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# Tandem reorganisation of 1,3-dipolar cycloadducts of C-(4-oxo-4*H*[1]benzopyran-3-yl)-*N*-phenylnitrone and allenic esters, leading to novel functionalized benzo[*b*]indolizines

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***Abstract*** : C-(4-oxo-4*H*[1]benzopyran-3-yl)-*N*-phenylnitrone (**1**) adds regiospecifically to the $C_2$-$C_3$ $\pi$-bond of allenic esters (**2a-c**) and the 1,3-dipolar cycloadducts formed undergo a series of intramolecular reorganisations including an intramolecular (4+2) cycloaddition, *in situ*, to yield novel functionalized benzo[*b*]indolizines (**3a-c**), in good yields. © 1998 Elsevier Science Ltd. All rights reserved.

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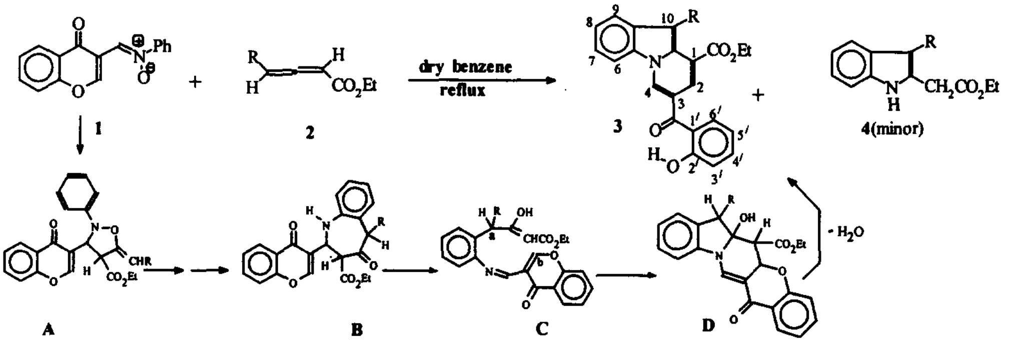
Allenes have been recognised as valuable synthons and are being extensively employed in the synthesis of a variety of molecules.[1] These are generally involved in synthesis through a cycloaddition step which provides easily functionalisable cyclic structures having an *exo*-alkylidene moiety. Recently, 1,3-dipolar cycloadducts of nitrones and allenes have been reported[2] to undergo rearrangements yielding a variety of heterocyclic systems. In continuation of our investigations on cycloadditions of allenes,[3] we report here that C-(4-oxo-4*H*[1]benzopyran-3-yl)-*N*-phenylnitrone (**1**) undergoes regiospecific cycloadditions to the $C_2$-$C_3$ $\pi$ bond of allenic esters (**2a-c**) and the formed cycloadducts undergo a series of tandem intramolecular transformations to afford novel functionalized benzo[*b*]indolizines (**3a-c**) in good yields; the minor products (scheme 1) include 2-ethoxycarbonylmethyl-indoles (**4a-c**).



| R | Reaction time/h | Product(% yield) | |
|---|---|---|---|
| H | 22 | 3a (35) | 4a (5) |
| Me | 16 | 3b (55) | 4b (~1) |
| Et | 14 | 3c (60) | 4c (<1) |

**Scheme 1**

Refluxing an equimolar solution of nitrone[4] and allenic ester (**2a-c**)[3] in dry benzene, under anhydrous conditions and column chromatographic separation of the residue obtained on evaporation of solvent, yielded **3a-c** as red to orange-red needles ($CCl_4$-hexane) along with indoles (**4a-c**).[5] The assigned structures of the benzoindolizines (**3a-c**) are based on rigorous spectroscopic analysis and microanalytical data; complete $^1H$ and $^{13}C$ NMR assignments for **3a** are included.[5b] A highly characteristic resonance in the $^{13}C$ NMR spectrum of **3a**

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was that of C10 which appeared at δ 97.94[cf.6]; in case of **3b,c** the C10 resonance (quat. carbon) appeared at δ 105.34 and 112.00, respectively.

Mechanistically, the plausible route to formation of the benzoindolizines involves rearrangement of initially formed 5-*exo*-alkylidene-isoxazolidines (**A**) to tetrahydrobenzazepinones (**B**)[cf.2] followed by cleavage of the azepinone ring by a retro-Mannich reaction[2a,b] leadimg to a ring-opened intermediate **C** which cyclizes to **D**, and the latter, after dehydration and chromone ring opening, yields benzoindolizine (**3a-c**); opening of chromone rings is reported to be quite facile.[7] Alternatively, hydrolytic cleavage of C=N in **C** followed by intramolecular condensation would lead to the indole (**4**).[cf.2] It may be mentioned here that in the proposed scheme the cyclization in **C** has been indicated as a concerted ($4\pi+2\pi$) process , however, a stepwise or highly non-synchronous cyclization cannot be ruled out; in the latter case the high electrophilicity of the C2 of chromone[7] ($C_b$ in **C**) may be crucial and experiments are being taken up to verify this.

To rationalize the higher yields of indolizines and shorter reaction times in the case of **2b** and **c** (scheme 1), molecular modeling, employing dtmm (version 2.0) of intermediate **C** was helpful. The energy minimized model of **C** revealed that in its lowest energy conformation the heterodienic component and the enol-π systems are parallel as required for cycloadditon. The molecular modeling further revealed that conformational constraints imposed by alkyl substituents at $C_a$ lead to further compacted structures, increasing the proximity between diene and dienophilic components in the intermediate **C**, and this may be responsible for enhanced yields of indolizines from allenic esters **2b** and **2c**; these observations are being further verified.

## References and Notes

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5 (a).These reactions are also completed at room temperature by constant stirring of reaction mixtures for extended periods ( 3-5 days) with same overall and relative yields of products.

(b) **3a:** Red needles ($CCl_4$:Hexane, 1: 9), mp 114-115°C, Anal. Calc. for $C_{22}H_{17}O_4N$: C, 73.54; H, 4.74; N, 3.89 %. Found : C, 73.74; H, 4.98; N 3.99 %. UV (Hexane): $\lambda_{max}$ 382.5, 330.5, 290.0, 285.0, 265.0 nm; IR (KBr):$\nu_{max}$ 3060 (-OH), 3015(s), 1715($CO_2Et$), 1624(C=O), 1600(br), 1483(s), 1458(s), 1422(m), 1352(m), 1333(m), 1304(m), 1288(s), 1265(m), 1213(m), 1198(s) $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): δ 11.51(s, 1H, -OH), 8.99(s, 1H, C4-H), 8.11(s, 1H, C2-H), 7.80 & 7.76 ( doublets, 1 H each, $J$ = 8.02 & 7.62 Hz, C6-H & C9 -H), 7.63( dd, 1H, $J$ = 1.35 & 7.91 Hz, C6′-H), 7.56(t, 1H, $J$ = 7.52 Hz, C4′-H), 7.48(t, 1H, $J$ = 6.65 Hz, C7-H), 7.46(s, 1H, C10-H), 7.39(t, 1H, $J$ = 7.60 Hz, C8-H), 7.03(d, 1H, $J$ = 8.24 Hz, C3′-H), 6.90(t, 1H, $J$ = 7.52 Hz, C5′-H), 4.40( q, 2H, $J$ = 7.12 Hz, $-OCH_2$), 1.41(t, 3H, $J$ = 7.12 Hz, $-CH_3$); $^{13}C$ nmr ($CDCl_3$): δ 195.10(C=O), 164.66( $CO_2$-), 162.61(C2′), 136.21(C4′), 133.97(C4), 132.37(C10a), 131.88(C6′), 131.26 & 130.50 (C5a & C9a), 128.02(C2), 125.19(C7), 121.86(C8), 121.62(C9), 120.12(C1) 119.27(C3), 119.06(C5′), 118.79(C3′), 117.49(C1′), 110.62(C6), 97.93(C10), 61.50($-OCH_2$), 14.38($-CH_3$); Mass m/z: 360 (20,$M^++1$), 359(50, $M^+$), 286 (20, $M^+-73$), 91(100). **4a**, a viscous oil, identified from its spectral data.[2a] **3b**, Orange red needles($CCl_4$:Hexane,1: 9), mp123-124°C; **3c**, Red needles($CCl_4$:Hexane,1:4), mp 68-69°C.

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