[3+2] Cycloadditions: Part XXXIV: Further Investigations of Cycloadditions of *C,N*-Diaryl- and *C*-Aryl-*N*-methyl Nitrones to α,β -Unsaturated Esters

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Investigations of [3+2] cycloadditions of *C,N*-diaryl and *C*-aryl-*N*-methyl nitrones as three atom components (TAC) to substituted methyl *E*-cinnamates and diethyl arylidene malonates have been further investigated. [3+2] Cycloadditions of cinnamates yielded mixtures of cycloadducts, the major products being the 3,4-*trans*-4,5-*trans*-2,3,5-triaryl-4-carbomethoxy products originating from the *endo*-carbonyl-*exo*-aryl *meta* channel approach of the cinnamate component. [3+2] Cycloadditions to diethyl arylidene malonates furnished single cycloadducts-3,5-*trans*-2-methyl-3,5-diaryl-4,4-dicarbomethoxy isoxazolidines by a *endo*-aryl *meta* channel approach of the 2π -component.

Keywords: [3+2] Cycloadditions, Methyl *E*-Cinnamate, Diarylidene malonate, Nitrone, Isoxazolidine, XRD.

INTRODUCTION

[3+2] Cycloadditions (32CA) of three atom components (TAC) to olefinic substrates by $[\pi 4_s + \pi 2_s]$ pathways form a useful protocol for construction of different 5-membered heterocyclic ring systems with regio- and stereochemical control [1-3]. The literature on 32CAs of nitrones have been reviewed regarding both experimental and theoretical aspects [4-11].

We have been carrying out systematic studies of 32CA of acyclic and cyclic nitrones to olefinic substrates conjugated to electron withdrawing groups *viz.* carboxamide, carboxylate ester, keto- and nitro. The regio- and stereoselectivities of these reactions have been studied and in several instances, the course of reactions analyzed by computational studies [1,2,9,11-21].

The present communication is an extension of our earlier studies. It was of interest to us to extend our investigations on the 32CA of nitrones to substituted methyl *E*-cinnamates and arylidene malonates to obtain a more complete picture of regio- and stereoselectivities of these processes. We had previously reported the 32CA of *C*-(4-nitrophenyl)-*N*-(4'-chlorophenyl) nitrone with methyl *E*-cinnamates [18]. Earlier to this work, only a single instance of 32CA of a nitrone to cinnamic acid

ester was reported [22,23]. We now report the 32CA of four *C,N*-diaryl nitrones, with different *C*-aryl substituents to differently substituted methyl *E*-cinnamates, to assess the influence of changing aryl substituents on regio- and stereoselectivities of the cycloadditions. We had observed earlier in the 32CA of nitrones to α,β -unsaturated amides, that changes in substituents do have a small but perceptive influence on the selectivities of the process [12]. 32CA reactions of *C*-aryl-*N*-methyl nitrones with diethyl arylidene malonates were investigated for the first time. We had earlier investigated the 32CA of *C,N*-diaryl nitrones to arylidene malonates [19]; a remarkable increase in regio- and stereoselectivity compared to cinnamic acid esters was observed leading to the exclusive formation in the uncatalyzed reactions of *trans*-3,5-diaryl-4,4-dicarbomethoxy isoxazolidines in nearly quantitative yields. It was of interest to us to find out whether there would be any changes in reactivity and selectivity if *C*-aryl-*N*-methyl nitrones were reacted.

EXPERIMENTAL

Melting points of the isolated cycloadducts were recorded on an electrically heated Kofler Block apparatus and are uncorrected. Column and thin layer chromatography were carried

out using neutral alumina (Qualigens), silica gel (Qualigens 60-120 mesh, Spectrochem 100-200 mesh) and silica gel G (Merck), respectively. Spots on TLC chromatograms were visualized with iodine vapour. Anhydrous sodium sulphate was used for drying extracts. Analytical samples were routinely dried over anhydrous CaCl_2 *in vacuo* at room temperature.

IR spectra were recorded in KBr discs on Perkin-Elmer FT-IR model RX-9. UV spectra were recorded with a Hitachi UV-vis-NIR model U 3501. ^1H NMR and ^{13}C NMR spectra were recorded with Bruker AM-300L and Avance 300 instruments at 300 MHz and 75.5 MHz and DRX 500 instruments at 500 MHz and 125.5 MHz respectively. Chemical shifts for NMR are reported in ppm, downfield from TMS, ^1H - ^1H coupling constants are given in Hz. ^{13}C NMR assignments were confirmed by DEPT spectra. COSY and DQF-COSY experiments were performed to unravel ^1H - ^1H coupling information.

All chemicals were from Merck, India. These were purified by recrystallization or by fractional distillation under reduced pressure. The purities of starting materials were verified from comparison of their melting points or boiling points with those recorded in literature as well as from their IR and ^1H NMR spectra.

Preparation of dipolarophiles: The cinnamic acid methyl esters (**5,6,7**) were prepared by esterification of the corresponding acids (0.4 mol) by refluxing with anhydrous methanol (162 mL)/concentrated sulphuric acid (6 mL) for 5 h. On cooling crystals of methyl 4-chlorocinnamate, m.p. 74–76 °C (yield 71.5 g, 91 %), methyl 4-nitrocinnamate, m.p. 162 °C (yield 77.6 g, 95 %), methyl 4-methoxycinnamate, m.p. 94 °C (yield 70.6 g, 92 %) respectively were obtained.

The arylidene malonate dipolarophiles (**18,19,20**) were prepared by standard experimental procedures [24–26] from diethyl malonates by condensation with the appropriate aromatic aldehydes in presence of piperidine in benzene solution. The structural integrities of the dipolarophiles were confirmed by IR and NMR spectra.

General procedure for the cycloaddition reactions: The [3+2] cycloadditions were carried out in refluxing dry thiophene-free toluene with three-fold molar excess of the dipolarophile under nitrogen atmosphere for 11–25 h, the reactions being monitored by TLC and ^1H NMR spectroscopy. The post-reaction mixture was worked up by removing the solvent under reduced pressure in a Büchi-type rotary evaporator, the residue was analyzed by ^1H NMR and TLC and then chromatographed over neutral alumina to resolve the components.

Reaction of C-(4-chlorophenyl)-N-phenyl nitron (1) (1.02 g, 0.0044 mol) with methyl 4-chlorocinnamate (6) (2.60 g, 3 × 0.0044 mol). Reaction time 11 h. 300 MHz ^1H NMR analysis revealed three products formed: total conversion ~ 94 %; ratio (**9a**), (**9b**), (**9c**) = 88:9:3.

3,4-trans-4,5-trans-2-Phenyl-3,5-di(4'-chlorophenyl)-4-carbmethoxy isoxazolidine (9a): Yellow solid, m.p. 78 °C, m.f.: $\text{C}_{23}\text{H}_{19}\text{NO}_3\text{Cl}_2$; yield 1.28 g (68 %), isolated from hexane eluates, R_f 0.44 (benzene). IR (KBr, ν_{max} , cm^{-1}): 2952, 2852, 1732 (ester CO), 1637, 1596, 1489, 1400, 1091 & 1013 (aryl Cl), 826 (1,4-disubstituted benzene ring), 758 & 695 (mono-substituted benzene ring). ^1H NMR (300 MHz, CDCl_3): δ 5.19 (d, J = 6.6 Hz, H3), 3.49 (dd, J = 6.6, 8.4 Hz, H4), 5.38 (d, J =

8.4 Hz, H5), 3.70 (s, OCH_3), 6.97–7.03 (m, ovl, A/H-2,4,6), 7.24 (t, J = 7.5 Hz, A/H-3,5), 7.30–7.45 (m, ovl, B,C/H-2,3,5,6); ^{13}C NMR (75.5 MHz, CDCl_3): δ 73.1 (C3), 66.2 (C4), 82.0 (C5), 52.3 (OCH_3), 170.5 (CO), 150.6 (A/C-1), 114.6 (A/C-2,6), 127.9, 128.1, 128.9, 129.15, 129.05 (A/C-3,5, B,C/C-2,6,3,5), 122.4 (A/C-4), 139.5 (B/C-1), 134.6, 133.7 (B,C/C-4), 135.5 (C/C-1). Anal. calcd. (found) (%) for $\text{C}_{23}\text{H}_{19}\text{NO}_3\text{Cl}_2$: C, 64.5 (64.2); H, 4.5 (4.3); N, 3.3 (3.1).

3,4-cis-4,5-trans-2-Phenyl-3,5-di(4'-chlorophenyl)-4-carbmethoxy isoxazolidine (9b): From later hexane eluates, a mixture of (**9a**) and (**9b**) were obtained, which were resolved further by rechromatography and PTLC using benzene:hexane (4:1) as developing solvent, with double development; pale yellow solid, m.p. 66 °C, m.f.: $\text{C}_{23}\text{H}_{19}\text{NO}_3\text{Cl}_2$; yield 114 mg (6 %). IR (KBr, ν_{max} , cm^{-1}): 2954, 2854, 1730 (ester CO), 1635, 1595, 1491, 1398, 1091 & 1010 (aryl Cl), 826 (1,4-disubstituted benzene ring), 755 & 695 (mono-substituted benzene ring). ^1H NMR (300 MHz, CDCl_3): δ 4.98 (d, J = 10.2 Hz, H3), 3.73 (br t, J = 9.9 Hz, H4), 5.72 (d, J = 9.6 Hz, H5), 3.30 (s, OCH_3), 6.94–7.01 (m, ovl, A/H-2,6), 7.20–7.28 (m, ovl, A/H-3,4,5), 7.30–7.45 (m, ovl, B,C/H-2,3,5,6); ^{13}C NMR (75.5 MHz, CDCl_3): δ 71.2 (C3), 60.1 (C4), 79.5 (C5), 52.6 (OCH_3), 168.8 (CO), 149.1 (A/C-1), 116.1 (A/C-2,6), 127.9, 128.3, 128.7, 129.4, 129.2 (A/C-3,5, B,C/C-2,6,3,5), 122.7 (A/C-4), 139.5 (B/C-1), 134.6, 134.2 (B,C/C-4), 136.1 (C/C-1). Anal. calcd. (found) (%) for $\text{C}_{23}\text{H}_{19}\text{NO}_3\text{Cl}_2$: C, 64.5 (64.3); H, 4.5 (4.6); N, 3.3 (3.1).

Detected by ^1H NMR in crude reaction mixture: Regioisomeric 3,4-trans-4,5-trans-2-phenyl-3,4-di(4'-chlorophenyl)-5-carbmethoxy isoxazolidine (**9c**): δ 4.81 (d, J = 7.5 Hz, H3), 4.07 (dd, J = 7.5, 8.5 Hz, H4), 4.49 (d, J = 8.5 Hz, H5).

Reaction of C-(4-nitrophenyl)-N-phenyl nitron (2) (0.655 g, 0.0027 mol) with methyl 4-chlorocinnamate (6) (1.59 g, 3 × 0.0027 mol): Reaction time 12 h. 300 MHz ^1H NMR analysis revealed three products formed: total conversion ~ 92 %; ratio **10a**:**10b**:**10c** = 89:7:4.

3,4-trans-4,5-trans-2-Phenyl-3-(4'-nitrophenyl)-5-(4''-chlorophenyl)-4-carbmethoxy isoxazolidine (10a): yellow solid, m.p. 62 °C, m.f.: $\text{C}_{23}\text{H}_{19}\text{N}_2\text{O}_5\text{Cl}$; yield 0.85 g (72 %), isolated from hexane eluates, R_f 0.62 (benzene). IR (KBr, ν_{max} , cm^{-1}): 3069, 2924, 2854, 1736 (ester CO), 1598, 1491, 1521 & 1346 (nitro), 1091, 1013 & 520 (aryl Cl), 825 (1,4-disubstituted benzene ring), 755 & 692 (mono-substituted benzene ring) cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ 5.41 (d, J = 6.0 Hz, H3), 3.54 (dd, J = 6.0, 9.0 Hz, H4), 5.45 (d, J = 9.0 Hz, H5), 3.73 (s, OCH_3), 7.02–7.07 (m, ovl, A/H-2,4,6), 7.33 (br t, J = 8.0 Hz, A/H-3,5), 7.79 (d, J = 8.7 Hz, B/H-2,6), 8.28 (d, J = 8.7 Hz, B/H-3,5), 7.28–7.49 (m, ovl, C/H-2,3,5,6); ^{13}C NMR (75.5 MHz, CDCl_3): δ 72.7 (C3), 65.9 (C4), 82.1 (C5), 52.8 (OCH_3), 170.2 (CO), 150.1 (A/C-1), 114.4 (A/C-2,6), 127.4 (A/C-3,5), 122.7 (A/C-4), 147.6 (B/C-1), 128.1 (B/C-2,6), 124.2 (B/C-3,5), 148.5 (B/C-4), 134.8, 134.7 (C/C-1,4), 129.0, 129.2 (C/C-2,6,3,5). Anal. calcd. (found) (%) for $\text{C}_{23}\text{H}_{19}\text{N}_2\text{O}_5\text{Cl}$: C, 62.9 (62.6); H, 4.4 (4.5); N, 6.4 (6.2).

Detected by ^1H NMR in crude reaction mixture. 3,4-cis-4,5-trans-2-Phenyl-3-(4'-nitrophenyl)-5-(4''-chlorophenyl)-4-carbmethoxy isoxazolidine (**10b**): δ 5.14 (d, J = 9.0 Hz, H3),

3.70 (obs., overlapped with methoxy signals), 5.74 (d, $J = 9.0$ Hz, H5); 3,4-*trans*-4,5-*trans*-2-phenyl-3-(4'-nitrophenyl)-4-(4''-chlorophenyl)-5-carbmethoxy isoxazolidine (**10c**): δ 4.83 (d, $J = 6.0$ Hz, H3), 4.07 (t, $J = 6.0$ Hz, H4), 4.67 (d, $J = 6.0$ Hz, H5).

Reaction of C,N-diphenyl nitrone (3) (0.591 g, 0.003 mol) with methyl 4-chlorocinnamate (6) (1.77g, 3×0.003 mol): Reaction time 15 h. 300 MHz ^1H NMR analysis revealed three products formed: total conversion $\sim 75\%$; ratio **11a:11b:11c** = 89:8:3.

3,4-*trans*-4,5-*trans*-2,3-Diphenyl-5-(4'-chlorophenyl)-4-carbmethoxy isoxazolidine (11a): Pale yellow waxy solid, m.f.: $\text{C}_{23}\text{H}_{20}\text{NO}_3\text{Cl}$; yield 0.70 g (60 %) isolated from hexane eluates, $R_f = 0.58$ (benzene:petroleum ether 1:1). IR (KBr, ν_{max} , cm^{-1}): 3070, 3033, 2951, 1731 (ester CO), 1400, 1091, 1016 & 511 (aryl Cl), 826 (1,4-disubstituted benzene ring), 759 & 696 (mono-substituted benzene ring). ^1H NMR (300 MHz, CDCl_3): δ 5.11 (d, $J = 6.8$ Hz, H3), 3.45 (dd, $J = 6.8$ Hz, 8.4, H4), 5.28 (d, $J = 8.4$ Hz, H5), 3.66 (s, OCH_3), 6.93 (d, $J = 8.8$ Hz, A/H-2,6), 7.13 (t, $J = 6.8$ Hz, A/H-3,5), 6.85 (t, $J = \sim 7.3$ Hz, A/H-4), 7.12-7.31 (m, ovl, B, C/H-2,3,5,6); ^{13}C NMR (75.5 MHz, CDCl_3): δ 73.9 (C3), 66.3 (C4), 82.1 (C5), 52.5 (OCH_3), 170.7 (CO), 150.9 (A/C-1), 114.5 (A/C-2,6), 126.5 (A/C-3,5), 122.3 (A/C-4), 140.9 (B/C-1), 128.9, 128.3 (B/C-2,6,3,5), 127.9 (B/C-4), 135.7 (C/C-1), 129.0, 129.1 (C/C-2,6,3,5), 134.5 (C/C-4). Anal. calcd. (found) (%) for $\text{C}_{23}\text{H}_{20}\text{NO}_3\text{Cl}$: C 70.1 (69.8); H 5.1 (4.9); N 3.6 (3.4).

Detected by ^1H NMR in crude reaction mixture. 3,4-*cis*-4,5-*trans*-2,3-Diphenyl-5-(4'-chlorophenyl)-4-carbmethoxy isoxazolidine (**11b**): δ 4.85 (d, $J = 10.4$ Hz, H3), 3.68 (br. t, $J = \sim 9.9$ Hz, H4), 5.61 (d, $J = 9.6$ Hz, H5); 3,4-*trans*-4,5-*trans*-2,3-Diphenyl-4-(4'-chlorophenyl)-5-carbmethoxy isoxazolidine (**11c**): δ 4.81 (d, $J = 6.6$ Hz, H3), 4.19 (br. t, $J = \sim 7.0$ Hz, H4), 4.51 (d, $J = 7.5$ Hz, H5).

Reaction of C-(4-chlorophenyl)-N-phenyl nitrone (1) (1.02 g, 0.0044 mol) with methyl 4-nitrocinnamate (7) (2.73 g, 3×0.0044 mol): Reaction time 23 h. 300 MHz ^1H NMR analysis revealed three products formed: total conversion $\sim 72\%$; ratio **12a:12b:12c** = 88:9:3.

3,4-*trans*-4,5-*trans*-2-Phenyl-3-(4'-chlorophenyl)-5-(4''-nitrophenyl)-4-carbmethoxy isoxazolidine (12a): pale yellow solid, m.p. 78°C , m.f.: $\text{C}_{23}\text{H}_{19}\text{N}_2\text{O}_5\text{Cl}$; yield 1.10 g (58 %) isolated from petroleum ether eluates, R_f 0.57 (petroleum ether:benzene 1:1). IR (KBr, ν_{max} , cm^{-1}): 3062, 2918, 2849, 1734 (ester CO), 1475, 1085, 1022 & 525 (aryl Cl), 809 (1,4-disubstituted benzene ring), 762 & 683 (mono-substituted benzene ring). ^1H NMR (300 MHz, CDCl_3): δ 5.07 (d, $J = 6.6$ Hz, H3), 3.43 (br. t, $J = \sim 7.1$ Hz, H4), 5.47 (d, $J = 7.6$ Hz, H5), 3.76 (s, OCH_3), 6.96-7.18 (m, ovl, A, B/H-2,3,5,6), 6.94 (t, $J = 7.4$ Hz, A/H-4), 7.44 (d, $J = 8.4$ Hz, C/H-2,6), 7.99 (d, $J = 8.4$ Hz, C/H-3,5); ^{13}C NMR (75.5 MHz, CDCl_3): δ 72.9 (C3), 66.2 (C4), 80.9 (C5), 52.8 (OCH_3), 170.3 (CO), 149.8 (A/C-1), 115.4 (A/C-2,6), 127.4 (A/C-3,5), 122.4 (A/C-4), 138.7 (B/C-1), 128.8, 128.7, 128.0 (B/C-2,6,3,5, C/C-2,6), 134.0 (B/C-4), 145.4 (C/C-1), 124.0 (C/C-3,5), 148.0 (C/C-4). Anal. calcd. (found) (%) for $\text{C}_{23}\text{H}_{19}\text{N}_2\text{O}_5\text{Cl}$: C 62.9 (62.6); H 4.3 (4.3); N 6.4 (6.3).

Detected by ^1H NMR in crude reaction mixture. 3,4-*cis*-4,5-*trans*-2-Phenyl-3-(4'-chlorophenyl)-5-(4''-nitrophenyl)-4-

carbmethoxy isoxazolidine (**12b**): δ 4.84 (d, $J = 10.2$ Hz, H3), 3.64 (br. t, $J = \sim 9.7$ Hz, H4), 5.70 (d, $J = 9.3$ Hz, H5); 3,4-*trans*-4,5-*trans*-2-phenyl-3-(4'-chlorophenyl)-4-(4''-nitrophenyl)-5-carbmethoxy isoxazolidine (**12c**): δ 4.64 (d, $J = 6.0$ Hz, H3), 4.07 (br. t, $J = \sim 6.5$ Hz, H4), 4.32 (d, $J = 7.2$ Hz, H5).

Reaction of C,N-diphenyl nitrone (3) (0.868 g, 0.0044 mol) with methyl cinnamate (8) (2.14 g, 3×0.0044 mol): Reaction time 16 h: 300 MHz ^1H NMR analysis revealed three products formed: total conversion $\sim 75\%$, ratio **13a:13b:13c** = 91:7:2.

3,4-*trans*-4,5-*trans*-2,3,5-Triphenyl-4-carbmethoxy isoxazolidine (13a): Pale yellow waxy solid, m.f.: $\text{C}_{23}\text{H}_{21}\text{NO}_3$; yield 0.94 g, 60 % isolated from hexane eluates, R_f 0.58 (benzene:petroleum ether 1:1). IR (KBr, ν_{max} , cm^{-1}): 3062, 3029, 2952, 1720 (ester CO), 1637, 1597, 1489, 1443, 763 & 697 (mono-substituted benzene ring). ^1H NMR (300 MHz, CDCl_3): δ 5.16 (d, $J = 6.8$ Hz, H3), 3.53 (dd, $J = 6.8, 8.8$ Hz, H4), 5.32 (d, $J = 8.8$ Hz, H5), 3.71 (s, OCH_3), 6.98 (d, $J = 7.8$ Hz, A/H-2,6), 6.87 (t, $J = 7.5$ Hz, A/H-3,5), 7.03 (t, $J = 7.3$ Hz, A/H-4), 7.15-7.40 (m ovl, B/H-2,3,4,5,6, C/H-3,4,5), 7.49 (d, $J = 7.2$ Hz, C/H-2,6); ^{13}C NMR (75.5 MHz, CDCl_3): δ 73.7 (C3), 66.0 (C4), 82.7 (C5), 51.9 (OCH_3), 170.5 (CO), 150.9 (A/C-1), 114.1 (A/C-2,6), 126.6, 126.1 (A, B/C-3,5), 121.6 (A/C-4), 141.1 (B/C-1), 128.7, 128.3, 128.7 (B/C-2,6, C/C-2,6,3,5), 127.9 (B/C-4), 137.3 (C/C-1), 128.6 (C/C-4). Anal. calcd. (found) (%) for $\text{C}_{23}\text{H}_{21}\text{NO}_3$: C 76.9 (76.6), H 5.9 (5.7), N 3.9 (3.7).

Detected by ^1H NMR in crude reaction mixture. 3,4-*cis*-4,5-*trans*-2,3,5-Triphenyl-4-carbmethoxy isoxazolidine (**13b**): δ 4.89 (d, $J = 10.3$, H3), 3.65 (observed ovl, methoxy signal, H4), 5.67 (d, $J = 9.7$, H5); 3,4-*trans*-4,5-*trans*-2,3,4-Triphenyl-5-carbmethoxy isoxazolidine (**13c**): δ 4.72 (d, $J = 6.7$ Hz, H3), 4.01 (br. t, $J = \sim 7.0$ Hz, H4), 4.45 (d, $J = 7.5$ Hz, H5).

Reaction of C-(4-nitrophenyl)-N-(4'-chlorophenyl)-nitrone (14) (1.217 g, 0.0044 mol) with methyl cinnamate (8) (2.14 g, 3×0.0044 mol): Reaction time 16 h. 300 MHz ^1H NMR analysis revealed three products formed: total conversion $\sim 71\%$, ratio **15a:15b:15c** = 89:7:4.

3,4-*trans*-4,5-*trans*-2-(4'-Chlorophenyl)-3-(4'-nitrophenyl)-5-phenyl-4-carbmethoxy isoxazolidine (15a): white crystals, m.p. 128°C , m.f.: $\text{C}_{23}\text{H}_{19}\text{N}_2\text{O}_5\text{Cl}$; yield 0.86 g (72 %), isolated from hexane eluates. UV: λ_{max} 250 nm ($\log \epsilon$ 4.22); IR (KBr, ν_{max} , cm^{-1}): 2954, 2830, 1736 (ester CO), 1495, 1343 (aromatic $-\text{NO}_2$), 1100 (aryl Cl), 825 (1,4-disubstituted benzene ring), 749, 695 (mono-substituted benzene ring). ^1H NMR (300 MHz, CDCl_3): δ 5.35 (d, $J = 6.1$ Hz, H3), 3.53 (dd, $J = 6.1, 8.5$ Hz, H4), 5.45 (d, $J = 8.5$ Hz, H5), 3.70 (s, OCH_3), 7.00 (d, $J = 8.9$ Hz, A/H-2,6), 7.25 (d, $J = 8.9$ Hz, A/H-3,5), 7.76 (d, $J = 8.7$ Hz, B/H-2,6), 8.26 (d, $J = 8.7$ Hz, B/H-3,5), 7.36-7.41 (m, ovl, C/H-2,3,5,6,4); ^{13}C NMR (75.5 MHz, CDCl_3): δ 72.9 (C3), 65.9 (C4), 83.2 (C5), 52.8 (OCH_3), 170.2 (CO), 148.9 (A/C-1), 115.8 (A/C-2,6), 128.7 (A/C-3,5), 136.2, 136.0 (A/C-4, C/C-1), 147.8 (B/C-1), 127.4 (B/C-2,6), 124.2 (B/C-3,5), 148.2 (B/C-4), 128.9, 129.1 (C/C-2,6,3,5), 126.7 (C/C-4). Anal. calcd. (found) (%) for $\text{C}_{23}\text{H}_{19}\text{N}_2\text{O}_5\text{Cl}$: C 62.9 (62.7), H 4.4 (4.5), N 6.4 (6.2).

Detected by ^1H NMR in crude reaction mixture. 3,4-*cis*-4,5-*trans*-2-(4'-Chlorophenyl)-3-(4''-nitrophenyl)-5-phenyl-4-carbmethoxy isoxazolidine (**15b**): δ 5.13 (d, $J = 10.1$ Hz, H3), 3.66 (br. t, $J = \sim 9.7$ Hz, H4), 5.68 (d, $J = 9.4$ Hz, H5); 3,4-*trans*-

4,5-*trans*-2-(4'-Chlorophenyl)-3-(4''-nitrophenyl)-4-phenyl-5-carbmethoxy isoxazolidine (**15c**): δ 4.96 (d, J = 6.1 Hz, H3), 4.12 (br. t, J = ~6.6 Hz, H4), 4.47 (d, J = 7.1 Hz, H5).

Reaction of C-(4-chlorophenyl)-N-methyl nitrone (16) (0.746 g, 0.0044 mol) with diethyl (4-nitrophenyl) methylene malonate (18) (3.86 g, 3 $\times$ 0.0044 mol): Reaction time 25 h. 300 MHz ^1H NMR analysis revealed only one product.

3,5-*trans*-2-Methyl-3-(4'-chlorophenyl)-5-(4''-nitrophenyl)-4,4-dicarbethoxy isoxazolidine, (21): Pale yellow crystals, m.p. 106-108 $^\circ\text{C}$; m.f.: $\text{C}_{22}\text{H}_{23}\text{N}_2\text{O}_7\text{Cl}$; yield 1.70 g (84 %), isolated from hexane eluates, R_f 0.59 (benzene). UV (λ_{max} , EtOH): 266 nm (log ϵ : 4.19). IR (KBr, ν_{max} , cm^{-1}): 2990, 1724 (ester CO), 1521 & 1346 (aromatic $-\text{NO}_2$), 1103, 1062 & 503 (aromatic Cl), 859 (1,4-disubstituted benzene ring), 750 & 692 (mono-substituted benzene ring). ^1H NMR (500 MHz, CDCl_3): δ 4.72 (s, H3), 6.10 (s, H-5), 3.83, 3.40 (dq, J = 10.7, 7.0 Hz, $\text{CO}_2\text{CH}_2\text{CH}_{3(\text{II})}$), 0.70 (t, J = 7.0 Hz, $\text{CO}_2\text{CH}_2\text{CH}_{3(\text{I})}$), 3.78, 3.29 (dq, J = 10.7, 7.2 Hz, $\text{CO}_2\text{CH}_2\text{CH}_{3(\text{III})}$), 0.75 (t, J = 7.2 Hz, $\text{CO}_2\text{CH}_2\text{CH}_{3(\text{II})}$), 2.75 (s, N-CH₃), 7.30-7.36 (close coupled AB system, A/H-2,6,3,5), 7.60 (d, J = 8.7, B/H-2,6), 8.18 (d, J = 8.7 Hz, B/H-3,5); ^{13}C NMR (125.5 MHz, CDCl_3): δ 78.3 (C3), 75.3 (C4), 83.2 (C5), 168.0, 167.9 (>CO (I,II)), 62.2, 62.1 ($\text{CO}_2\text{CH}_2\text{CH}_{3(\text{I,II})}$), 13.7, 13.6 ($\text{CO}_2\text{CH}_2\text{CH}_{3(\text{I,II})}$), 43.4 (N-CH₃), 134.9, 134.7 (A/C-1,4), 129.0, 128.8, 129.3 (A/C-2,6,3,5, B/C-3,5), 148.4 (B/C-1), 123.5 (B/C-2,6), 143.5 (B/C-4). Anal. calcd. (found) (%) for $\text{C}_{22}\text{H}_{23}\text{N}_2\text{O}_7\text{Cl}$: C 57.1 (56.8), H 5.0 (4.8), N 6.1 (5.9).

Reaction of C-(4-chlorophenyl)-N-methyl nitrone (16) (0.746 g, 0.0044 mol) with diethyl phenyl methylene malonate (20) (3.27 g, 3 $\times$ 0.0044 mol): Reaction time 18 h. 300 MHz ^1H NMR analysis revealed only one product.

3,5-*trans*-2-Methyl-3-(4'-chlorophenyl)-5-phenyl-4,4-dicarbethoxy isoxazolidine (22): White shining crystals, m.p. 112-114 $^\circ\text{C}$, m.f.: $\text{C}_{22}\text{H}_{24}\text{NO}_5\text{Cl}$; yield 1.61 g (88 %), isolated from hexane eluates, R_f 0.61 (benzene). IR (KBr, ν_{max} , cm^{-1}): 1728 (ester CO), 1591 (aromatic C=C), 1093, 1043 & 502 (aromatic -Cl), 861 (1,4-disubstituted benzene ring), 759 & 703 (mono substituted benzene ring); ^1H NMR (300 MHz, CDCl_3): δ 4.64 (s, H3), 5.96 (s, H-5), 3.66, 3.17 (dq, J = 10.7, 7.2 Hz, $\text{CO}_2\text{CH}_2\text{CH}_{3(\text{I})}$), 0.59 (t, J = 7.2 Hz, $\text{CO}_2\text{CH}_2\text{CH}_{3(\text{II})}$), 3.71, 3.33 (dq, J = 10.7, 7.2 Hz, $\text{CO}_2\text{CH}_2\text{CH}_{3(\text{III})}$), 0.67 (t, J = 7.2 Hz, $\text{CO}_2\text{CH}_2\text{CH}_{3(\text{II})}$), 2.67 (s, N-CH₃), 7.20-7.40 (m, A/B/H-2,6,3,5); ^{13}C NMR (75.5 MHz, CDCl_3): δ 77.9 (C-3), 74.9 (C-4), 84.1 (C-5), 168.1, 167.8 (>CO (I,II)), 61.4 ($\text{CO}_2\text{CH}_2\text{CH}_{3(\text{I,II})}$), 13.2, 13.1 ($\text{CO}_2\text{CH}_2\text{CH}_{3(\text{I,II})}$), 43.0 (N-CH₃), 134.2, 134.7 (A/C-1,4), 128.1, 128.6, 128.5 (A/C-2,6,3,5, B/C-3,5), 135.8 (B/C-1), 129.9 br. (B/C-2,6), 127.5 (B/C-4). Anal. calcd. (found) (%) for $\text{C}_{22}\text{H}_{24}\text{NO}_5\text{Cl}$: C 63.2 (63.0), H 5.7 (5.5), N 3.4 (3.4).

Reaction of C-(4-nitrophenyl)-N-methyl nitrone (17) (0.612 g, 0.0034 mol) with diethyl phenyl methylene malonate (20) (2.57 g, 3 $\times$ 0.0034 mol): Reaction time 15 h. 300 MHz ^1H NMR analysis revealed only one product.

3,5-*trans*-2-Methyl-3-(4'-nitrophenyl)-5-phenyl-4,4-dicarbethoxy isoxazolidine (23): yellow crystals, m.p. 108-110 $^\circ\text{C}$, m.f.: $\text{C}_{22}\text{H}_{24}\text{N}_2\text{O}_7$; yield 1.25g (85 %) isolated from 10 % benzene in petroleum ether eluates, R_f 0.48 (benzene). IR (KBr, ν_{max} , cm^{-1}): 2983, 1726 (ester CO), 1602, 1524 & 1354 (aromatic $-\text{NO}_2$), 1102, 1035 & 502 (aromatic -Cl), 852 (1,4-disubstituted

benzene ring), 746 & 691 (mono-substituted benzene ring). ^1H NMR (300 MHz, CDCl_3): δ 4.84 (s, H-3), 6.05 (s, H-5), 3.82, 3.34 (dq, J = 10.7, 7.2 Hz, $\text{CO}_2\text{CH}_2\text{CH}_{3(\text{I})}$), 0.67 (t, J = 6.3 Hz, $\text{CO}_2\text{CH}_2\text{CH}_{3(\text{II})}$), 3.75, 3.27 (dq, J = 10.7, 7.1 Hz, $\text{CO}_2\text{CH}_2\text{CH}_{3(\text{III})}$), 0.71 (t, J = 6.3 Hz, $\text{CO}_2\text{CH}_2\text{CH}_{3(\text{II})}$), 2.74 (s, N-CH₃), 8.21 (d, J = 8.8 Hz, A/H-2,6), 7.64 (d, J = 8.8 Hz, A/H-3,5), 7.30-7.43 (m, B/H-2,6,3,5,4), ^{13}C NMR (75.5 MHz, CDCl_3): δ 77.6 (C-3), 75.1 (C-4), 84.2 (C-5), 167.8, 167.4, (>CO (I,II)), 61.7, 61.5 ($\text{CO}_2\text{CH}_2\text{CH}_{3(\text{I,II})}$), 13.3, 13.1 ($\text{CO}_2\text{CH}_2\text{CH}_{3(\text{I,II})}$), 43.0 (N-CH₃), 147.9 (A/C-1), 130.0 br. (A/C-2,6), 123.4 (A/C-3,5), 143.8 (A/C-4), 135.5 (B/C-1), 128.7, 128.1 (B/C-2,6,3,5), 127.5 (B/C-4). Anal. calcd. (found) (%) for $\text{C}_{22}\text{H}_{24}\text{N}_2\text{O}_7$: C 61.7 (61.4), H 5.6 (5.4), N 6.5 (6.3).

X-ray crystallographic analysis of cycloadduct 22: Cycloadduct **22** was recrystallized by slow evaporation from methanol solution at room temperature to obtain single crystals. Diffraction data were recorded on a Bruker Smart Apex II CCD area detector diffractometer operating the Mo K α radiation (λ = 0.7107 $\text{\AA}$) at the Department of Chemistry, University of Calcutta. The structures were solved by direct methods (SHELXS) and refined using isotropic, then anisotropic thermal factors (SHELXL program) [27]. Hydrogens were gradually introduced in the calculations and kept riding on the bonded atom during all refinements. Figure is drawn using the PLATON program [28].

Crystals were orthorhombic (space group Pca21). Crystal data and structure refinement for cycloadduct **22** is given in Table-1. The X-ray crystallographic study showed an all *trans*-configuration: H-3 and H-5 were *trans*-oriented, additionally the N-lone pair was *trans*- to H-3. Two optical antipodes were present in the unit cell which had a two-fold alternating axis of symmetry.

Supplementary data contain - positional parameters ($\times 10^4$) and mean recalculated isotropic factors ($\times 10^3$) for non-hydrogen

TABLE-1
CRYSTAL DATA AND STRUCTURE
REFINEMENT FOR CYCLOADDUCT 22

Formula	$\text{C}_{22}\text{H}_{24}\text{NO}_5\text{Cl}$
m.w.	417.87
Temperature	150 $^\circ$ (2) K
Radiation	Mo K α - 0.71073 $\text{\AA}$
Crystal system, space group	Orthorhombic, Pca21
Cell parameters	a = 16.582(6) $\text{\AA}$; b = 10.482(4) $\text{\AA}$; c = 25.442(10) $\text{\AA}$; $\alpha = \beta = \gamma = 90^\circ$
Volume	4422(3) $\text{\AA}^3$
Z, Calculated density	8, 1.255 Mg/m^3
Absorption coefficient	0.204 mm^{-1}
F(000)	1760
Crystal size	0.22 $\times$ 0.16 $\times$ 0.09 mm
$\theta_{\text{min}} - \theta_{\text{max}}$	1.60 - 18.44 $^\circ$
Limiting indices	-14 $\leq h \leq$ 14, -9 $\leq k \leq$ 9, -22 $\leq l \leq$ 22
Reflections collected/unique	14738/3232 [R(int) = 0.1284]
Completeness to q	99.3 %
Refinement method	Full-matrix least-squares on F ²
Data/parameters	3232/530
Goodness-of-fit on F ²	1.032
Final R indices [I > 2 σ (I)]	R1 = 0.0510, wR2 = 0.1026
R indices (all data)	R1 = 0.0827, wR2 = 0.1185
Largest diff. peak and hole	0.162 and -0.172 e. $\text{\AA}^{-3}$

atoms; positional parameters ($\times 10^3$) and mean recalculated isotropic factors ($\times 10^3$) for hydrogen atoms; anisotropic thermal parameters.

RESULTS AND DISCUSSION

32CA of *C,N*-diaryl nitrones to substituted methyl *E*-cinnamates: The 32CA of four differently substituted nitrones (**1-4**) to various substituted methyl *E*-cinnamates are reported (Scheme-I). Additionally, the reaction of *C*-(4-nitrophenyl)-*N*-(4'-chlorophenyl) nitron (**14**) with **8**, reported earlier [19], was repeated to obtain further amounts of the resultant cycloadducts **15a-c**.

The following reactions were carried out in refluxing anhydrous toluene with three-fold molar excess of the cinnamates: (a) nitrones **1**, **2**, **3**, **4** with **6**; (b) nitron **4** with **5**; (c) nitron **1** with **7**; (d) nitron **3** with **8**; (e) nitron **14** with **8** (repetition of earlier work) [19].

The reactions were monitored by TLC and 300 MHz ^1H NMR analysis of aliquots taken from time to time. Work-up involved removal of the solvent under reduced pressure in a rotary evaporator, followed by ^1H NMR analysis of the post-reaction mixture for total overall yield and product ratios. The post-reaction mixture was then chromatographed over neutral alumina to isolate the products. Reactions of **4** with **5** and **6** did not proceed satisfactorily as evident from ^1H NMR monitoring of the reaction mixtures-extensive decomposition was

observed. The results of the other 32CA reactions are summarized in Scheme-I. All the reactions gave 3,4-*trans*-4,5-*trans*-2,3,5-triaryl-4-carbomethoxy isoxazolidine (series a) as major products, the corresponding diastereoisomeric 3,4-*cis*-4,5-*trans*-2,3,5-triaryl-4-carbomethoxy isoxazolidine (series b) were obtained as minor products, the regioisomeric 3,4-*trans*-4,5-*trans*-2,3,4-triaryl-5-carbomethoxy isoxazolidine (series c) were obtained in even lesser quantity. All the major products (**9a**, **10a**, **11a**, **12a**, **13a**) were isolated by chromatography in pure state. Of the minor compounds, only **9b** could be isolated in the pure state. The other diastereoisomeric products (**10b** to **13b**) and regioisomeric products (**9c** to **13c**) were detected by ^1H NMR of the crude reaction mixture. All the isolated products (**9a-13a**, **9b**) showed IR bands ($1736\text{--}1730\text{ cm}^{-1}$) characteristic of unconjugated ester; other characteristic bands could be assigned to substituted aromatic rings, aryl Cl and aryl nitro substituents.

Structure elucidation of the products were achieved by spectroscopic analysis, particularly by 300 MHz ^1H NMR and 75.5 MHz ^{13}C NMR and comparison of the values with those of the isoxazolidines generated by 32CA of nitrones to α,β -unsaturated amides [9-12]. We reported earlier that the 32CA of *C*-(4-nitrophenyl)-*N*-(4'-chlorophenyl) nitron (**14**) with methyl cinnamate (**8**) furnished **15a** as the major compound; this on mild hydrolysis afforded the corresponding acid **15d**. XRD analysis of **15d** established the structure as 3,4-*trans*-4,5-*trans*-

Scheme-I: 32CA of *C,N*-diaryl nitrones to substituted methyl cinnamates

TABLE-2
 300 MHz ^1H NMR ASSIGNMENTS OF CYCLOADDUCTS; CHEMICAL SHIFTS IN δ , COUPLING CONSTANTS IN Hz

Proton No.	9a	9b	9c	15a	15d
H-3	5.19 (d, 6.6)	4.98 (d, 10.2)	4.81 (d, 7.5)	5.35 (d, 6.1)	5.54 (d, 8.4)
H-4	3.49 (dd, 6.6, 8.4)	3.73 (br.t, ~9.9)	4.07 (dd, 7.5, 8.5)	3.53 (dd, 6.1, 8.5)	3.54 (dd, 8.4, 8.7)
H-5	5.38 (d, 8.4)	5.72 (d, 9.6)	4.49 (d, 8.5)	5.41 (d, 8.5)	5.33 (d, 8.7)

2-(4'-chlorophenyl)-3-(4''-nitrophenyl)-5-phenyl-4-carboxy isoxazolidine. The characteristic ^1H NMR and ^{13}C NMR signals relating to isoxazolidine ring of **15a** and **15d** are given in Tables 2 and 3. The chemical shifts and coupling constants of the isomeric cycloadducts (**9a**, **9b**, **9c**) are given in Table-2.

 TABLE-3
 75.5 MHz ^{13}C NMR ASSIGNMENTS OF
 CYCLOADDUCTS, CHEMICAL SHIFTS IN δ

Carbon No.	9a	9b	15a	15d [#]
C-3	73.1	71.2	72.9	72.3
C-4	66.2	60.1	65.9	65.0
C-5	82.0	79.5	83.2	83.1

[#]In DMSO- d_6

The signals in **9a** were similar to the corresponding signals of **15a** with small changes attendant upon changes in aromatic substituents which affect the ^1H - and ^{13}C NMR chemical shifts in the benzylic 3- and 5-positions. Hence cycloadduct **9a** was 3,4-*trans*-4,5-*trans*-2-phenyl-3,5-di(4'-chlorophenyl)-4-carbomethoxy isoxazolidine belonging to series a type of cycloadducts, arising out of *meta*-channel *endo*-carbonyl-*exo*-aryl approach of **6** to the nitrone [2].

The positions of attachment of aryl rings at C-3 and C-5 were confirmed from COSY-LR assignments of **9a** and **9b** which showed long range couplings of H-3 and H-5 with *ortho*-aryl protons. **9b** was therefore diastereoisomeric with **9a**, having a 3,4-*cis*-4,5-*trans* configuration arising from the *meta*-channel *exo*-carbonyl-*endo*-aryl approach of **6** to the nitrone [2]. The relative configuration of C-4 and C-5 were fixed from the *E*-configuration of the starting *E*-methyl cinnamate.

The structure and stereochemistry of the other cycloadducts of all three series were established by comparison of the ^1H - and ^{13}C NMR characteristics of the isoxazolidine ring carbons and protons with those of **9a**, **9b** and **9c**, respectively. The major series a (**10a**, **11a**, **12a**, **13a**) showed H-3 in the region δ 5.07-5.41, H-5 in the region δ 5.28-5.47, H-4 in the region δ 3.43-3.54, $J_{3,4}$ (6.0-6.8 Hz), $J_{4,5}$ (7.6-9.0Hz); C-3 in the region δ 72.7-73.9, C-4 in the region δ 65.9-66.3, C-5 in the region δ 80.9-82.7.

In the diastereoisomeric series (**9b**-**13b**, **15b**), the H-4 and H-5 signals were more differentiated with respect to each other, H-3 moving ~0.2 ppm upfield and H-5 ~0.3 ppm downfield; H-4 shifted ~0.2 ppm downfield. All three ^{13}C -signals moved upfield: C-3 by ~2 ppm, C-4 by ~6 ppm and C-5 by ~2.5 ppm in **9b** compared to **9a**. $J_{3,4}$ and $J_{4,5}$ coupling constants were enhanced to ~9.5-10.5 Hz in this series.

The proton shifts of **9c** were markedly different from those of **9a** – H-5 moved significantly upfield (~0.9 ppm) while H-4 moved downfield by ~0.6 ppm, consequent upon the interchange of the substituents between C-4 and C-5. The magnitude of $J_{3,4}$ and $J_{4,5}$ (7.5 and 8.5Hz) suggested a 3,4-*trans*-4,5-*trans* configuration in **9c**. In the other members of the regioisomeric series (**10c**-**13c**, **15c**), the ^1H - and ^{13}C NMR characteristics of the isoxazolidine ring carbons and protons were similar to those of compound **9c**.

32 CA of C,N-disubstituted nitrones to arylidene malonates: 32CA reactions of C-aryl-N-methyl nitrones with diethyl arylidene malonates were investigated (**Scheme-II**). Studies on 32CA of N-methyl nitrones to arylidene malonates had not been investigated earlier. Our earlier publication on 32CA of arylidene malonates involved C,N-diaryl nitrones only [20].

The reactions carried out were (i) **16** with **18**, **19**, **20**; (ii) **17** with **19**, **20**. Reactions were carried out with a three-fold molar excess of the arylidene malonates in refluxing anhydrous toluene with ^1H NMR and TLC monitoring. Work-up was similar to that described earlier. ^1H NMR analysis of the post reaction mixture showed the presence of a single cycloadduct; no other products were detected within limits of NMR detection (~0.5 %). Conversions were nearly quantitative.

A remarkable increase in regio- and stereoselectivity compared to cinnamic acid esters was observed leading to the exclusive formation in the reactions of the *trans*-3,5-diaryl-4,4-dicarbomethoxy isoxazolidines. These were obtained by *meta*-channel *exo*-aryl approach of the arylidene malonates to the nitrone. NMR monitoring of reactions (both **16** and **17** with **19**) showed that these reactions with arylidene malonates bearing the electron-releasing substituent methoxy were not

Scheme-II: 32CA of C-aryl-N-methyl nitrones to diethyl arylidene malonates

successful-extensive decomposition was observed. These were not followed up.

IR spectra of the cycloadducts exhibited bands corresponding to non-conjugated esters ($\sim 1730\text{ cm}^{-1}$), 300 MHz ^1H NMR spectra showed two singlets corresponding to H-3 and H-5 (δ 4.64 and δ 5.96 respectively for **22**), thus confirming the regiochemistry of these cycloadducts. Both these protons showed long range coupling with the *ortho*-protons of aryl rings attached to C-3 and C-5.

Both these protons showed long range coupling with the *ortho*-protons of aryl rings attached to C-3 and C-5 (Fig. 1; DQF-COSY of **21**). Two carboxyl groups are attached to the diastereotopic centre C-4. Consequently the methylene protons and the methyl protons in the ethyl ester units are differentiated. Further, within each methylene group the two protons are differentiated, the mutual relationships of which were confirmed by reference to the DQF-COSY of cycloadduct **21**. The relative stereochemistry of the *N*-methyl cycloadduct **22** and hence of the other cycloadducts was confirmed by XRD studies. Earlier we had reported the XRD analysis of *N*-phenyl cycloadduct having the same relative configuration [12].

Fig. 1. 500 MHz ^1H - ^1H DQF-COSY of cycloadduct **21** in CDCl_3

Compound **22** was recrystallized from methanol to obtain single crystals. Diffraction data were recorded on a Bruker Smart Apex II CCD area detector diffractometer operating the $\text{MoK}\alpha$ radiation ($\lambda = 0.7107\text{ \AA}$). Crystals were orthorhombic (space group $\text{Pca}21$) with cell parameters $a = 16.582(6)\text{ \AA}$; $b = 10.482(4)\text{ \AA}$; $c = 25.442(10)\text{ \AA}$; $\alpha = \beta = \gamma = 90^\circ$. The X-ray crystallographic study showed an all *trans*-configuration: H-3 and H-5 were *trans*-oriented, additionally the N-lone pair was *trans*- to H-3. Two optical antipodes were present in the unit cell which had a two-fold alternating axis of symmetry. The ORTEP projection is shown in Fig. 2. The numberings of structures as given in these projections are those provided in the X-ray crystallographic analysis outputs.

Conclusion

The results of 32CA reactions between four differently substituted *C,N*-diaryl nitrones with four methyl *E*-cinnamates, bearing different aryl substituents, were investigated. The results can be summarized as follows: (i) The reactions proceeded

Fig. 2. X-ray crystallographic analysis of cycloadduct **22**-ORTEP projection

with high regioselectivity to give mainly 2,3,5-triaryl isoxazolidine adducts; (ii) the major product belonged to the 3,4-*trans*-4,5-*trans* series, obtained by the *meta*-channel, *endo*-carbonyl-*exo*-aryl approach of the methyl cinnamate; (iii) stereoselectivity overwhelmingly favoured the 3,4-*trans*-4,5-*trans* adducts (*meta*-channel, *endo*-carbonyl-*exo*-aryl approach of the methyl *E*-cinnamate) over the 3,4-*cis*-4,5-*trans* adducts (*meta*-channel, *exo*-carbonyl-*endo*-aryl approach); (iv) the regioisomeric isomers (*ortho*-channel) were obtained only in slight amounts; (v) the product ratios of cycloadducts of series a:b:c were 88-91: 7-9: 2-4; (vi) product ratios were essentially similar even with changes of substituents on either of the reactants. This is in contrast to 32CAs of α,β -unsaturated amides to *C,N*-diaryl nitrones [12,16], where changes in aryl substituents affected the regioselectivities.

32CA reactions of *C*-aryl-*N*-methyl nitrones with diethyl arylidene malonates were investigated, as these had not been investigated earlier. A remarkable increase in regio- and stereoselectivity compared to cinnamic acid esters was observed leading to the exclusive formation in the reactions of the *trans*-3,5-diaryl-4,4-dicarboxy isoxazolidines by a *endo*-aryl *meta* channel approach of the 2π component.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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