with $F^2 > 3\sigma(F^2)$ were used during subsequent structure refinement. The structure was solved by direct methods (MULTAN11/82). Refinement was by full-matrix least-squares techniques based on F to minimize the quantity $\sum w(|F_o| - |F_c|)^2$ with $w = 1/\sigma^2(F)$. Non-hydrogen atoms were refined anisotropically, and hydrogen atoms were included as constant contributions to the structure factors and were not refined. Refinement converged to R_1 = 0.052 and R_2 = 0.094.

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Registry No. 1a, 136476-39-6; **1b**, 136476-38-5; **2**, 136476-32-9; **3**, 136476-33-0; **4a**, 136476-40-9; **5**, 136476-35-2; **6a**, 136476-42-1; **6b**, 136476-43-2; **7**, 136476-36-3; **8**, 136476-37-4; 1,1-cyclopropanedicarboxylic acid, 598-10-7; 1-(nitrometyyl)-1-cyclopropanecarboxaldehyde, 136476-34-1; 2benzaldehyde, 100-52-7; 1,1-bis(hydroxymethyl)cyclopropane, 39590-81-3; 1,1-cyclopropanedicarboxaldehyde, 136476-41-0.

Supplementary Material Available: Tables of crystallographic refined positional parameters, refined displacement (β) parameters, and bond distances and angles (4 pages). Ordering information is given on any current masthead page.

Electrochemical Generation and Reduction of Organic Free Radicals. α-Hydroxybenzyl Radicals from the Reduction of Benzaldehyde

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Abstract: Careful analysis of the kinetics of the electrochemical reduction of benzaldehyde in ethanolic buffers, paying particular attention to the second reduction step(s), shows that the α-hydroxybenzyl radicals formed upon protonation of the initial ketyl radicals are more difficult to reduce than the starting molecule. Thus, a clear example is provided of the lack of general validity of the commonly accepted view that radicals resulting from the addition of electrophiles onto anion radicals should be easier to reduce than the substrate from which they derive. There is then no general impediment to the generation and redox characterization of radicals by electrochemical means along this type of reaction sequence. The main thermodynamic and kinetic characteristics of the reduction, dimerization, and proton exchange interconversion of the α-hydroxybenzyl and benzaldehyde ketyl radicals are derived from the experimental data.

Neutral free radicals may be generated upon electrochemical reduction of organic substrates either directly by dissociative electron transfer or from chemical transformation of an initially formed anion radical. Once formed, these free radicals may in both cases undergo an electron transfer from the electrode surface, leading to the corresponding carbanions. In the second case, they may also be reduced in the solution by electron transfer from the parent anion radicals. The relative value of the reduction potentials of the substrate and of the resulting neutral radical is an essential factor governing the possibility of triggering either a radical or a carbanion chemistry by electrochemical reduction of organic substrates. More generally, gathering thermodynamic and kinetic data on the redox properties of organic free radicals is certainly an important task in radical chemistry from both a mechanistic and a synthetic point of view. For this purpose, an elegant method has been recently developed in which the radical is generated photochemically and characterized electrochemically.[2] If possible, i.e., in the case where the reduction potential of the radical would be more negative than that of the substrate, the use of standard electrochemical techniques such as cyclic voltammetry for both generating the radical and measuring its electrochemical properties would also be a quite valuable tool.[3]

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