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Direct methoxylation of nitroarenes and nitroazaarenes with alkaline methoxides *via* nucleophilic displacement of an aromatic hydrogen atom

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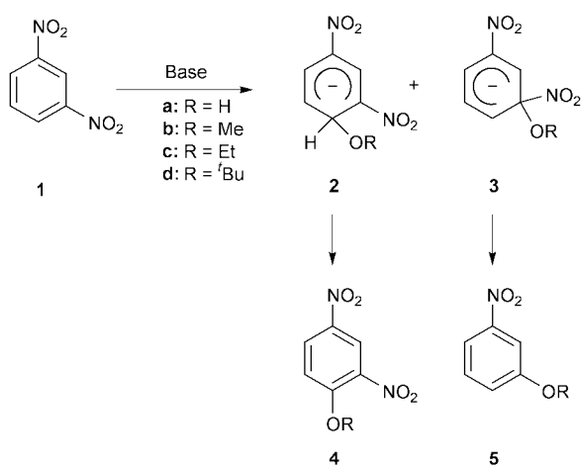
Treatment of 1,3-dinitrobenzene and 5-substituted derivatives with excess potassium or sodium methoxide in 1,3-dimethylimidazolidin-2-one (DMI) at room temperature results in the displacement of an aromatic hydrogen at the 4-position by methoxide, affording 2,4-dinitroanisole and its 6-substituted derivatives, respectively, in low to moderate yield. In contrast, an equimolar reaction under similar conditions leads to the replacement of the nitro group in preference to the ring hydrogen. The reaction does not take place with lithium methoxide as a base. Mono- and dinitronaphthalenes and nitroquinolines undergo similar displacement of a hydrogen atom at the position *ortho* or *para* to the nitro group, giving the corresponding methoxy derivatives in moderate yield. A slow addition of the nitro compound to a large excess of potassium methoxide under an oxygen atmosphere has been found to enhance the conversion and improve the product yield. On the basis of the product distribution as well as the kinetic isotope effect $k_H/k_D = 2.1$, direct displacement of a ring hydrogen atom by methoxide ion has been interpreted in terms of the rate-determining release of an *ipso*-hydrogen atom as a proton from the initially formed Meisenheimer adduct.

Introduction

Nucleophilic substitution of aromatic halides constitutes one of the most useful methodologies in organic synthesis. There have been numerous reports to date on the introduction of functional group(s) into aromatic rings *via* the route involving nucleophilic displacement of halogen atom(s). However, the versatility of this methodology is sometimes limited by the availability of starting aromatic halides. Nucleophilic displacement of a ring hydrogen atom in electron-deficient aromatic systems has been intensively investigated by Makosza and co-workers and become known as the vicarious nucleophilic substitution of hydrogen (VNS).[1,2] Since aromatic halides are usually prepared by electrophilic substitution of ring hydrogen atom(s), direct nucleophilic displacement of ring hydrogen(s), if possible, should provide the compounds whose substitution patterns are complementary to those obtained *via* electrophilic pathways. This type of nucleophilic aromatic substitution has been shown to be useful for the introduction of some types of carbon, nitrogen or oxygen nucleophiles into nitroarenes,[1] but it requires as a prerequisite the location of a good nucleofugal group as a vicarious leaving moiety at an appropriate position in the Meisenheimer adduct. This disadvantage considerably limits the scope of the VNS reaction as a synthetic tool.

The reaction of nitroarenes with alkoxide ions has previously been reported in a few papers, but its scope is limited and yields are often low due to the extensive formation of by-products.[3,4] It has long been known that the reaction between 1,3-dinitrobenzene **1** and alkali methoxide results in the alkoxy-denitration to give 3-nitroanisole **5b**, since the methoxide ion is not strong enough as a base to abstract a ring hydrogen from the initial Meisenheimer adduct **2b** and, therefore, it prefers to replace the nitro group as a nitrite ion from the second Meisenheimer adduct **3b** which forms in equilibrium with **2b** (Scheme 1). However, similar attempts to extend this methodology to the direct introduction of alkoxy groups were unsuccessful. In the present paper, we report an alternative approach to the direct displacement of a ring hydrogen atom by a methoxy group,



Scheme 1

which involves treatment of nitroarenes or nitroazaarenes with a large excess of potassium methoxide in a dipolar aprotic solvent at room temperature.

Results and discussion

When 1,3-dinitrobenzene **1** was treated with a slight excess (1.2 equiv.) of potassium methoxide in 1,3-dimethylimidazolidin-2-one (DMI) at room temperature, 3-nitroanisole **5b** was the sole product isolated in 65% yield in accordance with previous reports.[5,6] However, when the reaction was carried out in the presence of a large excess of the methoxide (8.0 equiv.), a small amount of 2,4-dinitroanisole **4b** was obtained in addition to the expected product **5b**. The unusual by-product **4b** could have been derived from the displacement of a hydrogen atom at the 4-position in **1**, jointly activated by two nitro groups present at *ortho* and *para* positions (Scheme 1). This unexpected finding led us to an idea that the use of a methoxide base in a large

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Table 1 Reaction of 1,3-dinitrobenzene **1** with alkoxide salts[a]

Run	Base (equiv.)	Solvent	Time/h	Product (%)[b]	
				4b	**5b**
1	KOMe (1.2)	DMI	12	—	65
2	KOMe (8.0)	DMI	8	10	51
3[c]	KOMe (8.0)	DMF	8	26	25
4[c]	KOMe (8.0)	DMI	8	44	—
5[c]	KOMe (8.0)	DMSO	8	—[e]	—
6[c]	NaOMe (8.0)	DMI	8	36	6
7[c]	LiOMe (8.0)	DMI	8	—[f]	—
8[cd]	KOMe (8.0)	DMI	8	61[g]	—
9[cd]	KOEt (8.0)	DMI	8	—[h]	—
10[cd]	KO^{t}Bu (8.0)	DMI	8	—[i]	—

[a] All reactions were carried out using **1** (3.0 mmol), alkoxide salt (1.2–8.0 mmol) and the given solvent (3.0 mL) at room temperature. [b] Isolated yield. [c] To a solution (10 mL) of the given base was added dropwise nitroarene **1** in the same solvent (20 mL) over 6 h. [d] The reaction was carried out under oxygen. [e] 3-Methyl-2,4-dinitroanisole was obtained in 18% yield. [f] Starting material was recovered in 86% yield. [g] 2,4-Dinitrophenol **4a** was obtained in 6% yield. [h] A complex mixture. [i] Phenol **4a** was obtained in 38% yield.

excess may facilitate the removal of an *ipso*-hydrogen atom as a proton from the initial Meisenheimer adduct **2b**. Thus, in order to see the effect of the increase in amount of alkoxide base, nitroarene **1** was added in small portions to a solution of 8 equiv. of potassium methoxide in DMI over 8 h at room temperature. This slight modification brought about a remarkable increase in yield of **4b** at the expense of **5b**, the yield of the former reaching as high as 44%. DMI was the solvent of choice; less polar *N*,*N*-dimethylformamide (DMF) and 1-methylpyrrolidin-2-one (NMP) proved to be unsatisfactory. When the reaction was carried out in tetrahydrofuran (THF) under similar conditions, substrate **1** was recovered almost intact. The reaction was found to depend on the counter cation of methoxide and the lithium salt proved to be ineffective for the present purpose. Thus, both sodium and potassium methoxides reacted similarly with compound **1**, but an attempted reaction using lithium methoxide failed, the starting material being recovered mostly unchanged (86%). When potassium methoxide was used as a base in dimethyl sulfoxide (DMSO), 3-methyl-2,4-dinitroanisole was obtained in 18% yield. This compound was no doubt derived from a further reaction of the initial product **4b**,[7] suggesting that the methylsulfinylmethyl anion ($MeSOCH_2^-$) generated *in situ* from DMSO worked better as a nucleophile than the methoxide ion. When the reaction was carried out under an oxygen atmosphere, the yield of **4b** rose to 61% and 2,4-dinitrophenol **4a** was isolated as an additional product in 6% yield (Table 1). Concurrent formation of **4a** suggests a possible involvement of an anion radical species generated from **1**, its oxidation by molecular oxygen leading to the phenolic by-product **4a**.[8]

When sodium ethoxide was used in place of potassium methoxide, however, there resulted a complex mixture of products, in which little or no ethoxylation products could be detected by ^{1}H-NMR. This could be attributed in part to the poor solubility of sodium ethoxide in the solvent employed. The attempted reactions were run in a suspension of sodium ethoxide in DMI at room temperature, so that the effective concentration of the ethoxide anion should have been low enough to exclude possible formation and subsequent conversion of the Meisenheimer adduct **2c** to aromatic ether **4c**. 1,3-Dinitrobenzene **1** and potassium *tert*-butoxide reacted under similar conditions to give 2,4-dinitrophenol in 38% isolated yield, the yield being better than those previously reported.[7]

Attempted reaction between nitrobenzene and potassium methoxide under similar conditions did not produce any nitroanisole. Instead, azoxybenzene and azobenzene were the major products obtained in 44 and 2% yields, respectively. The base-assisted conversion of nitrobenzene to azoxybenzene and/or azobenzene has been reported in the past.[9] Thus, the presence of at least two strongly electron-withdrawing groups on the benzene ring is indispensable for the nucleophilic displacement of a ring hydrogen by methoxide ion to take place to any appreciable extent.

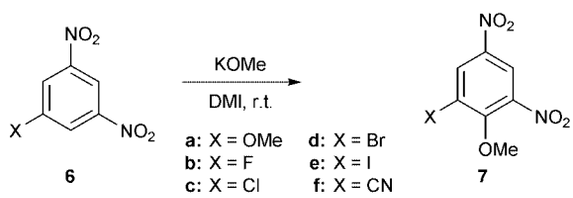
Table 2 Reaction of 5-substituted 1,3-dinitrobenzenes **6a–f** with potassium methoxide[a]

Substrate	X	Time/h	Product	Yield (%)[b]
1	H	12	**4b**	61
6a	OMe	12	**7a**	42
6b	F	8	**7b**	43
6c	Cl	8	**7c**	50
6d	Br	8	**7d**	25
6e	I	8	**7e**	18
6f	CN	8	**7f**	39

[a] All reactions were carried out using a substrate (3.0 mmol), potassium methoxide (24.0 mmol) and DMI (30 mL) at room temperature. [b] Isolated yield.

Reaction of 5-substituted 1,3-dinitrobenzenes 6a–f with potassium methoxide

An equimolar reaction between 1,3,5-trinitrobenzene and sodium methoxide has long been known to result in the preferential displacement of the nitro group, giving 3,5-dinitroanisole in good yield. However, treatment of 5-substituted 1,3-dinitrobenzenes **6a–f** with a large excess of potassium methoxide under similar conditions gave the corresponding methoxylation products **7a–f** in 18–50% yield (Scheme 2). Regardless of the



Scheme 2

electronic nature of substituent groups, the yields were always lower than that of the parent compound **1**. The decrease in yield may be attributed to the increase in steric congestion around the 4-position of compound **6**. A competition study made for a series of 5-halogeno-1,3-dinitrobenzenes **6b–e** revealed the yields of ethers **7** to decrease in the order F ≈ Cl > Br > I. This observation, together with the increasing trends towards phenolic by-product as well as dehalogenation product, suggests a possibility that the present methoxylation reaction may involve a radical anion species as an intermediate. Although a previous paper reported that the reaction of compound **6f** and methoxide ion occurs on the nitrile carbon atom to form an imido-ester,[10] the nitrile function remained intact under our conditions (Table 2).

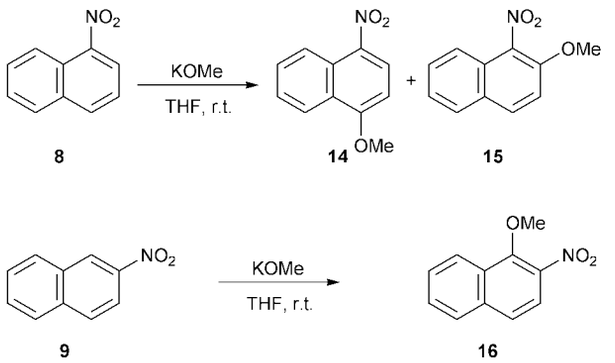
Reactions of mononitronaphthalenes 8, 9 and dinitronaphthalenes 10–13 with potassium methoxide

Since the benzo annulation gives considerable stabilization to the σ-adduct of electron-deficient aromatic systems, polycondensed nitroarenes are expected to be more reactive than monocyclic nitroarenes. In fact, the reaction of 1-nitronaphthalene **8** and potassium methoxide under the above-mentioned conditions gave only small amounts of the expected product and mainly intractable tarry substances. This could be understood since 1-nitronaphthalene **8** is more susceptible to the action of a strong base than 1,3-dinitrobenzene **1**. Thus, when the same reaction was carried out in less polar THF, 1-methoxy-4-nitronaphthalene **14** was obtained in 36% yield,

Table 3 Reaction of mono- and dinitronaphthalenes **8**–**13** with potassium methoxide[a]

Substrate	Position(s) of NO_2	Product	Position(s) of MeO	Yield (%)[b]
8	1-	**14**	4-	36
		15	2-	—[c]
9	2-	**16**	1-	59
10	1,5-	**17**	4-	18
		18	4,6-	30
11	1,6-	**19**	4-	23
12	1,7-	**20**	4,8-	46
13	1.8-	—	—	—[d]

[a] All reactions were carried out using a substrate (3.0 mmol), KOMe (24.0 mmol) and THF (30 mL) at room temperature for 14 h. [b] Isolated yield. [c] Trace. [d] A complex mixture.



Scheme 3

together with a trace amount of 2-methoxy-1-nitronaphthalene **15** (Scheme 3; Table 3). In contrast, 1-methoxy-2-nitronaphthalene **16** was obtained in 59% yield from 2-nitronaphthalene **9**. Compared with the 1-nitro isomer, however, more reaction time was needed for completion.

Dinitronaphthalenes are expected to be even more susceptible toward the action of potassium methoxide. Indeed, a similar reaction of 1,5-dinitronaphthalene **10** gave a mixture of 1-methoxy-4,8-dinitronaphthalene **17** and 1,7-dimethoxy-4,8-dinitronaphthalene **18**, in which the latter was predominant and could no doubt have been derived from a further reaction of the initial product **17** (Table 3). In this case, the first methoxylation took place at a position *para* to the nitro group, but the second one occurred at the position *ortho* to the nitro group in the opposite ring (Scheme 4). Under similar conditions, 1,7-dinitronaphthalene **12** gave 1,5-dimethoxy-4,6-dinitronaphthalene **20** as the major product. In these dinitronaphthalenes, the initially introduced methoxy group did not disturb the second methoxylation at the opposite ring. Interestingly, the reaction of 1,6-dinitronaphthalene **11** stopped at the monomethoxylation stage, giving compound **19** as the sole product. 1,8-Dinitronaphthalene **13** led only to an intractable tarry product, probably due to its inherent complexity in behavior arising from the spatial proximity of two nitro groups.

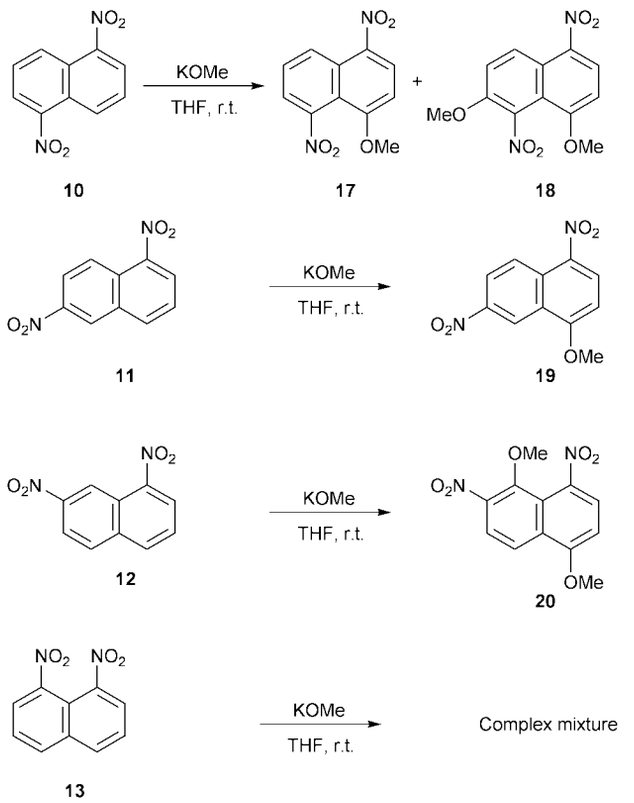
Reaction of nitroquinolines 21–24 with potassium methoxide

Nitroquinolines behaved better as an electrophile than nitronaphthalenes. Thus, treatment of isomeric nitroquinolines **21**–**24** with potassium methoxide in THF at room temperature produced the corresponding methoxylated nitroquinolines **25**–**28** in 32–46% isolated yields (Scheme 5). Similarly to the amination of nitroquinolines by potassium permanganate in liquid ammonia, the regioselectivity of the present displacement reaction has been found to obey the LUMO and LUMO + 1 orbital densities[11] and the starting materials were completely consumed under the conditions where the corresponding nitronaphthalene isomers remained almost intact (Table 4).

Table 4 Reaction of nitroquinolines **21**–**24** with potassium methoxide[a]

Substrate	Position of NO_2	Product	Position of OMe	Yield (%)[b]
21	5-	**25**	6-	43
22	6-	**26**	5-	32
23	7-	**27**	8-	38
24	8-	**28**	7-	46

[a] All reactions were carried out using a substrate (3.0 mmol), KOMe (24.0 mmol) and THF (30 mL) at room temperature for 14 h. [b] Isolated yield.

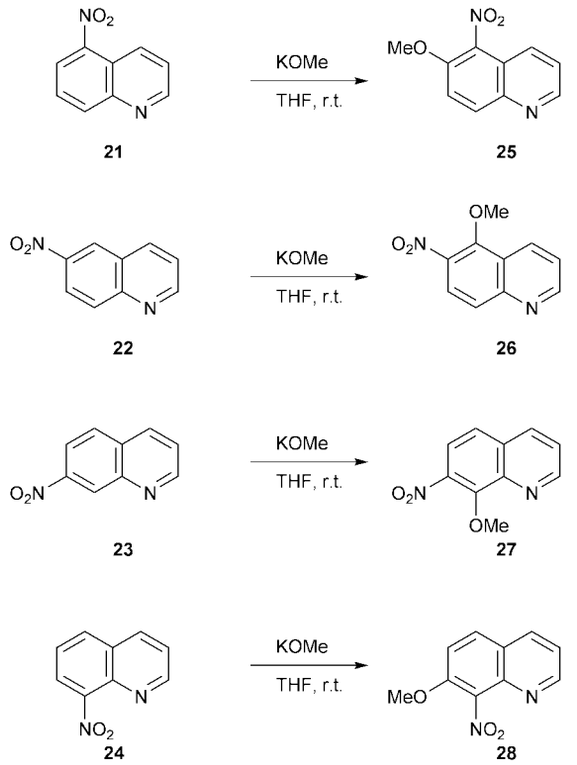


Scheme 4

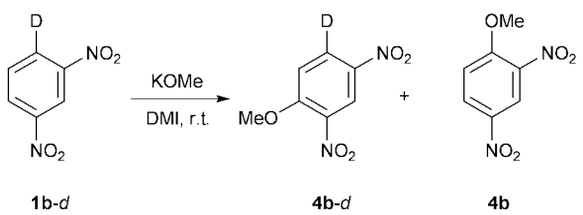
Isotopic effect and possible mechanism for the methoxylation reaction

The kinetic isotope effect of this reaction was investigated using 1-deuterio-2,4-dinitrobenzene **1b**-*d* as the substrate, where the intramolecular competition between 1-D and 5-H positions was observed as the ratio of the 5-H- and 1-D-substituted products, *i.e.*, 2,4-dinitroanisole **4b** *versus* 1-deuterio-5-methoxy-2,4-dinitrobenzene **4b**-*d* (Scheme 6). The value of the kinetic isotope effect k_H/k_D was 2.1 ± 0.2, as estimated by mass spectrometry, which is considerably lower than those observed in the reaction of nitrobenzene with potassium *tert*-butoxide (k_H/k_D = 4.2 for *para*-substitution and 6.4 for *ortho*-substitution).[12] This finding suggests that the removal of an *ipso*-hydrogen atom from the Meisenheimer complex **2** is slow and thus rate-determining.

The mechanism of the present reaction is probably more complex than it appears. A possible reaction pathway is depicted in Scheme 7, where the reaction between 1,3-dinitrobenzene **1** and potassium methoxide is taken as an example, assuming the one-electron transfer process involving a dianionic species **29** and a pair of radical anions **30** and **31** as the possible intermediates. Thus, compound **1** reacts with potassium methoxide to form an initial Meisenheimer adduct **2b** which,[13] in the absence of excess sodium methoxide, goes into equilibrium with



Scheme 5



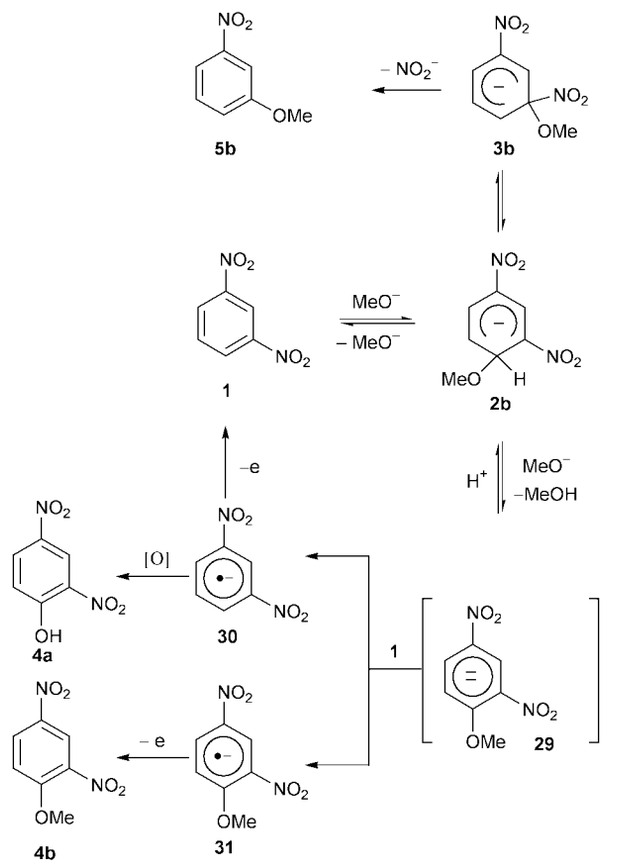
Scheme 6

the second Meisenheimer adduct **3b**, eventually releasing the nitro group as the nitrite anion to afford 3-nitroanisole **5b**. In the presence of a large excess of methoxide, however, the initial adduct **2b** would undergo partial deprotonation to generate an unstable dianion **29**,[14] which would then transfer an electron to an oncoming molecule of **1**, leading to a pair of radical anions **30** and **31**. The dianionic species is sometimes assumed as a possible intermediate in nucleophilic aromatic substitution,[12–15] but the exact nature of these reactive species remains to be clarified. Under an atmosphere of oxygen, radical anion **30** would be oxidized to produce 2,4-dinitrophenol **4a** and the starting material **1**, while radical anion **31** would lose an electron to afford 2,4-dinitroanisole **4b**.

Experimental

General

Melting points were determined on a Yanagimoto hot-plate apparatus and are uncorrected. ^{1}H NMR spectra were recorded in $CDCl_3$ and/or DMSO-d_6 on a Varian Gemini 200 MHz NMR spectrometer using TMS as an internal reference, unless otherwise mentioned. J values are given in Hz. Infrared spectra were measured as KBr pellets or liquid films with a Shimadzu FTIR-8100S infrared spectrophotometer and only prominent peaks were recorded. EI mass spectra were determined at 70 eV on a Shimadzu GCMS-QP2000A mass spectrometer. Elementary analyses were performed at Microanalysis Laboratory, Institute of Chemical Research, Kyoto University.



Scheme 7

1,3-Dimethylimidazolidin-2-one (DMI) was distilled from CaH_2 under reduced pressure and tetrahydrofuran (THF) from benzophenone ketyl prior to use. 3,5-Dinitroanisole **6a**,[16] 3,5-dinitrofluorobenzene **6b**,[5] 3,5-dinitrochlorobenzene **6c**,[17] 3,5-dinitrobromobenzene **6d**,[18] 3,5-dinitroiodobenzene **6e**,[19] 1,6-dinitronaphthalene **11**,[20] 1,7-dinitronaphthalene **12**,[21] and 7-nitroquinoline **23**[22] were prepared according to the literature procedures. All other nitro compounds were commercial products and used without further purification.

Reaction of 1,3-dinitrobenzene 1 and 5-substituted derivatives 6a–f with potassium methoxide. General procedure

To a stirred solution of potassium methoxide (24 mmol) in DMI (10 mL) was added slowly a given nitroarene (3.0 mmol) over 8 to 12 h at room temperature. The resulting reaction mixture was diluted with 1 M HCl (100 mL) and the organic phase was extracted with benzene (3 × 30 mL). The combined extracts were evaporated and the residue was chromatographed on silica-gel using hexane–ethyl acetate as the solvent, giving the corresponding 2,4-dinitroanisoles **4b** or **7a**–**f**.

2,4-Dinitroanisole 4b. Mp 97–98 °C (lit.,[23] 95 °C). ^{1}H NMR ($CDCl_3$) δ 4.11 (s, 3H), 7.23 (d, 1H, J = 9.2), 8.46 (dd, 1H, J = 9.2, 2.8), 8.76 (d, 1H, J = 2.8); MS m/z (EI) 198 (M^+, 84%), 168 (100), 151 (93); IR (KBr) 3455 (br), 3098, 1607, 1530, 1489, 1348, 1283, 1154, 1071, 1003, 920, 831, 743 cm^{-1}.

3-Methyl-2,4-dinitroanisole. Mp 116–117 °C. ^{1}H NMR ($CDCl_3$) δ 2.52 (s, 3H), 4.00 (s, 3H), 7.01 (d, 1H, J = 9.5); MS (EI) m/z 212 (M^+, 64%), 195 (100), 178 (99); IR (KBr) 3440 (br), 1613, 1584, 1551, 1518, 1480, 1439, 1343, 1294, 1082, 833, 662 cm^{-1}. Found: C, 45.16; H, 3.74; N, 13.32. $C_8H_8N_2O_5$ requires C, 45.29; H, 3.80; N, 13.20%.

3-Nitroanisole 5b. Mp 38–39 °C (lit.,[24] 39 °C). ^{1}H NMR ($CDCl_3$) δ 3.90 (s, 3H), 7.23 (ddd, 1H, J = 8.4, 2.3, 1.1), 7.44 (t,

1H, J = 8.2), 7.74 (t, 1H, J = 2.3), 7.83 (ddd, 1H, J = 8.2, 2.3, 1.0); MS m/z (EI) 153 (M^+, 72%), 107 (41), 92 (76), 77 (100); IR (KBr) 3445 (br), 1530, 1354, 1291, 1250, 1044, 901, 880, 799, 737 cm^{-1}.

1,2-Dimethoxy-3,5-dinitrobenzene 7a. Mp 100–101 °C (lit.,[25] 102 °C). ^1H NMR ($CDCl_3$) δ 4.04 (s, 3H), 4.10 (s, 3H), 7.96 (d, 1H, J = 2.6), 8.26 (d, 1H, J = 2.6); MS m/z (EI) 228 (M^+, 100%), 181 (75), 92 (59); IR (KBr) 3452 (br), 3104, 2957, 1595, 1545, 1522, 1352, 1297, 1096, 1055, 984, 920, 882, 806, 789, 749, 731 cm^{-1}.

2-Fluoro-4,6-dinitroanisole 7b. Bp 131–132 °C/0.1 mmHg (lit.,[26] 118–120 °C/0.025 Torr). ^1H NMR ($CDCl_3$) δ 4.25 (d, 3H, J = 3.8), 8.23 (dd, 1H, J = 3.3, 11.0), 8.49 (dd, 1H, J = 1.8, 3.3); MS (EI) m/z 216 (M^+, 38%), 186 (100), 156 (22), 140 (25), 94 (93); IR (KBr) 3108, 2959, 1615, 1539, 1495, 1347, 1291, 1078, 994, 901, 810 cm^{-1}.

2-Chloro-4,6-dinitroanisole 7c. Mp 34–35 °C (lit.,[27] 34.8–35.2 °C). ^1H NMR ($CDCl_3$) δ 4.20 (s, 3H), 8.66 (d, 1H, J = 2.2), 8.59 (d, 1H, J = 2.2); MS (EI) m/z 234 (M^+ + 2, 14%), 232 (M^+, 38), 204 (34), 202 (100); IR (KBr) 3098, 1597, 1538, 1478, 1426, 1345, 1269, 1076, 982, 932, 907, 758 cm^{-1}.

2-Bromo-4,6-dinitroanisole 7d. Mp 46–47 °C (lit.,[28] 45–46 °C). ^1H NMR ($CDCl_3$) δ 4.13 (s, 3H), 8.64 (d, 1H, J = 2.7), 8.68 (d, 1H, J = 2.7); MS (EI) m/z 278 (M^+ + 2, 21%), 276 (M^+, 22), 248 (50), 246 (52), 75 (100); IR (KBr) 3096, 1593, 1541, 1474, 1420, 1341, 1264, 1152, 1075, 978, 907 cm^{-1}.

2-Iodo-4,6-dinitroanisole 7e. Mp 66–67 °C. ^1H NMR ($CDCl_3$) δ 4.08 (s, 3H), 8.69 (d, 1H, J = 2.2), 8.84 (d, 1H, J = 2.2); MS (EI) m/z 324 (M^+, 45%), 294 (44), 75 (100), 62 (78); IR (KBr) 3447 (br), 1586, 1538, 1516, 1466, 1343, 1258, 982, 970, 716 cm^{-1}. Found: C, 26.15; H, 1.62; N, 8.42. $C_7H_8IN_2O_5$ requires C, 25.95; H, 1.56; N, 8.65%.

2-Methoxy-3,5-dinitrobenzonitrile 7f. Mp 72–73 °C (lit.,[29] 73 °C). ^1H NMR ($CDCl_3$) δ 4.37 (s, 3H), 8.69 (d, 1H, J = 2.2), 8.84 (d, 1H, J = 2.2); MS (EI) m/z 223 (M^+, 29%), 193 (100), 117 (22), 104 (68); IR (KBr) 3092, 2953, 2244, 1617, 1592, 1538, 1487, 1416, 1347, 1271, 1092, 978, 920 cm^{-1}.

Reaction of mono- and dinitronaphthalenes 8–13 with potassium methoxide. General procedure

To a stirred suspension of potassium methoxide (24 mmol) in THF (10 mL) was added slowly a given nitronaphthalene (3.0 mmol) over 6 h. The mixture was stirred for an additional 8 h at room temperature and then diluted with water. The organic phase was extracted with Et_2O (3 × 30 mL) and the combined extracts were evaporated to leave a residue, which was chromatographed on silica gel using a mixture of hexane and ethyl acetate as the solvent to give the methoxylated nitronaphthalenes **14**–**20**.

1-Methoxy-4-nitronaphthalene 14. Mp 83–84 °C (lit.[30] 83 °C). ^1H NMR ($CDCl_3$) δ 4.05 (s, 3H), 6.73 (d, 1H, J = 8.8), 7.49–7.80 (m, 2H), 8.25–8.40 (m, 2H), 8.76 (dd, 1H, J = 7.6, 1.2); MS (EI) m/z 203 (M^+, 72%), 107 (41), 92 (76), 77 (100); IR (KBr) 1569, 1513, 1499, 1461, 1423, 1307, 1268, 1095, 1005, 758 cm^{-1}.

1-Methoxy-2-nitronaphthalene 16. Mp 80–81 °C (lit.,[30] 80 °C). ^1H NMR ($CDCl_3$) δ 4.15 (s, 3H), 7.64–7.71 (m, 3H), 7.88–7.92 (m, 2H), 8.30–8.34 (m, 1H); MS (EI) m/z 203 (M^+, 78%), 156 (75), 127 (100), 114 (56); IR (KBr) 3442 (br), 1586, 1524, 1341, 1320, 1262, 1086, 976, 816, 760 cm^{-1}.

1-Methoxy-4,8-dinitronaphthalene 17. Mp 159–160 °C. ^1H NMR ($CDCl_3$) δ 4.05 (s, 3H), 7.00 (d, 1H, J = 8.8), 7.64 (dd, 1H, J = 1.1, 7.5), 7.77 (dd, 1H, J = 7.5, 8.8), 8.47 (d, 1H, J = 8.9), 8.90 (dd, 1H, J = 1.1, 8.8); MS (EI) m/z 248 (M^+, 100%), 218 (27), 155 (39), 126 (77), 114 (61); IR (KBr) 3454 (br), 1578, 1541, 1512, 1374, 1325, 1273, 1119, 1059, 967, 889, 743, 669 cm^{-1}. Found: C, 53.38; H, 3.21; N, 11.21. $C_{11}H_8N_2O_5$ requires C, 53.23; H, 3.25; N, 11.29%.

1,7-Dimethoxy-4,8-dinitronaphthalene 18. Mp 213–214 °C. ^1H NMR ($CDCl_3$) δ 4.01 (s, 3H), 4.06 (s, 3H), 6.91 (d, 1H, J = 8.7), 7.57 (d, 1H, J = 9.8), 8.31 (d, 1H, J = 8.7), 8.89 (d, 1H, J = 9.8); MS (EI) m/z 278 (M^+, 100%), 233 (23), 215 (13), 185 (34), 156 (22); IR (KBr) 3452 (br), 1609, 1568, 1543, 1516, 1321, 1271, 1053, 903, 818, 664 cm^{-1}. Found: C, 51.70; H, 3.54; N, 10.01. $C_{12}H_{10}N_2O_6$ requires C, 51.80; H, 3.62; N, 10.07%.

1-Methoxy-4,7-dinitronaphthalene 19. Mp 181–182 °C. ^1H NMR ($CDCl_3$) δ 4.20 (s, 3H), 7.00 (d, 1H, J = 8.8), 8.48 (dd, 1H, J = 9.6, 2.5), 8.62 (d, 1H, J = 8.8), 8.99 (d, 1H, J = 9.6), 9.32 (d, 1H, J = 2.5); MS (EI) m/z 248 (M^+, 100%), 218 (58), 202 (14), 172 (27), 155 (23), 126 (33); IR (KBr) 3450 (br), 1626, 1599, 1584, 1507, 1462, 1350, 1316, 1277, 1117, 1078, 1003, 822, 745 cm^{-1}. Found: C, 53.29; H, 3.25; N, 11.19. $C_{11}H_9N_2O_5$ requires C, 53.23; H, 3.25; N, 11.29%.

1,5-Dimethoxy-4,6-dinitronaphthalene 20. Mp 152–153 °C. ^1H NMR ($CDCl_3$) δ 3.91 (s, 3H), 4.05 (s, 3H), 7.52 (d, 1H, J = 9.2), 7.65 (d, 1H, J = 9.0), 7.81 (d, 1H, J = 9.0), 7.98 (d, 1H, J = 9.2); MS (EI) m/z 278 (M^+, 100%), 247 (15), 173 (18), 157 (21); IR (KBr) 3450 (br), 1599, 1534, 1509, 1464, 1368, 1347, 1277, 1071, 842 cm^{-1}. Found: C, 52.20; H, 3.45; N, 10.22. $C_{12}H_{10}N_2O_6$ requires C, 51.80; H, 3.62; N, 10.07%.

Reaction of nitroquinolines 21–24 with potassium methoxide. General procedure

To a stirred suspension of potassium methoxide (24 mmol) in THF (10 mL) was added slowly a nitroquinoline (3.0 mmol) over 6 h. The resulting mixture was stirred for an additional 8 h at room temperature and then diluted with water. The organic phase was extracted with Et_2O (3 × 30 mL), evaporated, and chromatographed on silica gel using a mixture of hexane and ethyl acetate as the solvent to obtain methoxynitroquinolines **25**–**28**.

6-Methoxy-5-nitroquinoline 25. Mp 104–105 °C (lit.,[31] 104–105 °C). ^1H NMR ($CDCl_3$) δ 4.22 (s, 3H), 7.09 (d, 1H, J = 8.9), 7.71 (dd, 1H, J = 4.2, 8.9), 8.56 (d, 1H, J = 8.9), 9.04 (dd, 1H, J = 1.6, 4.2), 9.25 (dd, 1H, J = 1.6, 8.9); MS (EI) m/z 204 (M^+, 64%), 174 (55), 157 (37), 128 (100); IR (KBr) 3453 (br), 1561, 1505, 1333, 1306, 1109, 830, 810 cm^{-1}.

5-Methoxy-6-nitroquinoline 26. Mp 130–131 °C (lit.,[32] 125–126.5 °C). ^1H NMR ($CDCl_3$) δ 4.16 (s, 3H), 7.58 (dd, 1H, J = 4.2, 8.6), 7.95 (d, 1H, J = 9.4), 8.15 (d, 1H, J = 9.4), 8.65 (dd, 1H, J = 1.7, 8.6), 9.07 (dd, 1H, J = 1.7, 4.2); MS (EI) m/z 204 (M^+, 83%), 157 (100), 128 (79), 115 (56); IR (KBr) 3456 (br), 1595, 1526, 1493, 1364, 1345, 1312, 1256, 1084, 970, 835, 822, 808, 789 cm^{-1}.

8-Methoxy-7-nitroquinoline 27. Mp 109–110 °C. ^1H NMR ($CDCl_3$) δ 4.38 (s, 3H), 7.57 (dd, 1H, J = 4.2, 8.3), 7.63 (d, 1H, J = 9.0), 7.87 (d, 1H, J = 9.0), 8.23 (dd, 1H, J = 1.6, 8.4), 9.07 (dd, 1H, J = 1.6, 4.2); MS (EI) m/z 204 (M^+, 3%), 174 (100), 144 (34), 116 (83); IR (KBr) 3455 (br), 1580, 1518, 1489, 1370, 1347, 1092, 976, 839, 803, 712 cm^{-1}. Found: C, 58.96; H, 3.78; N, 13.68. $C_{10}H_8N_2O_3$ requires C, 58.82; H, 3.95; N, 13.72%.

7-Methoxy-8-nitroquinoline 28. Mp 177–178 °C (lit.,[33] 178 °C). ^1H NMR ($CDCl_3$) δ 4.08 (s, 3H), 7.40 (dd, 1H, J = 4.3, 8.3), 7.43 (d, 1H, J = 9.2), 7.94 (d, 1H, J = 9.2), 8.17 (dd, 1H,

J = 1.7, 8.4), 9.07 (dd, 1H, J = 1.6, 4.2); MS (EI) m/z 204 (M^+, 100%), 174 (53), 146 (72), 128 (39), 115 (51); IR (KBr) 3446 (br), 1640, 1530, 1507, 1320, 1283, 1088, 878, 831, 793, 642 cm^{-1}.

Isotope experiment

1-Deuterio-2,4-dinitrobenzene **1**-*d* was prepared according to our modified procedure of the literature method;[34] 2,4-dinitroaniline was converted to 2,4-dinitrophenyldiazonium tetrafluoroborate (1.0 g)[35] and reduced by calcium hypophosphite (Nakarai, 2.0 g) in D_2SO_4–D_2O (2.0 mL : 30 mL) to obtain the deuterated product **1**-*d* (0.6 g, 93%). The isotopic purity of the product was 86.9%, as determined by mass spectrometry. The methoxylation of **1**-*d* was carried out under the conditions similar to those used for **1** and the kinetic isotopic effect was determined by mass spectrometric analysis of the isolated product.

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