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CONTROL OF REGIOCHEMISTRY IN NITRONE CYCLOADDITIONS. REGIOSELECTIVITY OF THE REACTIONS OF TRISUBSTITUTED NITRONES WITH ELECTRON-DEFICIENT AND CONJUGATED DIPOLAROPHILES

Marina Burdisso, Remo Gandolfi* and Paolo Grünanger

Dipartimento di Chimica Organica, Viale Taramelli, 10, 27100 Pavia (Italy)

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Abstract. Triphenylnitrone **1a** and C,C-diphenyl-N-methylnitrone **1b** reacted at r. t. with monosubstituted alkenes bearing an electron-attracting group (i.e., formyl, acetyl, cyano, methoxycarbonyl, sulfonyl and nitro groups) to give kinetically controlled mixtures of the two regioisomers. As a rule, the 4-substituted isoxazolidine was dominant over the 5-regioisomer (only the 4-regioisomer was obtained with nitroethylene) as a result of electronic control on regiochemistry. Owing to the easy reversibility of these reactions, thermodynamic control could be achieved at higher temperatures. Under these latter conditions the 5-substituted isoxazolidine was clearly prevalent owing to its being sterically less congested than the 4-substituted derivative. Evaluation of relative cycloaddition rates for **1a** showed that the activating effect of formyl (rel. rate = 1.5) and acetyl groups (1.00) is about five times higher than that of cyano (0.18) and methoxycarbonyl groups (0.22) whilst strikingly high was found the effect of the nitro group (1,155) in particular if compared to the quite low effect of the sulfonyl group (0.03).
Only 5-substituted derivatives were obtained in the reactions of **1a** and **1b** with styrene and 1,1-disubstituted derivatives (e.g., methacrolein) whereas only 4-substituted adducts were detected in the reactions of the same nitrones with monosubstituted acetylenes (e.g., methyl propiolate).
The reactions of N-phenyl and N-methyl-fluorenoneimine-N-oxide, **3a** and **3b**, and of C,C-tetramethylene-N-methyl nitrone **6a** with the same kind of dipolarophiles were also briefly investigated.

INTRODUCTION

On the basis of PMO theory Houk et al. predicted that in the reactions of nitrones with alkenes[1] the tendency to form 4-substituted isoxazolidines should increase as both electron-richness of the nitrone and electron deficiency of the monosubstituted dipolarophile increase.[2] An obvious way to test this theoretical prediction is to react trisubstituted (with electron donating or conjugating substituents) nitrones with monosubstituted electron-deficient dipolarophiles. Thus, Houk et al.[3] found that the electron-rich C,C-dicyclopropyl-N-methylnitrone reacts with styrene to give only the 5-substituted isoxazolidine whereas, in agreement with theoretical predictions, the 4-substituted isoxazolidine was the dominant or the sole adduct formed in the reactions of

the same nitrone with electron-deficient acrylonitrile and phenylvinylsulfone, respectively.

However, at first glance, the regiochemical outcome of the reactions of electron-rich C,C-diaryl-N-alkylnitrones with electron-deficient dipolarophiles reported so far seems rather erratic and not fully consistent with Houk's predictions. In fact, only 5-substituted isoxazolidines were obtained in the reactions of **1b** with (-)-menthyl acrylate,[4] of **1b** with methylvinylketone[5] and of **1c**[6] and **2**[7] with methyl acrylate (at ≥ 80°C). By contrast only 4-substituted isoxazolidines were isolated from the reactions of N-methyl-fluorenoneimine-N-oxide **3b** with methyl acrylate and acrylonitrile by Jones et al.[8] However, in a previous study with this latter nitrone and methyl acrylate Taylor et al. disclosed the formation of both regioisomers in a ratio [4-substituted:5-substituted = 4:1 at r. t.] almost independent of solvent polarity.[9]

As for trialkylnitrones, the reactions of the nitrones **4a** and **4b** (prepared in situ at ≥ 80°C) with acrylonitrile and methyl acrylate, respectively, afforded mixtures of the two regioisomers, wherein the 5-isoxazolidine predominated.[10] The sole 5-substituted regioisomer was isolated from the reaction of **5a** with acrylonitrile (at 25°C) whereas under similar conditions the 4-substituted isoxazolidine was prevalent in the adduct mixtures from the hetero-isomer **5b** and methyl acrylate or acrylonitrile (4-:5-regioisomer = 1.12 and 3.0, respectively).[11]

Finally, a further example of clear-cut dominance of the 5-regioisomer was recently reported by Funk et al. in the reaction of **6b** with methyl acrylate (at 25°C).[12]

It should be stressed that at least some of the above regiochemical data were produced in a context not aimed at a precise evaluation of regioisomer ratios and that in some instances authors did not thoroughly investigate whether or not the reaction was under strict kinetic control.[13] Consequently we felt that there was the need for a systematic investigation in order to definitely assess the regiochemical behavior of trisubstituted nitrones. Our own work, directed towards such a goal, started some years ago by reacting triphenylnitrone **1a** and C,C-diphenyl-N-methylnitrone **1b** with a complete series of conjugated electron-deficient monosubstituted alkenes, i.e. **7a-f**,[14] and with styrene.

The reactions of **1a** and **1b** with some 1,1-disubstituted alkenes and monosubstituted alkynes were then investigated. Finally, for sake of completeness, this study was briefly extended to the nitrones **3a** and **3b** and to the related "trialkylderivative" **6a**.

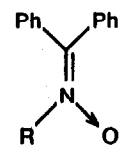
RESULTS

The reactions of triphenylnitrone **1a** with alkenes **7** were first carried out at room temperature (≃ 20°C) in order to secure a kinetic control as strict as possible on the regiochemistry. Nitroethylene **7f** reacted very readily with **1a** (100% conversion was achieved

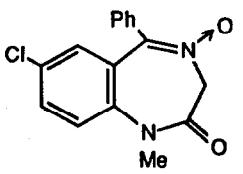
in less than 1h in benzene in the presence of excess dipolarophile) to afford only the 4-substituted isoxazolidine **8f**. The reaction of other electron-poor alkenes, i.e. **7a-e**, were found much more sluggish to give variable mixtures of regioisomers **8** and **9** (evaluated by column chromatography and/or ^{1}HNMR) in which the 4-substituted isoxazolidine, i.e. **8**, was highly dominant (Scheme 1 and Table 1). However, almost quantitative yields of adducts could be achieved for **7a-d** by stirring a slurry of the low soluble **1a** in neat dipolarophile for the appropriate time. For example the reaction of **1a** with acrolein reached 100% conversion in $\simeq$ 4 days. The regioisomer ratio did not change appreciably when the reactions of **7a-d** were carried out in a mixture benzene:dipolarophile (2:1) as reaction medium. In the case of phenylvinylsulfone **7e** reasonable yields could be obtained only by heating at $\geq$ 60°C, but here again the 4-regioisomer was dominant. By contrast, only the 5-substituted isoxazolidine **9g** could be detected in the reaction of **1a** with the relatively electron-rich styrene. This latter dipolarophile exhibited the lowest reactivity of alkenes **7**.

With the aim of quantitatively evaluating relative reaction rates for **7a-f**, competition reactions between triphenylnitrone **1a** and excess mixtures of pairs of these dipolarophiles were carried out. The ratio of products was measured by column chromatography and/or ^{1}HNMR and the rate ratios, calculated by Huisgen's method,[15] are reported in Table 1. Table 1 clearly discloses the strikingly high reactivity of nitroethylene as compared to all other dipolarophiles used, in particular to phenylvinylsulfone [k(**7f**): k(**7e**) $\simeq$ 41.000]. Methoxycarbonyl and cyano groups exhibit a comparable ability in promoting the 1,3-dipolar cycloaddition and formyl and acetyl groups are about five times more effective than them.

Having thus established the high regioselectivity of the reaction of **1a** with the alkenes **7a-f** to give, under kinetic control, the 4-isoxazolidine as dominant product, we tackled the problem of reversing the regiochemical outcome by taking advantage of the reversibility of these reactions. In fact, attempted purification of **8f** by crystallization from methanol resulted in a high yield recovery of the nitrone **1a**, thus showing how easily the adduct **8f** can enter the cycloreversion reaction. The propensity of **8f** to break down to **1a** and nitroethylene was confirmed by dissolving **8f** in benzene or 1,2-dichloroethane in the presence of 1,3-diphenylisobenzofuran as nitroethylene trapping agent. The yellow color of the diene was discharged within 43 h and 10 h in benzene and 1,2-dichloroethane, respectively, at 40°C. We then sought reversal of regiochemistry by heating **1a** and excess **7f** in toluene at 110°C. The adduct **9f** was formed but, disappointingly, even after 10 h the 4-regioisomer **8f** comprised the major adduct and decomposition processes (see also Experimental) were clearly apparent from darkening of the reaction mixture. However, the desired reversal of regiochemistry could satisfactorily be achieved for the alkenes **7a-e**. After heating **1a** with an excess of **7a-e**, respectively, for some hours at 120°C, we could



1a : R = Ph
b : R = Me
c : R = CH_2SMe



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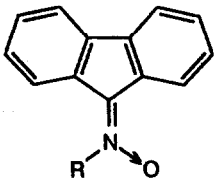
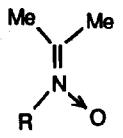
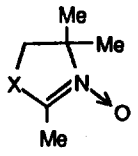


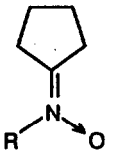
3a : R = Ph
b : R = Me



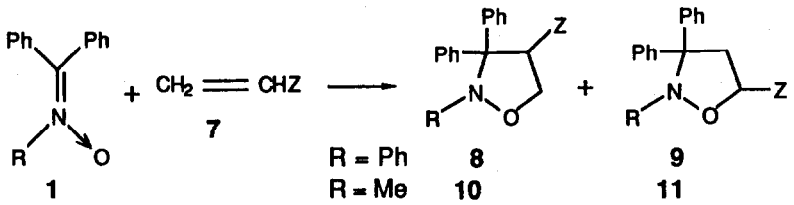
4a : R = CH_2CH_2CN
b : R = $CH_2CH_2CO_2Me$



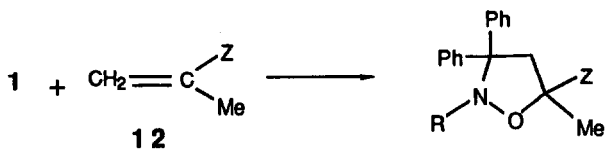
5a : X = CH_2
b : X = O



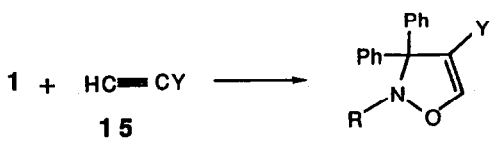
6a : R = Me
b : R = CH_2Ph



a : Z = CHO; **b** : Z = COMe; **c** : Z = CN; **d** : Z = CO_2Me;
e : Z = SO_2Ph; **f** : Z = NO_2; **g** : Z = Ph



13 : R = Ph
14 : R = Me



16 : R = Ph **a** : Y = COPh
17 : R = Me **b** : Y = CO_2Me

Scheme 1

Table 1. Regioisomer ratios under kinetic (benzene 20°C) and thermodynamic control (120°C) and relative rates (at 20°C) in the reactions of **1a** with alkenes **7**

Alkene	Kinetic ratios	Thermodynamic ratios	Relative rates
	8 : 9	**8 : 9**	
7a	97 : 3	5 : 95[b]	1.49
7b	88 : 12	- : 100[b]	1.00
7c	86 : 14	18 : 82[c]	0.18
7d	87 : 13	2 : 98[c]	0.22
7e	80 : 20[a]	5 : 95[d]	0.028
7f	100 : -	56 : 44[e]	1,155
7g	- : 100		

[a]At 60°C [b]2-3 h [c]≥6 h [d]At 110°C for 48 h [e]At 110°C for 10 h

Table 2. Regioisomer ratios in the reactions of **1b** with alkenes **7**.

Alkenes	Benzene:dipolar.(2:1) (20°C)	Acetonitrile (30°C)	Cyclohexane (30°C)	Neat dipolarophile (120°C)
	10 : 11	**10 : 11**	**10 : 11**	**10 : 11**
7a	77 : 23	70 : 30	80 : 20	-
7b	52 : 48	45 : 55	50 : 50	- : 100
7c	65 : 35	53 : 47	72 : 28	20 : 80
7d	60 : 40	48 : 52	62 : 38	2 : 98
7e	-	-	-	≤5 : 95
7f	100 : -	100 : -	100 : -	
7g	- : -	-	- : 100	

Table 3. Reactions of nitrones **3** with alkenes **7** under kinetic (20°C) and thermodynamic control (120°C).

Alkene	Benzene (20°C)	Neat dipolar. (120°C)	Benzene (20°C)	Neat dipolar. (120°C)
	18 : 19	**18 : 19**	**20 - 21**	**20 - 21**
7a	89 : 11	-	70 : 30	-
7b	89 : 11	-	78 : 22	-
7c	82 : 18	50 : 50	70 : 30	50 : 50
7d	92 : 8	22 : 78	78 : 22	21 : 79

recover good yields of the 5-regioisomers **9a-e**, respectively (Table 1). Only in the case of **7c** a substantial amount of the 4-regioisomer **8c** was present in the reaction mixture as a result of the low steric demand of the cyano group. In fact, the higher stability of the 5-substituted isoxazolidines **9** is steric in origin. Conversely, relief of steric compression certainly helps make the cycloreversion of the 4-regioisomers **8** an easy process.

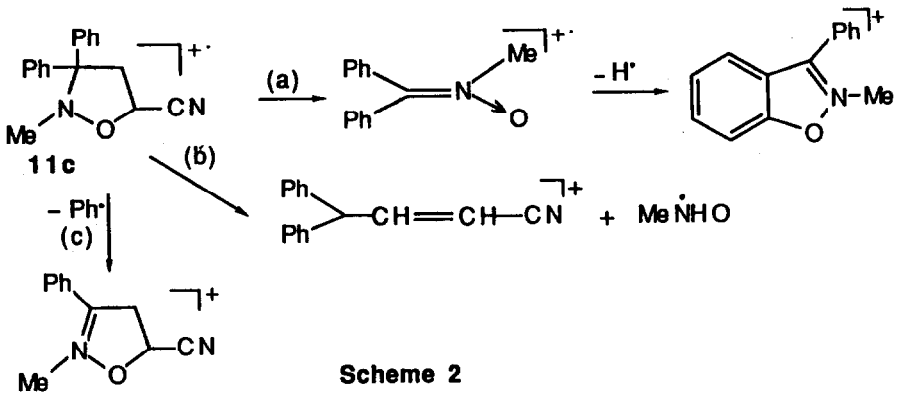
We emphasize that cycloreversion rates of the adducts **8a-e** are slower than that of **8f**

(see Experimental) and that **8a-d** did not appreciably cyclorevert under cycloaddition conditions whereas in the reaction of **8e** (at 60°C) a partial equilibration could well account for the relatively high yield of the 5-regioisomer.

Further details about the reactivity of trisubstituted nitrones were obtained by reacting the less reactive but more soluble C,C-diphenyl-N-methylnitrone **1b** with alkenes **7** (Table 2). Inspection of Table 2 clearly shows that there is a significant decrease in regioselectivity on passing from N-phenyl nitrone **1a** to N-methyl nitrone **1b**. Moreover, an increase in solvent polarity favoured the 5-regioisomer giving rise to a slight decrease in the **10:11** ratio so that in polar acetonitrile almost equimolar mixtures of the two regioisomers were formed in the reactions of **1b** with methylvinylketone, methyl acrylate and acrylonitrile. Noteworthy, nitroethylene **7f** kept on giving rise to a regiospecific reaction even in acetonitrile. The use of acetonitrile in place of cyclohexane as reaction medium also brought about a decrease in reaction rate for all of the alkenes **7**. Kinetic measurements allowed a quantitative evaluation of this solvent effect; the reaction of **1b** with acrolein in cyclohexane was found faster than that in acetonitrile by a factor of $\simeq 3$.

Finally the prevalence of the 5-regioisomer in the reactions of **1b** with **7b-e** under thermodynamic conditions fully confirm the data reported above for the related reactions of **1a**. In the reactions **1b+7a** and **1b+7f** decomposition processes (and in the latter case also a reluctance to reverse regiochemistry) hampered a satisfactory achievement of reversal of the regiochemical outcome.

The regiochemistry of isoxazolidines **8-11** is readily assigned on the basis of their spectroscopic data. The heterocyclic ring protons of 5-substituted isoxazolidines **9** and **11** give rise to ABX patterns in which the signals of H-4 and H-4' are well separated from that of H-5 [e.g., **11a**: δ ($CDCl_3$) 2.43 (s, NMe), 3.09 (dd, H-4', $J_{4,4'}$ = 12.5 Hz and $J_{4',5}$ = 5.5 Hz), 3.30 (dd, H-4, $J_{4,5}$ = 10.0 Hz), 4.38 (m, H-5), 9.43 (d, $J_{CHO,5}$ = 1.0 Hz)], whilst in 4-substituted isoxazolidines **8** and **10** these protons resonate, as a rule, at very similar fields and often merge in a complex unresolved signal [e.g., **10a**: δ ($CDCl_3$) 2.30 (s, NMe), 3.80-4.45 (m, H-4, H-5 and H-5'), 9.22 (d, CHO, $J_{CHO,4}$ = 3.5 Hz); δ (C_6D_6) 2.15 (s, NMe), 3.70 (ddd, H-4, $J_{CHO,4}$ = 3.5 Hz, $J_{4,5}$ = 7.5 Hz and $J_{4,5'}$ = 8.0 Hz), 3.90 (dd, H-5', $J_{5,5'}$ = 7.5 Hz), 4.06 (dd, H-5), 9.14 (d, CHO)]. The shift to lower fields of the methylene protons on passing from compounds **9** and **11** to **8** and **10**, respectively, is also clearly apparent in the case of the ABX patterns of the nitroderivatives **9f** [δ($CDCl_3$) 3.53 (dd, H4', $J_{4,4'}$ = 14.0 Hz and $J_{4',5}$ = 3.5 Hz), 4.00 (dd, H-4, $J_{4,5}$ = 7.5 Hz), 6.03 (dd, H-5)] and **8f** [δ ($CDCl_3$) 4.51 (dd, H-5', $J_{4,5'}$ = 7.8 Hz and $J_{5,5'}$ = 10.0 Hz), 4.84 (dd, H-5, $J_{4,5}$ = 5.6 Hz), 5.98 (dd, H-4)]. In agreement with the assigned structures the signals of COMe in **8b** and **10b**, of CO_2Me in **8d** and **10d** and of CHO in **8a** and **10a** are shifted to higher fields, owing to



Scheme 2

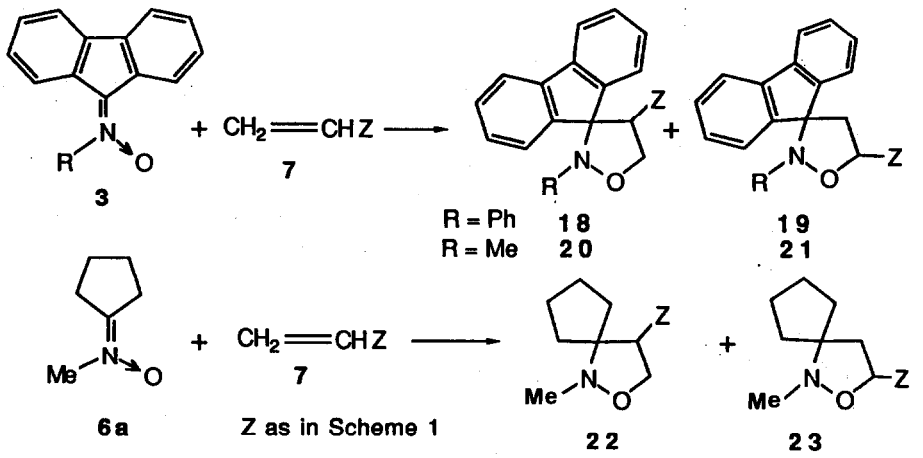
shielding by the cis-vicinal phenyl group, than the corresponding signals in the related adducts **9b** and **11b**, **9d** and **11d**, **9a** and **11a**, respectively.

The geminal coupling constant between the methylene protons is smaller in **8** and **10** than in **9** and **11** by > 4.0 Hz. This finding can easily be rationalized as due to the electron-attracting and lone pairs eclipsing effects of the oxygen atom on this geminal coupling in **8** and **10**. Moreover, in the ^{13}C-NMR spectrum of **10c** the triplet of the methylene carbon resonates at lower fieds than the doublet of the methine carbon whereas the reverse is true in the spectrum of **11c**. Finally, the C≡N stretching absorption in **11c** is much weaker than that in **10c** as a result of the vicinity of the electronegative oxygen atom to the cyano group in the former compound.

The mass spectra of **10c** and **11c** show that the important fragmentation pathways (reported in Scheme 2 for **11c**) are the same for both compounds. However in the case of the 5-substituted derivative **11c** the pathway (b)[16] comprises the dominant cleavage whilst the cycloreversion reaction [path (a)] predominates in the 4-regioisomer **10c**.

The reaction of **1a** and **1b** was then extended to 1,1-disubstituted alkenes, i.e **12a**, **12c** and **12d**. Only the reaction of **12a** could be carried out at room temperature whilst in the case of **12c** and **12d** heating (≥ 50°C) was necessary. The 5-substituted adduct (i.e., **13** and **14**) was the only detected product in all these reactions. By contrast, the acetylenic compounds **15** reacted smoothly at room temperature to only afford 4-substituted isoxazolines, i.e., **16** and **17** (Scheme 1).

In order to gain some insight into the repulsive steric interactions between the two phenyl groups on the carbon atom of the nitrones **1a** and **1b** and the substituent on the dipolarophile in the TS leading to the 4-substituted isoxazolidine, we then studied the reactions of N-phenyl- and N-methyl-fluorenoneimine-N-oxides **3a** and **3b** (Scheme 3 and Table 3). In these nitrones the two phenyl groups are locked in a coplanar conformation with a consequent decrease in their steric demand.



Scheme 3

However, the decrease in steric crowding of the TS leading to the 4-regioisomer, on passing from nitrones **1** to nitrones **3**, is not clearly reflected in the regiochemical outcome. Actually, either an increase (e.g., in the reaction of **3a** and **3b** with methyl acrylate) or a decrease (e.g., in the reaction of **3a** and **3b** with acrolein) in the 4-:5-regioisomer ratio was observed. Anyway, these results make it apparent that steric "non bonded" repulsions in the reactions of **1a** and **1b** are far from being dramatic.

The locking of the two phenyl groups should also bring about a lessening in steric compression between substituents at the 3-position and that at the 4-position in cycloadducts **18** and **20** as compared with **8** and **10**. The consequent prediction that the 4-:5-isoxazolidine equilibrium should be less shifted to the side of the 5-derivative in the reactions of **3a** and **3b** with respect to those of **1a** and **1b** is born out by the experimental data reported in Table 3. Moreover the equimolar regioisomer ratios found for the reactions of acrylonitrile with **3a** and **3b**, respectively, under thermodynamic control seem to suggest that 4-substituted isoxazolidines, when they lack steric congestion, are inherently at least as stable as related 5-substituted isomers.

Once again the N-methyl derivative **3b** exhibits a lower tendency than the N-phenyl derivative **3a** to produce the 4-substituted isoxazolidine. Our results confirm the previous report by Taylor et al.[9] on the reaction of **3b** with **7d** (see Introduction).

As for reaction rates, nitrones **3** reacted faster than nitrones **1** and a different reactivity order for acrolein vs methylvinylketone was observed [i.e., k (**3a** + **7a**) = 0.5, k (**3a** + **7b**) = 1.0, k (**3a** + **7d**) = 5.0].

As last topic we briefly investigated the reactions of the trialkylderivative **6a** with

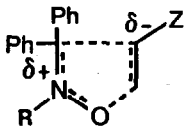
acrylonitrile and methyl acrylate. In contrast to the above reported data for **1a**, **1b**, **3a**, and **3b**, and in agreement with the data on the nitrone **6b** by Funk et al.,[12] the 5-regioisomer was clearly prevalent for both dipolarophiles (i.e., **22c**:**23c** = 0.67 and **22d**:**23d** = 0.30). We conclude that alkyl substituents, both at the nitrogen and carbon atom of the nitrone, are less effective than aromatic substituents in promoting formation of the 4-regioisomer.

DISCUSSION

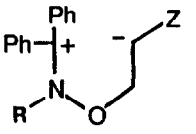
Our findings clearly show that C,C-diaryl-N-substituted nitrones, e.g. **1a**, **1b**, **3a** and **3b**, react with monosubstituted electron-deficient dipolarophiles to give mixtures of regioisomers in which the 4-regioisomer is, as a rule, dominant. In particular triphenylnitrone **1a** and N-phenyl-fluorenoneimine-N-oxide **3a** emerge as the nitrones which exhibit the highest tendency of all the nitrones studied so far to give 4-substituted isoxazolidines. Indeed, the 4-:5-regioisomer ratios found for **1a** and **3a** are, as a whole, higher than those reported for C,C-dicyclopropyl-N-methylnitrone.[3] The regiochemical results for the latter nitrone [e.g., 4-:5-isoxazolidine =1:1 and 3:1 for its reactions with methyl acrylate and acrylonitrile, respectively] are similar to those for **1b**, thus suggesting that the effect on regioselectivity of a cyclopropyl residue at the carbon atom of the nitrone is similar to that of a phenyl substituent.

The regiospecific formation of the 5-substituted isoxazolidine reported in the literature for some reactions of C,C-diaryl-N-alkylnitrones (see Introduction) could have been the result of thermodynamic control (e.g., the reaction of **1b** with **7b**) or of partial equilibration along with possible overlooking of the 4-regioisomer. Anyway, our results for the reactions of nitrones **1** and **3** with alkenes **7** fully confirm the theoretical predictions by Houk et al.[2,3] They can qualitatively be rationalized in the framework of occupied-unoccupied MO interactions, wherein the interactions between occupied MOs of the nitrone and unoccupied MOs of the dipolarophile prevail. The PMO arguments about this topic have been detailed several times by Houk[2,3,17] and need not to be repeated here.

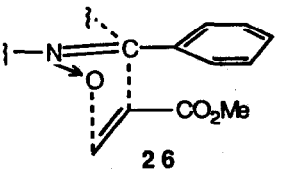
Suffice to say that the two aryl substituents on the carbon atom of the nitrone will tend, inter alia, to increase the HOMO coefficient on the oxygen atom while decreasing that on the carbon atom. Consequently we propose that in the asynchronous TS for nitrones **1** and **3** leading to the 4-isoxazolidine C·····O bond formation is more advanced than C·····C bond formation[18] with development of a partial positive charge on the 1,3-dipole and a partial negative one on the dipolarophile (i.e., **24**). Both charges can efficiently be dispersed by substituents. This asynchronism in bond formation (which, in our opinion, also holds for all the reactions of electron-rich trisubstituted nitrones with electron-poor dipolarophiles) along with the well known earliness of 1,3-dipolar cycloaddition TS[19] provides a rationale



24



25



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for the observation that steric effects on regioselectivity are not as important as one would have expected for these heavily substituted 1,3-dipoles. As a result a clear-cut emergence of electronic effects is observed in the case of electron-deficient monosubstituted alkenes.

It should be added that there can also be a stabilizing interaction between one of the phenyl groups and the substituent on the dipolarophile, which helps counteract repulsive steric effects. For example, the attractive interaction between a phenyl and a methoxycarbonyl group (e.g., **26**) is well documented in 1,3-dipolar cycloadditions.[20]

On the other hand steric effects, along with electronic effects, are certainly important factors in determining formation of the sole 5-substituted isoxazolidine in the reactions of nitrones **1** with 1,1-disubstituted alkenes **12** and with styrene.

The slight decrease in reaction rate as well as in the 4-:5-regioisomer ratio brought about by the increase in solvent polarity in the reactions of **1b** is in agreement with previous observations on solvent effect on nitrone 1,3-dipolar cycloadditions.[9,21] It provides compelling evidence against the presence of a true dipolar intermediate (i.e., **25**) and supports an efficient dispersal of the partial charges in the TS.

The regiospecific formation of the sole 4-regioisomer observed in the reactions of acetylenic dipolarophiles **15** with nitrones **1** should be classified as "expected" in view of the well known higher tendency of monosubstituted alkynes[1a,3,17,22] as compared with related alkenes to give 4-adducts in their reaction with nitrones.

Finally MO calculations needed to rationalize the interesting different effect of aryl vs alkyl nitrone substituents as well as the ranking of double bond activation towards cycloaddition by different groups will be reported at a later time.

EXPERIMENTAL

Melting points are uncorrected. Elemental analyses were made on a Carlo Erba CHN analyzer mod. 1106. IR spectra were measured as Nujol suspensions or as films on a Perkin Elmer 157 spectrophotometer. ^{1}H and ^{13}CNMR Spectra were recorded as $CDCl_3$ solutions (unless otherwise stated) on a Bruker WP80SY spectrometer (operating at 80 and 20.2 MHz) equipped with an Aspect 2000 computer with TMS as internal standard. Mass spectra were measured on a Du-Pont 21-492B using the electron impact mode (75 eV, compounds were vaporized at 45°C). Thin layer chromatography was carried on plates precoated with Silicagel 60 $6F_{254}$ Merck. Spots were

revealed either by spraying with 3% chromium (VI) oxide in sulfuric acid (50%) followed by heating at 120°C or under UV light (254 nm). The former method is very sensitive for N-phenylisoxazolidines owing to the appearance of a very intense purple-red colour. Column chromatography was performed with Silicagel 60 (70-230 mesh) Merck eluting either with cyclohexane-ethyl acetate mixtures or with benzene. The reagents used were either commercially available or prepared by literature method and were distilled or crystallized before use. Solid adducts were purified by crystallization from cyclohexane or petrol ether (**8c**, **9b**, **18a** and **18d** from MeOH) and oily products as well as unstable products by column chromatography. Adducts are colourless (slightly yellow in the case of nitroderivatives).

Reaction of triphenylnitrone **1a** with alkenes **7** at r.t.. A slurry of **1a** (500 mg) in the neat dipolarophile **7a**, **7b**, **7c**, and **7d**, respectively, (4 ml) was stirred at r.t. until 100% conversion was reached (TLC analysis; $\simeq$ 4 days for **7a**, 7 days for **7b**, $\geq$ 30 days for **7c** and **7d**). Then the dipolarophile was evaporated off and the residue column chromatographed (cyclohexane: AcOEt = 9:1 as eluant) to give the pure regioisomers in the case of **7a** (total yield:90%), **7b** (93%) and **7d** (95%). In the case of **7c** (91%) the two regioisomers could not be separated by chromatography but **8c** was obtained in a pure state from the kinetic mixture by fractional crystallization. A second set of reactions was carried out in a benzene/dipolarophile (2:1) mixture as solvent at 20°C $\mp$ 1. Longer reaction times were required to reach high conversions but the regioisomer ratios (evaluated by ^{1}HNMR and column chromatography and reported in Table 1) did not change appreciably. **8a**: δ 3.95-4.70 (m, H-5, H-5' and H-4), 9.40 (d, CHO, J4,CHO = 2.4 Hz); δ (C_6D_6) 3.74 (dt, H-4, J4,5 = J 4,5' = 8.0 Hz), 4.06 (t, H-5', J5,5' = 8.0 Hz), 4.33 (t, H-5), 9.13 (d, CHO, J4,CHO = 2.0) (Hz). **9a**: δ 3.14 (dd, H-4', J4,4' = 12.6 Hz and J4',5 = 3.0 Hz), 3.45 (dd, H-4, J4,5 = 9.5 Hz), 4.72 (dd, H-5), 9.50 (bs, CHO). **8b**: δ 1.75 (s, COMe), 4.20-4.70 (m, H-4, H-5 and H-5'). **9b**: δ 2.05 (s, COMe), 3.27 (m, H-4 and H-4'), 4.64 (t, J4,5 + J4',5 = 13.4 Hz). **8c**: δ 4.11 (dd, H-4, J4,5' and 9.0 Hz and J4,5 = 6.0 Hz), 4.37 (dd, H-5', J5,5' = 8.0 Hz), 4.76 (dd, H-5). **9c**: δ 3.32 (m, H-4 and H-4'), 4.77 (t, H-5, J4,5 + J4',5 = 15.0 Hz). **8d**: δ 3.25 (s, OMe), 4.20-4.65 (m, H-4, H-5 and H-5'). **9d**: δ 3.34 (m, H-4 and H-4'), 3.63 (s, OMe), 4.80 (t, H-5, J4,5 + J4',5 = 14.6 Hz).

The reaction of **1a** (200 mg) with **7e** (200 mg) was carried out in benzene (2 ml) at 60°C for 15 days. The crude mixture of **8e** and **9e** was analyzed by ^{1}H-NMR and the individual components separated by column chromatography (cyclohexane: AcOEt = 95:5). **8e**: δ 4.40, 4.57 and 4.99 (three triplets, H-4, H-5 and H-5', J = 8.3 Hz). **9e**: δ 3.53 (m, H-4 and H-4'), 5.21 (t, H-5, J4,5 + J4',5 = 14.6 Hz).

A slurry of **1a** (300 mg) and **7f** (0.5 ml) in benzene (5 ml) was stirred at r.t. for 1h. After that time the solvent and nitroethylene were evaporated under reduced pressure to give a solid residue which was purified by column chromatography. A quantitative yield of the slightly yellow **8f** was obtained. Attempted crystallization from methanol resulted in the recovery of pure **1a**. The very fast decomposition of **8f** upon heating prevented obtention of a reliable value for its m.p..

The reaction of **1a** (250 mg) with **7g** (3 ml) was conducted at 65°C for 8 days.[23] Usual work-up afforded pure (by ^{1}HNMR) **9g** in 20% yield. **9g**: δ 3.45 (m, H-4 and H-4'), 5.42 (dd, H-5, J4,5 + J4',5 = 15.5 Hz).

Competition reactions of **1a** with alkenes **7**. A slurry of the nitrone **1a** (200 mg, 0.73 mmol) in a mixture of a pair of dipolarophiles **7** [**7a**(22.2 mmol) + **7b**(28.2 mmol), **7b**(19.8 mmol) + **7c** (123.5 mmol), **7b** (21.7 mmol) + **7d** (87.6 mmol), **7a** (178.6 mmol) + **7f** (4.11 mmol), **7a** (17.86 mmol) + **7d** (88.56 mmol)] was kept at 20°C $\mp$ 2 under stirring until 100% conversion was reached (TLC analysis). In the case of **7c** + **7e** [**7c**(2.92 mmol) + **7e** (2.19 mmol)] the competition reaction was carried out at 60°C for 3 days. The ratio of adducts for the reactions of **7a** + **7b** [**8a** + **9a** (47.7%), **8b** + **9b** (39.3%)], **7b** + **7c** [**8b** + **9b** (47%), **8c** + **9c** (49.6%)], **7b** + **7d** [**8b** + **9b** (49%), **8d** + **9d** (41.8%)] and **7c** + **7e** [**8c** + **9c** (76%), **8e** (10%)] were evaluated by column chromatography (eluant: cyclohexane/AcOEt for the latter reaction

and benzene for the other reactions) whilst for the reactions of **7a** + **7f** [100%, **8a** ($\simeq$ 5.5%) and **8f** ($\simeq$ 94.5%)] and of **7a** + **7d** [92%, **8a** + **9a** (57.5%) and **8d** + **4d** (42.5%)] by ^{1}HNMR. A second set of reactions [**7a** + **7b**, **7b** + **7c**, **7b** + **7d**] was then carried out under the same conditions. Relative rate constants were calculated by Huisgen's method[15] : k(**7a**) = 1.49 $\mp$ 5%, k(**7b**) = 1.00, k(**7c**) = 0.177 $\mp$ 5%, k(**7d**) = 0.223 $\mp$ 6%, k(**7e**) $\simeq$ 0.028, k(**7f**) $\simeq$ 1155. The value of 6.74, for the ratio k(**7a**) : k(**7d**), obtained from the direct competition of **7a** vs **7d** compares well with the value of 6.68 calculated from the data reported above.

Reactions of **1a** with alkenes **7** under thermodynamic control. Cycloreversion reactions of adducts **8**. A mixture of **1a** (200 mg), the appropriate dipolarophile (2.5 ml) and hydroquinone (10 mg) was heated (2h for **7a**, 3h for **7b**, $\geq$ 6h for **7c** and **7d**) at 120°C in a sealed ampoule. Evaporation of the dipolarophile gave a residue which was column chromatographed to afford pure adducts [**8a** (4%) + **9a** (77%) **9b** (84%), and **8d** ($\simeq$ 1%) + **9d** (75%), respectively] or mixture of adducts [**8c** (13.5%) + **9C** (61.5%)].

A mixture of **1a** (100 mg) and **7e** (123 mg) was heated at 110°C for 48 h to give a mixture of **8e** + **9e** ($\simeq$ 5:95 by ^{1}HNMR after a fast column chromatography).

The reaction of **1a** (250 mg) with excess **7f** (130 mg) was carried out in toluene at reflux. Some more nitroethylene was added over the reaction period. After 10 h the solvent was evaporated off and the two spots separated by column chromatography (cyclohexane/AcOEt = 95:5). The faster moving component consisted of pure **8f** (76 mg) wilst the slower moving one (60 mg) was a mixture of two products. In fact, along with signals which clearly disclosed the presence of **9f** (see Results section), the ^{1}HNMR of the lower R_F component displayed a singlet at δ 3.68 and the IR spectrum an intense absorption at ν max 1750 cm^{-1}. These data are consistent with a triphenyl-ß-lactam structure derived from **9f** through a base induced rearrangement with elimination of HNO_2[24] (**9f**: ß-lactam $\simeq$ 2:1).

A solution of **8f** (20 mg) and 1,3-diphenylisobenzofuran (10 mg) in degassed benzene and 1,2-dichloroethane, respectively, was heated at 40°C $\mp$ 2. The yellow fluorescent color of the diene was discharged within $\simeq$ 10 h in 1,2-dichloroethane and 43 h in benzene. TLC analysis[25] showed the presence of triphenylnitrone and of the nitroethylene-isobenzofuran adduct. Likewise compounds **8a**, **8b**, **8c**,**8d** and **8e**, respectively, were kept at 31°C in benzene in the presence of diphenylisobenzofuran for 21 days. After that time no triphenylnitrone could be detected in the reactions of **8c** and **8d** whereas small amounts of the 1,3-dipole were present in the reactions of **8a**, **8b** and **8e**.

Reactions of **1b** with alkenes **7**. **1b** (250 mg) was dissolved in the appropriate solvent (cyclohexane, acetonitrile and benzene, respectively) in the presence of excess dipolarophile (2 ml for **7a-d** and 0.5 ml for **7f**) and the solution left aside for ten days. Then the solvent was evaporated off and the ratio of cycloadducts (Table 2) was established by ^{1}HNMR and/or column chromatography.

Preparative reactions for **7a-d** were carried out in neat dipolarophile at r.t. to give mixtures of adducts **10/11** in $\geq$ 80% yield. The individual components were obtained (with the exception of **10d** and **11d**) by column chromatography (benzene or cyclohexane/AcOEt mixtures). Attempted crystallization of **10f** from methanol led to decomposition to **1b**. Variable amounts of a by-product (m.p. 188-190°) derived from the nitrone but not fully characterized were isolated in several instances. On qualitative grounds the relative reaction rates of akenes **7** with **1b** were found similar to those with **1a** (i.e., **7f** $\gg$ **7a** $\simeq$ **7b** > **7c** $\simeq$ **7d**). A quantitative evaluation was carried out for the reaction of acrolein (2.98 g) with **1b** (0.116 g) both in cyclohexane and acetonitrile (total volume, 25 ml) under pseudo-first order conditions. Sealed ampoules for either solvent were thermostatted at 25°C $\mp$ 1 and the [nitrone]/[**10a** + **11a**] ratio was evaluated at appropriate time intervals by ^{1}HNMR (careful integration of the NMe signals after evaporation of the solvent and excess acrolein). Least-squares treatment of ln a/a-x (a is the initial concentration of **1b**) led to pseudo-first order constants from which second order rate constants (L mol^{-1} s^{-1}) of 3.64 $\mp$ 0.2 x 10^{-6} and 1.18 $\mp$ 0.1 x 10^{-6} were calculated for the reaction in cyclohexane and acetonitrile, respectively.

The reaction of **1b** with excess **7b** in benzene equilibrated readily both at 120°C (3 h, 70% yield of **11b**) and at 80°C (10 h, 95% yield of **11b**). Reversal of regiochemistry was achieved also for **1b** + **7a** (benzene at reflux for 10 h; **11a** : **10a** ≃ 5 : 1) but decomposition processes prevented a good yield recovery of the reaction products. A clean equilibrium, which consisted almost only of **11d** (80% after crystallization), set up upon heating a solution of **1b** in neat **7d** at 120°C for ≥ 6 h. Likewise (120°C, ≥ 6 h) a 90% yield of **10c** + **11c** was isolated from the reaction of **1b** in neat **7c**. Finally the adduct **11e** (100 mg) was obtained from the reaction of **1b** (120 mg) with phenylvinylsulfone (150 mg) after heating at 60°C for ten days and at 80°C for further two days.

10b: δ 1.68 (s, COMe), 2.25 (s, NMe), 4.38 (m, H-4, H-5 and H-5'). **11b**: δ 2.05 (s, COMe), 2.43 (s, NMe), 3.22 (m, H-4 and H-4'), 4.43 (t, H-5, J4,5 + J4',5 = 16.0 Hz). **10c**: ν max 2245 cm^{-1} (w, CN); δ 2.28 (s, NMe), 3.90-4.50 (m, H-4, H-5 and H-5'); ^{13}CNMR, δ 40.7 (q, Me), 42.2 (d, C-4), 68.2 (t, C-5), 78.2 (s, C-3), 117.7 (s, CN); mass spectrum, m/z 264 ($M^{+\cdot}$, 15), 218 ($C_{16}H_{12}N^{+}$, 18), 211 ($C_{14}H_{13}NO^{+\cdot}$, 52), 210 ($C_{14}H_{12}NO^{+}$, 100), 191 ($C_{15}H_{11}^{+}$, 12), 187 ($C_{11}H_{11}N_2O^{+\cdot}$, 17.5), 165(15), 140(12), 118(23), 91(15), 77(37). **11c**: ν max 2240 cm^{-1} (vw, CN); δ 2.47 (s, NMe), 3.32 (m, H-4 and H-4'), 4.49 (t, H-5, J4,5 + J4',5 = 16.0 Hz; ^{13}CNMR, δ 41.3 (q, Me), 43.5 (t, C-4), 64.5 (d, C-5), 77.8 (s, C-3), 119 (s, CN); mass spectrum, m/z 264 (68), 218(100), 211(12), 210(36), 191(34), 187(63), 165(25), 140(97), 118(23), 103(11), 91(24), 77(37). **10d**: δ 2.21(s, NMe), 3.30 (s, OMe), 4.40 (m, H-4, H-5 and H-5'). **11d**: δ 2.45 (s, NMe), 3.25 (m, H-4 and H-4'), 3.60 (s, OMe), 4.40 (t, H-5, J4,5 + J4',5 = 16.0 Hz). **11e**: δ 2.55 (s, NMe), 3.17 (dd, H-4', J4,4' = 13 Hz, J4',5 = 7.2 Hz) 3.73 (dd, H-4, J4,5 = 8.6 Hz), 4.72 (dd, H-5). ^{13}CNMR, δ 38.38 (t, C-4), 42.8 (q, Me), 77.78 (s, C-3), 94.05 (d, C-5). **10f**: δ 2.29 (s, NMe), 4.54 (dd, H-5', J5,5' = 10.0 Hz and J4,5' = 8.8 Hz), 4.74 (dd, H-5, J4,5 = 4.9 Hz), 6.12 (dd, H-4). ^{13}CNMR, δ 39.3 (q, Me), 68.8 (t, C-5), 80.5 (s, C-3), 97.2 (d, C-4). **11g**: δ 2.53 (s, NMe), 3.06 (dd, H-4', J4,4' = 12.0 Hz and J4',5 = 10.2 Hz), 3.25 (dd, H-4, J4',5 = 6.8 Hz).

Reactions of **1a** and **1b** with alkenes **12**. All the reactions of nitrones **1** with alkenes **12** were performed in neat dipolarophile: at r.t. for methacrolein [2 months], at 54°C for methyl methacrylate (10 days with **1a** and 5 days with **1b**), at 65°C (with **1a**, 10 h) and 80°C (with **1b**, 7 days) for methacrylonitrile. **13a** (48%): δ 1.50 (s, Me), 3.25 (d, CH2), 9.81 (s, CHO). **13c** (27%): ν max 2230 cm^{-1} (vw, CN) δ 1.70 (s, Me), 3.41 (d, CH2). **13d** (81%): δ 1.62 (s, Me), 3.13 (d, H-4', J4,4' = 13.0 Hz), 3.49 (s, OMe), 3.71 (d, H-4). **14a** (50%): δ 1.30 (s, Me), 2.40 (s, NMe), 3.00 (d, H-4', J4,4' = 13.0 Hz), 3.37 (d, H-4), 9.50 (s,CHO). **14c** (70%) ν max 2225 cm^{-1} (vw, CN); δ 1.35 (s, Me), 2.58 (s, NMe), 3.13 (d, H-4', J4,4' = 13.0 Hz), 3.72 (d, H-4'). **14d** (87%): δ 1.25 (s, Me), 2.40 (s, NMe), 2.98 (d, H-4', J4,4'= 13.0 Hz), 3.51 (s, OMe), 3.75 (d, H-4).

Reactions of nitrones **1** with alkynes **15**. The reactions of nitrones **1** (500 mg) with alkynes **15** (equimolar amounts of **15a** and a two-fold excess of **15b**, respectively) were carried out in benzene (5 ml) at r.t. (60 h for **1a** + **15a**, 80 h for **1a** + **15b**, 36 h for **1b** + **15a** and **1b** + **15b**). Yellow decomposition products, which we did not manage to fully characterize, were formed in the reaction of **1a** + **15b**. Adducts were isolated in a pure state by flash column chromatography (cyclohexane: AcOEt = 4:1 as eluant): **16a** (91%), **16b** (60%), **17a** (94%), **17b** (98%). **16a**: ν max 1570, 1590, 1608 and 1623 cm^{-1} (s, C=O and C=C); δ 6.80-8.00 (m, the signal of H-5 is buried under aromatic protons). **16b**: ν max 1620 cm^{-1} (s, C=C) and 1715 cm^{-1} (vs, C=O); δ 3.58 (s, OMe), 6.40-7.50 (m, aromatic protons), 7.65 (s, H-5). **17a**: ν max 1568, 1588 and 1618 cm^{-1} (s, C=O and C=C); δ 2.30 (s, NMe), 7.05-7.70 (m, aromatic protons and H-5); ^{13}CNMR, δ 42.2 (q, NMe), 80.6 (s, C-3), 120.95 (s, C-4), 158.3 (d, C-5), 189.4 (s, co). **17b**: ν max 1620 cm^{-1} (s, C=C), 1720 cm^{-1} (vs, C=O); δ 2.28 (s, NMe), 3.50 (s, OMe), 7.10-7.70 (m, aromatic protons and H-5). It is well known that H-4 in 5-substituted isoxazolines resonates at δ ≤ 6.0 whereas H-5 in 4-substituted isomers at δ ≥ 7.0.[17,21]

Reactions of nitrones **3** with alkenes **7**. Nitrones **3** (200 mg) were dissolved in a benzene:dipolarophile (2:1) mixture (5 ml) and kept at 20°C until 100% conversion was

Table 4. Physical and analytical data for adducts **8–23**.[a,b]

Adduct	M.p.(°C)	Found C	Found H	Found N	Formula	Required C	Required H	Required N
8a	120–121	80.2	5.8	4.1	C22H19NO2	80.2	5.8	4.3
9a	Oil	80.3	5.9	4.4				
8b	128–130	80.2	6.2	4.1	C23H21NO2	80.4	6.2	4.1
9b	85–86	80.5	6.4	4.3				
8c	112–114	80.7	5.8	8.4	C22H18N2O	81.0	5.6	8.6
8d	90–92	77.0	6.1	4.0	C23H21NO3	76.9	5.9	3.9
9d	90–93	76.6	6.0	4.0				
8e	149–151	73.7	5.3	3.3	C27H23NO3S	73.5	5.2	3.2
9e	136–139	73.3	5.4	3.4				
8f	-	72.6	5.4	8.0	C21H18N2O3	72.8	5.2	8.1
10a	64–66	76.3	6.5	5.1	C17H17NO2	76.4	6.4	5.2
11a	68–71	76.2	6.3	5.4				
10b	Oil	77.1	6.5	4.8	C18H19NO2	76.8	6.8	5.0
10c	100–104	77.6	6.0	10.5	C17H16N2O	77.3	6.1	10.6
11c	102–103	77.5	6.3	10.8				
11d	103–105	72.8	6.5	5.0	C18H19NO3	7.27	6.4	4.7
11e	126–128	70.0	5.3	3.9	C22H21NO3S	69.7	5.5	3.7
10f	100–105	67.6	5.6	9.7	C16H16N2O3	67.6	5.7	9.9
11g	102–104	84.0	6.8	4.4	C22H21NO	83.8	6.7	4.5
13a	Oil	80.6	6.1	4.0	C23H21NO2	80.4	6.2	4.1
13c	140–141	81.3	6.1	8.4	C23H20N2O	81.2	5.9	8.2
13d	79–80	77.5	6.0	3.9	C24H23NO3	77.2	6.2	3.8
14a	80–4	76.6	6.9	5.2	C18H19NO2	76.8	6.8	5.0
14c	122–124	77.8	6.6	10.1	C18H18N2O	77.7	6.5	10.1
14d	79–81	73.3	6.6	4.6	C19H21NO3	73.3	6.8	4.5
16a	118–121	83.4	5.3	3.6	C28H21NO2	83.4	5.3	3.5
16b	115–117	77.3	5.3	4.0	C23H19NO3	77.3	5.4	3.9
17a	124–127	80.6	5.9	4.3	C23H19NO2	80.9	5.6	4.1
17b	Oil	73.1	5.7	4.9	C18H17NO3	73.2	5.8	4.7
18a	133–136	80.7	5.4	4.2	C22H17NO2	80.7	5.2	4.3
18b	134–136	80.9	5.4	4.0	C23H19NO2	80.9	5.6	4.1
19b	120–123	80.8	5.5	4.3				
18c	140–142	81.3	5.2	8.3	C22N16N2O	81.5	5.0	8.6
19c	178–179	81.4	5.3	8.5				
18d	129–132	77.5	5.5	4.0	C23H19NO3	77.3	5.4	3.9
20a	Oil	77.1	5.5	5.5	C17H15NO2	77.0	5.7	5.3
20b	98–100	77.2	6.0	5.1	C18H17NO2	77.4	6.1	5.0
21b	Oil	77.1	5.9	5.2				
21c	Oil	77.9	5.5	10.8	C17H14N2O	77.8	5.4	10.7
22c	Oil	64.8	8.4	16.9	C9H14N2O	65.0	8.5	16.9
23c	Oil	65.1	8.4	17.0				
22d	Oil	60.3	8.4	7.1	C10H17NO3	60.3	8.6	7.0
23d	Oil	60.2	8.5	7.0				

[a] Compounds not reported in this Table either are known compounds (**9g**, **11b**, **20c**, **20d** and **21d**) or were not isolated in a pure state. [b] The IR spectra of compounds **8–23** displayed the absorption bands required by their functional groups.

reached (e.g.,48h for **7b** and 7 days for **7d**). The regioisomer ratio was determined by column chromatography (benzene or cyclohexane: AcOEt mixtures as eluant) and/or ^{1}H-NMR.

Competition reactions of **3a** with an excess mixture of **7a** + **7b** and **7b** + **7d**, respectively, were carried out in benzene at r.t. Competition reactions of acrolein (1 ml) and methylvinylketone (1 ml), respectively, with **1a** (50 mg) + **3a** (50 mg) were carried out in dichloromethane (2 ml) at r.t.. After 20 h the adduct ratios, **18a** + **19a** : **8a** + **9a** = 2 and **18b** + **19b** : **8b** + **9b** = 6, were determined by ^{1}HNMR analysis. Likewise the reactions of **1b** (50 mg) + **3b** (50 mg) with acrolein (1 ml, 20 h), acrylonitrile (1 ml, 48 h) and methyl acrylate (1 ml, 40 h) respectively, in benzene (2 ml) were interrupted before completion. The adduct ratio, i.e., **20+21:10+11** was found to be of $\simeq$ 2.0 for acrolein and of $\simeq$ 9 for methyl acrylate and acrylonitrile.

Thermodynamic ratios were obtained by heating nitrones **3** in neat dipolarophile at 120°C for $\geq$ 3 days ($\geq$ 85% yield).

18a: δ 4.17(ddd, H-4, J4,5' = 8.5 Hz, J4,5= 6.5 Hz, J4,CHO = 1.0 Hz), 4.60 (t, H-5' J5,5' = 8.5 Hz), 4.91 (dd, H-5), 9.02 (d, CHO). **19a**: δ 3.08 (dd, H-4', J4,4' = 13.5 Hz and J4'5= 10.2 Hz), 3.26 (dd, H-4, J4,5 = 2.8 Hz), 4.82 (dd, H-5), 10.15 (bs, CHO). **18b**: δ (C6D6) 1.02 (s, COMe), 3.83 (dd, H-4, J4,5' = 9.0 Hz and J4,5 = 6.0 Hz), 4.25 (dd, H-5', J5,5' = 8.0 Hz), 5.10 (dd, H-5). **19b**: δ 2.55 (s, COMe), 3.05 (dd, H-4', J4,4'= 13.0 Hz and J4',5 = 9.3 Hz), 3.35 (dd, H-4, J4,5 = 4.7 Hz), 4.85(dd, H-5). **18c**: νmax 2240 cm^{-1} (w, CN); δ 4.16 (dd, H-4, J4,5'= 7.0 Hz and J4,5= 9.0 Hz), 4.59 (dd, H-5', J5,5'= 9.0 Hz), 4.82 (t, H-5). **19c**: ν max 2235 cm^{-1} (vw, CN); δ 3.29 (d, H-4 and H-4'), 5.27 (t, H-5, J4,5= 12.5 Hz). **18d**: δ 4.18 (dd, H-4, J4,5'= 8.0 Hz and J4,5=6.8 Hz), 4.55 (t, H-5', J5,5'=8.0 Hz), 4.87 (dd, H-5). **19d**: δ 3.11 (dd, H-4', J4.4' = 13.0 Hz and J4',5 = 9.6 Hz), 3.28 (dd, H-4, J4,5 = 5.4 Hz), 3.84 (s, OMe), 5.08 (dd, H-5). **20a**: δ 2.07 (s, NMe), 3.98 (dd, H-4, J4,5 = 8.5 Hz and J4,5' = 6.0 Hz), 4.37 (t, H-5', J5,5' = 8.5 Hz), 4.67 (dd, H-5), 9.02 (bs, CHO). **21a**:δ 2.12 (s, NMe), 2.83 (dd, H-4', J4,4' = 13.0 Hz, J4',5 = 9.8 Hz), 3.02 (dd, H-4, J4,5 = 4.3), 4.60 (H-5), 10.0 (bs, CHO). **20b**: δ (C6D6) 1.03 (s, COMe), 2.04 (s, NMe), 3.77 (dd, H-4, J4,5' = 9.0 Hz and J4,5 = 5.5 Hz), 4.17 (dd, H-5', J5,5' = 8.0 Hz), 4.98 (dd, H-5). **21b**:δ 2.15 (s, NMe), 2.50 (s, COMe), 2.84 (dd, H-4', J4,4' = 13.0 Hz, J4',5 = 9.3 Hz), 3.12 (dd, H-4, J4,5 = 5.7 Hz), 4.65 (dd, H-5). **20c**: νmax 2240 cm^{-1} (w, CN); δ 2.15 (s, NMe), 3.98 (dd, H-4, J4,5' = 6.0 Hz and J4,5 = 9.5 Hz), 4.40 (dd, H-5', J5,5'= 8.0 Hz), 4.63 (dd, H-5). **21c**: ν max 2235 cm^{-1} (vw, CN); δ 2.18 (s, NMe), 3.15 (m, H-4 and H-4'), 5.08 (dd, H-5, J4,5 + J4',5 = 13.0 Hz). **20d**: δ 2.08 (s, NMe), 4.05 (dd, H-4, J4,5' = 8.0 Hz and J4,5 = 6.0 Hz), 4.40 (t, H-5', J5,5' = 8.0 Hz), 4.68 (dd, H-5). **21d**: δ 2.13 (s, NMe), 3.03 (m, H-4 and H-4'), 4.90 (t, H-5, J4,5 + J4,5' = 16.0 Hz).

Reaction of **6a** with acrylonitrile and methyl acrylate, respectively. A solution of **6a** (300 mg) and of acrylonitrile (1 ml) or methyl acrylate (1 ml) in benzene (3 ml) was kept at r.t. for 3 days. Usual work-up followed by column chromatography (cyclohexane: AcOEt = 7:3 as eluant) allowed isolation of the pure adducts ($\geq$ 80% yield; **22c**:**23c** = 40:60 and **22d**:**23d** = 23:77). **22c** δ (C_6D_6)2.25 (s, NMe) 2.42 (dd, H-4, J4,5 = 6.3 Hz and J4,5' = 8.7 Hz), 3.55 (t, H-5', J5,5' = 8.5 Hz), 3.75 (dd, H-5); ν max 2235 (w, CN) cm^{-1}. **23c**: δ (C6D6) 1.70 (dd, H-4', J4,4' = 13.0 Hz and J4',5 = 9.2 Hz), 1.99 (dd, H-4, J4,5 = 6.8 Hz), 2.35 (s, NMe), 4.00 (dd, H-5); νmax: 2230 cm^{-1} (vw, CN). **22d**: δ (C6D6) 2.38 (s, NMe), 3.09 (dd, H-4, J4,5' = 9.5 Hz, J4,5 = 8.0 Hz), 3.32 (s, OMe) 3.92 (dd, H-5', J5,5' = 8.0 Hz), 4.35 (t, H-5). **23d**: δ 2.46 (M, H-4 and H-4'), 2.63 (s, NMe), 3.78 (s, OMe), 4.59 (t, H-5, J4,5 + J4',5 = 16.5 Hz).

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