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Vicarious nucleophilic substitution of hydrogen (VNS) in 1,4-naphthoquinone derivatives—competition between VNS and vinylic nucleophilic substitution (S_NV)

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Abstract—Carbanions of dimethyl chloromalonate, ethyl 2-chloroacetoacetate and dimethyl malonate react with naphthoquinone derivatives mainly via vicarious nucleophilic substitution or oxidative nucleophilic substitution of hydrogen processes. These reactions in 2-halo substituted naphthoquinones are generally faster processes than vinylic nucleophilic substitution of halogen (S_NV). Introduction of one Cl substituent into position 2- of 1,4-naphthoquinone increases substantially its electrophilic activity resulting in much faster addition of the carbanion in the position occupied by hydrogen. On the other hand addition of the carbanions to 2,3-dichloro-1,4-naphthoquinone proceeds slower than to 1,4-naphthoquinone. © 2001 Published by Elsevier Science Ltd.

Vicarious nucleophilic substitution (VNS) of hydrogen is a general reaction between electrophilic arenes and nucleophiles containing leaving groups at the nucleophilic centre. A variety of carbon as well as amino and hydroxy substituents can be directly introduced into aromatic rings via this reaction.[1–4] A similar reaction may occur with electrophilic alkenes or aldimines.[5–10] Due to their strong electrophilic character quinones appear to be active potential reactants in this reaction. In the literature one example of VNS type reaction of quinones was reported, however mechanistic features of this process were not recognized.[11] We have already reported reactions of halomethyl aryl sulfone carbanions with anthraquinone derivatives, some of them proceeding along the VNS pathway when the aromatic ring was activated by the quinone moiety.[12] An intramolecular variant of such process had been reported earlier.[13,14]

In the course of exploring the scope and limitations of the VNS reaction it was of substantial interest to clarify a possibility of execution of this process in the quinone rings. Another interesting question was the relation between rates of nucleophilic addition at the carbon atom bonded with hydrogen and halogen of the quinone ring. It was already well recognized, that, as a rule, in the electrophilic aromatic systems carbanionic nucleophiles add faster at positions occupied by hydrogen, than at, equally activated, positions occupied by halogens,[15–18] however such data for quinones were not available. 1,4-Naphthoquinone (**1a**) was selected as the model quinone for these studies, because it is reasonably stable and readily available.

Our first attempts to execute the VNS reaction of **1a** with α-halocarbanions typically used for this process, such as chloromethyl *p*-tolyl sulfone or ethyl chloroacetate, carried out in the presence of *t*-BuOK in THF, even at −70°C, gave negative results. Apparently eventual VNS products were totally decomposed under the strongly basic reaction conditions.

On the other hand, less active carbanions, formed from more acidic precursors such as dimethyl chloromalonate (**2a**) or ethyl 2-chloroacetoacetate (**2b**) in the presence of DBU, a much milder base than *t*-BuOK, reacted smoothly with **1a** giving the expected VNS products **3a** or **3b** in good yields (Scheme 1).

The reaction of **2a** or **2b** with 2-chloro-1,4-naphthoquinone (**1b**) proceeded under similar conditions exclusively along the VNS pathway giving **3c** and **3d**. Nucleophilic replacement of the halogen, S_NV was not observed under such conditions (Scheme 1). These results indicate that the addition of the carbanions of **2a** and **2b** to 2-chloro-1,4-naphthoquinone proceeds much faster in the position occupied by hydrogen than in that occupied by Cl.

The VNS reactions in nitroarenes proceed via addition of nucleophiles bearing a leaving group X, in positions connected with the hydrogen of the ring, giving anionic σ^H-adducts, followed by base induced β-elimination of HX.[1–4] This mechanism has been experimentally verified,

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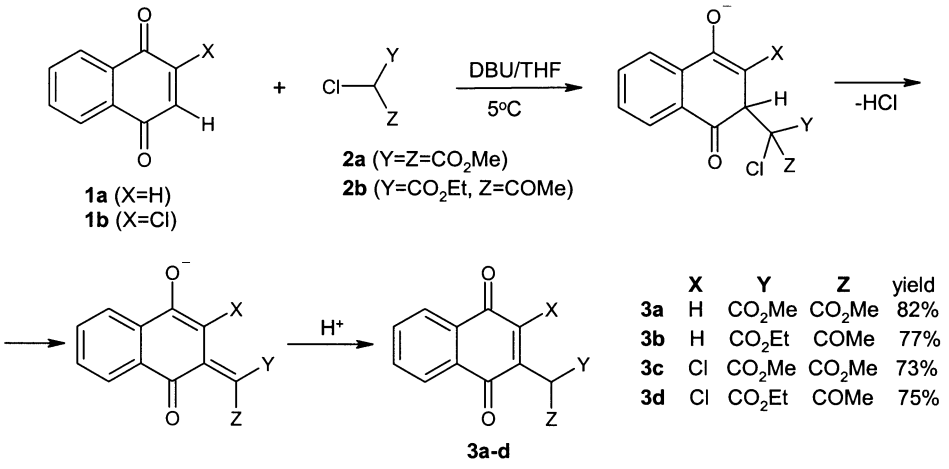


Scheme 1.

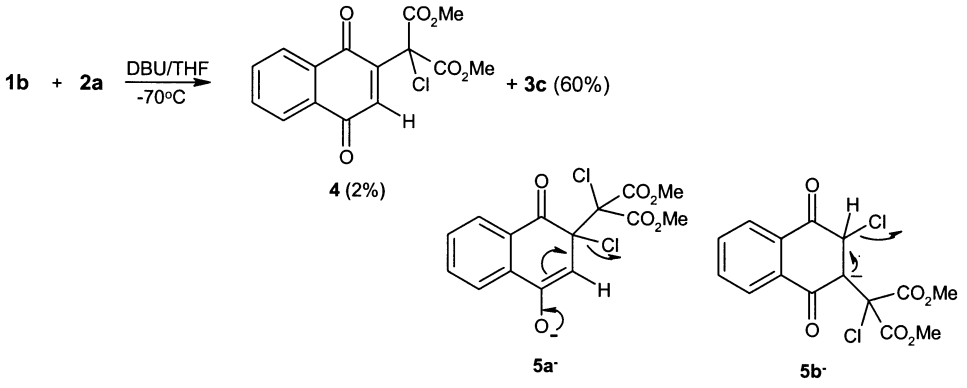
in particular it was shown that the reaction rate strongly depends on the strength and concentration of base. These conclusions were based on results of competitive experiments in which the ratio of competing nucleophilic substitution of halogen (S_NAr) and VNS was found to be a function of base concentration.[15–18] In order to elucidate the mechanism of VNS in quinones the same approach was attempted—namely studies of competition between vinylic nucleophilic substitution of Cl (S_NV)[19–23] and VNS in **1b** as a function of base concentration. It is well known that some carbanions replace readily the halogens in 2,3-dichloro-1,4-naphthoquinone,[24–28] a similar replacement of the halogen proceeds with enamines,[29] however not much is known about replacement of the halogen in 2-chloro-1,4-naphthoquinone (**1b**) with carbanions. Reactions of other nucleophiles: F^-, MeO^- and dialkyl amines with **1b** indicate that hard nucleophiles (F^-, MeO^-) add preferably to the carbon atom connected to Cl whereas dialkylamines add to that connected to hydrogen.[30]

When the reaction of **1b** with **2a** was carried out at −70°C with low base concentration, the only observed change was a decrease of yield of the VNS product **3c** (60%) whereas product S_NV (**4**) was formed in a negligible amount (2%) (Scheme 2). This product could be formed in two ways—the *ipso* substitution via intermediate **5a**$^-$ and *cine* substitution proceeding via addition of the carbanion in position 3- occupied by hydrogen to give an intermediate **5b**$^-$. Further proton shift and elimination of the chloride anion in **5b** could give **4**, whereas base induced β-elimination leads to the VNS product **3c**. The reaction with higher concentration of base led to the VNS product only (63%).

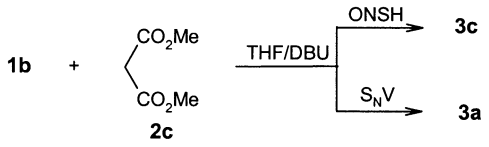
It seems however most likely that **4** was produced from σ^H adduct **5b** upon chromatographic purification. Indeed, when the reaction mixtures were separated using silicagel pretreated with AcOH/hexane before use, compound **4** was not observed and the yield of **3c** became lower.

Control of competing reactions of nucleophilic substitution of hydrogen and halogen by base concentration is possible provided that the formation of the σ^H adducts is truly a reversible process. One can therefore expect that this control can be more pronounced at a higher temperature when dissociation of the σ^H adducts is accelerated. However, when the reaction of **1b** with **2a** in the presence of a base in low concentration was carried out at higher temperature, the S_NV product **4** was not obtained.

Preferable formation of the σ^H adduct and acceleration of the equilibration process at higher temperature was observed in the reaction of **1b** with dimethyl malonate (**2c**) which is unable to enter VNS. When the reaction was carried out at −100°C, only the product of the oxidative nucleophilic substitution of hydrogen (ONSH) **3c** was



Scheme 2.



T, °C	3c (ONSH)	3a (S_NV)	substrate 1b	material balance
-100	50%	0	47%	97%
-70	36%	3%	26%	65%
0	32%	6%	16%	54%
+20	25%	13%	12%	50%
+40	17%	17%	2%	36%

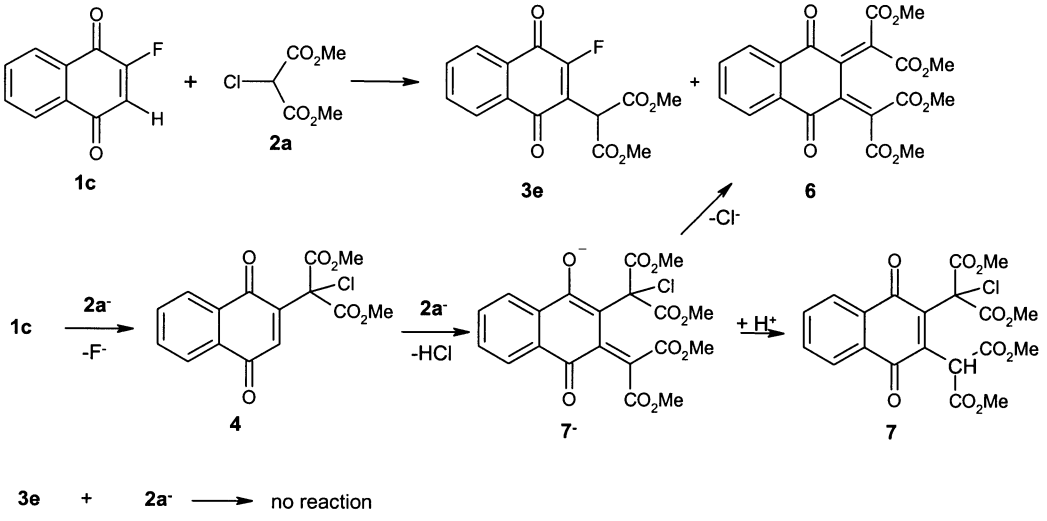
Scheme 3.

formed. Higher temperature of the reaction favoured formation of the S_NV product **3a** (Scheme 3).

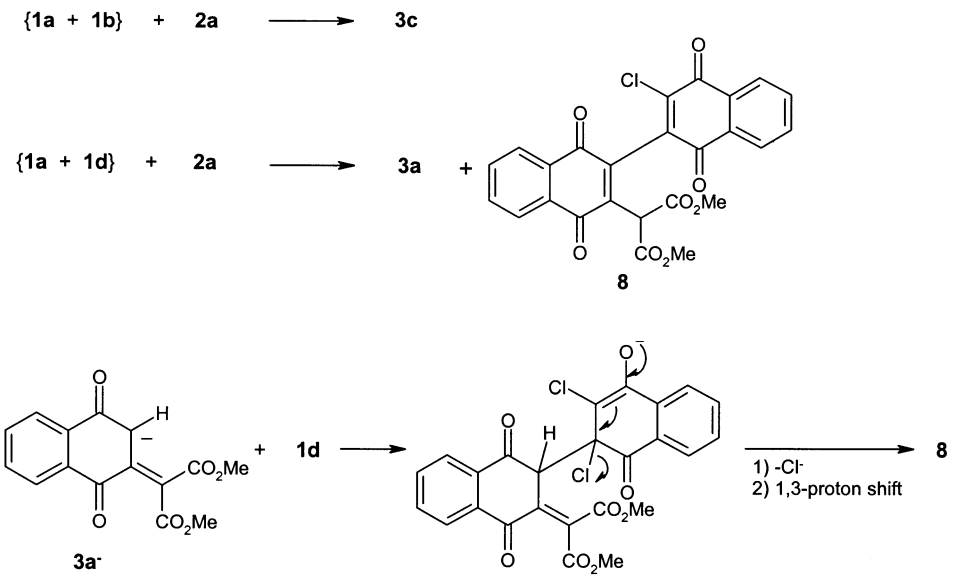
In halonitroarenes nucleophilic replacement of F occurs much faster than Cl when the halogens are located in equally activated positions.[31] In our studies we have observed that α-halocarboanions reacted with chloronitroarenes only via the VNS pathway, whereas the reaction with analogous fluoronitrobenzenes gave S_NAr and VNS products in a ratio depending on strength and concentration of the base.[1–4,15–18] We could, therefore, expect that ratio of VNS and S_NV should be a function of base concentration in the reaction of **2a** with 2-fluoro-1,4-naphthoquinone (**1c**). When this quinone was subjected to the reaction with **2a** in the presence of an excess of DBU at −70°C, two products were formed: the expected VNS product **3e** (33%) and compound **6** (8%) (Scheme 4).

Formation of **6** can be rationalised by a speculative mechanistic pathway in which the initial step is S_NV process giving **4** which reacts further with $\mathbf{2a}^-$ as shown in Scheme 4. Indeed, when DBU was added slowly to a mixture of **1c** (1 mmol) and **2a** (2 mmol), compound **6** was obtained in much higher yield (30%) and product **3e** was formed in yield 31%. In a separate experiment it was shown that compound **3e** does not react with the carbanion of **2a** under the reaction conditions. Moreover, when **1c** was treated with an equimolar amount of the carbanion of **2a**, and the reaction mixture was quenched after 5 min at −70°C intermediate **7** was observed by ^1H, ^{13}C and MS spectra. In this experiment product **3e** was obtained in low yield (6%), whereas two products of the S_NV reaction {**6**+**7**} were observed in combined yield about 30% (according to ^1H NMR spectra). Compound **7** was transformed into compound **6** during an attempt of purification by column chromatography and could not be separated from **6** by recrystallisation.

These results indicate that rates of addition of $\mathbf{2a}^-$ to **1c** in the positions occupied by hydrogen and fluorine giving σ^H and σ^F adducts are similar, the former adduct produces the VNS product **3e** whereas departure of F^- from the σ^F adduct gives **4** which reacts further producing **6**. In order to gain insight into how halogen substituents affect activity of naphthoquinone in reactions with carbanions, rates of the reactions of **1a**, **1b** and 2,3-dichloro-1,4-naphthoquinone (**1d**) with **2a** and **2c** were directly compared in competitive experiments. When a mixture of **1a** (1.5 mmol), **1b**



Scheme 4.



Scheme 5.

(1.5 mmol) and **2a** (1 mmol) was added to an excess of DBU at −70°C the only process was VNS in **1b** giving **3c** (76% yield based on **2a**) (Scheme 5). Unreacted **1a** (1.31 mmol) and **1b** (0.23 mmol) were recovered from the reaction mixture. Thus Cl substituent activates **1b** for the addition of carbanions in position 3- occupied by hydrogen, so it reacts much faster than 1,4-naphthoquinone (**1a**). On the other hand in the reaction of **1a** (1.5 mmol) and **1d** (1.5 mmol) with **2a** (1 mmol) in the presence of an excess of DBU at −70°C, the carbanion of **2a** reacted only with **1a** giving the VNS product **3a** (66%) and product **8** (17%) (Scheme 5).

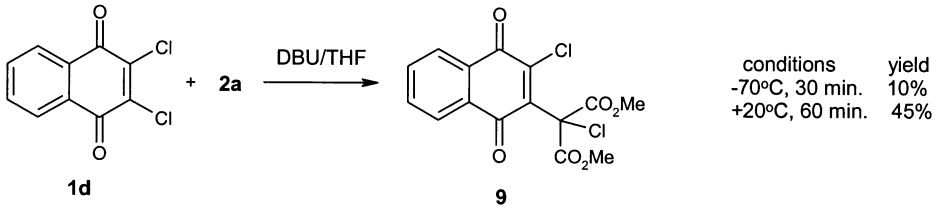
Compound **8** was apparently formed via a reaction of the carbanion of **3a** with **1d** proceeding as S_NV process (VNS+S_NV) (Scheme 5). Indeed, when the reaction between {**1a**+**1d**} and **2a** was finished at higher temperature (0°C) VNS product **3a** was obtained in low yield (5%), whereas product **8** was obtained in yield 69%. In addition to that, when a 1:1 mixture of **3a** and **1d** was treated with DBU product **8** was obtained in 75% yield.

Reaction S_NV in **1d** is a relatively slow process. For example, treatment of **1d** with **2a** in the presence of DBU at −70°C for 30 min gave the S_NV product **9** in 10% yield only, and about 75% of both educts were recovered. When this reaction was carried out at +20°C and quenched after 60 min product **9** was obtained in a higher yield (45%) (Scheme 6). These results indicate that the addition of the carbanion to **1a** proceeds faster than to **1d** in spite of the presence of two Cl substituents in **1d**.

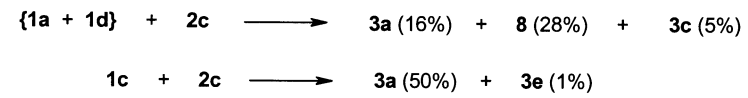
Results of these competitive experiments show a peculiar effect of Cl substituents on the electrophilic reactivity of naphthoquinones. The presence of one Cl increases substantially the electrophilic activity of **1b**, resulting in much faster addition of the carbanion to **1b** (than to **1a**) in the position occupied by hydrogen. There is no reason to suppose that the second Cl substituent would exert the opposite effect, however, in spite of the expected higher general electrophilicity of the molecule of **1d**, Cl substituents occupying the addition sites protect them against nucleophilic addition, thus it proceeds much slower than to **1b** and **1a**. Similarly, in nitroarenes the Cl substituents increase the general electrophilic activity of the ring and simultaneously protect positions they occupy against nucleophilic attack.

Since ONSH usually proceeds slower than VNS, we expected that the competition between S_NV in **1d** and ONSH in **1a** could give additional information concerning the relation of the electrophilic activities of **1a** and **1d**. When a mixture of **1a**, **1d** and dimethyl malonate (**2c**) in THF was added to a solution of DBU in THF at −70°C, the main process was ONSH in **1a** giving **3a** (16%) and **8** (28%), but S_NV process in **1d** also took place in this case giving **3c** in low 5% yield (Scheme 7).

In this connection it was of interest to compare the effects of



Scheme 6.



Scheme 7.

Cl and F substituents in 2-halo substituted naphthoquinones on the competition between S_NV and ONSH, in the reaction with $\mathbf{2c}^-$. The reaction of dimethyl malonate (**2c**) with 2-fluoro-1,4-naphthoquinone (**1c**) gave mostly S_NV product **3a** (50%) (Scheme 7) whereas the product of ONSH (**3e**) was formed in low amount (1%).

Although these results are purely qualitative one can conclude that similarly as in nitroarenes Cl activates the ring for nucleophilic addition, but protects the position it occupies, whereas similar effects of F are much weaker.

1. Experimental

Melting points are uncorrected. IR spectra were recorded in KBr on Beckmann IR-4240 spectrometer. ^{1}H- and ^{13}C NMR spectra were taken in $CDCl_3$ on Varian Gemini 200 (200 MHz) spectrometer, chemical shifts are given in δ ppm referred to TMS as internal standard. Mass spectra were recorded on AMD 604 spectrometer. Column chromatography was performed using silica gel 230–400 mesh (E. Merck). All reactions were performed under Ar. The following compounds were prepared by known methods: 2-chloro-1,4-naphthoquinone (**1b**),[32] 2-fluoro-1,4-naphthoquinone (**1c**),[33] 2,3-dichloro-1,4-naphthoquinone (**1d**).[34] Other reagents are commercially available.

1.1. General procedure for VNS reaction in naphthoquinones 1a–d

To a stirred solution of DBU (380 mg, 2.5 mmol) in THF (8 mL) a solution of the carbanion precursor (1 mmol) and the quinone (1 mmol) in THF (2 mL) was added dropwise at +5°C. The mixture was stirred for 5 min at +5°C, the cooling bath was removed and the reaction mixture was allowed to warm up to +20°C, and kept at this temperature for 10 min. The reaction mixture was then poured into cold 3% HCl solution and extracted with CH_2Cl_2. The combined extracts were dried with $MgSO_4$. The solvents were evaporated in vacuo and the products were isolated from the residue by column chromatography (hexane/CH_2Cl_2 eluent).

1.1.1. 2-[Di(methoxycarbonyl)]methyl-1,4-naphthoquinone (3a). Yield 237 mg (82%), yellow crystals, mp 110–111°C (hexane/AcOEt), lit.[35]: mp 135°C (methanol). ^{1}H NMR: 8.18–8.04 (m, 2H), 7.82–7.72 (m, 2H), 7.06 (d, 1H, J=0.9 Hz), 5.08 (d, 1H, J=0.9 Hz), 3.82 (s, 6H). IR ν_{max}: 1750, 1730, 1664, 1317, 1302, 1237, 752. Anal. calcd for $C_{15}H_{12}O_6$: C 62.50, H 4.20; found: C 62.46, H 4.05.

1.1.2. 2-[Acetyl-(ethoxycarbonyl)]methyl-1,4-naphthoquinone (3b). Yield 221 mg (77%), oil. ^{1}H NMR: 13.21 (s, 1H, enolic form), 8.18–8.04 (m, 2H, both forms), 7.83–7.71 (m, 2H, both forms), 7.08 (d, 1H, J=0.9 Hz, keto form), 6.84 (s, 1H, enolic form), 5.18 (d, 1H, J=0.9 Hz, keto form), 4.27 (q, 2H, J=7.1 Hz, enolic form), 4.19 (q, 2H, J=7.1 Hz, keto form), 2.41 (s, 3H, keto form), 2.00 (s, 3H, enolic form), 1.31 (t, 3H, J=7.1 Hz, keto form), 1.17 (t, 3H, J=7.1 Hz, enolic form). IR (film) ν_{max}: 2984, 1743, 1724, 1667, 1596, 1301, 1254, 1196. Anal. calcd for $C_{16}H_{14}O_5$: C 67.13, H 4.93; found: C 67.10, H 4.83.

1.1.3. 2-[Di(methoxycarbonyl)]methyl-3-chloro-1,4-naphthoquinone (3c). Yield 235 mg (73%), yellow crystals, mp 152–153°C (ethanol), lit.[35]: mp 153.5°C (methanol). ^{1}H NMR: 8.25–8.10 (m, 2H), 7.85–7.75 (m, 2H), 5.16 (s, 1H), 3.81 (s, 6H). IR ν_{max}: 1750, 1733, 1674, 1273, 1252, 1035, 753. Anal. calcd for $C_{15}H_{11}ClO_6$: C 55.83, H 3.44, Cl 10.99; found: C 55. 89, H 3.30, Cl 11.18.

1.1.4. 2-[(Acetyl-(ethoxycarbonyl)]methyl-3-chloro-1,4-naphthoquinone (3d). Yield 242 mg (75%), yellow crystals, mp 105–106°C (hexane/ether), lit.[26]: mp 106–107°C (ethanol). ^{1}H NMR (exists only in enolic form): 13.20 (s, 1H), 8.27–8.09 (m, 2H), 7.86–7.75 (m, 2H), 4.18 (q, 2H, J=7.1 Hz), 1.91 (s, 3H), 1.16 (t, 3H, J=7.1 Hz), lit.: IR ν_{max}: 1684, 1665, 1646, 1596, 1395, 1340, 1284, 1242, 710. Anal. calcd for $C_{16}H_{13}ClO_5$: C 59.92, H 4.08, Cl 11.06; found: C 60.01, H 3.97, Cl 11.16.

1.1.5. 2-[Di(methoxycarbonyl)]chloromethyl-1,4-naphthoquinone (4). To a stirred solution of dimethyl chloromalonate (333 mg, 2 mmol) and 2-chloro-1,4-naphthoquinone (385 mg, 2 mmol) in THF (15 mL) a solution of DBU (304 mg, 2 mmol) in THF (5 mL) was added dropwise at −70°C. The reaction mixture was kept at this temperature for 20 min and then poured into cold 3% HCl solution and extracted with CH_2Cl_2. The combined extracts were dried with $MgSO_4$. The solvents were evaporated in vacuo at room temperature and the products **3c** and **4** were isolated from the half of the residue by column chromatography (hexane/CH_2Cl_2/ether eluent) in yields 195 mg (60%) and 8 mg (2%) respectively. The second half of the residue was purified by column chromatography using silicagel pretreated with AcOH/hexane to give **3c** only (179 mg, 56%). **4**, brown oil: ^{1}H NMR: 8.16–8.06 (m, 2H), 7.85–7.74 (m, 2H), 7.29 (s, 1H), 3.89 (s, 6H). ^{13}C NMR: 184.2, 182.4, 165.2, 144.9, 136.3, 135.0, 134.5, 131.7 (2C), 127.2, 126.4, 72.4, 54.5. MS (CI): 662 (20) [$2M^+ + NH_4$], 340 (100) [$M^+ + NH_4$].

1.2. The reaction of dimethyl malonate (2c) with 2-chloro-1,4-naphthoquinone (1b) at various temperatures (competition between ONSH and S_NV) (Scheme 3)

To a stirred solution of dimethyl malonate (132 mg, 1 mmol) and 2-chloro-1,4-naphthoquinone (193 mg, 1 mmol) in THF (8 mL) a solution of DBU (152 mg, 1 mmol) in THF (2 mL) was added dropwise at temperature indicated in Scheme 3. After 30 min the reaction mixture

was poured into cold 3% HCl solution and extracted with CH_2Cl_2. The combined extracts were dried with $MgSO_4$. The solvents were evaporated in vacuo and after flash column chromatography (hexane/CH_2Cl_2/ether) educt and a mixture of products **3a** and **3c** were obtained. The ratio **3a/3c** was determined on the basis of ^{1}H NMR spectra.

1.3. Reaction of 2-fluoro-1,4-naphthoquinone (1c) with dimethyl chloromalonate (2a)

To a stirred solution of DBU (380 mg, 2.5 mmol) in THF (8 mL) a solution of **2a** (167 mg, 1 mmol) and 2-fluoro-1,4-naphthoquinone (176 mg, 1 mmol) in THF (2 mL) was added dropwise at −70°C. The mixture was stirred for 30 min at −70°C, then poured into cold 3% HCl solution and extracted with CH_2Cl_2. The combined extracts were dried with $MgSO_4$. The solvents were evaporated in vacuo and the residue separated by column chromatography (hexane/CH_2Cl_2/ether eluent, silicagel was washed with AcOH/hexane before use) to give **3e** (101 mg, 33%) and **6** (33 mg, 16%).

When DBU (2 mmol) was added to a mixture of **2a** (2 mmol) and **1c** (1 mmol), product **3e** was obtained in yield 95 mg (31%) and **6** was isolated in yield 124 mg (30%).

1.3.1. 2-[Di(methoxycarbonyl)]methyl-3-fluoro-1,4-naphthoquinone (3e). Yellow crystals, mp 130–131°C (hexane/CH_2Cl_2). ^{1}H NMR: 8.24–8.12 (m, 2H), 7.90–7.78 (m, 2H), 5.03 (s, 1H), 3.84 (s, 6H). ^{13}C NMR: 182.8 (J_{C-F}=11 Hz), 177.1 (J_{C-F}=23 Hz), 166.0 (J_{C-F}=2 Hz), 159.2 (J_{C-F}=292 Hz), 134.9, 134.4, 131.2, 130.2 (J_{C-F}=4 Hz), 127.2, 126.6 (J_{C-F}=3 Hz), 123.3 (J_{C-F}=4 Hz), 53.4, 46.7. IR ν_{max}: 1747, 1683, 1652, 1284, 1259, 1197, 747. Anal. calcd for $C_{15}H_{11}FO_6$: C 58.83, H 3.62, F 6.20; found: C 58.83, H 3.47, F 6.22.

1.3.2. 2,3-*bis*-[Di(methoxycarbonyl)]methylene-1,4-naphthoquinone (6). White powder, mp 148–150°C (dec.) (hexane/CH_2Cl_2). ^{1}H NMR: 8.22–8.12 (m, 2H), 7.90–7.80 (m, 2H), 3.91 (s, 6H), 3.83 (s, 6H). ^{13}C NMR: 183.8, 164.3, 162.0, 139.8, 135.6, 134.3, 133.1, 127.7, 53.33, 53.26. IR ν_{max}: 1732, 1721, 1701, 1691, 1310, 1246, 1116. MS (LSIMS HR): calcd for $C_{20}H_{17}O_{10}$ ($[M+H]^+$): 417.0821; found: 417.0805. Anal. calcd for $C_{20}H_{16}O_{10}$: C 57.69, H 3.87; found: C 56.92, H 3.90.

1.4. Reaction 1c with 2a and equimolar amount of DBU

To a stirred solution of 2-fluoro-1,4-naphthoquinone **1c** (176 mg, 1 mmol) in THF (8 mL) a solution of **2a** (167 mg, 1 mmol) and DBU (152 mg, 1 mmol) in THF (2 mL) was added dropwise at −70°C. The mixture was stirred for 5 min at −70°C, then poured into cold 3% HCl solution and extracted with CH_2Cl_2. The combined extracts were dried with $MgSO_4$. The solvents were evaporated in vacuo and the products **3e** (18 mg, 6%) and a mixture of **6**+**7** (1:3 from ^{1}H NMR spectra) (65 mg, ca. 30%) were isolated from the residue by column chromatography (hexane/CH_2Cl_2/ether eluent, silicagel was washed with AcOH/hexane before use). This mixture could not be separated neither by recrystallisation nor by chromatography. Thus spectral data for **7** were obtained after subtracting the spectra of **6** from the spectra of mixture **6**+**7**.

1.4.1. 2-[Di(methoxycarbonyl)]chloromethyl-3-[di-(methoxycarbonyl)]methyl-1,4-naphthoquinone (7). Pale pink powder, ^{1}H NMR: 8.15–8.02 (m, 2H), 7.84–7.75 (m, 2H), 6.15 (s, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.86 (s, 3H), 3.83 (s, 3H). ^{13}C NMR: 189.6, 185.7, 165.1, 165.0, 164.9, 162.9, 141.5, 135.5, 135.3, 134.9, 134.8, 134.7, 127.4, 126.8, 71.7, 55.2, 54.4, 54.2, 53.18, and 53.1. MS (LSIMS HR): calcd for $C_{20}H_{18}ClO_{10}$ ($[M+H]^+$): 453.0589; found: 453.0605.

1.5. Competitive reaction of 1,4-naphthoquinone (1a) and 2-chloro-1,4-naphtoquinone (1b) with dimethyl chloromalonate (2a)

To a stirred solution of DBU (380 mg, 2.5 mmol) in THF (8 mL) a solution of **1a** (237 mg, 1.5 mmol), **1b** (289 mg, 1.5 mmol) and **2a** (167 mg, 1 mmol) in THF (7 mL) was added slowly at −70°C. The mixture was stirred for 30 min at this temperature, then poured into cold 3% HCl solution and extracted with CH_2Cl_2. The combined extracts were dried with $MgSO_4$. The solvents were evaporated in vacuo and the residue was separated by column chromatography (hexane/CH_2Cl_2/ether eluent) to give **3c** (247 mg, 76% yield), **1b** (44 mg, 0.23 mmol) and **1a** (207 mg, 1.31 mmol).

1.6. Competitive reaction of 1,4-naphthoquinone (1a) and 2,3-dichloro-1,4-naphthoquinone (1d) with dimethyl chloromalonate (2a)

To a stirred solution of DBU (380 mg, 2.5 mmol) in THF (8 mL) a solution of **1a** (237 mg, 1.5 mmol), **1d** (341 mg, 1.5 mmol) and **2a** (167 mg, 1 mmol) in THF (7 mL) was added slowly at −70°C. After stirring for 30 min at −70°C the reaction mixture was poured into cold 3% HCl solution and extracted with CH_2Cl_2. The combined extracts were dried with $MgSO_4$ and evaporated in vacuo. The residue was separated by column chromatography (hexane/CH_2Cl_2/ether eluent) to give educts **1d** (237 mg, 1.04 mmol) and **1a** (90 mg, 0.57 mmol), and products **3a** (190 mg, 66% yield) and **8** (82 mg, 17% yield).

When this reaction was carried out for additional 30 min at 0°C products **3a** and **8** were obtained in yield 15 mg (6%) and 331 mg (69%), respectively.

In reaction **3a** (1 mmol) with **1d** (1 mmol) was carried out at −70 to +20°C for 30 min and the product **8** was obtained in yield 358 mg (75%).

1.6.1. *bis*-1,4-Naphthoquinone derivate (8). Yellow powder, mp 222–223°C (dec.) (hexane/CH_2Cl_2/AcOEt). ^{1}H NMR: 8.32–8.09 (m, 4H), 7.93–7.78 (m, 4H), 4.33 (s, 1H), 3.78 (s, 3H), 3.77 (s, 3H). ^{13}C NMR: 182.5, 181.8, 180.7, 177.1, 166.4, 166.2, 146.0, 142.1, 141.9, 140.5, 135.4, 135.2, 135.1, 134.9, 132.2, 132.0, 131.9, 131.7, 128.3, 128.0, 127.8, 127.5, 53.8 (2C), 52.9. MS (EI), *m/z* (%): 478 (8) [M^+], 444 (11), 353 (100), 213 (14). IR ν_{max}: 1750, 1733, 1673, 1656, 1321, 1277, 1244. Anal. calcd for

$C_{25}H_{15}ClO_8$: C 62.71, H 3.16, Cl 7.40; found: C 62.35, H 2.92, Cl 7.27.

1.6.2. 2-[Di(methoxycarbonyl)]chloromethyl-3-chloro-1,4-naphthoquinone (9). To a stirred solution of dimethyl chloromalonate (167 mg, 1 mmol) and 2,3-dichloro-1,4-naphtoquinone (227 mg, 1 mmol) in THF (15 mL) a solution of DBU (152 mg, 1 mmol) in THF (2 mL) was added drop wise at 0°C. The cooling bath was removed and the reaction mixture was allowed to warm up to +20°C, and kept at this temperature for 1 h. The reaction mixture was poured into cold 3% HCl solution and extracted with CH_2Cl_2. The combined extracts were dried with $MgSO_4$. The solvents were evaporated in vacuo and the product **9** (159 mg, 45%) was isolated from the residue by column chromatography (hexane/CH_2Cl_2/ether eluent, silicagel was washed with AcOH/hexane before use).

Yellow crystals, mp 193–194°C (hexane/CH_2Cl_2). ^{1}H NMR: 8.24–8.05 (m, 2H), 7.89–7.76 (m, 2H), 3.91 (s, 6H). ^{13}C NMR: 179.7, 176.7, 164.6, 146.4, 144.1, 135.0, 134.7, 131.4, 131.0, 127.6, 127.5, 69.2, 54.9. IR ν_{max}: 1766, 1737, 1683, 1664, 1285, 1209, 707. Anal. calcd for $C_{15}H_{10}Cl_2O_6$: C 50.44, H 2.82, Cl 19.85; found: C 50.30, H 2.80, Cl 19.95.

1.7. The competition between S_NV in 1d and ONSH in 1a with dimethyl malonate (2c)

To a stirred solution of **1a** (237 mg, 1.5 mmol), **1d** (341 mg, 1.5 mmol) and **2c** (132 mg, 1 mmol) in THF (15 mL) a solution of DBU (152 mg, 1 mmol) in THF (2 mL) was added slowly at −70°C. After stirring for 30 min at −70°C the reaction mixture was poured into cold 3% HCl solution and extracted with CH_2Cl_2. The combined extracts were dried with $MgSO_4$ and evaporated in vacuo. The residue was separated by column chromatography (hexane/CH_2Cl_2/ether eluent) to give educts **1a** (126 mg, 0.80 mmol) and **1d** (204 mg, 0.9 mmol), and products **3a** (45 mg, 16%), **3c** (15 mg, 5%) and **8** (135 mg, 28%).

1.8. The competition between S_NV and ONSH in 1c with dimethyl malonate

The reaction **1c** (176 mg, 1 mmol) with **2c** (132 mg, 1 mmol) was carried out analogously to described procedure for **1b** and **2c** at −70°C, and the products **3a** (143 mg, 50%) and **3e** (3 mg, 1%) were separated by column chromatography.

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