## Intramolecular 1,4-Dipolar Cycloadditions utilizing Heteroaromatic Betaines

## Kevin T. Potts\* and Maurice O. Dery

Department of Chemistry, Rensselaer Polytechnic Institute, Troy, New York 12180, U.S.A.

anhydro-2-(2-Allyloxyphenyl)-3,5-diphenyl-4-hydroxy-6-oxo-1,3-thiazinium hydroxide and the corresponding ethynyl derivative underwent ready thermal 1,4-dipolar cycloaddition to give a 1:1-cycloadduct (whose structure was determined by X-ray crystallography) in a highly regio- and stereo-selective cycloaddition and 1,3-diphenyl-2*H*-benzo[*h*]pyrano[4,3-*b*]pyrid-2(1*H*)-one, respectively; no cycloaddition was observed, however, on increasing the alkenyl chain by one carbon atom, rearrangement of the thiazinium nucleus to a substituted quinol-4-one being the preferred reaction pathway.

Although intramolecular 1,3-dipolar cycloadditions<sup>1</sup> are becoming an increasingly viable synthetic approach to a variety of complex ring systems, there have been no reports in the literature of the potentially equally as versatile intramolecular 1,4-dipolar cycloadditions. Closely related, however, are the intramolecular cycloadditions of several 4,6dihydroxypyrimidines<sup>2</sup> with alkenic–alkynic side-chains to give stable 1:1-cycloadducts as well as annulated pyridines by loss of HNCO from the intermediate cycloadduct. These cycloadditions may be rationalized either in terms of a heteroaromatic betaine containing a 1,4-dipole or as involving a cyclic azadiene.



We have found that the heteroaromatic betaine (3) containing a 1,4-dipole readily undergoes intramolecular cycloaddition with suitably situated alkenyl and alkynyl side-chains and that the cycloaddition is very sensitive to the alkenyl chain length. Reaction of salicylanilide with allyl bromide in acetone- $K_2CO_3$  readily gave the allyl derivative  $\dagger$  (1; X = O, R = H, n = 1) [m.p. 58—60 °C;  $v_{CO}$  1655 cm<sup>-1</sup>;  $M^+$  253 (77%)] which was converted into the thioamide (1; X = S, R = H, n = H)1) with Lawesson's reagent<sup>3</sup> [yellow irregular prisms, hexane, 71%, m.p 90–92 °C;  $M^+$  269 (100%)]. The thioamide (1; X = S, R = H, n = 1) and (chlorocarbonyl)phenylketene (2) in dry tetrahydrofuran (THF)-Et<sub>3</sub>N at room temperature readily formed anhydro-2-(2-allyloxyphenyl)-3,5-diphenyl-4-hydroxy-6-oxo-1,3-thiazinium hydroxide (3; R = H, n = 1) [orange prisms, acetone, 46%; m.p. 184 °C decomp.; v<sub>CO</sub> 1655, 1600 cm<sup>-1</sup>; (M + 1) 414 (9%)], which when refluxed in toluene (3 h) gave in a highly regio- and stereo-selective cycloaddition colourless plates of the cycloadduct (4; R = H)[EtOH; 84%, m.p. 198-200 °C; (M + 1) 414 (25%); <sup>1</sup>H n.m.r. (CDCl<sub>3</sub>, 200 MHz) & 2.22 (dd, 1, J<sub>8a,8b</sub> 12.90, J<sub>7,8b</sub> 4.89 Hz, H<sub>8b</sub>), 3.23 (m, 2, J<sub>7,8a</sub> 11.56 Hz, H<sub>8a</sub>, H<sub>7</sub>), 4.27 (m, 1, J<sub>gem</sub> 11.6,  $J_{7,CH_{2O}}$  11.4 Hz, OCH<sub>2</sub>), 4.53 (dd, 1,  $J_{7,CH_{2O}}$  4.29 Hz, OCH<sub>2</sub>), 6.50–7.50 (m, 14, aromatic)]. The structure of this product, especially the configuration at C-7, was confirmed by a single crystal X-ray determination which is shown in Figure 1.‡ Increase in the alkenyl chain length by one carbon atom

‡ Crystal data: C<sub>25</sub>H<sub>19</sub>NO<sub>3</sub>S, M = 413, space group  $P2_1/a$  (no. 14), a = 9.450(2), b = 10.498(2), c = 20.048(4) Å,  $\beta = 95.54(2)^\circ$ , U = 1979.5(7) Å<sup>3</sup>, Z = 4,  $D_c = 1.39$  g cm<sup>-3</sup>, crystal size  $= 0.1 \times 0.34 \times 0.32$  mm, Mo- $K_{\alpha}$  radiation,  $\lambda = 0.71069$  Å,  $\mu = 1.9$  cm<sup>-1</sup>,  $\omega$ -scan range  $= 2^\circ + [2\theta(K_{\alpha 1}) - 2\theta(K_{\alpha 2})]$ ,  $2\theta_{max} = 48^\circ$ , 3749 observed reflections; 3117 with  $I > 3\sigma(I)$  used in the structure refinement to obtain R = 5.44,  $R_w = 4.29\%$ .

Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1, 1986.



Figure 1. Molecular structure of (4). Some selected bond lengths (Å) and angles(°): N(1)-C(1b), 1.440(4); N(1)-C(10b), 1.476(4); C(1b)-C(6b), 1.378(5); C(2)-C(3), 1.554(4); C(3)-C(4), 1.557(4); C(4)-C(4), 1.557(4); CC(4a), 1.522(5); C(4a)-C(10b), 1.529(5); O(6)-C(6a), 1.366(4); C(10b)-S(12), 1.859(3); C(11)-S(12), 1.776(4); N(1)-C(2), 1.375(4); C(2)-O(2), 1.206(4); C(3)-C(31), 1.522(5); C(3)-C(11), 1.552(5); C(4a)-C(5), 1.499(5); C(5)-O(6), 1.432(5); C(11)-O(11), 1.202(4); C(1b)-N(1)-C(2), 117.9(2); C(2)-N(1)-C(10b), 117.3(2); N(1)-C(10b), N(1)-C(10b), 117.3(2); N(1)-C(10b), 117.3( C(1b)-C(6b), 119.7(3); N(1)-C(2)-C(3), 113.3(3); C(2)-C(3)-C(31),110.5(3); C(31)-C(3)-C(4), 113.6(3); C(31)-C(3)-C(11), 111.5(3); C(3)-C(4)-C(4a), 112.2(3); C(4)-C(4a)-C(10b), 111.1(3); C(4a)-C(4a)-C(4a)-C(4a), 112.2(3); C(4a)-C(4a)-C(4a)-C(4a)-C(4a), 112.2(3); C(4a)-C(4a)C(5)-O(6), 112.4(3); C(6a)-C(10a)-C(10b), 119.4(3); N(1)-C(10b)- $\begin{array}{l} C(4a), \ 109.3(2); \ C(4a)-C(10b)-C(10a), \ 111.1(3); \ C(4a)-C(10b)-S(12), \ 106.1(2); \ C(3)-C(11)-O(11), \ 124.5(3); \ O(11)-C(11)-S(12), \end{array}$ 120.5(3); N(1)-C(2)-O(2), 123.4(3); O(2)-C(2)-C(3), 123.3(3);C(11), 107.5(3); C(4)-C(4a)-C(5), 110.6(3); C(5)-C(4a)-C(10b), 108.6(3); C(5)-O(6)-C(6a), 115.4(3); O(6)-C(6a)-C(10a), 124.6(3); N(1)-C(10b)-C(10a), 113.4(3); N(1)-C(10b)-S(12), 107.9(2);C(10a)-C(10b)-S(12), 108.8(2); C(3)-C(11)-S(12), 115.0(2): C(10b)-S(12)-C(11), 96.3(2).

apparently distorted the geometry of the cycloaddition transition state sufficiently so that orbital overlap did not occur, and no cycloadduct was obtained. Instead, thermal rearrangement of the thiazinium nucleus to the quinol-4-one (5) resulted, this rearrangement being analogous to that observed<sup>4</sup> previously in intermolecular cycloadditions. Thus, salicylanilide and 4-bromobut-1-ene gave (1; X = O, R = H, n = 2) [colourless prisms, Et<sub>2</sub>O-hexane, 80%, m.p. 58—60 °C; (M + 1) 268 (100%)] which was converted into the corresponding thioamide (1; X = S, R = H, n = 2) [yellow needles, hexane, 53%, m.p. 57—58 °C; v<sub>NH</sub> 3280 cm<sup>-1</sup>; (M + 1) 284 (100%)]. Reaction of this with (2) gave the thiazinium betaine (3; R = H, n = 2) [orange prisms, acetone, 52%, m.p. 172—174 °C

 $<sup>^{\</sup>dagger}$  All products reported gave satisfactory (±0.4% for C, H, N) analytical values.



decomp.;  $v_{CO}$  1655, 1600 cm<sup>-1</sup>; (M + 1) 428 (0.4%)]. When this betaine was heated in boiling toluene for 24 h, the quinol-4-one (5) was obtained [colourless needles, CHCl<sub>3</sub>hexane, 23%, m.p., 262–263 °C;  $v_{CO}$  1615 cm<sup>-1</sup>; (M + 1) 368 (100%)]. Although a methyl group attached to C-2 of the alkenyl chain *viz.*, (3; R = Me, n = 1) did not prevent cycloaddition, the yield of the corresponding cycloadduct was reduced to <10%.

The behaviour of (4; R = H) on heating at its melting point is of particular interest. Carbonyl sulphide was extruded and the tricyclic system (6) was obtained in 78% yield via a 1,5-sigmatropic shift of 7-H [colourless microprisms, EtOH, m.p. 150—152 °C; v<sub>CO</sub> 1665 cm<sup>-1</sup>;  $M^{+*}$  353 (34%); <sup>1</sup>H n.m.r. (CDCl<sub>3</sub>, 200 MHz)  $\delta$  2.78 (d, 2,  $J_{3,4}$  7.80 Hz, 4-H), 4.00 (m, 1, 3-H), 4.71 (br.q, 2,  $J_{gem}$  14.90 Hz, OCH<sub>2</sub>), 6.45—7.38 (m, 14, aromatic)].

An alkynyl side chain in (3) underwent cycloaddition more readily than the corresponding alkenyl group. Salicylanilide and prop-2-ynyl bromide in acetone- $K_2CO_3$  gave (7; X = O) 565

[colourless needles, 85%, m.p. 120-122 °C; v<sub>NH</sub> 3360 cm<sup>-1</sup>,  $\delta_{C=C}$  2121 cm<sup>-1</sup>; v<sub>CO</sub> 1715 cm<sup>-1</sup>; (M + 1) 252 (100%); <sup>1</sup>H n.m.r. (CDCl<sub>3</sub>, 200 MHz) & 2.70 (t, 1, C=CH), 4.91 (d, 2, OCH<sub>2</sub>) 8.50-6.84 (m, 9, aromatic), 9.82 (s, 1, NH)] which with Lawesson's reagent gave (7; X = S) [yellow prisms, hexane, 40%, m.p. 69–70 °C;  $v_{C=C}$  2130 cm<sup>-1</sup>; <sup>1</sup>H n.m.r. (CDCl<sub>3</sub>, 200 MHz) & 2.55 (t, 1, C=CH), 4.81 (d, 2, OCH<sub>2</sub>), 7.80–7.13 (m, 9, aromatic), 10.90 (s, 1, NH); (M + 1) 268 (100%)]. This thioamide was readily converted into (8) with (2) [orange prisms, benzene, 81%, m.p. 176-177 °C decomp.;  $v_{C=C}$  2110 cm<sup>-1</sup>;  $v_{CO}$  1655, 1600 cm<sup>-1</sup>; (*M* + 1) 412 (7%)], and on heating at 105 °C for 1.5 h (8) gave 1,3diphenyl-2*H*-benzo[*h*]pyrano[4,3-*b*]pyrid-2(1*H*)-one (10)[yellow, irregular prisms, EtOH, 66%, m.p. 167–168 °C; v<sub>CO</sub>  $1640 \text{ cm}^{-1}$ ; (M + 1) 352 (100%); <sup>1</sup>H n.m.r. (CDCl<sub>3</sub>, 200 MHz)  $\delta$  4.95 (s, 2, OCH<sub>2</sub>), 6.31–7.81 (m, 15, aromatic)], formed by thermal elimination of COS from the intermediate cycloadduct (9).

The above cycloadditions illustrate the potential of this approach to carbon–carbon bond formation as a route to complex systems as well as polycyclic heterocycles. These cycloadditions are particularly striking as intermolecular cycloadditions of thiazinium betaines with alkynic and alkenic dipolarophiles do not occur.<sup>4</sup> Numerous other ring systems analogous to (3) are known,<sup>5</sup> giving this synthetic approach considerable potential for further development.

Received, 6th January 1986; Com. 018

## References

- 1 For a recent review, see '1,3-Dipolar Cycloaddition Chemistry,' vols. 1-2, ed. A. Padwa, John Wiley & Sons, New York, 1984.
- 2 P. G. Sammes and R. A. Watt, J. Chem. Soc., Chem. Commun., 1975, 502; L. B. Davies, P. G. Sammes, and R. A. Watt, *ibid.*, 1977, 664.
- 3 S. Scheibye, B. S. Pederson, and S.-O. Lawesson, *Bull. Soc. Chim. Belg.*, 1978, **87**, 229, 299; see also I. Thomsen, K. Clausen, S. Scheihye, and S.-O. Lawesson, *Org. Synth.*, **62**, 158.
- 4 K. T. Potts, R. Ehlinger, and W. M. Nichols, J. Org. Chem., 1975, 40, 2596.
- 5 For a review see W. Friedrichsen, T. Kappe, and A. Bottcher, *Heterocycles*, 1982, **19**, 1083.