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Cycloaddition of substituted spiroepoxycyclohexa-2,4-dienones: synthesis and X-ray crystal structure of the adducts[†]

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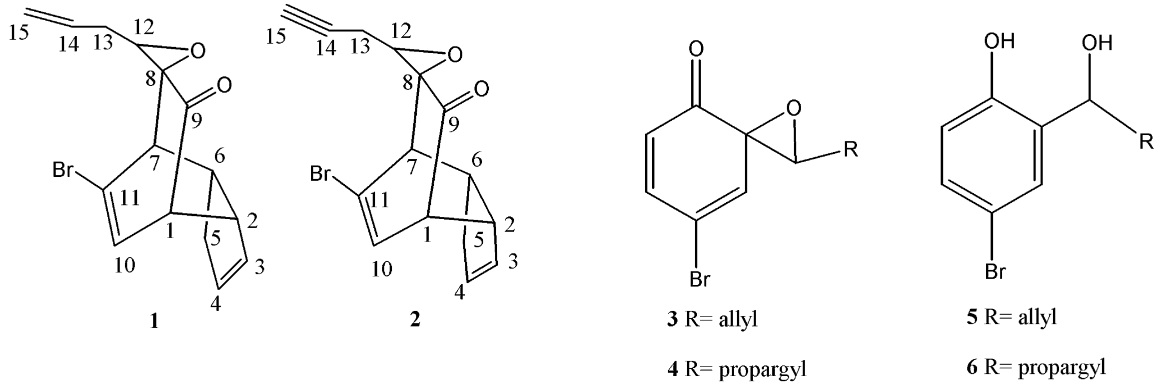
Abstract—The syntheses of the tricyclic ketoepoxides **1** and **2** from the readily available aromatic precursors **5** and **6** via cycloaddition of the spiroepoxycyclohexa-2,4-dienones **3** and **4** are described. The crystal structures of **1** and **2** were determined.

There has been a recent renewed interest in the chemistry of cyclohexa-2,4-dienones[1,2] and masked *o*-benzoquinones.[3] In particular, $\pi^{4s}+\pi^{2s}$ cycloaddition of these systems provides an efficient route to a variety of bicyclo[2.2.2]octenones that undergo a variety of reactions in the ground and excited states, leading to complex polycyclic systems which have served as precursors for diverse natural products.[1–3] In continuation of our studies in this area,[2] we required tetracyclic structures **1** and **2** containing a vinyl bromide and an alkene or alkyne tether attached to the oxirane ring. Our aim was to generate vinyl radicals by treating bromo compounds **1** and **2** with Bu_3SnH/AIBN and to probe for the intramolecular cyclization of these radicals by reaction with the allyl or propargyl multiple bonds. This did not occur. Further, it was of interest to study the compatibility of the bromo substituent and the allyl or propargyl group in the same molecule with the reaction conditions of the $NaIO_4$ oxidation described below. We wish to report here a facile synthesis of tetracyclic compounds **1** and **2** from readily available aromatic precursors **5** and **6** via their oxidation to the spiroepoxycyclohexa-2,4-dienones **3**, **4** followed by in situ trapping with cyclopentadiene (Scheme 1).

For the synthesis of compounds **1** and **2**, the aromatic precursors **5** and **6** were readily prepared from 5-bromosalicylaldehyde **7** by addition of allyl bromide[4] and



1

2

3 R= allyl

4 R= propargyl

5 R= allyl

6 R= propargyl

Scheme 1.

Keywords: tetracyclic vinyl bromides with alkene or alkyne tether; 2D NMR; X-ray crystallography.

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[†] We dedicate this communication to the memory of Professor Walter Grahn (1942–2001).

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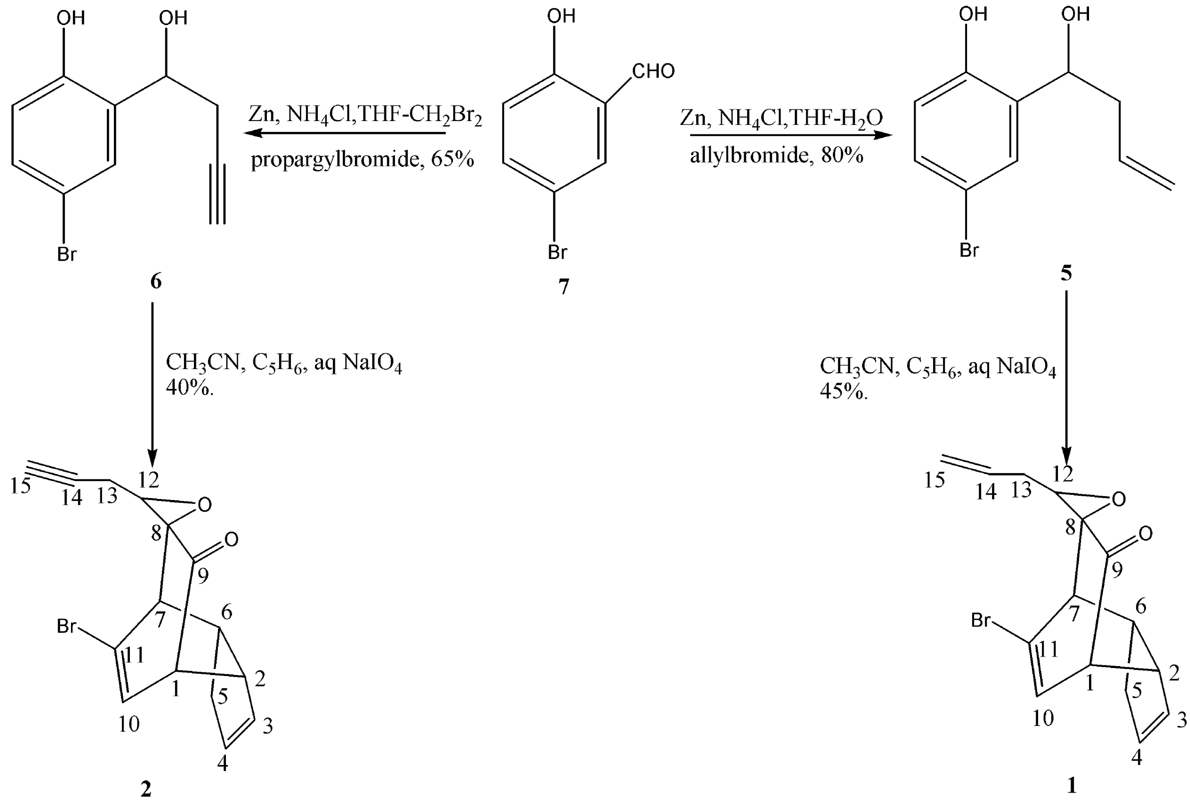

Scheme 2.

propargyl bromide,[5] respectively, in the presence of Zn–NH_4Cl (Scheme 2). Precursors **5** and **6** were oxidized with $NaIO_4$ in the presence of freshly cracked cyclopentadiene following a procedure developed in our laboratory.[2a,6] Chromatography of these products on silica gel gave the adducts **1** and **2** as crystalline solids in 45 and 40% yield, respectively. Although the spectral data of these adducts[7] (full ^1H and ^{13}C NMR assignments by 2D techniques, Table 1) clearly suggested their gross structure, their configurations, especially the orientation of the allyl and propargyl chains and the spirocentre in the oxirane ring were not easily discernible. Therefore, X-ray crystal structures of these adducts were determined (Figs. 1 and 2) that confirmed their stereochemical formulation.[8]

It may be mentioned that, although both adducts are formed as a result of regio- and stereoselective cycloaddition wherein the spiroepoxycyclohexa-2,4-dienones generated in situ behave as the 4π partners and cyclopentadiene as the dienophile 2π partner, the reaction could, in principle, give a number of products due to various possible modes of addition.[9]

In summary, the synthesis of the new tetracyclic compounds **1** and **2** from simple and readily available aromatic compounds via in situ generated spiroepoxycyclohexa-2,4-dienones followed by cycloaddition with cyclopentadiene, is described. The structure and stereochemistry of the adducts were established by X-ray single crystal analysis. This cycloaddition represents a precise example of generation of molecular complexity

Table 1. NMR data of compounds **1** and **2** [$CDCl_3$/TMS; $\delta(CDCl_3 = 77.0)$]

Compound **1**		Position	Compound **2**	
δ_C[a]	δ_H[b]		δ_C	δ_H[c]
54.3 d	3.44 dd	1	54.2 d	3.46 dd
49.7 d	3.38 m	2	49.5 d	3.37 dm
134.2 d	5.81 dq	3	134.2 d	5.81 dq
129.1 d	5.45 dq	4	129.0 d	5.45 dq
37.6 t	2.35 (α) dtt 2.71 (β) ddq	5	37.6 t	2.35 (α) dddt 2.71 (β) ddtd
37.2 d	3.10 dddd	6	37.1 d	3.09 dddd
50.7 d	2.97 t	7	50.5 d	2.95 t
61.8 s		8	61.6 s	
204.0 s		9	203.0 s	
127.6 d	6.25 dd	10	127.6 d	6.26 dd
120.9 s		11	120.6 s	
62.4 d	3.37 t	12	60.8 d	3.52 t
33.3 t	2.47 tt	13	19.6 t	2.59 (a) ddd 2.68 (b) ddd
132.2 d	5.89 ddt	14	77.9 s	
118.4 t	5.17 (*E*) dq 5.24 (*Z*) dq	15	71.5 d	2.11 t

[a] ^{13}C chemical shifts and multiplicity information from DEPT-135: C (s), CH (d), CH_2 (t).

[b] $J_{1,2}$ 2.7, $J_{1,10}$ 6.9, $J_{2,3}$ 2.2, $J_{2,4}$ 2.3, $J_{2,5\alpha(?)}$ 4.0, $J_{2,5\beta(?)}$ 2.1, $J_{2,6}$ 9.0, $J_{3,4}$ 5.6, $J_{3,5\alpha}$ 2.2, $J_{3,5\beta}$ 2.2, $J_{4,5\alpha}$ 2.3, $J_{4,5\beta}$ 2.3, $J_{5\alpha,5\beta}$ 17.6, $J_{5\alpha,6}$ 3.9, $J_{5\beta,6}$ 9.9, $J_{6,7}$ 3.5, $J_{7,10}$ 2.4, $J_{12,13}$ 6.2, $J_{13,14}$ 6.6, $J_{13,15E}$ 1.5, $J_{13,15Z}$ 1.2, $J_{14,15E}$ 10.2, $J_{14,15Z}$ 17.2, $J_{15E,15Z}$ 1.4 Hz.

[c] $J_{1,2}$ 2.6, $J_{1,10}$ 6.9, $J_{2,3}$ 2.2, $J_{2,4}$ 2.3, $J_{2,5\alpha(?)}$ 3.9, $J_{2,6}$ 8.9, $J_{3,4}$ 5.7, $J_{3,5\alpha}$ 2.2, $J_{3,5\beta}$ 2.2, $J_{4,5\alpha}$ 2.3, $J_{4,5\beta}$ 2.3, $J_{5\alpha,5\beta}$ 17.6, $J_{5\alpha,6}$ 4.2, $J_{5\beta,6}$ 10.1, $J_{6,7}$ 3.2, $J_{7,10}$ 2.5, $J_{12,13a}$ 6.0, $J_{12,13b}$ 5.9, $J_{13a,13b}$ 17.5, $J_{13a,15}$ 2.8, $J_{13b,15}$ 2.8 Hz.

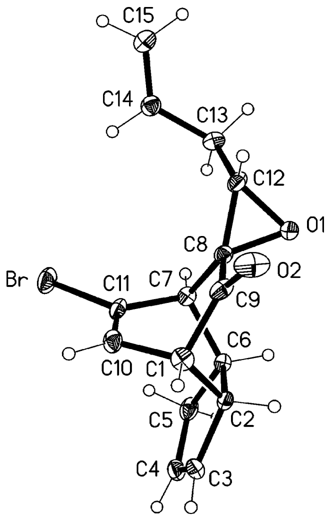

Figure 1. ORTEP diagram for compound **1**.

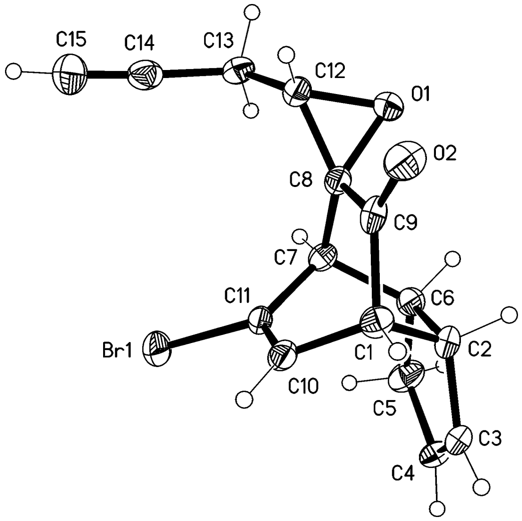

Figure 2. ORTEP diagram for compound **2**.

from simple precursors, which is an important aspect of synthetic design.[10]

Acknowledgements

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7. Data for **1**: mp 63–65°C. IR(KBr) ν_{max}: 1725 cm^{-1}. Found C, 58.43; H, 4.89%; $C_{15}H_{15}BrO_2$ requires C, 58.82; H, 4.90%. Data for **2**: mp 60–62°C. IR(KBr) ν_{max}: 1739 cm^{-1}. Found C, 59.09; H, 4.36%; $C_{15}H_{13}BrO_2$ requires C, 59.01; H, 4.20%.
8. Crystal structure determinations. Compound **1**: *Crystal data*: orthorhombic, space group *Pbca*, $a=10.3437(8)$, $b=15.5376(16)$, $c=16.4484(16)$ Å, $U=2643.5$ Å^3, $Z=8$, $T=-100$°C. *Data collection*: A crystal ca. 0.45×0.4×0.12 mm was used to record 3260 intensities on a Siemens P4 diffractometer (Mo Kα radiation, $2\theta_{max}$ 50°). *Structure refinement*: The structure was refined anisotropically on F^2 (program SHELXL-97, G.M. Sheldrick, University of Göttingen) to wR_2 0.059, R_1 0.032 for 164 parameters and 2315 unique reflections. The hydrogens were refined using a riding model or rigid methyl groups. Compound **2**: *Crystal data*: Triclinic, space group $P\bar{1}$, $a=8.0530(10)$, $b=8.1604(10)$, $c=19.766(2)$ Å, $\alpha=86.716(8)$, $\beta=85.357(10)$, $\gamma=82.766(10)$°, $U=1282.9$ Å^3, $Z=4$, $T=-100$°C. *Data collection*: A crystal ca. 0.4×0.4×0.15 mm was used to record 5169 intensities as above. *Structure refinement*: The structure was refined as above to wR_2 0.057, R_1 0.028 for 333 parameters and 4482 unique reflections.
Complete crystallographic data (excluding structure factors) have been deposited at the Cambridge Crystallographic Data Centre under the numbers CCDC-184661 (**1**), -184662 (**2**). Copies may be requested free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, England (E-mail: deposit@ccdc.cam.ac.uk), or via www.ccdc.cam.ac.uk/conts/retrieving.html
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