Tetrahedron Letters, Vol.31, No.39, pp 5669-5672, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

UNUSUAL TRANSFORMATIONS IN OXABICYCLOOCTANONES. AN APPARENT OXY-PROMOTED ELECTROCYCLIC OPENING INVOLVING FUSED CYCLOBUTANOLS[1]

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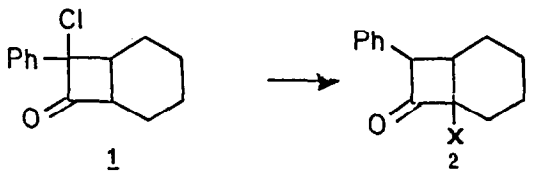
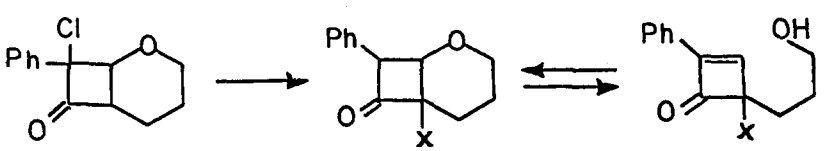
Abstract: Reaction of oxabicyclooctanone **3** with nucleophiles involves not only cine substitution but ring opening to cyclobutenones which are capable of further transformations. With azide as a nucleophile, further reactions occur, among them an oxy-promoted electrocyclic cyclobutane opening, with final formation of **8**, the structure of which was verified by X-ray diffraction.

Recently,[2] we have shown that chlorocyclobutanone **1** underwent cine substitution with a variety of nucleophiles to produce bicyclic cyclobutanones of type **2.** These reactions proceed via oxyallyl cation intermediates that react with nucleophiles at the ring junction.[3]



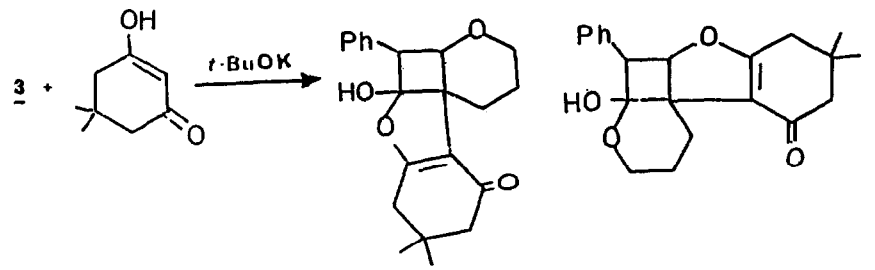
1 **2**

When we applied these reactions to the oxa analog **3**, we discovered an interesting participation by the oxygen function, that can lead first to cyclobutenones, which are of interest as vinyl ketene precursors[4], and further to unusual rearrangements. For instance, reaction of **3** with 1 equiv. of phenylthiol in the presence of Et_3N produced a cine substitution product **4**, which in the presence of acid or base exists in equilibrium with the ring opened cyclobutenone **5a** (indicated by NMR). Similarly, **3** reacted with



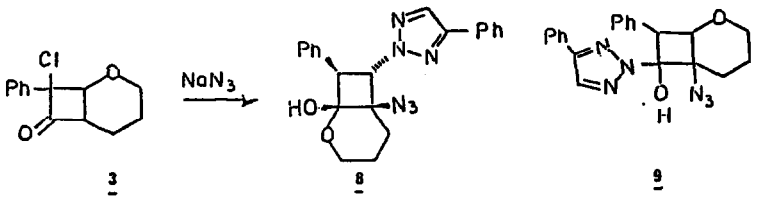
3 **4a**, X=SPh; **4b**, X=N_3 **5a**, X = SPh; **5b**, X = OMe; **5c**, X = N_3

methanol in the presence of triethylamine to produce directly the cyclobutenone **5b** (IR: 3400, 1770 cm^{-1}; NMR: vinyl singlet at 8.56, C=O at 195 ppm) in quantitative yield. By contrast, related oxabicyclooctanones underwent acid catalyzed ring opening of the cyclobutanone ring, with the 6-membered ring ether staying intact.[5]

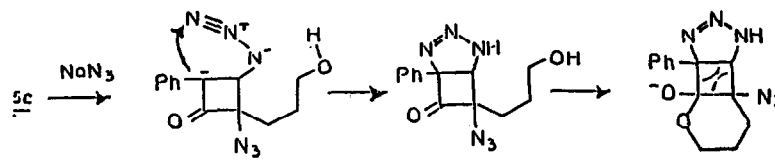


3 **6** **7**

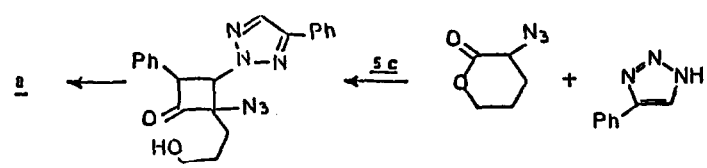
The sodium enolate of dimedone also reacted with **3** but the cine substitution product was shown by NMR to be an equilibrium mixture of the unusual hemiketals **6** and **7**,[6] of which the rearranged **7** (identified by 2D-NMR) was isolated in pure form. **7** apparently results via a cyclobutenone of type **5** (X=dimedone) which undergoes an intramolecular Michael addition by the enol of the dimedone unit followed by hemiketalization.



3 **8** **9**



11 **12** **13**



8 **16** **15a** **14**

b (SPh instead of N_3)

An unexpected transformation was observed when **3** was treated with an excess of NaN_3 in acetone at room temperature. The major product (formed together with 2 isomers) analyzed for: **3** (-Cl + N_6 + a styrene unit). IR indicated the presence of an azide function and absence of the ketone carbonyl. NMR showed the presence of two phenyl groups and what could be a triazole unit. Based on heteroCOSY experiments two structures **8** and **9**[7] fit all the data[6] and **8** proved to be the correct one as shown by X-ray diffraction studies (see Fig 1.). To explain the formation of 4-phenyl-1,2,3-triazole, the following mechanism appears plausible. The first step, formation of **4b** by cine substitution of **3** with azide ion, was followed by ring opening to the cylobutenone **5c**. Addition of NaN_3 to this conjugated ketone produced the β-azidoketone enolate **11**, which underwent cycloaddition to triazoline **12**. The latter exists in equilibrium with the hemiketal **13**. The driving force for the next step, an interesting oxy-promoted electrocyclic opening of the cyclobutane ring at room temperature, probably comes from formation of the aromatic triazole ring **14** as well as of the enol form of lactone **15**. Next it is postulated that the phenyltriazole **14** added, in a Michael addition, to another molecule of **5c**, followed by hemiketalization of **16** to **8**. As already shown for **6** and **7**, hemiketal formation appears to be favored in these cyclobutanone systems containing an appropriate hydroxy side chain.

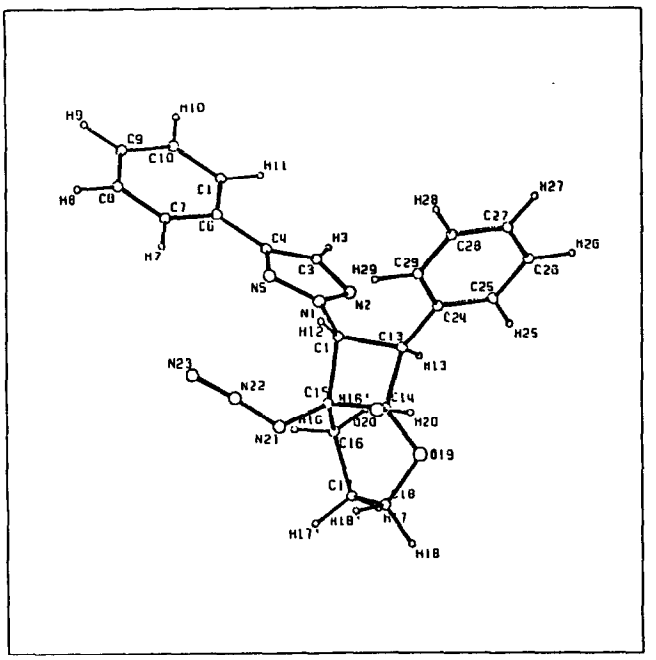


Fig 1.

CRYSTAL DATA: $C_{22}H_{20}N_6O_2$ transparent, prismatic, 0.4 x 0.3 x 0.3mm, triclinic, P1, (No. 2), a = 11.330(2), b = 14.750(2), c = 5.605(1)Å, α = 91.19(2), β = 99.25(2), γ = 81.54(2)°, from 25 reflections, T = 90K, V = 914.5(3)Å^3, Z = 2, Fw = 368.428, Dc = 1.41g/cc, μ = 0.892cm^{-1}.

To obtain further evidence for this unusual pathway, we subjected the thioether **4a** to NaN_3, as in the formation of **8**, and were able to isolate the phenylthiolactone **15b** (the analog of **15a**) and 4-phenyl-1,2,3-triazole **14**. Apparently, here **5a** got consumed before addition of phenyltriazole **14** took place. Furthermore, the methoxycyclobutenone **5b** underwent reaction with azide ions to produce an analog of **8** (MeO instead of N_3).

All compounds were completely identified by correlated ^1H and ^{13}C NMR spectra, IR, MS and in the case of **6**, **7** and **8** also by 2D-NMR experiments and **8** by X-ray diffraction studies.

Further studies on these systems are in progress.

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6. **6**, ^{13}C NMR 112.1 (C-hemiketal), 74.6 (CHO), 60.5 (CHPh); ^1H NMR 5.04 (d, J=5.5 Hz, CHO); 3.75 ppm (d, J=5.5 Hz, CHPh). **7**, ^{13}C NMR 96.2 (C-hemiketal), 83.7 (CHO), 59.7 (CHPh); ^1H NMR 4.28 (d, J=4 Hz, CHO), 3.96 (d, J=4 Hz, CHPh). **8**, **IR** 3351, 2110 cm^{-1}; ^{13}C NMR 148.4 and 131.7 (C and CH of triazole), 96.8 (C-hemiketal); ^1H NMR 5.48 (d, J=10 Hz, CH), 4.78 (d, J=10 Hz, CHPh).
7. The structure of **9** is plausible since phenyltriazole in acetone solution has been shown to exist in equilibrium with the acetone hemiaminal. Toppet, S.; Woutes, G.; Smets, G. *Org. Magn. Res.* **1978**, *11*, 578..

(Received in UK 30 July 1990)