Tetrahedron Vol. 47, No. 26, pp. 4603-4610, 1991
Printed in Great Britain

0040-4020/91 $3.00+.00

1-OXA-2,3-CYCLOHEXADIENE ("2*H*-ISOPYRAN") : A STRAINED HETEROCYCLIC ALLENE UNDERGOING CYCLOADDITION REACTIONS WITH CHARACTERISTIC TYPO-, REGIO- AND STEREOSELECTIVITIES

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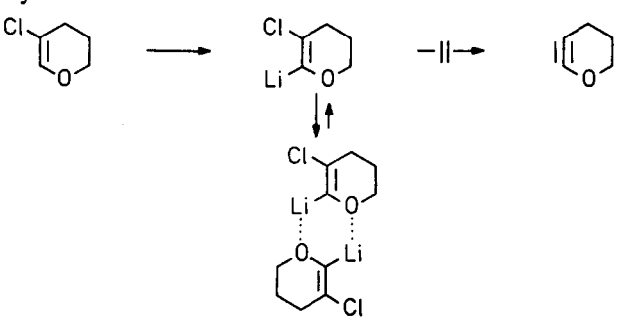
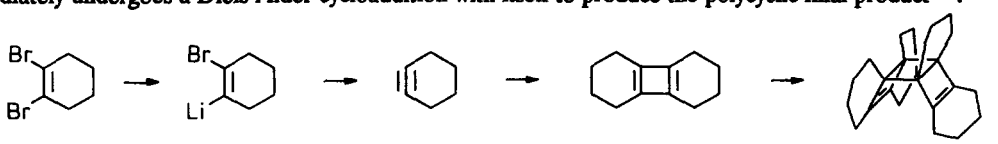
(*Received in Belgium* 21 *February* 1991)

Summary : 1-Oxa-2,3-cyclohexadiene can be readily generated by treatment of 5-bromo-3,4-dihydro-2*H*-pyran with potassium *tert*-butoxide in the presence of "18-crown-6" and can be trapped with dienes or olefins. The remarkable regio- and stereoselectivities with which [4+2] and [2+2] adducts are formed suggests a concerted, non-radical cycloaddition mechanism.

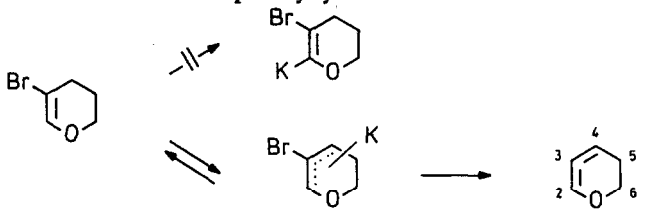
Neighboring oxygen atoms not only facilitate the replacement of carbon attached hydrogens by metal atoms but also stabilize the resulting organometallic species. Thus, if treated a few minutes with butyllithium at -75 °C, 5-chloro-3,4-dihydro-2*H*-pyran is quantitatively converted to the 6-lithiated derivative. The latter was found to be amazingly inert towards β-elimination of lithium chloride : the sole mode of decomposition observed at +80 °C is slow attack on the tetrahydrofuran solvent. [1]



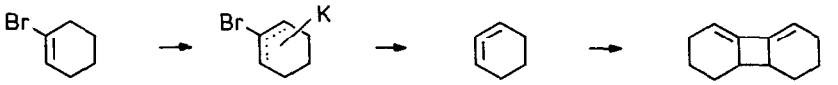
The remarkable chemical stability of this counter-polarized organometallic species may be attributed to its dimerization (or oligomerization) involving intraaggregate solvation by the ring oxygen atoms. In contrast, the carbocyclic analog 2-bromo-1-cyclohexenyllithium instantaneously loses lithium bromide even at very low temperatures. The cyclohexyne thus released dimerizes to afford a cyclobutadiene derivative which for its part immediately undergoes a Diels-Alder cycloaddition with itself to produce the polycyclic final product [2].



We wondered whether the replacement of lithium by potassium would sufficiently labilize the metalated heterocyclic intermediate to set free the 1-oxa-2-cyclohexyne. No such species, however, could be trapped when 5-*chloro*-3,4-dihydro-2*H*-pyran was heated with potassium *tert*-butoxide in dimethyl sulfoxide or, if activated by 1,4,7,10,13,16-hexaoxacyclooctadecane ("18-crown-6"), in tetrahydrofuran. On the other hand, the 5-*bromo*-3,4-dihydro-2*H*-pyran did react under such conditions although deprotonation occurred at the allylic rather than the hetero-adjacent olefinic position. Subsequent elimination of potassium bromide gave rise to an 1-oxa-2,3-cyclohexadiene intermediate which could be intercepted by cycloaddition with alkenes and dienes.

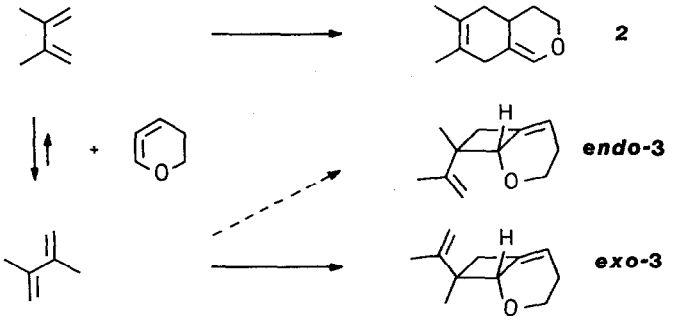


In a similar manner, Wittig *et al.* [3] had succeeded in generating 1,2-cyclohexadiene. In the absence of dienes or other efficient trapping agents this transient species dimerizes to form a 1,2-dimethylenecyclobutane derivative.

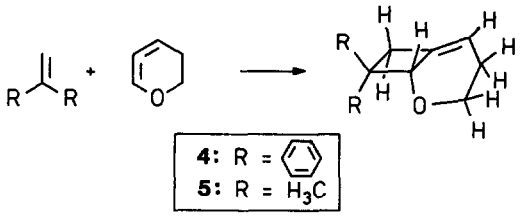


The 1-oxa-2,3-cyclohexadiene intermediate reacts particularly smoothly with furan. If the latter was employed as a cosolvent, the Diels-Alder cycloadduct 1 (50%) was obtained as the sole product. The *endo* configuration was assigned on the basis of a spectral comparison with the 1,2-cyclohexadiene derived carboanalogue. [4]

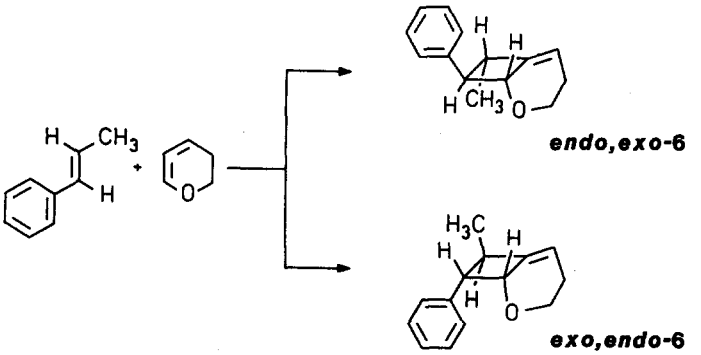
With 2,3-dimethyl-1,3-butadiene as the substrate, a [2 + 4] and [2 + 2] cycloaddition mode were found to compete with each other leading to 4,4a,5,8-tetrahydro-6,7-dimethyl-3*H*-2-benzopyran (2, 9%) and 3,5,6,6a-tetrahydro-6-methyl-6-(2-propenyl)-2*H*-cyclobuta[b]pyran (3, 37%). Nuclear spin transfer experiments revealed the *exo* configuration for the latter compound (the 1-methylvinyl group occupying a *trans* position with respect to the oxygen atom). The *endo* isomer was detected only as a minor impurity.



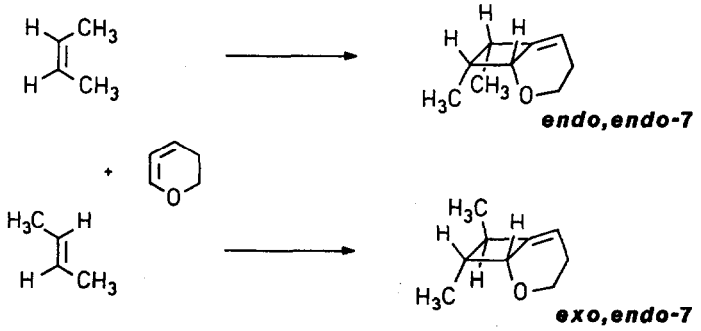
The 1,1-diphenylethylene cycloadduct **4** (43%) was again isolated with reasonable yield. In contrast, with isobutene only trace amounts of the corresponding adduct **5** (< 10%) were formed and attempts to separate it from the reaction mixture failed.



With *trans*-1-phenyl-1-propene two stereoisomers were produced, one of them having the methyl in the *exo* and the phenyl group in the *endo* position (*exo, endo*-**6**, 12%). The minor component (7%) had the two substituents displayed in the opposite way (*endo, exo*-**6**).

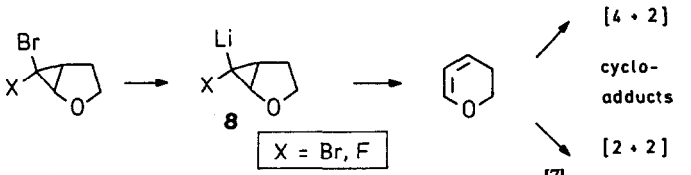


Finally, the reactions of *cis*- and *trans*-2-butene were investigated. Each of them gave a single product : the *endo, endo* and, respectively, the *exo, endo* isomer of 3,5,6,6a-tetrahydro-5,6-dimethyl-2*H*-cyclobuta[b]pyran (**7** , 8% and 6%, respectively). Within the limits of detection the two stereoisomers *endo,endo*-**7** and *exo,endo*-**7** were mutually uncontaminated. Evidently, the configuration of the olefinic components has been fully or at least predominantly retained.

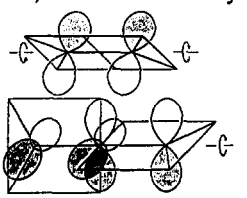


Support for the intermediacy of free (*i. e.*, uncomplexed) 1-oxa-2,3-cyclohexadiene comes from an elegant study by Christl *et al.* [5, 6]. These authors have generated the heterocyclic allene *via* carbenoid **8** by treating 6,6-dibromo- or, better, 6-bromo-6-fluoro-2-oxabicyclo[3,1,0]-hexane with methyllithium and have intercepted it in

24 - 80% yield with styrene, α-methylstyrene, 1,3-butadiene, 2,3-dimethyl-1,3-butadiene, furan and 2,5-dimethylfuran. The observed selectivities are in perfect qualitative and even semi-quantitative agreement with ours.



The views differ a bit as far as the mechanistic interpretation is concerned [7]. In our opinion, some of the observed typoselectivities (discrimination between the [4+2] and the [2+2] mode), regioselectivities (cycloaddition involving the oxygen adjacent or distant double bond of the "isopyran") and the retention of the olefin configuration in the cycloadducts as well as the "masochistic" [8] stereoselectivities are hardly compatible with the intermediacy of a biradical having a finite lifetime. While styrene type substrates may well choose a radical pathway, we favor instead a concerted, though certainly asynchronous [$2_s+2_s+2_s$] cycloaddition [9] (transition state **9** in the case of a straight-chain allene or ketene) in the case of simple alkenes which do not offer resonance stabilization to potential intermediates. As molecular models reveal, a least hindrance approach must then lead to those stereoisomers of **3**, **6** and **7**, which were actually found to be preponderant.



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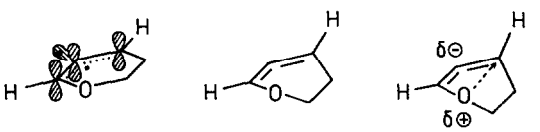
We do not know, of course, the accurate structure of the 1-oxa-2,3-cyclohexadiene intermediate, in particular not what dihedral angle the C(2),O and the C(4),C(5) bonds adopt with respect to each other. The two extreme situations, the planar [10] (**10a** : 0° twist) and the orthogonal (**10c** : 90° twist) geometry, appear equally unlikely, although the latter conformation could benefit from a through-space interaction with charge transfer from the oxygen to the carbon(3) atom. Presumably the molecule is moderately distorted (**10b**). Indeed, Huisgen *et al.* [11] have recently reported a twist angle of 58° for a seven-membered cyclic ketene imine.



10a **10b** **10c**

The observed regioselectivities can be plausibly rationalized. Since in [4+2] cycloadditions the oxacyclohexadiene acts as a dienophile, the electron poor C(3),C(4) double bond should participate preferentially. This offers the additional advantage of leaving the conjugation between the oxygen atom and the adjacent C(2),C(3) double bond intact. On the other hand, when alkene, 1,3-butadiene and styrene type olefins are employed as components in [2+2] cycloadditions they evidently want to be matched with the electron-rich, oxygen adjacent double bond. The regioselectivity may possibly be reversed again, if the oxacyclohexadiene is intercepted with donor substituted olefins such as enethers or enamines.

EXPERIMENTAL PART

1. General

For standard laboratory practice, see previous articles [12].

2. Starting Material and Material for Comparison

5-Bromo-3,4-dihydro-2*H*-pyran [13] : At -75 °C, bromine (0.10 L, 0.32 kg, 2.0 mol) was added dropwise to 3,4-dihydro-2*H*-pyran (0.18 L, 0.17 kg, 2.0 mol) dissolved in dichloromethane (0.10 L). *N,N*-Diethylaniline (0.34 L, 0.33 kg, 2.2 mol) was added, the solvent evaporated and the residue distilled as rapidly as possible. The fraction boiling in the range of 54 - 60 °C/15 mmHg was distilled again using a 20 cm long Widmer column; bp 58 -59 °C /15 mmHg. The product collected was found to be pure by gas chromatography (30 m C-20 M, 85 °C; 30 m SP-2340, 70 °C) and was stored in a deep freeze (-20 °C); 0.22 kg (67%); bp 59 - 60 °C/15 mmHg; n_D^{20} 1.5073. - ^{1}H-NMR : 6.67 (1 H, t, *J* 1.7), 4.0 (2 H, m), 2.44 (2 H, dt, *J* 5.2, 1.7), 2.0 (2 H, m).

(*Z*)-1-Ethylidene-2-methoxycyclobutane : 2-(2-Tetrahydropyranyloxy)cyclobutanone [14] (3.4 g, 20 mmol) was added to the "instant ylid" [15] prepared from ethyltriphenylphosphonium bromide (7.4 g, 20 mmol) and sodium amide (0.78 g, 20 mmol) in tetrahydrofuran. The mixture was kept 12 h at 25 °C, concentrated to one third of its volume, poured into ice-cold hexane (50 mL) and filtered. The solution was absorbed on silica gel (25 mL) which was evaporated to dryness and eluted with a 1 : 9 v/v diethyl ether/hexane mixture. After evaporation of the solvents a colorless oil (2.1 g) remained which was dissolved in methanol (20 mL) and treated 15 min at 25 °C with 20% aqueous sulfuric acid (2 mL). The solution was neutralized with sodium hydrogen carbonate and extracted with dichloromethane (3 × 25 mL). The combined organic layers were absorbed on silica gel (10 mL) which was poured on top of a column filled with fresh silica gel (15 mL). Elution with a 1 : 4 v/v mixture of diethyl ether/hexane afforded a colorless oil (1.45 g, 74%), which according to ^{1}H-NMR and MS was 2-ethylidenecyclobutanol. The (*Z*)-isomer was preponderant. - The alcohol (0.49 g, 5.0 mmol) and methyl iodide (0.35 mL, 0.80 g, 5.6 mmol) were added to anhydrous dimethylsulfoxide (10 mL) in which hexane washed sodium hydride (0.12 g, 5.0 mmol) had been dissolved under gentle warming (2 h 50 °C). After 30 min at 25 °C, the mixture was poured into water and extracted with pentane (3 × 10 mL). Distillation afforded the product (0.33 g, 58%) as a colorless liquid; bp 127 - 128 °C; n_D^{20} 1.4442; ^{1}H-NMR : 5.28 (1 H, qq, *J* 7.0, 2.3), 4.55 (1 H, dtdq, *J* 7.6, 3.3, 2.3, 2.0), 3.29 (3 H, s), 2.47 (1 H, symm. m), 2.28 (1 H, ddddq, *J* 15.6, 9.3, 7.7, 2.3, 2.0), 2.14 (1 H, dddd, *J* 12.0, 9.2, 7.3, 4.8), 1.93 (1 H, tdd, *J* 11.3, 7.9, 6.0), 1.68 (3 H, dq, *J* 7.0, 2.0).

3. Reaction between 5-Bromo-3,4-dihydro-2*H*-pyran and Potassium *tert*-Butoxide

At 25 °C, potassium *tert*-butoxide (11.2 g, 100 mmol) was added, in the course of 30 min and under stirring, to a solution of 5-bromo-3,4-dihydro-2*H*-pyran (8.2 g, 50 mmol) in dimethylsulfoxide (50 mL). After 4 h, water (0.5 L) was added and the mixture was extracted with hexane (3 × 50 mL). The combined organic layers were evaporated and the residue absorbed on silica gel (5 g). Elution with a 1 : 9 v/v mixture of diethyl ether and hexane from a column filled with fresh silica gel (100 g) gave access to two new products : **4-*tert*-butoxy-3,4-dihydro-2*H*-pyran** [7%; ^{1}H-NMR : 6.42 (1 H, dm, *J* 6.5), 4.73 (1 H, t, *J* 3.8), 4.0 (3 H, m), 1.9 (2 H, m), 1.20 (9 H, s); MS : 156 (M^+, 6%), 100 (22%), 83 (100%)] and **3-*tert*-butoxy-5,6-dihydro-2*H*-pyran** [6%; ^{1}H-NMR : 5.13 (1 H, tt, *J* 4.5, 1.7), 3.87 (2 H, symm. m), 3.71 (2 H, t, *J* 6.0), 2.2 (2 H, m), 1.31 (9 H, s); MS : (M^+, 6%), 100 (48%), 70 (100%)]. - Attempts to isolate and purify also the minor products failed. Nevertheless, a few of them, such as 5-*tert*-butoxy-3,4-dihydro-2*H*-pyran, 2-*tert*-butoxy-5,6-dihydro-2*H*-pyran and 1-oxa-2,3-cyclohexadiene [2+2] cyclodimers (or dihydrodimers) were identified by NMR spectroscopy and gas chromatograph-coupled mass spectrometry in the crude fractions.

4. Base Promoted Reaction between 5-Bromo-3,4-dihydro-2*H*-pyran and Dienes or Olefins

(4aα,5α,8α)-4,4a,5,8-Tetrahydro-5,8-epoxy-3*H*-2-benzopyran (1) : At 25 °C, potassium *tert*-butoxide (11.2 g, 100 mmol) was added, in the course of 30 min and under stirring, to a solution of 5-bromo-3,4-dihydro-2*H*-pyran (8.2 g, 50 mmol) in dimethylsulfoxide (50 mL) and furan (36 mL, 34 g, 0.50 mol). After 4 h, the mixture was poured into water (0.5 L) and extracted with hexane. The combined organic layers were evaporated and the residue absorbed on silica gel (20 g). Elution from a column filled with fresh silica gel (80 g) with a 1 : 4 v/v mixture of

diethyl ether and hexane afforded 3.75 g (50%) of a colorless, crystalline solid; mp 38.0 - 38.5 °C (from diethyl ether/pentane 1 : 5 v/v). - ^{1}H-NMR (C_6D_6) : 6.40 (1 H, d, *J* 1.8), 5.97 (1 H, dd, *J* 5.8, 1.7), 5.55 (1 H, dd, *J* 5.8, 1.5), 4.85 (1 H, d, *J* ~ 1.0), 4.75 (1 H, dd, *J* 4.5, ~ 1.5), 3.83 (1 H, ddd, *J* 11.4, 4.5, 2.0), 3.44 (1 H, ddd, *J* 12.4, 10.9, 2.7), 2.29 (1 H, dtd, *J* 11.5, 4.5, 2.2) 1.32 (1 H, dm, *J* 12.5), 0.28 (1 H, qd, *J* 12.3, 4.5). - Analysis : calc. for $C_9H_{10}O_2$ (150.18) C 71.98, H 6.71, found C 72.14, H 6.63%.

6,7-Dimethyl-4,4a,5,8-tetrahydro-3*H*-2-benzopyran (2) and **6α-methyl-6β-(2-propenyl)-(6aβ)-3,5,6,6a-tetrahydro-2*H*-cyclobuta[b]pyran** (*exo*-3) : The reaction was carried out as described above, but with 2,3-dimethyl-1,3-butadiene (25 mL, 18 g, 0.21 mol) instead of furan. After the extraction with hexane, the product mixture consisting of 2 and 3 in the ratio of 1 : 4 was isolated by bulb-to-bulb distillation; bp 120 - 140 °C; 3.75 g (46%). Separation was achieved using a Merck Lobar Lichroprep SI-50 column which was eluted with a 1 : 20 v/v diethyl ether/hexane mixture. - 2 : ^{1}H-NMR : 6.36 (1 H, t, *J* 1.7), 3.86 (2 H, symm. m), 2.74 (1 H, d, broad, *J* 18.0), 2.36 (1 H, d, broad, *J* 18.0), 2.29 (1 H, hext, *J* 5.6, 1.5), 2.07 (2 H, symm. m), 1.9 (1 H, m), 1.63 (3 H, s, broad), 1.62 (1 H, s ?, m ?), 1.61 (3 H, s, broad). - Analysis : calc. for $C_{11}H_{16}O$ (164.25) C 80..44, H 9.82; found C 80.38, H 9.75%. - *exo*-3 : ^{1}H-NMR : 5.53 (1 H, s-like, broad), 4.76 (1 H, pent, *J* 1.0), 4.71 (1 H, m, s-like), 4.24 (1 H, pent, *J* 2.5), 3.98 (1 H, ddd, *J* 11.9, 6.5, 2.3), 3.70 (1 H, ddd, *J* 11.8, 10.5, 4.4), 2.61 (1 H, dq, *J* 13.2, 2.6), 2.3 (1 H, m), 2.25 (1 H, d hex, *J* 13.0, 1.0), 2.00 (1 H, dm, *J* 17.0), 1.74 (3 H, dd, *J* ~ 1.5, 1.0), 1.14 (3 H, s). - Analysis : calc. for $C_{11}H_{16}O$ (164.25) C 80.44, H 9.82; found C 80.22, H 9.83%.

6,6-Diphenyl-3,5,6,6a-tetrahydro-2*H*-cyclobuta[b]pyran (4) : At 25 °C and under vigorous stirring, potassium *tert*-butoxide (11.2 g, 100 mmol) was added in the course of 30 min to a solution of 5-bromo-3,4-dihydro-2*H*-pyran (8.2 g, 50 mmol), 1,1-diphenylethylene (8.8 mL, 9.0 g, 50 mmol) and 1,4,7,10,13,16-hexaoxacyclooctadecane ("18-crown-6", 13.2 g, 50 mmol), in tetrahydrofuran (20 mL). After additional 5 min at 25 °C, the mixture was concentrated under reduced pressure and absorbed an silica gel (20 mL). Elution from a column filled with fresh silica gel (80 mL) with neat hexane (0.10 L) and later a 1 : 4 v/v diethyl ether/hexane mixture (0.25 L) afforded 5.6 g (43%) of a colorless crystalline product; mp 83.0 - 83.5 °C (from diethyl ether/pentane 1 : 2 v/v). - ^{1}H-NMR : 7.2 (10 H, m), 5.60 (1 H, m), 5.10 (1 H, pent, *J* 2.0), 3.64 (1 H, ddd, *J* 11.5, 6.8, 5.1), 3.53 (1 H, dq, *J* 14.1, 1.2), 3.32 (1 H, dt, *J* 11.5, 5.5), 2.97 (1 H, dm, *J* 14.1), 2.02 (2 H, symm. m). - Analysis : calc. for $C_{19}H_{18}O$ (262.35) C 86.99, H 6.92; found C 86.17, H 6.99.

5-Methyl-6-phenyl-(5α,6β,6aα)- and -(5α,6β,6aβ)-3,5,6,6a-tetrahydro-2*H*-cyclobuta[b]pyran (*endo,exo*- and *exo,endo*-6) : The reaction was carried out as described for the preparation of 1 with the exception of using *trans*-1-phenylpropene (13.0 mL, 11.8 g, 100 mmol) instead of furan. Elution from silica gel with a 1 : 9 v/v mixture of diethyl ether/hexane allowed to recover starting material (~10%) and to isolate a crude product (1.9 g, 19%) which consisted of *endo,exo*- and *exo,endo*-6 in the ratio of 63 : 37. - Analysis : calc. for $C_{14}H_{16}O$ (200.28) C 83.96, H 8.05; found C 83.84, H 7.74%.

The two components were separated by repetitive chromatography under the conditions specified above. - *endo, exo*-6 : ^{1}H-NMR : (C_6D_6) : 7.20 (2 H, dd, *J* ~ 7, 1.4), 7.15 (2 H, tt, *J* 7.5, 1.7), 7.07 (1 H, tt, *J* 7.2, 1.7), 5.38 (1 H, ~ ddt, *J* ~ 3.5, 3.0, 2.5), 4.38 (1 H, dq, *J* 6.6, 2.8), 3.84 (1 H, ddd, *J* 11.6, 6.2, 2.0), 3.55 (1 H, ddd, *J* 11.6, 10.1, 4.4), 2.89 (1 H, dd, *J* 8.8, 6.6), 2.82 (1 H, dqdt, *J* 8.9, ~ 7, 3.4, 2.6), 2.13 (1 H, symm. m), 1.74 (1 H, dm, *J* 17.0), 1.16 (3 H, d, *J* 6.2). - *exo,endo*-6 : ^{1}H-NMR : (C_6D_6) : 7.35 (2 H, dd, *J* 6.9, 1.7), 7.21 (2 H, tt, *J* 7.5, 1.8), 7.09 (1 H, tt, *J* 7.3, 1.5), 5.36 (1 H, dddd, *J* ~ 3.5, 3.0, 2.5, 1.0), 4.79 (1 H, d pent, *J* 8.5, 2.8), 3.52 (1 H, ddd, *J* 11.3, 6.0, 3.0), 3.42 (1 H, ddd, *J* 11.3, 9.2, 4.5), 3.16 (1 H, dd, *J* 8.5, 2.8), 2.99 (1 H, qqd, *J* 7.4, ~ 2.5, 1.0), 1.93 (1 H, symm. m), 1.66 (1 H, dm, *J* 17.0), 1.17 (3 H, d, *J* 7.3). - The structural assignments were corroborated by an Overhauser spin transfer experiment : the δ 4.79 signal of *exo,endo*-6 was enhanced to the extent of 3.7% upon irradiation at δ 1.17, while δ 4.38 of *endo,exo*-6 remained unaffected upon irradiation at δ 1.16.

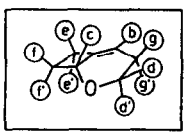
5,6-Dimethyl-(5α,6α6aα)-3,5,6,6a-tetrahydro-2*H*-cyclobuta[b]pyran (*endo,endo*-7) : In a salt-ice bath (-18 °C), an ampoule was filled with 5-bromo-3,4-dihydro-2*H*-pyran (2.4 g, 15 mmol), 1,4,7,10,13,16-hexaoxacyclooctadecane (4.0 g, 15 mmol), potassium 5-butyl-5-nonanolate (7.2 g, 30 mmol), *cis*-2-butene (20 mL, 14 g, 0.25 mol) and tetrahydrofuran (25 mL) and was sealed. The mixture was magnetically stirred 24 h at 25 °C. Chromatography on silica gel using a 1 : 20 diethyl ether/hexane mixture as the eluent permitted to collect 0.16 g (8%) of the cycloadduct *endo,endo*-7. - ^{1}H-NMR : 5.40 (1 H, m, s-like), 4.40 (1 H, ddd, *J* 8.0, 2.7, 2.2), 3.96 (1 H, ddd, *J* 11.3, 6.1, 1.7), 3.71 (1 H, ddd, *J* 11.3, 10.8, 4.4), 2.92 (1 H, symm. m), 2.58 (1 H, hex, *J* 7.6), 2.30 (1 H, symm. m), 1.96 (1 H, dm, *J* 17.0), 1.00 (3 H, d, *J* 6.9), 0.88 (3 H, d, *J* 7.0). - MS : 138 (M^+, 15%), 123 (91%), 109 (100%).

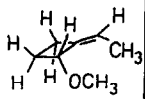
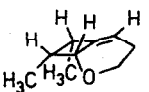
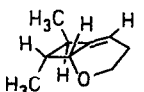
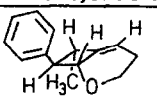
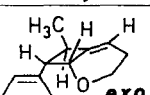
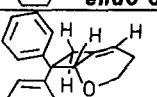
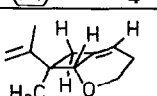
5,6-Dimethyl-(5α,6β6aβ)-3,5,6,6a-tetrahydro-2*H*-cyclobuta[b]pyran (*exo,endo*-7) : A similar reaction was performed with *trans*-2-butene, the potassium 5-butyl-5-nonanolate, however, being replaced by potassium *tert*-butoxide (30 mmol). The cycloadduct was again isolated by liquid chromatography; 0.12 g (6%). According to gas chromatography (30 m, SPB-5, 40 → 70 °C) it was not contaminated to any detectable extent by stereoisomer *endo,endo*-7. - ^{1}H-NMR : 5.50 (1 H, m, s-like), 4.60 (1 H, d pent, *J* 8.0, 2.7), 3.97 (1 H, ddd, *J* 11.5, 6.0, 1.8), 3.67 (1 H, ddd, *J* 11.5, 10.2, 4.5), 2.36 (1 H, qm, *J* 7.4), 2.3 (1 H, m), 2.23 (1 H, pent d, *J* 7.3, 2.0), 1.96 (1 H, dm, *J* 17.5), 1.23 (3 H, d, *J* 7.0), 1.02 (3 H, d, *J* 7.0). - MS : 138 (M^+, 12%), 123 (98%), 109 (95%), 67 (100%).

5. Synopsis of NMR Data

Despite the relatively small size of the cycloadducts 1 - 7, their ^{1}H-NMR spectra proved to be fairly complex. Moreover, coupling constants are known to be unreliable criteria for the stereoassignment of cyclobutane and

Table. ^{1}H-NMR comparison of the cycloadducts 3, 4, 6, 7 and 1-ethylidene-2-methoxycyclobutane : selected chemical shifts δ [in ppm] and coupling constants *J* [in Hz].



compound	δ_b	δ_c	δ_e	$\delta_{e'}$	δ_f	$\delta_{f'}$	$J_{c,f}$	$J_{c,f'}$	$J_{e,f}$	$J_{e',f}$	$J_{f',e}$	$J_{f',e'}$
	5.29	4.55	2.47	2.29	1.94	2.14	6.6	4.5	10.6	7.8	7.5	9.3
 **endo,endo-7**	5.40	4.40	2.92	-	2.58	-	8.0	-	7.8	-	-	-
 **exo,endo-7**	5.50	4.60	-	2.36	2.23	-	8.0	-	-	2.0	-	-
 **endo,exo-6**	5.38	4.38	2.82	-	-	2.89	-	6.6	-	-	8.8	-
 **exo, endo-6**	5.36	4.79	-	2.99	3.16	-	8.5	-	-	2.8	-	-
 **4**	5.60	5.10	3.53	2.97	-	-	-	-	-	-	-	-
 **exo-3**	5.53	4.24	2.61	2.25	-	-	-	-	-	-	-	-

cyclobutanone derivatives [16, 17]. Therefore, we had to resort to extensive spin polarization transfer (nuclear Overhauser effect) and double irradiation experiments. The most relevant chemical shifts and coupling constants of the [2+2] cycloadducts **3**, **4**, *endo,exo*-**6**, *exo,endo*-**6**, *endo,endo*-**7**, *exo,endo*-**7** and of a monocyclic compound (see Chapter 2) are compiled in the Table.

Acknowledgment : The authors express their gratitude to Prof. Geoffrey Bodenhausen (Lausanne), Prof. Paolo Ceccherelli (Perugia) and Dr. Stephen Wimperis (Lausanne) for help with the nmr spectroscopy, to Prof. Manfred Christl (Würzburg) for spectra comparisons and stimulating discussions, to Prof. Rolf Huisgen (München) for many valuable suggestions, to Prof. Jacques Salaün (Orsay) for starting material and advice regarding the preparation of 2-hydroxycyclobutanone, to Prof. Hisashi Yamamoto (Nagoya) for offering Y.N. the opportunity of a stay in Lausanne and, finally, to the Schweizerische Nationalfonds zur Förderung der wissenschaftlichen Forschung, Bern, for financial support (grants 2-446-084, 2-000-5'099 and 2-25'577).

REFERENCES

[1] M. Schlosser, Nguyen Dinh Ly, unpublished (1973); Nguyen Dinh Ly, diploma and doctoral theses, University of Lausanne, 1973 and 1984; K.S.Y. Lau, M. Schlosser, *J. Org. Chem.* **43** (1978), 1595, footnote 13; see also : O. Riobé, A. Lebouc, J. Delaunay, *C.R. Séances Acad. Sci., Ser. C* **284** (1977), 281; *Chem. Abstr.* **86** (1977), 189'646 e; M.A. Hassan, *J. Chem. Soc. Pak.* **5** (1983), 103; *Chem. Abstr.* **99** (1983), 212'107 j.

[2] G. Wittig, J. Weinlich, *Chem. Ber.* **98** (1965), 471; see also: G. Wittig, U. Meyer, *Chem. Ber.* **96** (1963), 329, 342.

[3] G. Wittig, P. Fritze, *Angew. Chem.* **78** (1966), 905; *Angew. Chem. Int. Ed. Engl.* **5** (1966), 846; *Liebigs Ann.Chem.* **711** (1968), 82.

[4] A.T. Bottini, L.L. Hilton, J. Plott, *Tetrahedron* **31** (1975), 1997.

[5] M. Christl, M. Braun, *Chem. Ber.* **122** (1989), 1939.

[6] See also : M. Christl, M. Schreck, *Angew. Chem.* **99** (1987), 474; *Angew. Chem. Int. Ed. Engl.* **26** (1987), 449 [1,2-cyclohexadiene]; M. Schreck, M. Christl, *Angew. Chem.* **99** (1987), 720; *Angew. Chem. Int. Ed. Engl.* **26** (1987), 690 [1-oxa-3,4-cyclohexadiene]; M. Christl, M. Braun, in : *Strain and Its Implications in Organic Chemistry* (NATO Workshop Proceedings, editors : A. de Meijere, S. Blechert), Kluwer Acad. Publ., Dordrecht 1989 [1,2,4-cyclohexatriene].

[7] M. Schlosser, *Proceeding by Elimination*, Nozaki Conference, Vol. **2** (1987), 1; M. Schlosser, Y. Naruse, *Yuki Gosei Kagaku Kyokaishi* **46** (1988), 528 [*J. Synth. Org. Chem. (Japan)*]; *Chem. Abstr.* **109** (1988), 229'688 x.

[8] J. March, *Advanced Organic Chemistry*, 3rd edition, J. Wiley & Sons, New York 1985, p. 762.

[9] R. Huisgen, L.A. Feiler, G. Binsch, *Chem. Ber.* **102** (1969), 3460; s.a.: G. Binsch, L.A. Feiler, R. Huisgen, *Tetrahedron Lett.* **9** (1968), 4497, last section; D.J. Pasto, *J. Am. Chem. Soc.* **101** (1979), 37; X.-b. Wang, K.N. Houk, *J. Am. Chem. Soc.* **112** (1990), 1754; E. Valentí, M.A. Pericàs, A. Moyano, *J. Org. Chem.* **55** (1990), 3582.

[10] P.W. Dillon, G.R. Underwood, *J. Am. Chem. Soc.* **96** (1974), 779; M. Balci, W.M. Jones, *J. Am. Chem. Soc.* **102** (1080), 7607.

[11] R. Huisgen, E. Langhals, H. Nöth, *J. Org. Chem.* **55** (1990), 1412.

[12] *E.g.*, M. Schlosser, J.H. Choi, S. Takagishi, *Tetrahedron* **46** (1990), 5633.

[13] R. Paul, *Bull. Soc. Chim. Fr.* [5] **1** (1934), 1397.

[14] J.P. Barnier, J.M. Denis, J. Salaün, J.M. Conia, *Tetrahedron* **30** (1974), 1405.

[15] M. Schlosser, B. Schaub, *Chimia* **36** (1982), 396.

[16] I. Fleming, D.H. Williams, *Tetrahedron* **23** (1967), 2747.

[17] H. Mayr, R. Huisgen, *Tetrahedron Lett.* **16** (1975), 1349: R. Huisgen, G. Steiner, H. Graf, unpublished results (doctoral dissertations G. Steiner and H. Graf, University of Munich, 1973 and 1980, respectively).