Dihalomethylation of Nitroarenes via Vicarious Nucleophilic Substitution of Hydrogen with Trihalomethyl Carbanions[1]

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Trichloro- and tribromomethyl carbanions generated by deprotonation of haloforms with potassium *tert*-butoxide in a THF–DMF mixture at ca. −70 °C react with a variety of carbocyclic and heterocyclic nitroarenes according to the vicarious nucleophilic substitution scheme. The reaction provides an efficient and convenient way for the direct introduction of dihalomethyl substituents ortho and para to the nitro group, which in turn can be hydrolyzed to produce nitroaryl aldehydes.

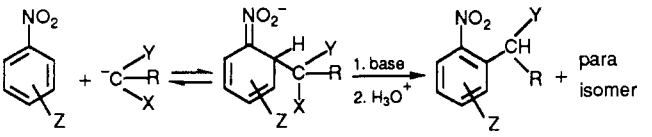
Introduction

Vicarious nucleophilic substitution (VNS) of hydrogen in nitroarenes is a reaction with carbanions containing leaving groups X at the carbanion center which proceeds according to Scheme I.

This is a general process in the sense of both aromatic partners and carbanions.[2] Indeed, there is practically no limitation concerning substituents Z in the aromatic rings,[3,4] which can be heterocyclic as well;[5,6] also, a large variety of carbanions containing leaving groups such as Cl, Br, PhO, PhS, >NCSS, etc., enter the reaction.[7] Some limitations concerning the scope are due to low nucleophilicity of highly stabilized carbanions, insufficient stability of some carbanions, or fast base-induced self-condensation of a carbanion precursor when the VNS proceeds with insufficient rate.

Trihalomethyl carbanions are well known to be intrinsically unstable due to their rapid dissociation to dihalocarbenes.[8] Nevertheless, they are able to react with such active electrophiles as aldehydes, ketones, and some Michael acceptors.[9] The availability of haloforms as well as the attractiveness of CHX_2 groups for further transformations prompted us to investigate dihalomethylation of nitroarenes via VNS. In 1971, McBee reported that *o*-dichloromethyl substituents can be introduced into *p*-halonitrobenzenes in the reaction with (trichloromethyl)lithium at −100 °C to −70 °C, suggesting a dichlorocarbene insertion mechanism.[10] In our preliminary communication, we reported the possibility of dichloromethylation of some nitroarenes with trichloromethyl anions via a typical VNS mechanism, namely addition of the carbanion followed by base-induced elimination of HCl from the initially formed σ-adduct.[11] Here we would like to present a full account of this study, including the reaction with tribromomethyl anions and also the conversion

Scheme I



of some dihalomethyl derivatives into aldehydes.

Results and Discussion

Reaction of Trihalomethyl Anions with Carbocyclic Nitroarenes. In this reaction there are two crucial problems connected with stability. The first problem is the intrinsic instability of the trihalomethyl anions which dissociate rapidly to dihalocarbenes. This dissociation can compete with the addition of the anions to nitroarenes and therefore prevent the VNS. The second problem is the instability of nitrobenzylidene dihalide carbanions, produced in the VNS reaction. They are known to undergo a variety of reactions, mainly via single-electron transfer, which would result in dimerization, polymerization, etc.[12] The selection of the reaction mode of the trihalomethyl carbanions (dissociation vs addition) should strongly depend on the electrophilic properties of the nitroarenes. Thus, the success of the VNS reaction requires that the CX_3^- addition to $ArNO_2$ should dominate over the dissociation, the elimination should be a very fast process, and the nitrobenzylidene dihalide carbanions which are produced should be converted rapidly into the neutral products. For both of the stability reasons the VNS with CX_3^- anions should be carried out at low temperature and at the same time the conditions should assure a high rate. From many of our earlier observations, and also the preliminary results of this process,[11] it seemed necessary to have conditions in which the carbanion cation ion pairs are relatively loose. Screening a variety of possibilities resulted in the selection of potassium *tert*-butoxide in a mixture of tetrahydrofuran–dimethylformamide (ca. 1:1 per volume) as the most efficient and general base/solvent system for the reaction of haloforms with nitroarenes. Additionally, the reaction should be carried out around −70 °C. Under such conditions the reaction usually proceeds rapidly with a strong exothermic effect; hence effective cooling and stirring is important. On the other hand stability of the nitrobenzylidene dihalide anions, even at such low temperature, requires that the reaction mixture should be quenched with an acid as soon as possible, 1–2 min after

(1) Part 161 in the series Reactions of Organic Anions. For part 160, see: Ostrowski, S.; Mąkosza, M. *Justus Liebigs Ann. Chem.* **1989**, 95.
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(5) (a) Mąkosza, M.; Chylińska, B.; Mudryk, B. *Justus Liebigs Ann. Chem.* **1984**, 8. (b) Mąkosza, M.; Kinowski, A.; Danikiewicz, W.; Mudryk, B. *Justus Liebigs Ann. Chem.* **1986**, 69.
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(10) Mc Bee, E. T.; Wesseler, E. D.; Hodgins, T. *J. Org. Chem.* **1971**, *36*, 2907.
(11) Mąkosza, M.; Owczarczyk, Z. *Tetrahedron Lett.* **1987**, 3021.
(12) Ida, H.; Ooki, N.; Takahashi, K. *Nippon Kagaku Kaishi* **1974**, 2127; *Chem. Abstr.* **1975**, *83*, 27739. Rothberg, I.; Thornton, E. R. *J. Am. Chem. Soc.* **1964**, *86*, 3296 and 3302. Closs, G. L.; Gosh, S. H. *J. Chem. Soc., Perkin Trans. 2* **1972**, 1473. Burt, L. B.; Freeman, D. I.; Gray, P. G.; Norris, R. K.; Randles, D. *Tetrahedron Lett.* **1977**, 3063.

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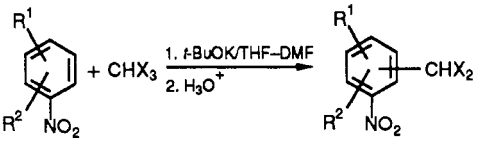
Table I. Reactions of Nitroarenes with Haloforms



entry	R^1	R^2	X	position of CHX_2	product	yield,[a] %
1	H	H	Cl	2, 4	**2a, 3a**	52, 13
2	H	H	Br	2, 4	**2b, 3b**	16, 15
3	4-F	H	Cl	2	**4a**	59
4	4-F	H	Br	–	–	–
5	3-F	H	Cl	2	**5a**	62
				4, 6	**6a, 7a**	12, 2[b]
6	3-F	H	Br	2	**5b**	43
				4, 6	**6b, 7b**	26, 2[b]
7	4-Cl	H	Cl	2	**8a**	94[c]
8	4-Cl	H	Br	2	**8b**	69
9	2-Cl	H	Cl	4, 6	**9a, 10a**	38, 32
10	2-Cl	H	Br	4, 6	**9b, 10b**	45, 10
11	2-Cl	4-Cl	Cl	6	**11a**	78
12	2-Cl	4-Cl	Br	6	**11b**	76
13	4-Br	H	Cl	2	**12a**	77[c]
14	4-Br	H	Br	2	**12b**	88[c]
15	4-J	H	Cl	2	**13a**	91[c]
16	4-J	H	Br	2	**13b**	80[c]
17	4-Ph	H	Cl	2	**14a**	83
18	4-Ph	H	Br	–	–	–
19	$4\text{-}OCH_3$	H	Cl, Br	–	–	–
20	$4\text{-}OCH_2Ph$	H	Cl	2	**15a**	59
21	$4\text{-}OCH_2Ph$	H	Br	–	–	–
22	4-(OPh-4-Cl)	H	Cl	2	**16a**	78
23	4-(OPh-4-Cl)	H	Br	–	–	–
24	$4\text{-}OCH_2CH{=}CH_2$	H	Cl	2	**17a**	58
25	$4\text{-}OCH_2CH{=}CH_2$	H	Br	2	**17b**	22
26	$2\text{-}OCH_2CH{=}CH_2$	H	Cl	4	**18a**	30
27	$2\text{-}OCH_2CH{=}CH_2$	H	Br	–	–	–
28	4-SPh	H	Cl	2	**19a**	29
29	4-SPh	H	Br	–	–	–
30	4-SOPh	H	Cl	2	**20a**	65
31	4-SOPh	H	Br	–	–	–
32	$4\text{-}SO_2Ph$	H	Cl	2	**21a**	40
33	$4\text{-}SO_2Ph$	H	Br	–	–	–
34	4-CN	H	Cl	2	**22a**	14
35	4-CN	H	Br	–	–	–
36	3-CN	H	Cl	2	**23a**	29
				4, 6	**24a, 25a**	8, 26[b]
37	3-CN	H	Br	2	**23b**	19
				4, 6	**24b, 25b**	18, 31[b]
38	$4\text{-}CF_3$	H	Cl	2	**26a**	76
39	$4\text{-}CF_3$	H	Br	2	**26b**	64
40	$3\text{-}CF_3$	H	Cl	4, 6	**27a, 28a**	6, 48
41	$3\text{-}CF_3$	H	Br	4, 6	**27b, 28b**	6, 40
42	1-nitronaphthalene		Cl	2	**29a**	67
43	1-nitronaphthalene		Br	2	**29b**	70

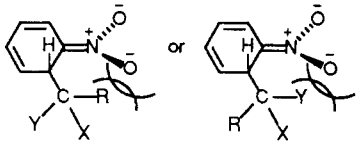
[a] Yields of isolated products. [b] Mixture of the isomers, composition determined by ^1H NMR spectroscopy. [c] CHX_3 were used in 25% molar excess.

mixing of the reactants. Small deviations from these optimal conditions often result in a dramatic decrease in the yield of the VNS product. Results of the reaction of chloroform **1a** and bromoform **1b** with nitrobenzene and its derivatives are shown in Table I.

Two interesting specific features should be emphasized and discussed in connection with the results shown in Table I. First is the orientation pattern. In our previous papers we have shown that the orientation is strongly affected by the steric requirements of the carbanions. Secondary carbanions (X-$\bar{C}$H-Y) usually react in both the ortho and para positions, whereas tertiary carbanions (X$\bar{C}$RY), which usually are more sterically demanding, react exclusively or preferentially in the para position.[2,3] Only when the para position is occupied or sterically hindered can tertiary carbanions react at the position ortho, although some times unsatisfactorily.[13] Both CCl_3^- and CBr_3^- are tertiary carbanions, nevertheless they react with nitrobenzene and even with *o*-chloronitrobenzene, giving substantial amounts of the ortho isomers, for CCl_3^- substitution in the ortho position was even preferred over that in the para. The sensitivity of the VNS toward steric effects is mainly due to difficulties in attaining the antiperiplanar configuration of H–C–C–X bonds necessary for the elimination of HX from the initially formed σ-adducts, as shown below. Such difficulties do not exist when R = H.

In the case of CX_3^- anions all three substituents are equally efficient leaving groups so there is substantial statistical facilitation of attaining the configuration necessary for the elimination. This should accelerate the

(13) Mudryk, B.; Mąkosza, M. *Tetrahedron* **1988**, 209.
(14) Stock, L. M.; Brown, H. C. *J. Am. Chem. Soc.* **1962**, *84*, 1668.



elimination, hence the orientation more nearly reflects the addition pattern.

The second feature is even more interesting. The already mentioned high intrinsic instability of the CX_3^- anions, which dissociate rapidly to the corresponding dihalocarbenes, makes these anions sensitive probes for estimating the activity of the nitroarenes in the VNS. Moreover, differences in the stabilities of $\bar{C}Cl_3$ and $\bar{C}Br_3$ provides the insight for even more subtle differences in these activities. Although all of these differences are manifested in yields of the products which are, in fact, an interplay of many factors, in the case of such unstable carbanions they should correlate somewhat with the activity of the nitroarenes toward the VNS. Results shown in Table I are in general in agreement with the expectation based on our many previous observations concerning activity of the nitroarenes in the VNS: $PhNO_2$, less active than *o*-$ClPhNO_2$ and *p*-$ClPhNO_2$, etc., but there are a few unexpected results. The most interesting is the low activity of *p*-fluoronitrobenzene, which is less active than $PhNO_2$ as it is apparent from the reaction with CCl_3^- and particularly CBr_3^- (entries 3 and 4). These results were confirmed by parallel experiments and are far beyond simple experimental error. Unchanged *p*-$FPhNO_2$ is recovered almost quantitatively. Thus, surprisingly, *p*-F deactivates nitroarenes toward nucleophilic substitution. This effect could not be detected in the classical S_NAr, due to the high rate of F substitution.[15] We have observed a similar situation in our attempts to use the Hammett correlation approach to observe the effect of substituents on the rate of VNS. The reaction of 4-X-nitrobenzenes with chloromethyl phenyl sulfone was strongly accelerated when X = Cl, Br, and I and much less when X = F.[16] Taking into account that Cl, Br, and I exhibit weaker inductive effects than F, we should suppose that conjugation of the latter with the NO_2 group through the ring is much more efficient due to a good correlation of the p orbital size.

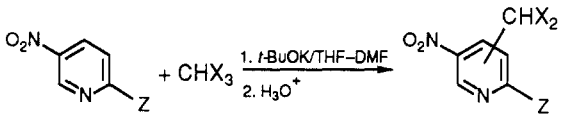
This supposition is strongly supported by the results of the reaction of CX_3^- anions with *m*-halonitrobenzenes, in which there is no conjugation between the halogens and the nitro group. Thus *m*-fluoronitrobenzene reacts efficiently with $\bar{C}Cl_3$ and $\bar{C}Br_3$ to produce corresponding dihalomethyl derivatives in good yield (entries 5 and 6).

Much stronger electron-donating conjugation abilities of F than Cl have often been observed in electrophilic aromatic substitution. Such reactions as nitration or halogenation of arenes are substantially decelerated by Cl or Br but not F substituents.[14]

The reaction with *p*-alkoxynitrobenzenes gives very interesting results, too. Whereas *p*-nitroanisole does not react with either $\bar{C}Cl_3$ or $\bar{C}Br_3$, *p*-benzyloxynitrobenzene and *p*-(4-chlorophenoxy)nitrobenzene do react satisfactorily with $\bar{C}Cl_3$ but not with $\bar{C}Br_3$. A substantial effect of alkyl group character on the reactivity of *p*-nitrophenol ethers in the VNS was already reported,[17] but only in the reaction with $\bar{C}Cl_3$ is it so strongly pronounced. Moreover (*p*-allyloxy)nitrobenzene reacted with both $\bar{C}Cl_3$ and $\bar{C}Br_3$,

(15) Miller, J. *Aromatic Nucleophilic Substitution*; Elsevier: Amsterdam, 1968.
(16) Unpublished results from our laboratory.
(17) Mąkosza, M.; Danikiewicz, W.; Wojciechowski, K. *Justus Liebigs Ann. Chem.* **1988**, 203.

Table II. Reactions of Nitropyridine Derivatives with Haloforms



entry	Z	X	position of CHX_2	product	yield, %
1	H	Cl	4	**30a**	72
2	H	Br	4	**30b**	63
3	CH_3O	Cl	6	**31a**	56 (34)
4	CH_3O	Br	6	**31b**	70 (30)
5	Cl	Cl	4, 6	**32a**, **33a**	54, 36
6	Cl	Br	4, 6	**32b**, **33b**	65, 24

[a] Yields of isolated products. Yields when 40% molar excess of CHX_3 was used are in parentheses.

although the yield of the dibromomethylated product was moderate. It is surprising that the *p*-allyloxy group deactivates the nitroarene toward nucleophilic substitution to a smaller extend than does F. Fast consumption of the trihalomethyl anions and the absence of dihalocarbenes was evidenced by observation that the eventual dichlorocarbene adduct to the allyloxy group was not detected.

Surprisingly, nitrobenzene derivatives containing strong electron- withdrawing groups such as CN or SO_2Ph in the para position did not react satisfactorily with CX_3^- anions. The yields of the dichloromethylated products were low, dibromomethylation was not observed, and the majority of the nitroarenes were recovered unchanged. It is also surprising that the presence of these groups para to the NO_2 group deactivates the nitrobenzene ring toward the reaction with CX_3^-, whereas in the meta position they exert a strong activating effect. As was expected the CF_3 substituent, which exerts a strong electron-withdrawing inductive effect, activates the nitrobenzene ring when located para and meta to the nitro group.

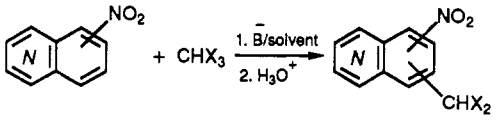
1-Nitronaphthalene is known to be one of the most active nitroarenes in the VNS process.[7,18] These observations were confirmed in the reaction with trihalomethyl anions: both of the carbanions studied reacted satisfactorily, giving the corresponding 2-dihalomethyl derivatives. Also in these cases a strong preference for the ortho substitution in the reaction with CX_3^- anions was observed; no 4-isomers of the dihalomethylated products, even in the reaction with CBr_3^-, were detected.

On the other hand, steric hindrance in the reaction with 2-nitronaphthalene prevents its reaction with trihalomethyl carbanions. None of them entered the reaction with it, which is similar to other tertiary carbanions. Lack of the desired VNS reaction between tertiary carbanions and 2-nitronaphthalene has been reported and explained by a substantial steric hindrance for the elimination created by the neighboring nitro group and the peri-hydrogen atom.[18]

Reaction of Trihalomethyl Anions with Nitro Heterocycles. In our previous papers we have shown that nitro derivatives of pyridine, quinoline, and five-membered aromatic heterocycles are active electrophilic partners in the VNS reaction.[5,6] The high activity of these compounds in the VNS was fully confirmed by the results of the reaction with trihalomethyl anions. 3-Nitropyridine and its derivatives 2-methoxy- and 2-chloro-5-nitropyridine reacted satisfactorily with both CCl_3^- and CBr_3^- anions (Table II). The orientation pattern of these reactions

(18) Mąkosza, M.; Danikiewicz, W.; Wojciechowski, K. *Justus Liebigs Ann. Chem.* **1987**, 711.

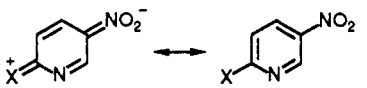
Table III. Reactions of Nitroquinolines and Nitroisoquinoline with Haloforms



entry	position of N	position of NO_2	X	position of CHX_2	product	yield,[a] %, and procedures A	B	C
1	1	5	Cl	6	**34a**	90	90	67
2	1	5	Br	6	**34b**	92	91	60
3	1	8	Cl	7	**35a**	59	60	34
4	1	8	Br	7	**35b**	40	35	16
5	1	6	Cl, Br	–	–	–	–	–
6	2	5	Cl	6	**36a**	81	85	72
7	2	5	Br	6	**36b**	89	93	80

[a] Yields of isolated products. A: CHX_3 were used in 6% molar excess (*t*-BuOK/TMF–DMF). B: $NaOCH_3/NH_3$ liquid system. C: CHX_3 were used in 40% molar excess (*t*-BuOK/TMF–DMF).

deserves some discussion. In 3-nitropyridine both of these carbanions have hydrogen replaced at position 4-, 2-methoxy-5-nitropyridine reacted exclusively at position 6-, whereas in 2-chloro-5-nitropyridine the substitution occured at both the 4- and 6- positions. Rationalization of such peculiar orientation patterns is based on the conjugation between the NO_2 group and the substitution para to it, which can be pictured by the dipolar resonance structure below. Contribution of this resonance structure



X = OMe and Cl but not H

for Z = Cl and particularly Z = OCH_3 explains partial and exclusive addition of the carbanions at C-6, respectively, whereas in the case of Z = H, when such conjugation does not exist, the reaction proceeds via addition to C-4. Here we would like to show another interesting aspect of this process: in spite of the instability of CX_3 and therefore the natural tendency to use an excess of CHX_3 in order to increase the yield of the dihalomethyl derivatives, excess of CHX_3 should be limited to 6–25%. Larger excess results in a substantial decrease of the yield because CX_3^- anions which have not reacted with $ArNO_2$ dissociate to dihalocarbenes which can subsequently react with the nitroarylidene dihalide anions, usually giving tars, hence the yields of the final products are substantially decreased.

The reaction of CX_3^- with 5-, 6-, 8-nitroquinolines and 5-nitroisoquinoline (Table III) follows the pattern observed earlier for the VNS of nitroquinolines[5b] and nitronaphthalenes[7,18] with sulfone and nitrile carbanions. In all these cases except 6-nitroquinoline, the reaction resulted in the formation of a single product in which the dihalomethyl substituent entered the position ortho to the nitro group, namely positions 6 and 7 in 5- and 8-nitroquinolines and position 6 in 5-nitroisoquinoline. 6-Nitroquinoline, similar to 2-nitronaphthalene, did not reacted with CX_3^- according to the VNS scheme, apparently for the identical sterical reasons.

The high activity of nitroquinolines in the reaction with trichloromethyl anions makes it possible to apply less sophisticated reaction conditions, namely to work in liquid ammonia using sodium methoxide. For the majority of nitroarenes mentioned earlier these conditions were unsuitable, the reaction was not observed at all, or only low yields of dichloromethylated products were obtained. One of the reasons for this is probably rapid and reversible dissociation of CX_3^- into CX_2 and X^-. Perhaps such a process precedes to some extent the VNS reaction but remains unnoticed in THF–DMF solution. On the other hand, in liquid ammonia solution dihalocarbenes are instantaneously quenched, so the fraction of $\bar{C}X_3$ which dissociated to CX_2 is irreversibly lost for the VNS. With very active nitroquinolines, the addition occurs rapidly and perhaps irreversibly, thus eventual quenching of CX_2 does not affect the reaction and hence it proceeds satisfactorily in liquid ammonia. The unfavorable effect of excess haloform on the yield of the VNS products is shown in Table III (column C).

Table IV. Reactions of Haloforms with Nitro Derivatives of 5-Membered Heterocycles and Indazole

entry	nitro compd	haloform	position of CHX_3	product	yield,[a] %
1	A	$CHCl_3$	3	**37a**	74[b] (70)[c]
2	A	$CHBr_3$	3	**37b**	64[b]
3	B	$CHCl_3$	3, 5	**38a, 39a**	20, 58[b]
4	B	$CHCl_3$	3, 5	**38a, 39a**	58[d]
5	B	$CHBr_3$	3, 5	**38b, 39b**	17, 66[b]
6	B	$CHBr_3$	3, 5	**38b, 39b**	75[e]
7	C	$CHCl_3$	5	**40a**	61[b]
8	C	$CHBr_3$	5	**40b**	50[b]
9	D	$CHCl_3$	4	**41a**	57[b]
10	D	$CHBr_3$	–	–	–

[a] Yields of isolated products. [b] *t*-BuOK/DMF–TMF system. [c] CH_3ONa/NH_3 liquid system. [d] *t*-BuOK/TMF system: **38a:39a** = 1.0 (GLC). [e] *t*-BuOK/TMF system: **39b:38b** = 1.65. A: 2-Nitrothiophene. B: 2-Nitrofuran. C: 1-Benzyl-4-nitroimidazole. D: 1-Ethyl-5-nitroindazole.

We have reported that N-protected nitroindoles enter satisfactorily the VNS reaction.[19] However our attempts to dihalomethylate 1,2-dimethyl-5-nitroindole in the reaction with CX_3 anions have failed. There are two possible reasons for this: decrease of the electrophilicity of the nitroaromatic ring by conjugation with donating N-Me substituent and/or steric hindrance in position 4 similar to those observed in 2-nitronaphthalene. Since 1-ethyl-5-nitroindazole reacted with $\bar{C}Cl_3$ (but not $\bar{C}Br_3$) satisfactorily, the former reason seems more important.

Very useful and interesting results were obtained in the reaction of CX_3^- anions with nitro derivatives of 5-membered heterocycles (Table IV). 2-Nitrothiophene reacted with both $\bar{C}Cl_3$ and $\bar{C}Br_3$ satisfactorily to form a single product from the VNS of the 3-hydrogen. No 5-dihalomethylated products were observed. Due to the known high activity of 2-nitrothiophene in the VNS, the dichloromethylation (but not dibromomethylation) also proceeded nicely in the liquid ammonia–sodium methoxide system. Actually, dibromomethylation of 2-nitrothiophene does occur in liquid ammonia too, but due to the high

(19) Wojciechowski, K.; Mąkosza, M. *Synthesis* **1989**, 106.

Table V. Hydrolysis of Nitroarylidene Dihalides into Nitroarylaldehydes

$$O_2NArCHX_2 \xrightarrow{[H_2O]} O_2NArCHO$$

entry	$O_2NArCHX_2$ no.	reaction conditions procedure/time, h	products no.	products yield,[a] %	$O_2NArCHO$ mp, °C	lit. mp, °C
1	**29a (29b)**	A/100 (10)	**42**	89 (97)	99–100	99[b]
2	**34a (34b)**	A/100 (10)	**43**	52 (95)	157–158	156–158[b]
3	**35b**	A/12	**44**	51	174–176	172–174[b]
4	**8a**	B/72	**45**	60	74	77[c]
5	**37a**	C/12	**46**	85	54	–
6	**38a (38b)**	D/6 (6)	**47**	78 (85)	81–82	–

[a] Yield of isolated products. [b] Reference 22. [c] Reference 23. A: $AgClO_4/CH_3CN/H_2O$. B: 85% $HCO_2H/ZnCl_2$. C: 75% HCO_2H. D: $AgClO_4/PhCH_3/H_2O$.

acidity of the product it cannot be protonated in this solvent and therefore undergoes decomposition.

Unexpectedly 2-nitrofuran reacted in high yield with trihalomethyl anions to give two isomeric dihalomethylated products in which the 5-isomers dominated over the 3-isomers in a ratio of 2.9 and 3.9 for CCl_3^- and CBr_3^-, respectively. In our preliminary paper we erronously reported that the dichloromethylation of 2-nitrofurane occurs mainly in position 3.[11] It should be stressed that in the reaction of chloromethyl phenyl sulfone with 2-nitrofuran, 2-nitro-3-[(phenylsulfonyl)methyl]furan was obtained in low yield.[6] The yield of this product also remained low under the conditions applied in this work for the reaction with haloforms. A strong tendency for the reaction in position 5 of 2-nitrofuran can also be seen from its reaction with CX_3^- carried out in THF (without DMF). Although these conditions are known to favor the ortho substitution,[20] the ratio of 5- to 3-isomer is still 1 for X = Cl and 1.65 for X = Br. The discrepancies in yields and orientation of the VNS in 2-nitrofuran with haloforms and chloromethyl phenyl sulfone is difficult to rationalize. Perhaps facile β-elimination of HX in the δ-adducts of CX_3^- anions assures fast conversion of the adducts to C-5 along the VNS pathway, whereas the elimination from the δ-adducts of other carbanions proceeds much slower, hence decomposition become the main process.

Conversion of Dihalomethylated Nitroarenes into Aldehydes. The VNS with haloforms provides an easy access to a great variety of dihalomethylated nitroarenes. They obviously appear to be good intermediates in the synthesis of the corresponding substituted nitroarylaldehydes via hydrolysis of the CHX_2 group. Hydrolysis of nitrobenzylidene dihalides is not, however, an easy task. Alkaline conditions cannot be applied. On the other hand acidic hydrolysis, proceeding via a carbocationic pathway, is strongly deccelerated by the electron-withdrawing nitro group. For example conversion of *p*-nitrobenzylidene dichloride into *p*-nitrobenzaldehyde requires treatment with concentrated sulfuric acid at 100 °C for 1 h whereas benzylidenedichloride is quantitatively hydrolyzed in a few minutes.[21] We have found that treatment with boiling 75% formic acid converts 3-(dichloromethyl)-2-nitrothiophene into the corresponding aldehyde. These conditions were too mild for hydrolysis of 5-chloro-2-nitrobenzylidene dichloride, addition of $ZnCl_2$ accelerates the procees sufficiently. The most general procedure for the hydrolysis of dihalomethylated nitroarenes is treatment with $AgClO_4$ in boiling aqueous acetonitrile (Table V), although for acid-sensitive furan derivatives a two-phase water–toluene system should be applied.

Experimental Section

Melting points are uncorrected. When no melting point is reported the products isolated and purified by column chromatography were oils. ^1H NMR spectra were recorded with Varian EM-360 (60 MHz), Brucker WP-100 (100 MHz), and Brucker AM-500 (500 MHz) spectrometers in $(CD_3)CO$ with TMS as an internal standard. In NMR data of the products **2a–3b** and **15a–28b** the positions of substituent and hydrogen in benzene ring are shown in relation to the dihalomethyl group.

For GLC analysis a Chromatotron GCHF 18.3 instrument equipped with 1.25-m stainless steel column packed with 5% OV-17 on 100 Chromosorb was used. Column chromatography was accomphished on silica gel, Merck, 230–400 mesh, with hexane–chloroform or hexane–ethyl acetate mixtures as eluents. TLC analysis were made on foil plates Merck 60 F254. All compounds had NMR spectra consistent with the structures and gave satisfactory C, H, and N microanalyses.

Materials. Commercially available aromatic nitro compounds were purified when necessary. The following nitro compounds were prepared according to know methods: benzyl 4-nitrophenyl ether,[17] allyl 2-nitrophenyl ether,[17] allyl 4-nitrophenyl ether,[17] 4-chlorophenyl 4-nitrophenyl ether,[24] 3-nitropyridine,[25] and 1,2-dimethyl-5-nitroindole.[26]

4-Nitrophenyl phenyl sulfoxide was prepared by oxidation of 4-nitrophenyl sulfide with equimolar amount of hydrogen peroxide in glacial acetic acid at room temperature for 60 h: yield 80%, mp 106–108 °C (methanol) (lit.[27] mp 107 °C).

4-Nitrophenyl phenyl sulfone was prepared by oxidation of 4-nitrophenyl phenyl sulfoxide with excess of hydrogen peroxide in glacial acetic acid at 60 °C for 5 h: yield 97%, mp 140–142 °C (methanol) (lit.[28a] mp 142 °C).

1-Benzyl-4-nitroimidazole was prepared by alkylation of 4(5)-nitroimidazole with benzyl bromide using KOH in DMSO (0.7 h, 35 °C): yield 87%, mp 72–74 °C (hexane–ethyl acetate) (lit.[28b] mp 76 °C).

1-Ethyl-5-nitroindazole was prepared by alkylation of 5-nitroindazole with ethyl bromide using K_2CO_3 in DMF 0.7 h, 35 °C, and isolation of the desired isomer by column chromatography using chloroform: yield 52%, mp 67 °C (chloroform–hexane) (lit.[28c] mp 70 °C).

1. Reactions of Haloforms with Nitroarenes in a *t*-BuOK/TMF–DMF System. General Procedure A. To a vigorously stirred solution of potassium *tert*-butoxide (1.44 g, 12 mmol) in a mixture of dry THF (5 mL) and dry DMF (4 mL) cooled to about −73 °C under argon, a solution of nitroarene (3 mmol) and haloform (3.3 mmol) in dry DMF (1–2 mL) was added

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dropwise with a maximum rate whereas the temperature should not exceed −68 °C. The mixture was then stirred at this temperature for 1 min and acidified with acetic acid (1.5 mL) or concentrated hydrochloric acid (2 mL) dissolved in methanol (3 mL). The mixture after reaching room temperature was poured into water (150 mL), and the products were extracted with dichloromethane (3 × 30 mL). The extracts were washed with water (3 × 50 mL) and dried with anhydrous Na_2SO_4, the solvent was evaporated, and the residue was chromatographed. The solid products were subsequently recrystallized.

Procedure B. The reactions of some nitrobenzene (Table I) and nitroquinoline (Table III) derivatives with haloforms were carried out according to procedure A, using 6% or 25% molar excess of haloform.

2. Reactions of Haloforms with Some Nitro Heterocycles in a $NaOCH_3/NH_3$ Liquid System. A solution of nitroarene (3 mmol) and haloform (3.3 mmol) in dry DMF (2 mL) was added quickly dropwise to a vigorously stirred mixture of sodium methoxide (0.65 g, 12 mmol) in ca. 10 mL of liquid ammonia at −70 to −68 °C. After that, the mixture was stirred at −70 to −68 °C for 1 min, neutralized with ammonium chloride (1.2 g), and left for evaporation of ammonia. The residue was treated with water (50 mL). The products were isolated and purified as in procedure A except for **34a**, **34b**, **36a**, and **36b**, which were solids isolated by filtration, washed with water, and dried on air, to give practically pure product (GLC, TLC), finally recrystallized from ethanol.

3. Hydrolysis of 5-Chloro-2-nitrobenzylidene Dichloride to 5-Chloro-2-nitrobenzaldehyde. A mixture of 5-chloro-2-nitrobenzylidene dichloride (0.84 g, 3.5 mmol), zinc chloride (2.0 g), and 85% formic acid (16 mL) was refluxed under argon for 72h. After cooling the mixture was poured into water (150 mL) and extracted with dichloromethane (3 × 30 mL). The combined extracts were dried, the solvent was evaporated, and the residue was purified by column chromatography to give 0.39 g (60% of the product): mp 74 °C (hexane–ethyl acetate) (lit[23] mp 77 °C); NMR (60 MHz) δ 7.9–8.5 (m, 3 H), 10.45 (s, 1 H).

4. Hydrolysis of 3-(Dichloromethyl)-2-nitrothiophene to 3-Formyl-2-nitrothiophene. A mixture of 3-(dichloromethyl)-2-nitrothiophene (2.12 g, 10 mmol) and 75% formic acid (50 mL) was refluxed under argon for 12 h. After this, the solution was concentrated under vacum, poured into water (150 mL), and extracted with dichloromethane (3 × 30 mL). The combined extracts were dried, the solvent was evaporated, and the residue was purified by column chromatography to give 1.33 g (85%) of the product: mp 53–54 °C (hexane–ethyl acetate); NMR (100 MHz) δ 7.67 (d, J = 5.8 Hz, 4-H), 8.13 (d, J = 5.8 Hz, 5-H), 10.70 (s, 1 H).

5. Hydrolysis of Nitroarylidene Dihalides to Nitroaryl Aldehydes in an Aqueous Acetonitrile Silver Perchlorate System. To a solution of **34b** (1.38 g, 4 mmol) in acetonitrile (20 mL) was added a solution of silver perchlorate (2.07 g, 10 mmol) in distilled water (8 mL), and the mixture was refluxed under argon for 10 h. After cooling silver bromide was filtered off and washed with dichloromethane (3 × 20 mL), and the filtrate was washed with distilled water (20 mL) and dried. The solvent was evaporated, and the residue was purified on a small amount of silica gel to give 0.77 g (95%) of the product: mp 157–158 °C (hexane-ethyl acetate) (lit.[22] mp 156–158 °C).

6. Hydrolysis of 3-(Dihalomethyl)-2-nitrofuran into 2-Nitro-3-furaldehyde. A mixture of 3-(dibromomethyl)-2-nitrofuran (0.86g, 3 mmol), toluene (10 mL), distilled water (5 mL), and silver perchlorate (1.56 g, 7 mmol) was refluxed under argon for 6 h. After cooling silver bromide was filtered off and washed with toluene (7 mL) and distilled water (5 mL). After separation the organic layer was dried. The solvent was evaporated, and the residue was purified on silica gel to give 0.39 g (85%) of the product: mp 81–82 °C; NMR (500 MHz) δ 7.10 (dd, J = 2.00 Hz, J = 0.35 Hz, 5-H), 7.96 (J = 2.01 Hz, J = 0.65 Hz, H-4), 10.47 (t, J = 0.50 Hz, 1 H).

Physical properties and ^1H NMR data of products listed in Tables I-IV are as follows.

2a: mp 26–27 °C (hexane–ethyl acetate) (lit[29] mp 27 °C).

2b: mp 46 °C (hexane–ethyl acetate) (lit[31] mp 46 °C).

3a: mp 45–46 °C (hexane–ethyl acetate) (lit.[30] mp 78 °C).

3b: mp 77–79 °C (hexane–ethyl acetate) (lit.[32] mp 78 °C).

4a: NMR (500 MHz) δ 7.56 (ddd, $^3H_{H-H}$ = 9.2 Hz, $^3J_{H-F}$ = 7.3 Hz, $^1J_{H-H}$ = 2.8 Hz, 4-H), 7.22 (d, $^5J_{H-F}$ = 1.3 Hz, 1 H), 7.98 (dd, $^3J_{H-F}$ = 9.4 Hz, $^4J_{H-H}$ = 2.8 Hz, 6-H), 8.25 (dd, $^4J_{H-F}$ = 5.0 Hz, $^3J_{H-H}$ = 9.2 Hz, 3-H).

5a: mp 67–68 °C (hexane–ethyl acetate); NMR (500 MHz) δ 7.53 (d, J = 3.0 Hz, 1 H), 7.75 (t, 3-H), 7.85 (td, $^3J_{H-H}$ = 8.2 Hz, $^4J_{H-F}$ = 5.1 Hz, 4-H), 7.89 (dt, $^3J_{H-H}$ = 8.0 Hz, J = 1.3 Hz, 5-H).

5b: mp 61–62 °C (hexane–ethyl acetate); NMR (500 MHz) δ 7.39 (d, J_{H-F} = 3.0 Hz, 1 H), 7.73 (t, 3-H), 7.80 (td, $^3J_{H-H}$ = 8.2 Hz, $^4J_{H-F}$ = 5.1 Hz, 4-H), 7.84 (dt, $^3J_{H-H}$ = 8.0 Hz, J = 10.2 Hz, 1.3 Hz, 5-H).

6a: NMR δ 7.52 (s, 1 H), 8.15 (dd, $^3J_{H-F}$ = 10.2 Hz, $^4J_{H-H}$ = 2.2 Hz, 3-H), 8.17 (dd, $^3J_{H-H}$ = 8.6 Hz, $^4J_{H-F}$ = 7.3 Hz, 6-H), 8.25 (ddd, $^3J_{H-H}$ = 8.6 Hz, $^4J_{H-H}$ = 2.2 Hz, $^4J_{H-H}$ = 0.9 Hz, 5-H).

6b: NMR (500 MHz) δ 7.37 (s, 1 H), 8.11 (dd, $^3J_{H-H}$ = 10.2 Hz, $^4J_{H-H}$ = 2.2 Hz, 3-H), 8.15 (dd, $^3J_{H-H}$ = 8.6 Hz), $^4J_{H-F}$ = 7.3 Hz, 6-H), 8.22 (ddd, $^3J_{H-H}$ = 8.6 Hz, $^4J_{H-H}$ = 2.2 Hz, $^5J_{H-F}$ = 0.9 Hz, 5-H).

7a: NMR (500 MHz) δ 7.65 (s, 1 H), 7.77 (ddd, $^3J_{H-H}$ = 8.9 Hz, $^3J_{H-F}$ = 7.7 Hz, $^3J_{H-H}$ = 2.7 Hz, 5-H), 7.92 (dd, $^3J_{H-F}$ = 8.5 Hz, $^4J_{H-H}$ = 2.7 Hz, 3-H), 8.33 (dd, $^3J_{H-H}$ = 8.9 Hz, $^4J_{H-F}$ = 5.3 Hz, 6-H).

7b: NMR (500 MHz) δ 7.52 (s, 1 H), 7.67 (ddd, $^3J_{H-H}$ = 8.9 Hz, $^3J_{H-F}$ = 7.7 Hz, $^4J_{H-H}$ = 2.7 Hz, 5-H), 7.84 (dd, $^3J_{H-F}$ = 8.5 Hz, $^4J_{H-H}$ = 2.7 Hz, 3-H), 8.28 (dd, $^3J_{H-H}$ = 8.9 Hz, $^4J_{H-F}$ = 5.3 Hz, 6-H).

8a: mp 34–35 °C (hexane–ethyl acetate); NMR (100 MHz) δ 7.70 (s, 1 H), 7.81 (dd, J = 8.8 Hz, J = 2.2 Hz, 5-H), 8.16 (d, J = 8.8 Hz, 3-H), 8.21 (d, J = 2.2 Hz, 6-H).

8b: mp 48–49 °C (hexane–ethyl acetate); NMR (60 MHz) δ 7.55 (s, 1 H), 7.8–8.2 (m, 3 H).

9a: mp 44–46 °C (hexane–ethyl acetate); NMR (100 MHz) δ 7.35 (s, 1 H), 7.39 (dd, J = 8.4 Hz, J = 1.9 Hz, 6-H), 8.00 (d, J = 1.9 Hz, 2-H), 8.15 (d, J = 8.4 Hz, 5-H).

9b: mp 49–51 °C (hexane–ethsyl acetate); NMR (100 MHz) δ 7.27 (s, 1 H), 7.93 (dd, J = 8.5 Hz, J = 2.0 Hz, 6-H), 8.00 (d, J = 2.0 Hz, 2-H), 8.13 (d, J = 8.5 Hz, 5-H).

10a: mp 60–62 °C (hexane–ethyl acetate); NMR (500 MHz) δ 7.09 (s, 1 H), 7.83, 7.60, 8.20 (ABX, J_{A-B} = 8.14 Hz, J_{A-X} = −1.07 Hz, J_{B-X} = −8.27 Hz).

10b: mp 64–66 °C (hexane–ethyl acetate); NMR (60 MHz) δ 7.00 (s, 1 H), 7.5–8.2 (m, 3 H).

11a: mp 40–41 °C (hexane–ethyl acetate); NMR (100 MHz) δ 7.26 (s, 1 H), 8.10 (d, J = 1.9 Hz, 1 H), 8.21 (d, J = 1.9 Hz, 1 H).

12a: mp 45–46 °C (hexane–ethyl acetate); NMR (100 MHz) δ 7.65 (s, 1 H), 7.90 (dd, J = 8.7 Hz, J = 1.9 Hz, 4-H); 8.05 (d, J = 8.7 Hz, 3-H), 8.30 (d, J = 1.9 Hz, 6-H).

12b: mp 52–53 °C (hexane–ethyl acetate); NMR (60 MHz) δ 7.50 (s, 1 H), 7.9–8.3 (m, 3 H).

13a: mp 57–58 °C (hexane–ethyl acetate); NMR (100 MHz) δ 7.61 (s, 1 H), 7.83 (d, J = 8.6 Hz, 3-H), 8.11 (dd, J = 8.6 Hz, J = 1.7 Hz, 4-H), 8.50 (d, J = 1.7 Hz, 6-H).

13b: mp 69–70 °C (hexane–ethyl acetate); NMR (60 MHz) δ 7.50 (s, 1 H), 7.8–8.4 (m, 3 H).

14a: mp 101–102 °C (hexane–ethyl acetate); NMR (100 MHz) δ 7.49–7.63 (m, 3 H), 7.77–7.86 (m, 3-H), 8.12 (d, 6-H, J = 1.9 Hz), 8.19 (d, J = 8.8 Hz, 5-H), 8.44 (d, J = 1.9 Hz, 2-H).

15a: mp 75–76 °C (hexane–ethyl acetate); NMR (100 MHz) δ 5.35 (s, 2 H), 7.32 (dd, J = 9.2 Hz, J = 2.8 Hz, 4-H), 7.35–7.57 (m, 5 H), 7.75 (d, J = 2.8 Hz, 6-H), 7.79 (s, 1 H), 8.14 (d, J = 9.2 Hz, 3-H).

16a: mp 65–67 °C (hexane–ethyl acetate); NMR (500 MHz) δ 7.22 (dd, J = 9.1 Hz, J = 2.8 Hz, 4-H), 7.25 (dd, J = 8.9 Hz, J = 2.1 Hz, 2 H), 7.55 (dd, J = 8.9 Hz, J = 2.2 Hz, 2 H), 7.73 (d, J = 2.8 Hz, 6-H), 7.75 (s, 1 H), 8.16 (d, J = 9.1 Hz, 3-H).

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17a: NMR (500 MHz) δ 4.85 (dt, J = 4.9 Hz, J = 1.4 Hz, 2 H), 5.51 (ddd, J = 17.2 Hz, J = 3.2 Hz, J = 1.4 Hz, 2 H), 6.12 (m, 1 H); 7.27 (dd, J = 9.1 Hz, J = 2.7 Hz, 4-H), 7.69 (d, J = 2.7 Hz, 6-H), 7.80 (s, 1 H), 8.16 (d, J = 9.1 Hz, 3-H).

17b: NMR (500 MHz) δ 4.85 (dt, J = 4.9 Hz, J = 1.4 Hz, 2 H), 5.51 (ddd, J = 17.2 Hz, J = 3.2 Hz, J = 1.4 Hz, 2 H), 6.12 (m, 1 H), 7.26 (dd, J = 9.1 Hz, J = 2.7 Hz, 4-H), 7.67 (d, J = 2.7 Hz, 6-H), 7.81 (s, 1 H), 8.01 (d, J = 9.1 Hz, 3-H).

18a: mp 41–43 °C (hexane–ethyl acetate); NMR (100 MHz) δ 4.7–4.9 (m, 2 H), 5.2–5.6 (m, 2 H), 5.8–6.3 (m, 1 H), 7.23 (s, 1 H), 7.24 (d, J = 8.5 Hz, J = 1.9 Hz, 6-H), 7.59 (d, J = 1.9 Hz, 2-H), 7.91 (d, J = 8.5 Hz, 5-H).

19a: mp 94–96 °C (hexane–ethyl acetate); NMR (100 MHz) δ 7.44 (dd, J = 8.7 Hz, J = 1.9 Hz, 4-H), 7.65 (s, 5 H), 7.78 (s, 1 H), 7.93 (d, J = 1.9 Hz, 6-H), 8.08 (d, J = 8.7 Hz, 3-H).

20a: mp 99–100 °C (hexane–ethyl acetate); NMR (500 MHz) δ 7.55–7.63 (m, 3 H), 7.67 (m, 1 H), 7.85–7.89 (m, 2 H), 8.05 (dd, J = 8.6 Hz, J = 1.9 Hz, 4-H), 8.21 (d, J = 8.6 Hz, 3-H), 8.60 (d, J = 1.9 Hz, 6-H).

21a: mp 135–136 °C (hexane–ethyl acetate); NMR (60 MHz) δ 7.5–8.7 (m, 9 H).

22a: mp 173–175 °C (hexane–ethjyl acetate); NMR (60 MHz) δ 7.81 (s, 1 H), 8.2–8.4 (m, 3 H).

23a: mp 149–151 °C (hexane–ethyl acetate); NMR (500 MHz) δ 7.63 (s, 1 H), 8.00 (t, 4-H), 8.31 (dd, J = 8.33 Hz, J = 1.3 Hz, 3-H), 8.36 (dd, J = 8.8 Hz, J = 1.3 Hz, 5-H).

23b: mp 145–146 °C (hexane–ethyl acetate); NMR (500 MHz) δ 7.49 (s, 1 H), 7.91 (t, 1-H), 8.22 (dd, J = 8.3 Hz, J = 1.3 Hz, 3-H), 8.32 (dd, J = 8.8 Hz, J = 1.3 Hz, 5-H).

24a: NMR (500 MHz) δ 7.54 (s, 1 H), 8.35 (d, J = 8.7 Hz, 6-H), 8.69 (dd, J = 8.72, J = 2.3 Hz, 5-H), 8.79 (d, J = 2.3 Hz, 3-H).

24b: NMR (500 MHz) δ 7.40 (s, 1 H), 8.33 (d, J = 8.8 Hz, 6-H), 8.63 (dd, J = 8.8 Hz, J = 2.4 Hz, 5-H), 8.73 (d, J = 2.3 Hz, 3-H).

25a: NMR (500 MHz) δ 7.71 (s, 1 H), 8.37 (dd, J = 8.3 Hz, J = 2.3 Hz, 5-H), 8.47 (d, J = 8.3 Hz, 6-H), 8.56 (d, J = 2.3 Hz, 3-H).

25b: NMR (500 MHz) δ 7.54 (s, 1 H), 8.29 (d, J = 8.4 Hz, J = 1.6 Hz, 5-H), 8.43 (d, J = 1.6 Hz, 3-H), 8949 (d, J = 8.4 Hz, 6-H).

26a: NMR (60 MHz) δ 7.70 (s, 1 H), 7.9–8.7 (m, 3 H).

26b: NMR (60 MHz) δ 7.63 (s, 1 H), 8.0–8.8 (m, 3 H).

27a: NMR (500 MHz) δ 7.44 (s, 1 H), 8.54 (m, 3-H, 6-H), 8.71 (dd, J = 8.8 Hz, J = 2.3 Hz, 5-H).

27b: NMR (500 MHz) δ 7.29 (s, 1 H), 8.49 (d, J = 2.3 Hz, 3-H), 8.59 (d, J = 8.8 Hz, 6-H), 8.68 (dd, J = 8.8 Hz, J = 2.3 Hz, 5-H).

28a: NMR (500 MHz) δ 7.73 (s, 1 H), 8.29 (dd, J = 8.3 Hz, J = 1.3 Hz, 5-H), 8.40 (d, J = 1.3 Hz, 3-H), 8.50 (d, J = 8.3 Hz, 6-H).

28b: NMR (500 MHz) δ 7.58 (s, 1 H), 8.26 (dd, J = 8.3 Hz, J = 1.3 Hz, 5-H), 8.34 (d, J = 1.3 Hz, 3-H), 8.55 (d, J = 8.3 Hz, 6-H).

29a: mp 88–89 °C (hexane–ethyl acetate); NMR (100 MHz) δ 7.38 (s, 1 H), 7.75–7.87 (m, 3 H), 8.12–8.21 (m, 1 H), 8.12 (d, J = 8.8 Hz, 3-H), 8.38 (d, J = 8.8 Hz, 4-H).

29b: mp 102–103 °C (hexane–ethyl acetate); NMR (100 MHz) δ 7.24 (s, 1 H), 7.74–7.80 (m, 3 H), 8.07–8.18 (m, 1 H), 8.13 (d, J = 8.8 Hz, 3-H), 8.33 (d, J = 8.8 Hz, 4-H).

30a: NMR (100 MHz) δ 7.74 (s, 1 H), 8.20 (d, J = 5.1 Hz, 5-H), 9.00 (d, J = 5.1 Hz, 6-H), 9.24 (s, 2-H).

30b: NMR (100 MHz) δ 7.55 (s, 1 H), 8.21 (d, J = 5.1 Hz, 5-H), 9.02 (d, J = 5.1 Hz, 6-H).

31a: mp 76–77 °C (hexane–ethyl acetate); NMR (100 MHz δ 4.13 (s, 3 H), 7.09 (d, J = 9.0 Hz, 3-H), 7.75 (s, 1 H), 8.46 (d, J = 9.0 Hz, 4-H).

31b: mp 62–64 °C (hexane–ethyl acetate); NMR (100 MHz) δ 4.12 (s, 3 H), 7.55 (s, 1 H), 8.38 (d, J = 9.0 Hz, 4-H).

32a: NMR (100 MHz) δ 7.83 (s, 1 H), 8.26 (s, 3-H), 9.30 (s, 6-H).

32b: mp 46–47 °C (hexane–ethyl acetate); NMR (100 MHz) δ 7.56 (s, 1 H), 8.25 (s, 3-H), 9.10 (s, 6-H).

33a: NMR (100 MHz) δ 7.78 (s, 1 H), 8.00 (d, J = 8.6 Hz, 3-H), 8.71 (d, J = 8.6 Hz, 4-H).

33b: mp 81–82 °C (hexane–ethyl acetate); NMR (100 MHz) δ 7.59 (s, 1 H), 7.85 (d, J = 8.6 Hz, 3-H), 8.58 (d, J = 8.6 Hz, 4-H).

34a: mp 95–96 °C (ethanol); NMR (100 MHz) δ 7.47 (s, 1 H), 7.83 (dd, J = 8.7 Hz, J = 4.2 Hz, 3-H), 8.29 (dd, J = 8.7 Hz, J = 1.6 Hz, 4-H), 8.44 (d, 2 H), 9.15 (dd, J = 4.2 Hz, J = 1.6 Hz, 2-H).

34b: mp 108–109 °C (ethanol); NMR (100 MHz) δ 7.32 (s, 1 H), 7.80 (dd, J = 8.7 Hz, J. = 4.2 Hz, 3-H), 8.24 (dd, J = 8.7 Hz, J = 1.6 Hz, 4-H), 8.43 (s, 7-H, 8-H), 9.12 (dd, J = 4.2 Hz, J = 1.6 Hz, 2-H).

35a: mp 136–137 °C (ethanol); NMR (100 MHz) δ 7.40 (s, 1 H), 7.79 (dd, J = 8.4 Hz, J = 4.2 Hz, 3-H), 3-H), 8.19 (d, J = 8.8 Hz, 6-H), 8.40 (d, J = 8.8 Hz, 5-H), 8.58 (dd, J = 8.4 Hz, J = 1.6 Hz, 4-H), 9.07 (dd, J = 4.2 Hz, J = 1.6 Hz, 2-H).

35b: mp 185–186 °C (ethanol); NMR (100 MHz) δ 7.24 (s, 1 H), 7.76 (dd, J = 8.4 Hz, J = 4.2 Hz, 3-H), 8.21 (d, J = 8.9 Hz, 1 H), 8.37 (d, J = 8.9 Hz, 1 H), 8.54 (dd, J = 8.4 Hz, J = 1.6 Hz, 4-H), 9.03 (dd, J = 4.2 Hz, J = 1.7 Hz, 2-H).

36a: mp 107–108 °C (ethanol); NMR (100 MHz) δ 7.49 (s, 1 H), 7.74 (d, J = 6.1 Hz, 4-H), 8.33 (d, J = 8.8 Hz, 7-H) 8.64 (d, J = 8.8 Hz, 8-H), 8.81 (d, J = 6.1 Hz, 3-H), 9.56 (s, 1-H).

36b: mp 128–129 °C (ethanol); NMR (100 MHz) δ 7.35 (s, 1 H), 7.69 (d, J = 6.1 Hz, 4-H), 8.35 (d, J = 8.8 Hz, 7-H), 8.59 (d, J = 8.8 Hz, 8-H), 8.80 (d, J = 6.1 Hz, 3-H), 9.53 (s, 1).

37a: mp 86–87 °C (hexane–chloroform); NMR (100 MHz) δ 7.67 (d, J = 5.8 Hz, 4-H), 7.76 (s, 1 H), 8.01 (d, J = 5.8 Hz, 5-H).

37b: mp 84–86 °C (hexane–chloroform); NMR (100 MHz) δ 7.65 (s, 1 H), 7.71 (d, J = 5.8 Hz, 4-H), 8.01 (d, J = 5.8 Hz, 5-H).

38a: mp 43–44 °C (hexane–chloroform); NMR (100 MHz) δ 7.24 (d, J = 2.1 Hz, 4-H), 7.43 (s, 1 H), 7.95 (d, J = 2.1 Hz, 5-H).

38b: mp 35–36 °C (hexane–chloroform); NMR (100 MHz) δ 7.25 (d, J = 2.1 Hz, 4-H), 7.43 (s, 1 H), 7.95 (d, J = 2.1 Hz, 5-H).

39a: mp 61–63 °C (hexane–chloroform); NMR (100 MHz) δ 7.03 (d, J = 3.8 Hz, 3-H), 7.27 (s, 1 H), 7.53 (d, J = 3.8 Hz, 4-H).

39b: mp 87–88 °C (hexane–chloroform); NMR (100 MHz) δ 7.05 (d, J = 3.8 Hz, 3-H), 7.27 (s, 1 H), 7.53 (d, J = 3.8 Hz, 4-H).

40a: mp 115 °C (hexane–chloroform); NMR (60 MHz) δ 5.85 (s, 1 H), 7.49 (s, 5 H), 7.83 (s, 2-H), 8.13 (s, 5-H).

40b: mp 140 °C (hexane–chloroform); NMR (60 MHz) δ 5.83 (s, 1 H), 7.50 (s, 5 H), 7.82 (s, 2-H), 7.95 (s, 5-H).

41a: NMR (500 MHz) δ 1.53 (t, J = 7.2 Hz, 3 H), 4.61 (q, J = 7.2 Hz, 2 H), 7.90 (s, 1 H), 7.96 (dd, J = 9.1 Hz, J = 0.7 Hz, 7-H), 8.00 (d, J = 9.1 Hz, 6-H), 8.72 (d, J = 0.7 Hz, 3-H).