

Synthesis of γ -disubstituted nitroalkyl compounds through a new solvomercuration- $S_{RN}1$ reaction sequence

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Dedicated to Rosa M. de Lederkremer

Abstract

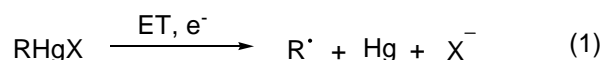
The synthesis of γ -disubstituted nitroalkanes using alkenes as starting materials is described. The synthetic strategy involves a first step of solvomercuration followed by an $S_{RN}1$ substitution reaction in DMSO as solvent under photoinitiation. The target compounds are obtained in good yields and the factors governing the distribution of substitution products are discussed.

Keywords: Nitroalkanes, nitranions, $S_{RN}1$ reactions, solvomercuration, radicals, electron transfer

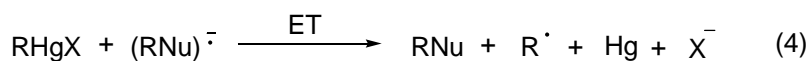
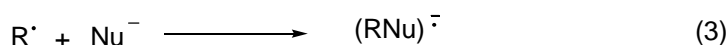
Introduction

The organic compounds of mercury are known from the middle 1800 and are probably the first established family of organometallics.¹ Organomercury compounds are usually stable to air, water and temperature and this contributed to the early development of their chemistry. Among their synthetic applications, the solvomercuration-demercuration process is one of the most studied and used method for the selective Markovnikov addition of different nucleophiles to olefins,² which leads to the formation of alcohols, ethers, amines, etc.

Organomercury hydrides have a weak Hg-H bond and the mercury hydride method has been widely used in radical chemistry.³ Organomercury halides does not react with nucleophiles by polar nucleophilic substitution reactions ($C^{\delta-}-Hg^{\delta+}X$), but are easily reduced ($-0.6V$)⁴ to alkyl radical ($R\cdot$), mercury metal and halide ion by electron donors (eq. 1).



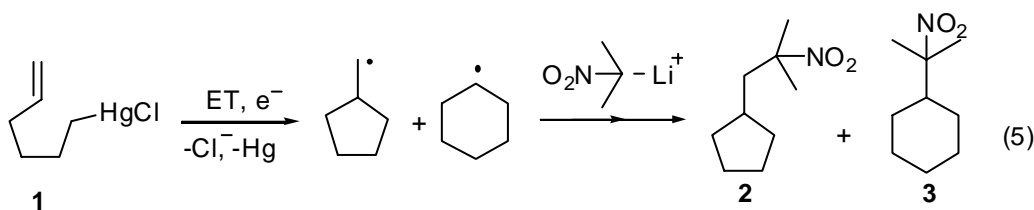
The ET from the electron donor to the organomercurial is proposed to be dissociative.⁵ The unimolecular radical nucleophilic substitution reaction, or $S_{RN}1$,⁶ is a chain process that has radical and radical anions as intermediates and has been shown that organomercury halides react with carbanions by this mechanism.⁷ The main steps of the $S_{RN}1$ reaction of organomercury halides are shown in Scheme 1. This chain process requires an initiation step. In a few systems, spontaneous electron transfer (ET) from the nucleophile to the substrate has been observed. When the ET does not occur spontaneously, it can be induced by light stimulation. In the initiation step (eq. 2) the ET to the substrate (RHgX) gives an alkyl radical (R^\cdot) which couples with the Nu^- in the first step of the propagation cycle (eq. 3). The radical anion of the substitution product (RNu^\cdot) transfers the odd electron to the substrate to give the substitution product, RNu , and the alkyl radical that propagates the chain reaction (eq. 4).



Scheme 1

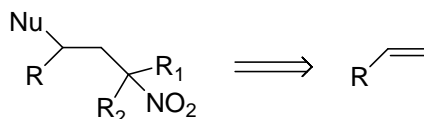
Different alkylmercury halides react by the $S_{RN}1$ mechanism with nitronate salts under photostimulation in DMSO to give substitution products from low to excellent yields (0-100%).⁸

Under irradiation, the radical probe 5-hexenylmercury chloride (**1**) reacts with the lithium salt of 2-nitropropane anion to give 5-*exo* (**2**) and 6-*endo* (**3**) cyclization products with a ratio 2/3 of 25 (eq. 5).⁸



On the other hand, nitro compounds have been widely used in organic synthesis as key intermediates or as final synthetic products.⁹

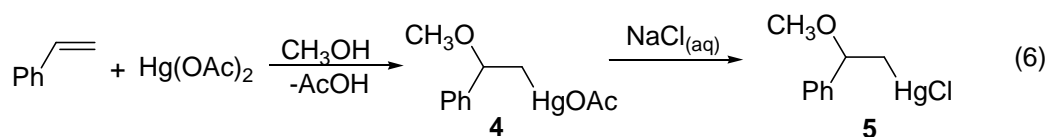
The easy access to organomercury chlorides through the solvomercuration reaction and the usefulness of nitroalkyl compounds in organic synthesis induced us to study a new and readily available method for the synthesis of γ -disubstituted nitroalkanes by a sequence of solvomercuration- $S_{RN}1$ reaction using alkenes as starting materials, and anions of nitroalkyl compounds as nucleophiles (Scheme 2).



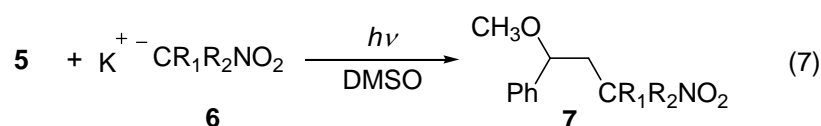
Scheme 2

Results and Discussion

Styrene reacts with $\text{Hg}(\text{OAc})_2$ in methanol to give 2-methoxy-2-phenyl-ethylmercury acetate (**4**) which precipitates as the chloride **5** when aqueous NaCl is added (eq. 6).¹⁰



Organomercurial compound **5** reacts with the potassium salt of nitromethane anion under photostimulation in DMSO to give 1-(1-methoxy-3-nitropropyl)benzene (**7a**) in 60% yield (eq. 7, entry 1 in Table 1).



6a: $\text{R}_1 = \text{R}_2 = \text{H}$, **6b:** $\text{R}_1 = \text{H}$, $\text{R}_2 = \text{CH}_3$, **6c:** $\text{R}_1 = \text{R}_2 = \text{CH}_3$, **7a:** $\text{R}_1 = \text{R}_2 = \text{H}$, **7b:** $\text{R}_1 = \text{H}$, $\text{R}_2 = \text{CH}_3$, **7c:** $\text{R}_1 = \text{R}_2 = \text{CH}_3$

With an irradiation time of 180 min and using six folds of the nucleophile, the yield of **7a** increases up to 75% (entry 2 in Table 1). The reaction does not occur in the dark and the photostimulated reaction is completely inhibited in the presence of a good radical scavenger as di-*tert*-butylnitroxide⁶ (entries 3 and 4 in Table 1). These results indicate that the substitution reaction proceeds by the $\text{S}_{\text{RN}}1$ mechanism.

As liquid ammonia is one of the best solvents for $\text{S}_{\text{RN}}1$ reactions, since the H abstraction by radicals is a slow process, we studied the reaction in this solvent. It is known that nitronate anion does not initiate $\text{S}_{\text{RN}}1$ reactions under irradiation in liquid ammonia due to its low lying HOMO, however, it reacts efficiently at the coupling step of the propagation cycle due to the low lying SOMO of the radical anion of the substitution product that is formed. On the other hand, the enolate anion of acetone initiates the photostimulated reactions in liquid ammonia, but does not couple with primary alkyl radicals (*Entrainment Reagent*).¹¹ A mixture of nitromethane anion **6a**

and acetone enolate anion in liquid ammonia react with organomercury chloride **5** under photostimulation to give disubstituted nitroalkane **7a** with excellent yield (entry 5, Table 1).

In order to extend the scope of the reaction, other nitronate anions salts were tested. In the reaction of **5** with nitroethane anion (**6b**) the formation of the two different diastereomers of **7b** are anticipated. These two compounds, which are formed in almost the same ratio, have similar retention time and fragmentation pattern by GC/MS. However, the most volatile one could be isolated as pure oil by column chromatography, and the ^1H NMR decoupling experiments suggested that it is formed by 1*S*-3*S* and 1*R*-3*R* pairs of enantiomers (see Experimental Section, entry 6 in Table 1).

Table 1. Photostimulated reactions of organomercury chlorides with carbanions^a

Entry	Substrate	Nucleophile	Product (%)
1 ^b	5	6a	7a (60)
2	5	6a	7a (75)
3 ^c	5	6a	7a (0)
4 ^d	5	6a	7a (0)
5 ^e	5	6a	7a (86)
6	5	6b	7b^f (73)
7	5	6c	7c (71)
8	8	6a	9^g (57)
9	10	6a	11 (30)
10 ^e	10	6a	11 (55)
11	12	6a	13 (74)
12	10	$\text{^-CH}_2\text{COPh}$	14 (10)
13 ^h	10	$\text{^-CH}_2\text{COPh}$	14 (20)

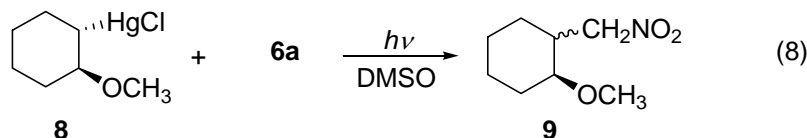
^a Reaction conditions: DMSO, 0.05 M on the substrates and 0.3 M on the nucleophiles, irradiation time was 180 min, otherwise indicated. All yields were determined by GC using the internal standard method. ^b Nucleophile concentration was 0.15 M and the irradiation time was 120 min. ^c Dark conditions. ^d 10 mol% of di-*tert*-butylnitroxide was added. ^e In liquid ammonia with 0.01 M of acetone enolate anion, the substrate concentration was 0.005 M and the nucleophile was 0.03 M, irradiation time was 150 min. ^f Mixture of the two diastereomers formed with a 1:1 ratio. ^g Mixture of *trans* and *cis* isomers (*trans/cis*: ca. 1.4). ^h With 1 equivalent of 18-crown-6.

The organomercury compound **5** reacts with 2-nitropropane anion (**6c**) to give the expected substitution product **7c** with good yield (entry 7 in Table 1).

In the same fashion, *trans*-2-methoxy-cyclohexylmercury chloride (**8**) was easily obtained from cyclohexene.¹² Russell found that the reaction of **8** with the lithium salt of 2-nitropropane

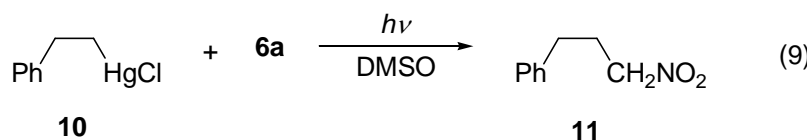
gives the *cis-trans* mixture of products with a ratio of 1/8. This reaction is slow and very long time (47 hours) is required, however, substitution products are obtained in poor yields (14.5%).^{8b}

We performed the photostimulated reaction of substrate **8** with the potassium salt **6a** in only three hours. This reaction affords the expected mixture of nitroalkanes **9** in 57% yield (eq. 8, entry 8 in Table 1).



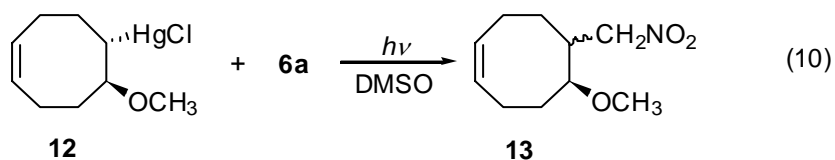
We obtained a *cis/trans* ratio of 1/1.4 which agrees with the expected lower selectivity but higher reactivity from the primary nitromethane anion compared to the tertiary 2-nitropropane anion.

In order to test the influence of the β -OCH₃ group, substrate **10** was prepared from styrene by reaction with BH₃/THF complex in THF followed by mercuration.¹³ Organomercurial **10** reacts with **6a** to give 1-(3-nitropropyl)benzene (**11**) in 30% yield (eq. 9, entry 9 in Table 1).

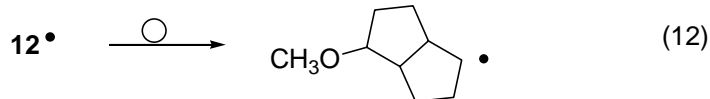
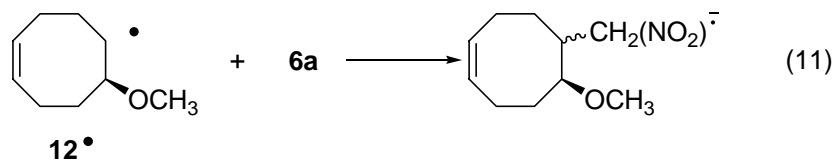


Substrate **10** reacts with **6a** in liquid ammonia under photostimulation to yield **11** in 55% (entry 10 in Table 1).

Radical probes have been used to demonstrate the presence of radicals along the propagation cycle of the S_{RN}1 mechanism.¹⁴ In order to trap intermediate radicals, the radical probe **12** was prepared from 1,5-cyclooctadiene. Conversely, in the reaction of **12** with nucleophile **6a** only uncyclized product **13** was formed in a 74% yield (entry 11 in Table 1) and no 5-*exo* ring closure compound could be observed (eq. 10).



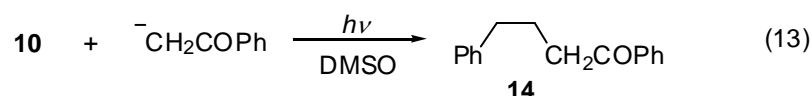
This result indicate that the intermediate radical **12**[·] couples faster with **6a** (eq.11) than the intramolecular 5-*exo* cyclization (eq. 12), in agreement with the expected high reactivity of carbanions derived from nitroalkyl compounds.¹⁵



In this reaction two different substitution products are formed. The ^1H NMR of the mixture of compounds clearly shows the vinylic protons signals, indicating that no cyclization occurred and that they are probably *cis/trans* isomers. The most volatile product was isolated by column chromatography and the ^1H NMR suggests that this compound is the *cis* isomer (See Experimental Section).

The enolate anions of ketones are probably the most studied nucleophiles in $\text{S}_{\text{RN}}1$ reactions,⁶ however, substrate **5** does not react with the enolate anion of acetophenone in DMSO or liquid ammonia under photoinitiation. It is known that 18-crown-6 increases the reactivity of enolate anion of acetophenone in the $\text{S}_{\text{RN}}1$ mechanism.¹⁶ No substitution product was formed in the reaction performed in the presence of 18-crown-6, or acetone enolate anion and only small amounts of styrene were detected by GC/MS.

Acetophenone enolate anion reacts with substrate **10** which lacks the $\beta\text{-OCH}_3$ group, to give 1,4-diphenylbutan-1-one (**14**) in 10% yield (eq. 13, entry 12 in Table 1). The ketone **14** is obtained in a 20% yield when the reaction is performed with 1 equivalent of 18-crown-6 (entry 13 in Table 1).

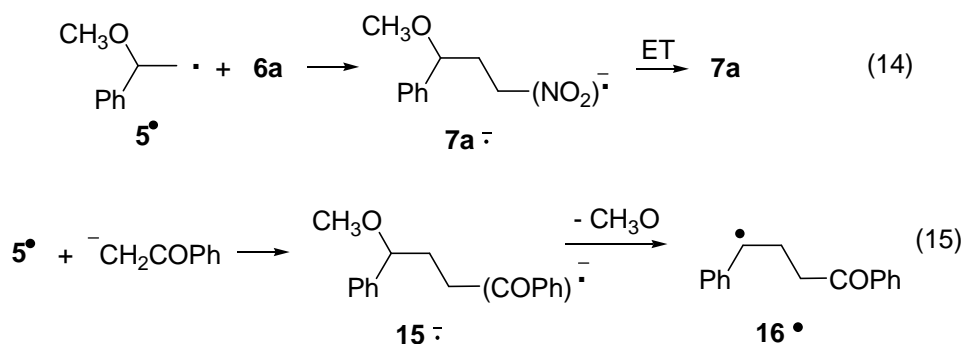


These results suggest that the $\beta\text{-OCH}_3$ plays a central role in the reaction of substrate **5** with acetophenone enolate anion.

The fragmentation of the C-O bond in radical anions of diphenyl and phenyl alkyl ethers is a well recognized process that had theoretically and experimentally been studied. The reaction is seen as the intramolecular ET from π^* MO to the σ^* C-O MO bond followed by homolytic or heterolytic fragmentation.¹⁷

Nitromethane anion **6a** is a low lying HOMO nucleophile that, when coupling with intermediate radical **5** \cdot , gives radical anion **7a** \cdot^- which has a low lying SOMO which is mainly located on the nitro group. Probably, this fact prevents fragmentation of the intermediate radical anion **7a** \cdot^- . ET from **7a** \cdot^- to the substrate propagates the chain reaction (eq. 14). On the other hand, coupling of radical **5** \cdot with acetophenone enolate ion would afford radical anion **15** \cdot^- that

may fragment to give radical **16**· which can not propagate the chain reaction (termination step) and the substitution product is not formed (eq. 15).



In summary, in this work we present a simple and readily available method for the synthesis of γ -disubstituted nitroalkyl compounds using alkenes as starting materials. The $S_{\text{RN}}1$ mechanism accounts for the substitution reactions and the products are obtained in good yields. More work is in progress in order to extend the scope of this new synthetic strategy.

Experimental Section

General Procedures. The internal standard method was used for all quantitative GC analyses with authentic samples and HP-1 (30 m x 0.32 mm) column. ^1H NMR (200.13 MHz) and ^{13}C NMR (50.32 MHz) were conducted in deuteriochloroform as a solvent otherwise indicated, and referenced with residual solvent signal. Coupling constants (J) are given in Hertz. GC/MS analyses were carried out on a Shimadzu QP-5050 apparatus coupled with a mass selective detector and a DB-5 (30 m x 0.25 mm ID) capillary column. High resolution mass spectra were performed at the Mass Spectrometry Facility of the University of California, Riverside, United States.

Materials. In radial thin layer chromatography purifications, 2 mm plates (silica gel 60 PF ₂₅₄) were used. DMSO was distilled under vacuum and stored over molecular sieves (4 Å). Acetone, acetophenone, styrene, cyclohexene, 1,5-cyclooctadiene, nitromethane, nitroethane, and 2-nitropropane were doubly distilled and stored over molecular sieves (4Å). In all purifications analytical grade solvents were employed and used as received from the suppliers.

Substrates

2-Methoxy-2-phenylethylmercury chloride (5). This compound was prepared as previously indicated¹⁰ (pf: 71.2-72°C. Lit¹⁰: 67-70°C).

trans-2-Methoxy-ciclohexylmercury chloride (8). This compound was prepared as previously indicated¹² (pf: 113-115°C. Lit¹²: 114-115°C).

2-Phenylethylmercury chloride (10). This substrate was prepared by a reported method¹³ (pf: 165.5-166°C. Lit: 165.5-166°C¹³).

8-Methoxycyclooct-4-enyl-mercury chloride (12). This compound was prepared following a procedure previously indicated,¹⁸ but switching acetate to chloride ion by adding aqueous sodium chloride (pf: 44-46°C).

S_{RN}1 Reactions in DMSO as solvent. In a previously flame dried three necked 25 mL round bottomed flask equipped with a magnetic stirrer were added 10 mL of DMSO under nitrogen. The solvent was degassed with vacuum and then *t*-BuOK and the conjugated acids of the nucleophiles were added. After 10 min of waiting for the nucleophiles formation, solid organomercury compounds were added. The reactions were irradiated using two medium pressure mercury lamps (λ_{max} : 400 nm) for the times indicated in Table 1. After irradiation, the reactions were quenched by adding ammonium nitrate and water in excess. The aqueous phase was extracted thrice with dichloromethane (50 mL) and the organic phase was washed with water and dried with magnesium sulfate. The solvent was removed under reduced pressure and the products were purified as indicated. When the reactions were performed with quantitative purposes, an adequate internal standard was added previous to the extraction with dichloromethane.

Reactions of in liquid ammonia. The reaction of **6a** with **5** is representative: In a previously flame dried three necked 250 mL round bottomed flask equipped with a cold finger condenser charged with ethanol, a nitrogen inlet and a magnetic stirrer were distilled 200 mL of sodium dried liquid ammonia. *t*-BuOK (8.8 mmol) was added and then nitromethane (6.0 mmol) and acetone (2.0 mmol) waiting 10 min for the nucleophile and entrainment formation. Organomercury compound **5** was added and the reaction irradiated 150 min with two medium pressure mercury lamps (λ_{max} : 400 nm) and quenched by adding ammonium nitrate in excess. After solvent evaporation, water was added (50 mL), and the work up was similar to previously indicated.

1-(1-Methoxy-3-nitropropyl)benzene (7a). Slightly yellow liquid purified by radial thin layer chromatography using dichloromethane-hexane mixture as solvent. ¹H RMN: 2.35 (q, 2H ³J: 6.85 Hz), 3.21 (s, 3H), 4.23 (t, 1H, ³J: 6.85 Hz), 4.34-4.65 (m, 2H), 7.25-7.36 (m, 5H). ¹³C RMN: 35.47; 56.76; 72.28; 80.20; 126.32; 128.16; 128.69; 140.31. GC/MS EI, *m/z* (%): 51 (18); 77 (40); 91(33); 105 (21); 115 (12); 121 (100); 149 (3, M⁺-NO₂). HRMS (CI/NH₃) calc for C₁₀H₁₇N₂O₃, 213.1239 found, 213.1243.

1-(1-Methoxy-3-nitrobutyl)benzene (7b). Slightly yellow liquid purified by radial thin layer chromatography using dichloromethane-hexane mixture as solvent. ¹H RMN: 1.56 (d, 3H, ³J: 6.94 Hz); 2.00 (dq, 1H, ³J: 3.3, 10.2, *J*_{gem}: 15.7 Hz); 2.31 (dq, 1H, ³J: 2.92, 10.2, *J*_{gem}: 15.7 Hz); 3.20 (s, 3H); 4.10 (dd, 1H, ³J: 2.92, 10.2 Hz); 4.90-5.06 (m, 1H), 7.22-7.33 (m, 5 H). ¹³C RMN: 20.02; 43.82; 56.94; 79.91; 80.45; 126.24; 128.04; 129.69; 140.74. GC/MS EI, *m/z* (%): 51 (16); 59 (21); 77 (23); 91 (22); 105 (18); 121 (100); 137 (11); 163 (1, M⁺-NO₂).^{19,20}

The other diastereomer was not obtained pure, but it was quantified assuming identical response as **7b** in the FID of the GC, GC/MS EI, m/z (%): 51 (15); 59 (13); 77 (21); 91 (18); 105 (13); 121 (100); 137 (7); 163 (1) (M^+-NO_2).

1-(1-Methoxy-3-methyl-3-nitrobutyl)benzene (7c). Slightly yellow liquid purified by radial thin layer chromatography using dichloromethane-hexane mixture as solvent. 1H RMN: 1.63 (s, 6H); 2.06 (dd, 1H, 3J : 2.56, J_{gem} : 15.16 Hz); 2.46 (dd, 1H, 3J : 9.86, J_{gem} : 15.16 Hz); 3.09 (s, 3H), 4.16 (dd, 1H, 3J : 2.56, 9.86 Hz), 7.22-7.33 (m, 5H). ^{13}C RMN: 26.17; 26.76; 48.59; 56.43; 80.29; 86.95; 126.32; 127.94; 128.61; 141.39. GC/MS EI, m/z (%): 41 (11); 73 (27); 77 (28); 91 (21); 105 (17); 121 (100); 137 (13); 176 (2, M^+-HNO_2).²¹

trans 1-Methoxy-2-(nitromethyl)cyclohexane (9). Slightly yellow liquid purified by radial thin layer chromatography using dichloromethane-hexane mixture as solvent. 1H RMN: 0.84-1.25 (m, 6H); 1.66-1.84 (m, 2H); 2.11-2.23 (m, 1H); 2.91 (td, 1H, 3J : 4.02; 9.86 Hz); 3.32 (s, 3H); 4.28 (dd, 1H, 3J : 7.85, J_{gem} : 11.87 Hz); 4.65 (dd, 1H, 3J : 4.93, J_{gem} : 11.87 Hz) ^{13}C RMN: 24.17; 24.87; 28.59; 30.18; 42.64; 55.98; 78.64; 80.53. GC/MS EI, m/z (%): 41 (81); 45 (100); 55 (43); 67 (37); 71 (17); 95 (66); 127 (2, M^+-NO_2). HRMS (CI/NH₃) calc for C₈H₁₉N₂O₃, 191.1396 found, 191.1403.²²

cis 1-Methoxy-2-(nitromethyl)cyclohexane (9). This compound was not obtained pure, but it was quantified assuming identical response as the *trans* isomer in the FID of the GC. GC/MS EI, m/z (%): 41 (69); 45 (100); 55 (44); 67 (31); 71 (16); 95 (60); 127 (2, M^+-NO_2).

1-(3-Nitropropyl)benzene. This compound was identified by an Spike test using an authentic sample prepared as previously reported.²³

cis 5-Methoxy-6-(nitromethyl)cyclooct-1-ene (13). Slightly yellow liquid purified by radial thin layer chromatography using dichloromethane-hexane mixture as solvent. 1H RMN: 1.26-1.48 (m, 2H); 1.58-2.14 (m, 5H); 2.37-3.77 (m, 3H); 3.42 (s, 3H); 3.39 (ddd, 1H, J_{ax-ax} : 7.3, J_{ax-eq} : 4.02, J_{ax-eq} : 1.46 Hz); 4.26 (dd, 1H, J_{gem} : 12.4, 3J : 6.40 Hz); 4.48 (dd, 1H, J_{gem} : 12.4, 3J : 8.03 Hz); 5.66 (m, 2H). ^{13}C RMN: 22.13; 24.12; 27.52; 30.16; 39.11; 57.14; 79.88; 80.29; 128.61; 130.71. GC/MS EI, m/z (%): 41 (100); 43 (26); 45 (30); 53 (19); 58 (10); 67 (72); 71 (15); 77 (14); 79 (48); 81 (12); 91 (24); 93 (30); 153 (5, M^+-NO_2). HRMS (CI/NH₃) calc for C₁₀H₂₁N₂O₃, 217.1552 found, 217.1550.²⁴

trans 5-Methoxy-6-(nitromethyl)cyclooct-1-ene (13). This compound was not obtained pure, but was quantified assuming identical response as the *cis* isomer in the FID of the GC. GC/MS EI, m/z (%): 41 (100); 43 (27); 45 (32); 53 (20); 55 (38); 71 (13); 79 (46); 81 (13); 85 (14); 93 (28); 95 (12); 153 (16, M^+-NO_2).

1,4-Diphenylbutan-1-one (14). This compound was identified using an authentic sample prepared as previously indicated.²⁵

Acknowledgments

This work was supported in part by Agencia Córdoba Ciencia de la Provincia de Córdoba, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), SeCyT Universidad Nacional de Córdoba and FONCYT. MEB and SEV gratefully acknowledge the receipt of fellowships from CONICET.

References and Footnotes

1. (a) Makarova, L. G.; Nesmeyanov, A. N. In *Methods of Elemento-Organic Chemistry. The Organic Compounds of Mercury*, North Holland Publishing Co.: Amsterdam, 1967. (b) Staub, H.; Zeller, K. P.; Leditsche, H. In *Houben-Weyl: Methoden der Organischen Chemie*. 4th Edit. Vol. 13/2b. Thieme: Stuttgart, 1974.
2. (a) Larock, R. C. *Angew. Chem. Int. Ed.* **1978**, *17*, 27. (b) Larock, R. C. In *Organomercury Compounds in Organic Synthesis*, Springer-Verlag: Heidelberg and New York 1985. (c) Chatt, J. *Chem. Rev.* **1951**, *48*, 7.
3. (a) Barluenga, J.; Yus, M. *Chem. Rev.* **1988**, *88*, 487. (b) Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541. (c) Giese, B. In *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*; Pergamon: Oxford, 1986.
4. (a) Kurosawa, H.; Okada, H.; Hattori, T. *Tetrahedron Lett.* **1981**, *22*, 4495. (b) Hush, N. S.; Oldham, K. B. *J. Electroanal. Chem.* **1963**, *6*, 34.
5. Russell, G. A. In *Advances in Free Radical Chemistry*, JAI Press Inc.: London, 1990; Vol. 1, p1.
6. (a) Rossi, R. A.; Pierini, A. B.; Peñeñory, A. B. *Chem. Rev.* **2003**, *103*, 71. (b) Rossi, R. A.; Pierini, A. B.; Santiago, A. N. *Aromatic Substitution by the S_{RN}1 Reaction*, In *Organic Reactions*; Paquette, L.A.; Bittman, R., Eds; Wiley: New York, 1999, p. 1. (c) Rossi, R. A.; de Rossi, R. H. In *Aromatic Substitution by the S_{RN}1 Mechanism*, ACS: Washington D.C., 1983. (d) Rossi, R. A. In *Synthetic Organic Photochemistry*; Griesberck, A. G., Mattay, J. Eds.; Marcel Dekker: New York, 2005; Vol. 12, Ch. 15. p 495.
7. Russell, G. A. *Acc. Chem. Res.* **1989**, *22*, 1.
8. (a) Russell, G. A.; Hershberger, J.; Owens, K. *J. Am. Chem. Soc.* **1979**, *101*, 1312. (b) Russell, G. A.; Hershberger, J.; Owens, K. *J. Organomet. Chem.* **1982**, *225*, 43.
9. (a) Kornblum, N. *Aldrichim. Acta* **1990**, *23*, 71. (b) Ono, N. In *The Nitro Group in Organic Synthesis*, Wiley-VCH, 2001.
10. Lewis, A.; Azoro, J. *J. Org. Chem.* **1981**, *46*, 1764.
11. (a) Peñeñory, A. B.; Rossi, R. A. *Gazz. Chim. Ital.* **1995**, *125*, 605. (b) Vaillard, S. E.; Postigo, A.; Rossi, R. A. *J. Org. Chem.* **2002**, *67*, 8500.
12. Brown, H. C.; Rei, M.H. *J. Am. Chem. Soc.* **1969**, *91*, 5646.
13. Larock, R. C.; Brown, H. C. *J. Am. Chem. Soc.* **1970**, *92*, 2467.

14. (a) Santiago, A. N.; Rossi, R. A. *J. Chem. Soc., Chem. Commun.* **1990**, 206. (b) Ashby, E. C.; DePriest, R. N.; Su, W. *Organometallics* **1984**, *3*, 1718. (c) Beckwith, A. L. J.; Palacios, S. M. *J. Phys. Org. Chem.* **1991**, *4*, 404. (d) Annunziata, A.; Galli, C.; Marinelli, M.; Pau, T. *Eur. J. Org. Chem.* **2001**, 1323.
15. The estimate coupling rate constant of neophyl radicals with anion **6a** is at least of the order of 106 M⁻¹ s⁻¹. Argüello, J. E.; Peñéñory, A. B.; Rossi, R. A. *J. Org. Chem.* **2000**, *65*, 7175.
16. Rossi, R. A.; Pierini, A. B.; Borosky, G. L. *J. Chem. Soc. Perkin Trans. 2* **1994**, 2577.
17. (a) Asensio, X.; Gonzalez-Lafont, A.; Marquet, J.; Lluch, J. M. *J. Org. Chem.* **2005**, *70*, 540. (b) Casado, F.; Pisano, L.; Farriol, M.; Gallardo, I.; Marquet, J.; Melloni, G. *J. Org. Chem.* **2000**, *65*, 322. (c) Cayón, E.; Marquet, J.; Lluch, J. M.; Martin, X. *J. Am. Chem. Soc.* **1991**, *113*, 8970. (d) Marquet, J.; Cayón, E.; Martin, X.; Casado, F.; Gallardo, I.; Moreno, M.; Lluch, J. M. *J. Org. Chem.* **1995**, *60*, 3814. (e) Pisano, L.; Farriol, M.; Asensio, X.; Gallardo, I.; Gonzalez-Lafont, A.; Lluch, J. M.; Marquet, J. *J. Am. Chem. Soc.* **2002**, *124*, 4708.
18. Franz, H. J.; Höbold, R.; Höhn, G.; Müller-Hagen, R.; Müller, W.; Pritzkow, W.; Schmidt, J. *J. Prakt. Chem.* **1970**, *312*, 622.
19. The structure of this compound was assigned as the diastereomer former by *1S-3S* and *1R-3R* pair of enantiomers based on decoupling experiments. Both dq belong to the signals of protons at C2 which are diastereotopic. The dq at 2.31 is given by a proton *gauche* to the nitro group (H2b), and dq at 2.00 by the remaining proton (H2a). The dd at 4.10 belongs to the proton at C1 and the m at 4.98 to the proton at C3. When the signal at 4.10 is decoupled, the signal of H2b gives a dd with a ³J: 10.2 Hz, J_{gem}: 15.7 Hz and H2a a dd with a ³J: 3.3 Hz, J_{gem}: 15.7 Hz; this indicates that H2b, that is *gauche* with de nitro group, is *anti* to the proton at C3. When the signal at 4.98 is decoupled, the dq of H2b gives a dd with ³J: 2.92 Hz, J_{gem}: 15.7 Hz and H2a a dd with ³J: 10.2 Hz y J_{gem}: 15, 7 Hz; this indicates that H2a is *anti* with the proton at C1. If we assume that the biggest groups at C1 and C2, namely the phenyl and the CH(CH₃)NO₂ groups, must be *anti* to each other, this diastereomer only can be that formed by the *1S-3S* and *1R-3R* pair of enantiomers.
20. Dilman, A. D.; Lyapkalo, I. M.; Ioffe, S. L.; Strelenko, Y. A.; Tartakovskiy, V. A. *J. Org. Chem.* **2000**, *65*, 8826
21. Kurosawa, H.; Okada, H.; Sato, M.; Hattori, T. *J. Organomet. Chem.* **1983**, *250*, 83.
22. The *trans* structure to this compound was assigned based on td at 2.91 which correspond to the proton at C1. A value of ³J: 9.87 Hz is characteristic of an axial proton in a cyclohexane ring that has two axial vicinal protons too. If protons at C1 and C2 are axial, the OCH₃ and the CH₂NO₂ groups must be equatorial and so it is *trans* isomer.
23. Bordwell, F. G.; Bartmess, J. E. *J. Org. Chem.* **1978**, *43*, 3101.
24. The suggested *cis* structure to this compound was assigned based to the ddd at 3.39 which correspond to the proton at carbon 5. A coupling constant of 7.3 Hz indicates a proton that is axial which is coupled to other axial proton. Since one proton at carbon 4 must be axial, then the proton at carbon 6 must be equatorial and so the compound is the *cis* isomer.

25. (a) Auwers, K.; Möller, K.; *J. Prakt. Chem.*; **1925**, 109, 124. (b) Perkins, M.; Peynircioğlu, N. B.; Smith, B. V. *J. Chem. Soc., Perkin Trans. 2* **1978**, 1025.