Cycloaddition of Cyclic Vinyl Ethers to an Isoquinolinium Salt: Application to the Preparation of a Model *C*-Naphthylglycoside

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The cycloaddition of cyclic enol ethers, including sugar glycals, to 2-(2,4-dinitrophenyl)isoquinolinium chloride leads to new substituted naphthaldehydes in useful yields.

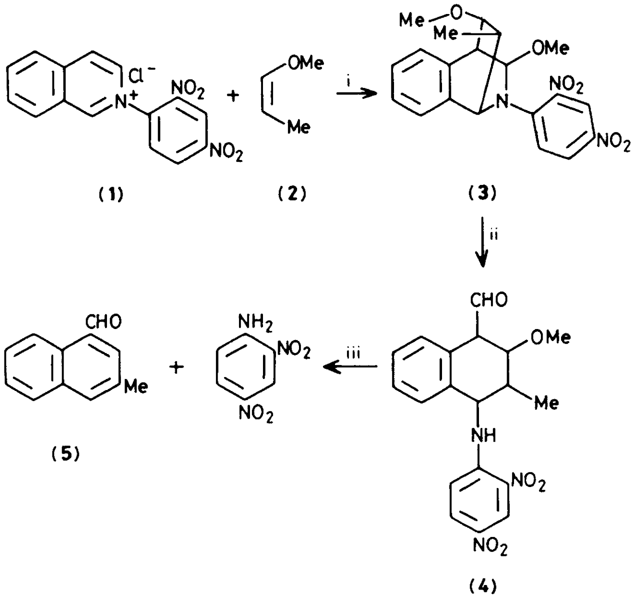
The preparation of *C*-glycosides is a research problem of current interest.[1] Of major importance are the *C*-arylglycosides such as nogalamycin, averufin, carminic acid, and vineomycin.[2] Recently, Sammes has reported a synthesis of a fragment of nogalamycin where the glycoside portion is constructed *de novo* from an acetophenone.[3] We report a simple method that permits the merger of an intact carbohydrate with an aromatic species to create an additional functionalized aromatic ring under mild conditions.

Our method is an extension of the Bradsher–Falck cycloaddition of vinyl ethers to isoquinolinium salts.[4] Thus, isoquinolinium salt (**1**) and vinyl ether (**2**) react to form Diels–Alder adduct (**3**) which is opened to amino aldehyde (**4**) which aromatizes to (**5**). Our contribution, outlined in Table 1, was

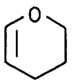
Table 1. Reactions of cyclic enol ethers with isoquinolinium salt (**1**).

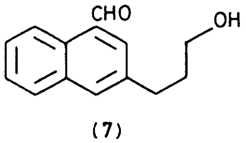
Vinyl ether	Temp./°C	Time	Product[e]	Yield[f]/%
(**6**)	40	24 h	(**7**)	82
(**8**)[a]	0	15 min	(**9**)	86
(**10**)	40	24 h	(**11**)	72
(**12**)	60	60 h	(**13**)	58
(**14**)[b]	No reaction			
(**15**)	40	8 h	(**16**)	73
(**17**)[a]	0—R.t.[d]	24 h	(**18**)	77
(**19**)[c]	50	60 h	(**13**)	55

[a] Ref. 10. [b] Ref. 11. [c] Ref. 7. [d] R.t. = room temperature. [e] Structures were assigned from n.m.r. data. In addition, the tetra-acetate of (**13**) had the expected high resolution mass spectrum. [f] Overall yield based on isoquinolinium salt as limiting reagent.



Scheme 1. i, MeOH, $CaCO_3$; ii, Amberlyst 15 resin, aqueous tetrahydrofuran; iii, aqueous MeOH and either NaOH or K_2CO_3.


(**6**)



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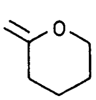
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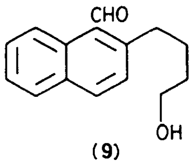

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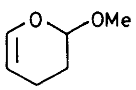
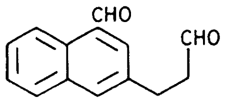
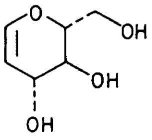


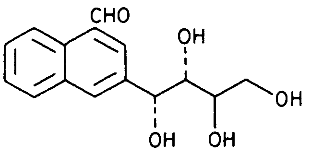
(**10**)



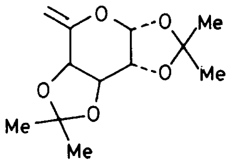
(**11**)



(**12**)

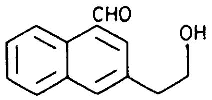


(**13**)

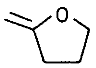


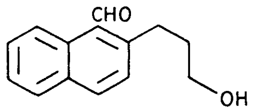
(**14**)


(**15**)

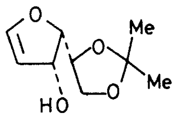


(**16**)


(**17**)



(**18**)



(**19**)

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to demonstrate that cyclic vinyl ethers, including sugar glycals,[5] are useful substrates for this reaction, Scheme 1.

Hence, the new naphthalenes that are the end result of the simple procedure have a functionalized side-chain. We have shown that endocyclic and exocyclic vinyl ethers in both five- and six-membered rings are suitable reactants. Generally the exocyclic methylene substrates react more rapidly than the endocyclic vinyl examples. In example (**10**), we show that a vinyl ether with an oxygen which is also part of an acetal is sufficiently reactive. The one case of no useful reaction is the 5,6-dehydrogalactose derivative (**14**). Since (**10**) did react the failure may be steric in origin.[6] The reactions of the two different endocyclic sugar glycals (**12**) and (**19**) were uneventful, and after workup, afforded the same model *C*-naphthylglycoside (**13**).

With general methods for preparing sugar glycals either from other sugars[7] or by the Diels–Alder reaction of aldehydes,[8] and with a wide assortment of isoquinolines available,[9] the potential for preparing *C*-arylglycosides appears to be unlimited.

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References

1 L. A. Reed, III, Y. Ito, S. Masamune, and K. B. Sharpless, *J. Am. Chem. Soc.*, 1982, **104**, 6468; M. D. Lewis, J. K. Cha, and Y. Kishi, *ibid.*, p. 4976; S. Danishefsky and J. F. Kerwin, Jr., *J. Org. Chem.*, 1982, **47**, 3803; A. P. Kozikowski and K. L. Sorgi, *Tetrahedron Lett.*, 1982, 2281; H. Ohrui, G. H. Jones, J. G. Moffatt, M. L. Maddox, A. T. Christensen, and S. K. Byram, *J. Am. Chem. Soc.*, 1975, **97**, 4602; S. Czernecki and V. Dechavanne, *Can. J. Chem.*, 1983, **61**, 533; U. Hacksell and G. D. Davies, Jr., *J. Org. Chem.*, 1983, **48**, 4144; R. M. Williams and A. O. Stewart, *Tetrahedron Lett.*, 1983, 2715, and references therein.

2 Nogalamycin: P. F. Wiley, D. W. Elrod, D. J. Hauser, and F. J. Richard, *J. Med. Chem.*, 1982, **25**, 560; averufin: C. A. Townsend, S. G. Davis, S. B. Christensen, J. C. Link, and C. P. Lewis, *J. Am. Chem. Soc.*, 1981, **103**, 6885; carminic acid: J. C. Overeem and G. J. M. van der Kerk, *Recl. Trav. Chim. Pays-Bas*, 1964, **83**, 1023; vineomycin: K. Ohta, H. Okazaki, and T. Kishi, *Chem. Pharm. Bull.*, 1982, **30**, 762.

3 M. A. Bates and P. G. Sammes, *J. Chem. Soc., Chem. Commun.*, 1983, 896.

4 C. K. Bradsher and F. H. Day, *J. Heterocycl. Chem.*, 1974, **11**, 23; M. Sukumar and J. R. Falck, *J. Org. Chem.*, 1982, **47**, 5021, and references therein; for the intramolecular version: G. P. Gisby, P. G. Sammes, and R. A. Watt, *J. Chem. Soc., Perkin Trans. 1*, 1982, 249; D. L. Fields, T. H. Regan, and J. C. Dignan, *J. Org. Chem.*, 1968, **33**, 390; addition of dihydropyran to an acridizinium salt.

5 For a compilation of Diels–Alder reactions of carbohydrates, see R. W. Franck and T. V. John, *J. Org. Chem.*, 1983, **48**, 3269; relevant articles not included in this ref. are: P. J. Card, *ibid.*, 1982, **47**, 2169; D. D. Ward and F. Shafizadeh, *Carbohydr. Res.*, 1981, **95**, 155; D. Horton, T. Machinami, Y. Takagi, C. W. Bergmann, and G. C. Christoph, *J. Chem. Soc., Chem. Commun.*, 1983, 1164, and references cited therein; J. L. Primeau, R. C. Anderson, and B. Fraser-Reid, *J. Am. Chem. Soc.*, 1983, **105**, 5874.

6 A. J. Kirby, 'The Anomeric Effect and Related Stereoelectronic Effects at Oxygen,' Springer Verlag, Berlin, 1983, P. Deslongchamps, 'Stereoelectronic Effects in Organic Chemistry,' Pergamon Press, Oxford, 1983.

7 R. E. Ireland, S. Thaisrivongs, N. Vanier, and C. S. Wilcox, *J. Org. Chem.*, 1980, **45**, 48.

8 S. Danishefsky, J. F. Kerwin, Jr., and J. Kobayashi, *J. Am. Chem. Soc.*, 1982, **104**, 358.

9 G. Grethe, 'The Chemistry of Heterocyclic Compounds,' vol. 38, John Wiley & Sons, New York, 1981.

10 R. E. Ireland and D. Habich, *Chem. Ber.*, 1981, **114**, 1418.

11 B. Helferich and E. Himmer, *Chem. Ber.*, 1929, **62**, 2136.