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High intensity ultrasound-assisted reduction of sterically demanding nitroaromatics

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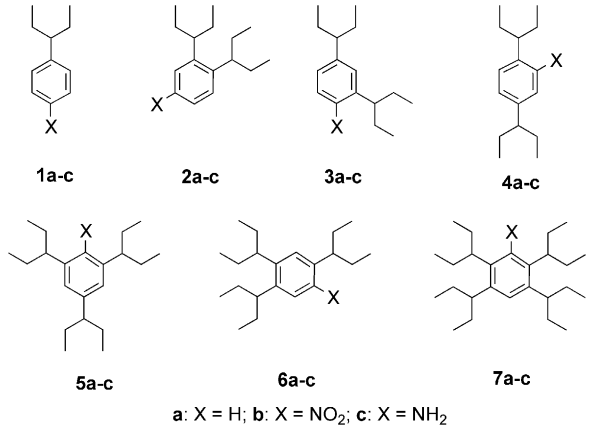
Abstract—Sterically demanding nitroaromatic compounds have been prepared and reduced to their corresponding amines with high intensity ultrasound using hydrazine in the presence of a Raney nickel catalyst. These reactions were dependent on catalyst quality, solvent and ultrasonic amplitude and, in comparison to their silent reactions, proceeded much faster and afforded higher yields.

1. Introduction

Sterically demanding molecules are of great interest in many applications where control of the spatial environment is an important consideration,[1–3] while an additional useful property often associated with the presence of bulky organic groups is increased lipophilicity, which makes for more amenable handling with organic solvents.[4] We have developed a simple procedure for the production of certain crowded aromatic molecules using a catalytic system for the clean addition of ethylene to a series of alkylaromatics,[5] and we are now actively developing the chemistry of these compounds further.[6] We report here the preparation of a series of nitroaromatics and their reduction to the corresponding anilines. The latter should be versatile starting materials for the preparation of other aromatics and, in particular, of bulky Schiff bases which are currently of great interest for their potential applications to catalytic processes of great industrial importance such as olefin polymerisation and metathesis, asymmetric catalysis and epoxide–carbon dioxide co-polymerisation.[2]

2. Results and discussion

The nitration of crowded aromatic molecules is often problematic due to competing electrophilic substitution of the alkyl groups.[7] This is particularly so when using a nitric acid/sulfuric acid nitration mixture. These complications can be largely avoided using nitric acid in acetic anhydride and we have applied this procedure to hydrocarbons **1a**–**7a**.



Fuming nitric acid gave the best results, especially with the more crowded substrates and side reactions were significant only for the nitrations of **4a**, **6a** and **7a** where cleavage of an alkyl group occurred to an extent of about 50% (Eqs. 1, 2).[8] It seems that two factors combine to make the cleavage of an alkyl group significant: (1) when this group is *ortho* or *para* (or both) to another alkyl group and (2) when the expected position for nitration is *ortho* to an alkyl group. The side reaction can be minimised if the reaction temperature is kept below 10 °C. The by-products could be readily separated from the desired product by recrystallisation from hexane.

Keywords: Bulky molecules; Ultrasound; Nitroaromatics; Reduction; Nitration; Anilines.
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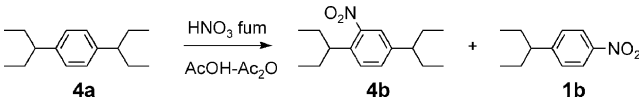
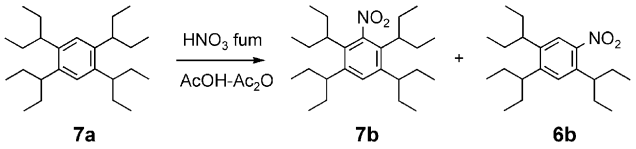
The orientation of the nitration was confirmed in all cases by ^{1}H and ^{13}C NMR measurements. The results for the nitrations are presented in Table 1.



(1)



(2)

Raney nickel catalysed hydrazine reduction of nitroaromatics is a generally useful procedure,[10] and in our hands gave satisfactory results for the less hindered nitroaromatics reported here, but highly variable results for the more hindered compounds, **5b** and **7b**, which were of particular interest to us for our further work.[11]

High energy techniques (ultrasound, microwaves) have found increasing interest in synthetic organic chemistry, showing good results for reactions that otherwise were practically impossible, giving pure products in good yield and in short reaction times.[12] Ultrasound techniques have been applied to many reactions involving metals,[13] and we therefore examined the use of high intensity ultrasound for the reduction of our nitrocompounds. These reactions were dependent on solvent, catalyst quality and ultrasound intensity dependent and, in comparison to their silent reactions, proceeded much faster and afforded higher yields (Table 2; due to its somewhat lower purity, compound **6b** was not examined in this series of experiments). In heterogeneous reactions the most important action by sonication is erosion, which implies the removal of impurities and oxide layers together with pitting of metal surfaces. This procedure is believed to remove reactive intermediates away from the metal surface and keep the metal clean and active during the reaction, thus accounting for the improvements observed for sonochemical reactions in comparison to the silent ones.[11] In comparative experiments methanol was used as solvent and the temperature was kept between 45 °C and 50 °C (Eq. 3). *t*-BuOH and toluene were also tested as solvents but the results were unsatisfactory. With ethanol no reaction occurred even after 3 h with heating or 1 h with sonication for compound **7b**, although for **1b**–**4b**, the results were similar for both methods.

Table 1. Yields of nitroaromatic compounds (**1b**–**7b**)[a]

Alkylbenzene	Nitrocompound	Yield (isolated)[b] (%)
1a	**1b**	82
2a	**2b**	95
3a	**3b**	87
4a	**4b**	48
5a	**5b**	62
6a	**6b**	66[b]
7a[c]	**7b**	40

[a] Prepared from alkyl-benzenes (**1a**–**7a**) with fuming nitric acid in 1:1 v/v acetic anhydride–acetic acid at 10 °C.[8] Compound **1b** has been reported previously.[9] NMR data for all compounds are provided below.

[b] All compounds except for **6b** could be obtained in >97% purity by distillation or recrystallisation. Compound **6b** could not be completely freed of by-products and was obtained with 90% purity.

[c] $CHCl_3$ was also added to aid dissolution of the starting material.

Table 2. Yields of anilines (**1c**–**7c**) from reduction of nitroaromatics (**1b**–**7b**)[a]

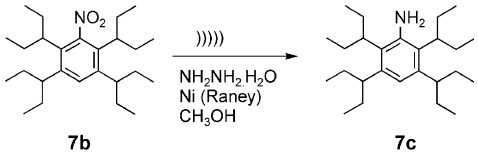
Starting material	Product	Heating[b]		Ultrasound[c]	
		Yield[d] (%)	Time (h)	Yield[d] (%)	Time (min)
1b	**1c**	97	2.0	96	5
2b	**2c**	95	2.5	97	7
3b	**3c**	96	2.5	95	7
4b	**4c**	91	2.5	93	7
5b	**5c**	84	20	90	10
7b	**7c**	77	20	93	15

[a] Compound **1c** has been reported previously.[9,14] NMR data for all compounds are provided below.

[b] With $N_2H_4{\cdot}H_2O$ and catalyst Ni (Raney) in methanol with heating only (45–50 °C).

[c] With $N_2H_4{\cdot}H_2O$ and catalyst Ni (Raney) in methanol with sonication. Temperature maintained at 45–50 °C.

[d] By GC.



(3)

Another very important parameter is the catalyst. The quality of the Raney nickel was found to be very important for good yields for the more difficult reductions and although care was taken to prepare and store it the same way to maintain consistent reactivity, it was found to vary from batch to batch. The yields presented in Table 2 are the highest that we observed.

From Table 2 one can see that, for both methods, in the case of molecules of low steric demand (**1b**–**4b**), the yields are similar although the reaction times differ greatly, from 5 min with ultrasound to 2 h with heating. In contrast, for the compounds with the greatest steric demand, (**5b** and **7b**), not only are the reaction times very short with ultrasound, but the yields are also higher.

In order to tackle the problem of reproducibility, we also tried Ni–Al alloy as a catalyst under the same conditions,[15] since, if successful, this should have excellent reproducibility being a commercial product. The results, however, were very poor (6% for **7c**). We also tried a 'green chemistry' approach, substituting the organic solvent with water, but no reaction occurred. Using Ni–Al alloy and hydrazine hydrate with ultrasound (10 min), we did, however, manage to reduce nitrobenzene itself to aniline in 65% yield in water and in 82% in methanol.

Table 3. Product yield dependence on ultrasound intensity

Product	Sonication time (min)	Yield [a] (%)		Yield ratio
		A[b]	B[c]	
1c	5	21	96	1:4.5
2c	7	17	97	1:5.7
3c	7	18	95	1:5.3
4c	7	15	93	1:6.2
5c	10	13	90	1:6.9
7c	15	7	93	1:13.3

[a] By GC.
[b] Ultrasound intensity 30% of maximum, temperature 45–50 °C.
[c] Ultrasound intensity 90% of maximum, temperature 45–50 °C.

Ammonium chloride in water has been used as an alternative to hydrazine hydrate but under our conditions it gave only a low yield (8% aniline).[16] Although not suitable for our substrates, water has many advantages as a solvent and so we also examined its possible use for less demanding substrates. Indeed 1-nitronaphthalene was reduced using a catalytic amount of Raney nickel and an excess of hydrazine hydrate to the corresponding amine in water with high intensity ultrasound in a 97% yield.

Another parameter that was considered was the intensity of sonication, although at this point it must be mentioned that the measurement of the absorbed acoustic power in a liquid is something that has not yet been defined.[17] Experiments performed with different typical intensities (30% and 90% of the max), but under otherwise identical conditions, led to markedly different reaction yields. A complete comparison of the results is listed in Table 3. Although the intensities are in 1:3 ratios (30% and 90%, respectively), the corresponding yields are in ratios between 1:4.6 for the least crowded (**1c**) and 1:13.3 for the most bulky (**7c**). It is clear that the higher intensity influences all the reactions and this beneficial effect is most evident for the most crowded molecules.

All the compounds reported here have been characterised by ^{1}H and ^{13}C NMR and gave spectra consistent with the proposed structures.

In conclusion, we have synthesised a series of bulky nitroaromatic compounds, which were reduced to the corresponding anilines using hydrazine hydrate in the presence of Raney nickel as catalyst with the assistance of high intensity ultrasound. Parameters such as the catalyst and solvent were examined. It has been demonstrated that the application of high intensity ultrasound is very beneficial for these reductions to proceed in good yield and in short reaction times in comparison with classical methods. Further development of the chemistry of these compounds is in progress.

3. Data for all compounds

3.1. 1-(1-Ethylpropyl)-4-nitrobenzene, 1b

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.72 (t, $J = 7.5$ Hz, 6H, CH_3), 1.52 (m, 2H, CH_2), 1.70 (m, 2H, CH_2), 2.43 (m, 1H, CH), 7.27 (d, $J = 8.9$ Hz, 2H, CH), 8.12 (d, $J = 8.9$ Hz, 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.0, 29.0, 49.7, 123.5, 128.5, 146.3, 154.0; HR-MS (EI) *m/z* calcd for $C_{11}H_{15}NO_2$: 193.1103. Found 193.1099; IR (cm^{-1}) 1516 (vs), 1346 (vs).

3.2. 1,2-Di(1-ethylpropyl)-4-nitrobenzene, 2b

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.76 (m, 12H, CH_3), 1.54 (m, 4H, CH_2), 1.69 (m, 4H, CH_2), 2.88 (m, 2H, CH), 7.29 (d, $J = 8.7$ Hz, 1H, CH), 7.96 (d, $J = 8.7$ Hz, 1H, CH), 8.00 (s, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.3, 29.2, 41.5, 41.9, 112.6, 113.3, 126.7, 134.6, 143.6, 145.2; HR-MS (EI) *m/z* calcd for $C_{16}H_{25}NO_2$: 263.1885. Found 263.1882; IR (cm^{-1}) 1516 (vs), 1351 (vs).

3.3. 2,4-Di(1-ethylpropyl)-1-nitrobenzene, 3b

Mp 27 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.76 (m, 12H, CH_3), 1.58 (m, 4H, CH_2), 1.71 (m, 4H, CH_2), 2.38 (m, 1H, CH), 3.02 (m, 1H, CH), 7.06 (d, $J = 8.9$ Hz, 1H, CH), 7.09 (s, 1H, CH), 7.63 (d, $J = 8.9$ Hz, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.7, 11.9, 28.9, 42.1, 49.7, 123.7, 125.5, 127.4, 139.5, 149.6, 150.7; HR-MS (EI) *m/z* calcd for $C_{16}H_{25}NO_2$: 263.1885. Found 263.1881; IR (cm^{-1}) 1526 (vs), 1366 (vs).

3.4. 1,4-Di(1-ethylpropyl)-2-nitrobenzene, 4b

Mp 42 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.75 (t, $J = 8.9$ Hz, 6H, CH_3), 0.80 (t, $J = 8.9$ Hz, 6H, CH_3), 1.55 (m, 4H, CH_2), 1.70 (m, 4H, CH_2), 2.37 (m, 1H, CH), 2.89 (m, 1H, CH), 7.27 (s, 1H, CH), 7.28 (d, $J = 2.3$ Hz, 1H, CH), 7.40 (d, $J = 2.3$ Hz, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.9, 28.9, 29.0, 42.2, 49.0, 65.0, 122.3, 127.6, 131.6, 136.9, 144.7, 151.6; HR-MS (EI) *m/z* calcd for $C_{16}H_{25}NO_2$: 263.1885. Found 263.1880; IR (cm^{-1}) 1526 (vs),1356 (vs).

3.5. 1,3,5,-Tri(1-ethylpropyl)-2-nitrobenzene, 5b

Mp 38 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.73 (t, $J = 7.5$ Hz, 18H, CH_3), 1.52 (m, 6H, CH_2), 1.67 (m, 6H, CH_2), 2.26 (m, 3H, CH), 6.84 (s, 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.7, 11.9, 29.1, 29.3, 43.6, 49.6, 123.6, 135.9, 147.4, 151.9; HR-MS (EI) *m/z* calcd for $C_{21}H_{35}NO_2$: 333.2668. Found 333.2664; IR (cm^{-1}) 1526 (vs), 1381 (vs).

3.6. 1,2,4,-Tri(1-ethylpropyl)-5-nitrobenzene, 6b

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.80 (m, 18H, CH_3), 1.56 (m, 6H, CH_2), 1.70 (m, 6H, CH_2), 2.85 (m, 2H, CH), 3.03 (m, 1H, CH), 7.09 (s, 1H, CH), 7.49 (s, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.8, 28.9, 41.8, 121.4, 125.5, 136.4, 143.2, 149.3; HR-MS (EI) *m/z* calcd for $C_{21}H_{35}NO_2$: 333.2668. Found 333.2663; IR (cm^{-1}) 1521 (vs), 1345 (vs).

3.7. 1,2,4,5-Tetra(1-ethylpropyl)-3-nitrobenzene, 7b

Mp 157 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.81 (m, 24H, CH_3), 1.52 (m, 4H, CH_2), 1.71 (m, 12H, CH_2),

2.20 (m, 2H, CH), 2.91 (m, 2H, CH), 7.08 (s, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.0, 12.9, 28.1, 29.0, 42.3, 45.8, 126.9, 129.7, 144.2, 156.3; HR-MS (EI) *m/z* calcd for $C_{26}H_{45}NO_2$: 403.3450. Found 403.3446; IR (cm^{-1}) 1526 (vs), 1381 (vs).

3.8. 4-(1-Ethylpropyl)phenylamine, 1c

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, J = 7.3 Hz, 3H, CH_3), 0.88 (t, J = 7.3 Hz, 3H, CH_3), 1.59 (m, 2H, CH_2), 1.72 (m, 2H, CH_2), 2.28 (m, 1H, CH), 3.59 (s, 2H, NH_2), 6.71 (d, J = 7.2 Hz, 2H, CH), 7.00 (d, J = 7.2 Hz, 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.3, 29.5, 48.9, 115.3, 128.6, 135.9, 144.3; HR-MS (EI) *m/z* calcd for $C_{11}H_{17}N$: 163.1361. Found 163.1359; IR (cm^{-1}) 3440 (m), 3354 (m), 3219 (w).

3.9. 3,4-Di(1-ethylpropyl)phenylamine, 2c

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.83 (m, 12H, CH_3), 1.53 (m, 4H, CH_2), 1.65 (m, 4H, CH_2), 2.74 (m, 2H, CH), 3.45 (br s, 2H, NH_2), 6.52 (m, 2H, CH), 6.95 (m, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.3, 29.2, 41.4, 41.9, 112.6, 113.2, 126.6, 134.6, 143.6, 145.2; HR-MS (EI) *m/z* calcd for $C_{16}H_{27}N$: 233.2143. Found 233.2140; IR (cm^{-1}) 3450 (m), 3359 (m), 3219 (w).

3.10. 2,4-Di(1-ethylpropyl)phenylamine, 3c

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.82 (m, 12H, CH_3), 1.6 (m, 8H, CH_2), 2.16 (m, 1H, CH), 2.49 (m, 1H, CH), 3.07 (br s, 2H, NH_2), 6.65 (d, J = 7.5 Hz, 1H, CH), 6.76 (d, J = 7.5 Hz, 1H, CH), 7.04 (d, J = 7.5 Hz, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.9, 12.2, 27.6, 29.2, 41.9, 49.0, 123.1, 126.5, 129.5, 136.1, 142.1, 146.4; HR-MS (EI) *m/z* calcd for $C_{16}H_{27}N$: 233.2143. Found 233.2138; IR (cm^{-1}) 3465 (m), 3374 (m), 3219 (w).

3.11. 2,5-Di(1-ethylpropyl)phenylamine, 4c

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.83 (t, J = 7.3 Hz, 6H, CH_3), 0.87 (t, J = 7.3 Hz, 6H, CH_3), 1.69 (m, 8H, CH_2), 2.22 (m, 1H, CH), 2.47 (m, 1H, CH), 3.65 (br s, 2H, NH_2), 6.49 (s, 1H, CH), 6.60 (d, J = 7.7 Hz, 1H, CH), 6.98 (d, J = 7.7 Hz, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.0, 12.3, 27.9, 29.3, 41.8, 49.4, 115.6, 118.8, 126.5, 127.4, 143.8, 144.0; HR-MS (EI) *m/z* calcd for $C_{16}H_{27}N$: 233.2143. Found 233.2139; IR (cm^{-1}) 3470 (m), 3379 (m), 3219 (w).

3.12. 2,4,6-Tri(1-ethylpropyl)phenylamine, 5c

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.73 (t, J = 7.3 Hz, 6H, CH_3), 0.81 (t, J = 7.3 Hz, 12H, CH_3), 1.61 (m, 12H, CH_2), 2.16 (m, 1H, CH), 2.50 (m, 2H, CH), 3.39 (br s, 2H, NH_2) 6.61 (s, 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.8, 12.1, 27.8, 42.2, 49.2, 123.3, 129.6, 135.1, 139.9; HR-MS (EI) *m/z* calcd for $C_{21}H_{37}N$: 303.2926. Found 303.2922; IR (cm^{-1}) 3480 (m), 3394 (w), 3219 (vw).

3.13. 2,3,5,6-Tetra(1-ethylpropyl)phenylamine, 7c

Mp 70 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.78 (t, J = 7.3 Hz, 12H, CH_3), 0.87 (t, J = 7.3 Hz, 12H, CH_3), 1.58 (m, 8H, CH_2), 1.79 (m, 8H, CH_2), 2.79 (m, 2H, CH), 3.00 (m, 2H, CH), 3.47 (s, 2H, NH_2), 6.38 (s, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.0, 13.4, 26.2, 28.8, 41.1, 42.7, 125.3, 141.5, 143.6; HR-MS (EI) *m/z* calcd for $C_{26}H_{47}N$: 373.3708. Found 373.3703; IR (cm^{-1}) 3500 (m), 3424 (w).

Acknowledgments

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References and notes

1. Tokitoh, N.; Okazaki, R. *Coord. Chem. Rev.* **2000**, *210*, 251–277; Power, P. P. *Chem. Commun.* **2003**, 2091–2101; Toyota, K.; Kawasaki, S.; Yoshifuji, M. *J. Org. Chem.* **2004**, *69*, 5065–5070; Weidenbruch, M. *Organometallics* **2003**, *22*, 4348–4360; Kobayashi, K.; Takagi, N.; Nagase, S. *Organometallics* **2001**, *20*, 234–236; Dutan, C.; Shah, S.; Smith, R. C.; Choua, S.; Berclaz, T.; Geoffroy, M.; Protasiewicz, J. D. *Inorg. Chem.* **2003**, *42*, 6241–6251; Hu, Y. H.; Su, M. D. *Chem. Phys. Lett.* **2003**, *378*, 289–298.
2. Catsoulacos, D. P.; Steele, B. R.; Heropoulos, G. A.; Micha-Screttas, M.; Screttas, C. G. *Tetrahedron Lett.* **2003**, *44*, 4575–4578; Connor, E. F.; Younkin, T. R.; Henderson, J. I.; Waltman, A. W.; Grubbs, R. H. *Chem. Commun.* **2003**, 2272–2273; Gonsalvi, L.; Gaunt, J. A.; Adams, H.; Castro, A.; Sunley, G. J.; Haynes, A. *Organometallics* **2003**, *22*, 1047–1054; Dove, A. P.; Gibson, V. C.; Hormnirun, P.; Marshall, E. L.; Segal, J. A.; White, A. J. P.; Williams, D. J. *Dalton Trans.* **2003**, 3088–3097; Jenkins, J. C.; Brookhart, M. *J. Am. Chem. Soc.* **2004**, *126*, 5827–5842; Roder, J. C.; Meyer, F.; Kaifer, E.; Pritzkow, H. *Eur. J. Inorg. Chem.* **2004**, 1646–1660; Krajete, A.; Steiner, G.; Kopacka, H.; Ongania, H. K.; Wurst, K.; Kristen, M. O.; Preishuber-Pflugl, P.; Bildstein, B. *Eur. J. Inorg. Chem.* **2004**, 1740–1752; Axenov, K. V.; Kotov, V. V.; Klinga, M.; Leskela, M.; Repo, T. *Eur. J. Inorg. Chem.* **2004**, 695–706; van der Vlugt, J. T.; Hewat, A. C.; Neto, S.; Sablong, R.; Mills, A. M.; Lutz, M.; Spek, A. L.; Muller, C.; Vogt, D. *Adv. Synth. Catal.* **2004**, *346*, 993–1003.
3. Groysman, S.; Segal, S.; Goldberg, I.; Kol, M.; Goldschmidt, Z. *Inorg. Chem. Commun.* **2004**, *7*, 938–941; Hamilton, C. W.; Laitar, D. S.; Sadighi, J. P. *Chem. Commun.* **2004**, 1628–1629; Roder, J. C.; Meyer, F.; Kaifer, E.; Pritzkow, H. *Eur. J. Inorg. Chem.* **2004**, 1646–1660; Vol'eva, V. B.; Karmilov, A. Y.; Belostotskaya, I. S.; Komissarova, N. L.; Prokof'ev, A. I. *Polym. Sci. A* **2004**, *46*, 264–269; Shivanyuk, A.; Saadioui, M.; Broda, F.; Thondorf, I.; Vysotsky, M. O.; Rissanen, K.; Kolehmainen, E.; Bohmer, V. *Chem. Eur. J.* **2004**, *10*, 2138–2148.
4. Siraki, A. G.; Chan, T. S.; O'Brien, P. J. *Toxicol. Sci.* **2004**, *81*, 148–159; Seifert, S.; Kunstler, J. U.; Schiller, E.; Pietzsch, H. J.; Pawelke, B.; Bergmann, R.; Spies, H. *Bioconjugate Chem.* **2004**, *15*, 856–863; Durand, G.; Polidori, A.; Ouari, O.; Tordo, P.; Geromel, V.; Rustin, P.; Pucci, B. *J. Med. Chem.* **2003**, *46*, 5230–5237; Kara-

nikolopoulos, G.; Batis, C.; Pitsikalis, M.; Hadjichristidis, N. *Macromol. Chem. Phys.* **2003**, *204*, 831–840; Blum, P.; Mohr, G. J.; Matern, K.; Reichert, J.; Spichiger-Keller, U. E. *Anal. Chim. Acta* **2001**, *432*, 269–275.

5. Steele, B. R.; Screttas, C. G. *J. Am. Chem. Soc.* **2000**, *122*, 2391–2392.
6. Steele, B. R.; Micha-Screttas, M.; Screttas, C. G. *Tetrahedron Lett.* **2004**, *45*, 9537–9540; Steele, B. R.; Micha-Screttas, M.; Screttas, C. G. *Appl. Organomet. Chem.* **2002**, *16*, 501–505.
7. Nightingale, D. V. *Chem. Rev.* **1947**, *40*, 117–140; Saleh, S. A.; Tashtoush, H. I. *Tetrahedron* **1998**, *54*, 14157–14177.
8. In a typical reaction 17.9 g (50 mmol) of **7a** was added to a mixture of 10 mL Ac_2O and 50 mL $CHCl_3$ in a flask cooled by an ice bath. To this mixture was added a mixture of 10 mL Ac_2O and 3 mL HNO_3 (100%) prepared below 10 °C and the reaction mixture was stirred overnight at room temperature. The reaction mixture was neutralised with 10% NaOH, extracted with (3×100 mL CH_2Cl_2), dried over Na_2SO_4 and evaporated. The product was recrystallised from hexane. Yield 9.3 g **7b** (46%, mp 157 °C). The other nitrocompounds were prepared in a similar way.
9. Huston, R. C.; Kaye, I. A. *J. Am. Chem. Soc.* **1942**, *64*, 1576–1580.
10. Furst, A.; Berlo, R. C.; Hooton, S. *Chem. Rev.* **1965**, *65*, 51–68; Gowda, S.; Gowda, D. C. *Tetrahedron* **2002**, *58*, 2211–2213; Yuste, F.; Saldana, M.; Walls, F. *Tetrahedron Lett.* **1982**, *23*, 147–148.
11. Sonication experiments were carried out in a 250 mL sonochemical reaction vessel fitted with a thermometer, a reflux condenser and probe (length 254 mm, diameter 13 mm) and controlled by a 400 W ultrasonic processor Sonics & Materials. This processor allows the ultrasonic vibrations at the probe (titanium alloy) tip to be set at 90% and 30% amplitude. The system was operated in the non-pulse mode. In a typical reaction 0.403 g (1.0 mmol) of **7b** and 1.0 mL of $N_2H_4{\cdot}H_2O$ and a catalytic amount (ca. 0.15 mmol) of Raney nickel were sonicated in 30 mL of absolute MeOH at 45–50 °C for 15 min. CH_2Cl_2 was added after sonication and the whole reaction mixture was filtered through Celite. The filtrate was washed three times with 30 mL of water, dried over Na_2SO_4 and evaporated. The product was analysed by GC and GC-MS; The comparative silent, thermal reactions were carried out using the same quantities of materials at 40–50 °C for the times indicated in Table 2. Work-up and analysis as above.
12. Mason, T.; Lorimer, J. *Applied Sonochemistry: Uses of Power Ultrasound in Chemistry and Processing*; Wiley, 2002.
13. Luche, J. L.; Cintas, P. In *Active Metals*; Fürstner, A., Ed.; VCH: Weinheim, 1996; pp 133–190.
14. Cram, D. J. *J. Am. Chem. Soc.* **1952**, *74*, 2152–2159.
15. Keefer, L. K. *Chem. Rev.* **1989**, *89*, 459–502.
16. Bhaumik, K.; Akamanchi, K. *Can. J. Chem.* **2003**, *81*, 197–198.
17. Margulis, M. A.; Margulis, I. M. *Russ. J. Phys. Chem.* **2003**, *77*, 1183–1190.