The Reaction of Saccharin Derivatives with *N,N*-Diethylprop-1-ynamine: Formation of Cyclobutenyl Saccharinates and of a Spiro-oxete

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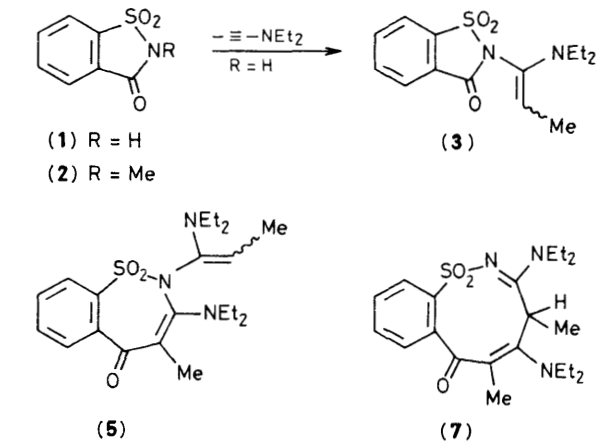
Saccharin and two equivalents of *N,N*-diethylprop-1-ynamine give a cyclobutenyl saccharinate (**4**) which, on bromination, gives the *N*-(cyclobutenyl cation)saccharin derivative (**8**), whose structure was established by *X*-ray crystallography [only preliminary *X*-ray data are available for (**4**)]; *N*-methylsaccharin reacts with one equivalent of ynamine to yield the spiro-oxete (**9**): this represents the second isolation of such a stable oxete from reaction of an ynamine with a carbonyl group.

In continuation of our studies on the reaction of 1,2-benzisothiazole 1,1-dioxides with ynamines[1] in which we observed interesting ring expansions we have examined the reaction of saccharin (**1**), its 5-chloro derivative, and *N*-methylsaccharin (**2**), with *N,N*-diethylprop-1-ynamine and now report some interesting transformations.

Saccharin (**1**) and the ynamine in acetonitrile at room temperature gave the 1-(*N*-saccharino)enamine (**3**), m.p. 105—106 °C (76.2%) [ν(CO) 1 730 cm^{-1}]† which reverted back to saccharin and *N,N*-diethylpropionamide with moisture. It had been hoped that a second molecule of ynamine could be induced to add to the carbonyl group of (**3**) and that, following ring-expansion, the *N*-enamine protecting group could be removed. Boiling a solution of (**3**) in acetonitrile (48 h) with an additional equivalent of ynamine gave a 1 : 2 adduct (**4**) (28.9%), m.p. 117.5—118 °C. Its n.m.r. spectra (^{1}H and ^{13}C) clearly eliminated structure (**5**) as well as the *N*-cyclobutenylsaccharin (**6**) (or the corresponding open-chain butadiene) possibility. Indeed, the presence of an *N*-substituted but otherwise unmodified saccharin ring system *seemed* to be ruled out by the i.r. spectrum [ν(CO) 1 640 cm^{-1}]‡ (as was a 6–5–6 fused system). On the other hand, a fused 9-membered ring structure (**7**) would have fitted all the data§ except the mass spectrum which showed the absence of a parent ion, the base peak being at *m/z* 223 ($C_{14}H_{27}N_2$). 5-Chlorosaccharin behaved similarly to give the chlorinated (**4**) (24%), m.p. 99—99.5 °C (from ethyl acetate) [ν(CO) 1 650 cm^{-1}].

Compound (**4**) and its chlorinated derivative did not give 2,4-dinitrophenylhydrazone derivatives. On the other hand, bromination of (**4**) in CCl_4–$CHCl_3$ (3 : 1 v/v) with *N*-bromosuccinimide (NBS) and benzoyl peroxide as catalyst gave orange crystals of (**8**) ($C_{21}H_{30}Br_3N_3O_3S$), (49%), m.p. 166—166.5 °C [ν(CO) 1 745 cm^{-1}],† whose structure was determined by a full single-crystal *X*-ray structure analysis, see Figure 1.

Scheme 1 is proposed to explain the results. The salt formulation for (**4**) is consistent with all its properties



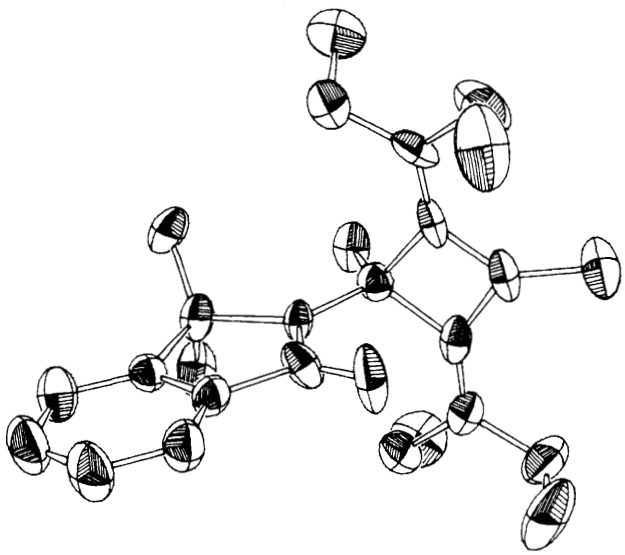
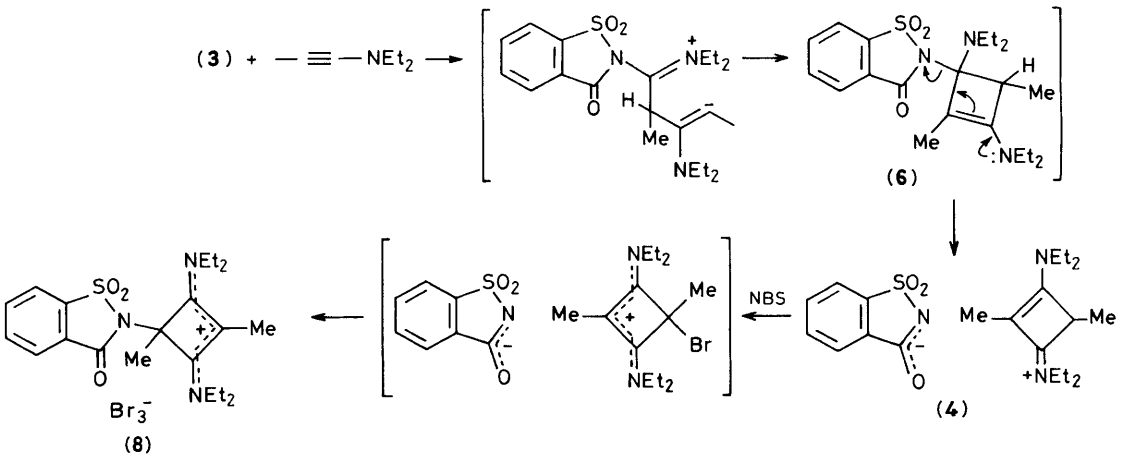


Figure 1. Molecular structure of bromination product (**8**). *Crystal data:* $C_{21}H_{30}N_3O_3S^+Br_3^-$, space group $P2_1/c$, a = 8.8950(25), b = 15.1252(97), c = 19.9853(96) Å, β = 99.42 (3)°, spherical crystal (diameter: 0.20 mm), $F(000)$ = 1288, μ(Mo-K_α) = 46.19 cm^{-1}, M_r = 644, Z = 4, D_c = 1.613 g/cm^3, U = 2652.5 Å^3, (sin θ/λ)$_{max}$ = 0.5937 Å^{-1}. A total of 4771 intensities were collected and 1495 with $I>3\sigma(I)$ were used in the analysis; R = 0.33, R_w = 0.036. The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

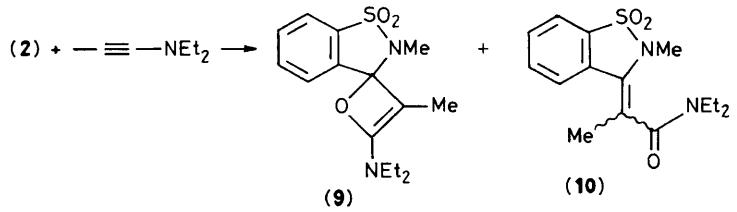
† All new compounds gave correct microanalytical, i.r., n.m.r., and mass spectral data.

‡ Saccharin and all its *N*-substituted derivatives we have studied exhibit ν(CO) at 1730 cm^{-1}.

§ The ^{13}C n.m.r. spectrum shows the presence of the disubstituted phenyl ring, a C=O and a C=N group (δ 169.6 and 167.7), two vinylic C [145.6 (=C–NEt$_2$), 101.0 (=C–Me)], and the >CHMe group [43.9 (d)], while the ^{1}H n.m.r. spectrum confirmed the presence of the latter group [δ 1.37 (d, 3H, *J* 14 Hz, Me), 4.0 (qd, 1 H, *J* 14, 1.9 Hz, >CH– coupled with α- and γ-Me groups)].



Scheme 1



including the low ν(CO) (O=C–N̄– ⟷ Ō–C=N) and its reaction with dry HCl gas to give saccharin. [Chlorinated (**4**) gives 5-chlorosaccharin, m.p. 185—186 °C, under these conditions.] The relatively low melting point of (**4**) finds precedence in a number of salts of saccharin with amines, *e.g.* aniline salt, m.p. 90 °C,[2] 1-naphthylamine salt, m.p. 105 °C.[3] Formation of stabilized cyclobutenyl cations from ynamines in the presence of nucleophiles is known.[4] A crystallographic study of (**4**) established its structure beyond doubt although the resolution is poor (R = 0.15) for the saccharinate ion.

N-Methylsaccharin (which no longer has an acidic hydrogen) reacted with ynamine to give spiro-oxete (**9**) (15.3%),¶ m.p. 116—117 °C, and the amide (**10**) (12.7%), m.p. 131—132 °C.†[6] The formation of an oxete intermediate in the reaction of ynamines with ketones which leads to α,β-unsaturated amides has been proposed often but, to our knowledge, only one example of its isolation has been reported.[7]

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¶ I.r. (KBr) 1360, 1190 cm^{-1} (SO_2); ^{1}H n.m.r. ($CDCl_3$) δ 8.0—7.4 (4H, m, ArH), 3.45—3.00 (4H, 2q, J 7 Hz, $2CH_2$), 2.8 (3H, s, CH_3), 1.95 (3H, s, CH_3), 1.15 (6H, t, J 7 Hz, $2CH_2CH_3$); ^{13}C n.m.r. ($CDCl_3$) δ 187.8 (s, C-2 of oxete; *cf.* ref. 5), 154.2 (s, C-3 of oxete), 137.9 (s), 137.0 (s), 133.5 (d), 132.5 (d), 130.6 (d), 125.5 (d, six aromatic carbons), 110.2 (s, C-3 of benzisothiazole dioxide), 44.9 (t), 35.8 (q), 16.4 (q), 13.6 (q); mass spectrum m/z 308 ($M^{\cdot+}$).

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6 An authentic sample was prepared by treatment of saccharin *pseudo*chloride with *N,N*-diethylprop-1-ynamine to give the propionamide followed by methylation of the corresponding anion (NaOEt/EtOH) with MeI (R. A. Abramovitch and K. M. More, unpublished results).
7 M. E. Kuehne and P. J. Sheeran, *J. Org. Chem.*, 1968, **33**, 4406. However, by carrying out the reaction in diethyl ether at −50 °C instead of acetonitrile at −27 °C M. Delaunois and L. Ghosez (*Angew. Chem., Int. Ed. Engl.*, 1969, **8**, 72) isolated only the allene resulting from ring-opening of the oxete intermediate.