249. π-Participation in Diazoketone Hydrolysis II: *Exo-endo* Cyclization Ratio in the Hydrolyses of 7-*syn*- and 5-*endo*-Diazoacetyl-2-norbornene[1])

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Summary

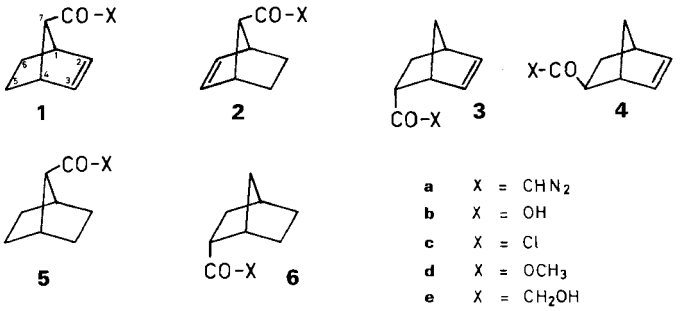
The rate of the acid-catalysed hydrolysis of 7-*syn*-diazoacetyl-2-norbornene (**1a**) is enhanced relative to that of the saturated analogue **5a** by a factor of 835. In contrast to the behaviour of other primary diazoketones, the substitution step is no longer rate-determining (mechanism *A-2*), but so much accelerated that the preceding proton transfer becomes the slow step (mechanism *A-S*$_E$*2*, demonstrated by a solvent isotope effect $k_H/k_D = 1.76$). Product analysis shows 100% cyclization; the product formation is explained in terms of brexyl and brendyl type carbenium ions (or ion pairs). – 5-*endo*-Diazoacetyl-2-norbornene (**3a**) shows very slight acceleration, and forms only 27% cyclization products (identical to those formed from **1a**). Thus, in spite of the absence of steric hindrance by hydrogen atoms, the *exo-endo* rate ratio for anchimeric assistance is $\geqslant 10^3$.

Acid-catalysed hydrolysis of primary diazoketones follows the *A-2* mechanism, rapid preequilibrium protonation forming a diazonium ion, followed by rate-determining substitution [2] by a nucleophile. As the diazonium group is very sensitive, a weak nucleophile, for instance H_2O [3], is sufficient.

$$R{-}CO{-}CHN_2 \overset{H^+,\ \text{rapid}}{\rightleftharpoons} R{-}CO{-}CH_2N_2^+ \xrightarrow[\text{rate-det.}]{H_2O} R{-}CO{-}CH_2OH + N_2 + H^+$$

A double bond in 5,6-position relative to the diazomethyl group can compete with a weak external nucleophile and form *cyclic* products [1] [4] [5]. The neighbouring group participation can furthermore result in a rate enhancement; we found this particularly with methylated cyclic olefins: 4-diazoacetyl-1,2-dimethylcyclopent-1-ene is hydrolysed about ten times more rapidly than diazoacetylcyclopentane [5]. We now present the results of a study of the hydrolyses of compounds in which the diazoacetyl group is kept in a rigid framework; 7-*syn*-diazoacetyl-2-norbornene (**1a**) and its *anti* isomer (**2a**), 5-*endo*-diazoacetyl-2-norbornene (**3a**) and its *exo* isomer (**4a**) have been compared with the saturated analogues 7-diazoacetyl- and 2-*endo*-diazoacetyl-norbornanes (**5a**, **6a**).

[1]) From the Doctoral Thesis by *R. Malherbe*, Lausanne 1972. – Preliminary communication: [1].



The diazoketones **1a** [6] and **2a** were prepared from the 2-norbornene-7-*syn*- and 7-*anti*-carboxylic acids (**1b**, **2b**) of known configuration [7]: the 1:3 mixture of the methyl esters [7] was separated by chromatography [8] and hydrolysed. **2b** was hydrogenated to **5b** [9]. The diazoketones **1a**, **2a** and **5a** were obtained *via* the acid chlorides **1c**, **2c** and **5c**, respectively.

Reaction of cyclopentadiene with acrylic acid [11] gave the acids **3b** [10] and **4b**; their configurations have been determined chemically and by NMR. [12]. Catalytic hydrogenation of **3b** gave **6b** [13]. Conversion to the diazoketones **3a**, **4a** and **6a** was performed *via* the acid chlorides **3c**, **4c** and **6c**, respectively.

1a and **3a** have previously been studied with respect to carbenic cyclization [6] [10].

Kinetics. – The rates of hydrolysis (k_1) in aqueous dioxane (60:40 *v/v*) in the presence of $HClO_4$ were measured by following the decrease in the UV. absorption at 273 nm. The individual runs were first order for at least 90% reaction. For **1a**, acid catalysis was confirmed by variation of the acid concentration at constant ionic force *(Table 1)*. The other diazoketones were hydrolysed by 0.10N $HClO_4$ *(Table 2)*; k_H is the second order rate constant ($=k_1/[H^+]$).

Table 1. *Rates of hydrolysis of* **1a** *as function of acid concentration* ($HClO_4$, dioxane/H_2O 60:40 *v/v*, 25.0°, $\mu = 0.1$; each k_1 value is the mean of 3–4 runs)

$10^3[H^+]$	$10^2 k_1 (s^{-1})$	$k_H (M^{-1}s^{-1})$
8.0	1.33	1.67
20.2	3.32	1.65
40.4	6.84	1.69

Table 2. *Rates of hydrolysis and isotope effects* (dioxane/H_2O and dioxane/D_2O 60:40 *v/v*, $HClO_4$ = 0.10N, 25.0°)

Substrate	$10^3 k_H (M^{-1}s^{-1})$	$k_{rel.}$	$10^3 k_D (M^{-1}s^{-1})$	k_H/k_D
5a	2.00±0.01	(1.00)	8.50	0.24
1a	1670±15	835	958	1.76
2a	0.85±0.01	0.47	3.01	0.28
6a	3.40±0.02	(1.00)	1.14	0.30
3a	4.25±0.05	1.25	1.35	0.31
4a	2.95±0.05	0.87	1.08	0.27

The unsaturated diazoketones 7-*anti* (**2a**) and 5-*exo* (**4a**), in which the configuration excludes π-participation, are hydrolysed slightly more slowly than the corresponding saturated diazoketones **5a** and **6a**. A similar rate reduction (about 2-fold), due to the inductive effect of the double bond, has been observed in cases of nucleophilic substitution in the absence of anchimeric assistance [6] [14]; therefore the double bond may exert this influence also on the substitution step of the hydrolysis of **2a** and **4a**. **2a** is least reactive, probably as a consequence of an additional effect of steric hindrance; another steric effect is present in the saturated compounds too: **5a** reacts 1.7 times more slowly than **6a**.

Compared with analogous open-chain compounds, the monocyclic and bicyclic diazoketones are in general hydrolysed more slowly, *e.g.:* 1-diazo-heptanone $k_H = 5.19 \cdot 10^{-3}$ $M^{-1}s^{-1}$ [5]; diazoacetyl-cyclopentane $k_H = 2{,}94 \cdot 10^{-3}$ $M^{-1}s^{-1}$ [5]; **5a** $2.00 \cdot 10^{-3}$ $M^{-1}s^{-1}$. In the cyclic compounds the solvation of the α-ketodiazonium ion formed in the preequilibrium step is probably sterically hindered; the concentration of this intermediate is therefore decreased.

Of the two diazoketones which are *a priori* susceptible to π-participation, the 5-*endo* isomer **3a** shows only very slight acceleration, just sufficient to compensate the rate reduction by the inductive effect of the double bond. On the contrary the 7-*syn* isomer **1a** reacts 835 times faster than its saturated analogue **5a**; this too must be due to an effect on the substitution step.

We have shown [15] by isotope exchange measurements that in the hydrolysis of primary diazoketones (mechanism *A-2*) the preequilibrium protonation-step is only 500–1000 times more rapid than the substitution step. So, if substitution is strongly accelerated in the hydrolysis of **1a**, one might ask whether this step is still rate-limiting or whether its velocity has overtaken that of protonation, so that the latter would become the slow step; instead of reversible preequilibrium protonation one might find irreversible, rate-determining protonation.

In order to test this hypothesis we measured the kinetic solvent isotope effect. Most of the compounds of *Table 2* show an isotope effect k_H/k_D about 0.3, a value characteristic for preequilibrium protonation normally found with primary diazoketones [2]. The only exception is **1a** with $k_H/k_D = 1.76$, a value typical for rate-determining proton transfer [16]. This means that the anchimeric effect has effectively so much accelerated the substitution step that it no longer limits the rate of the overall reaction; this is the first case of a primary diazoketone hydrolysed by a

Table 3. *Activation parameters for the hydrolysis of* **1a** *and* **2a** (dioxane/H_2O 60:40 *v/v*; $[HClO_4] = 0.10$; each k_1 value represents the mean of 2–3 runs)

Substrate	t	$10^3 k_1$ (s^{-1})	$\Delta H^{\neq}$ (kcal/mol)	$\Delta S^{\neq}$ (e.u.)
1a *(syn)*	5.0°	29.8		
	10.0°	66.5		
	25.0°	165		
	34.0°	402	15.6 ± 1	−7.6
2a *(anti)*	25.0°	0.084		
	34.0°	0.219		
	44.7°	0.592		
	60.2°	2.65	18.6 ± 1	−9.9

A-S_E2 mechanism. Thus the 835-fold acceleration of the global reaction rate represents only the minimum value of the anchimeric effect; the true acceleration of the substitution step cannot be measured.

In comparison, *Bly et al.* [17] have found in the rate of the acetolysis of 7-*syn*-brosyloxyethyl-2-norbornene a 140,000-fold acceleration over that of the saturated analogue.

In the hydrolysis of secondary diazoketones by the mechanism *A-S_E2*, the substitution step has been shown [18] to be *S_N2*-like. For the hydrolysis of **1a**, the very existence of the anchimeric effect proves its bimolecular character.

To complete our results, we measured the activation parameters for the hydrolysis of **1a** and its *anti*-isomer **2a** *(Table 3)*. In spite of the change in the rate-determining step, the entropies of activation are rather similar[2]).

Table 4. *Products formed by the acid-catalysed hydrolysis of* **1a** *and* **3a** *and by acetolysis of* **7**

Substrate	**9**	**7**	**8**	**3e**
1a $+H_3O^+$ [a][b])	47%	25%	28%	–
3a $+H_3O^+$ [a][b])	3%	1%	23%	73%
7 $+AcOH_2^+$ [c])	54% **9**-acetate	–	43% **8**-acetate	–
[d])	35% **9**-acetate	–	65% **8**-acetate	–

[a]) External standard; [b]) The volatile fraction represents > 95% yield (by NMR. with internal standard); [c]) After 16 h at 70°; [d]) After 120 h at 70°; at the same time the total yield of 8 + 9 diminishes.

Product analysis. – To facilitate the extraction of products, **1a** and **3a** have been hydrolysed in aqueous acetone (4:1 *v/v*) 1N in sulfuric acid (RT.). The reaction mixture was extracted with CH_2Cl_2, the volatile products were analysed by GC., the compounds isolated and identified. The diazoketones **2a**, **4a**, **5a** and **6a**, in which π-participation is excluded, can give only the hydroxy-ketones **2e**, **4e**, **5e** and **6e** which were not isolated.

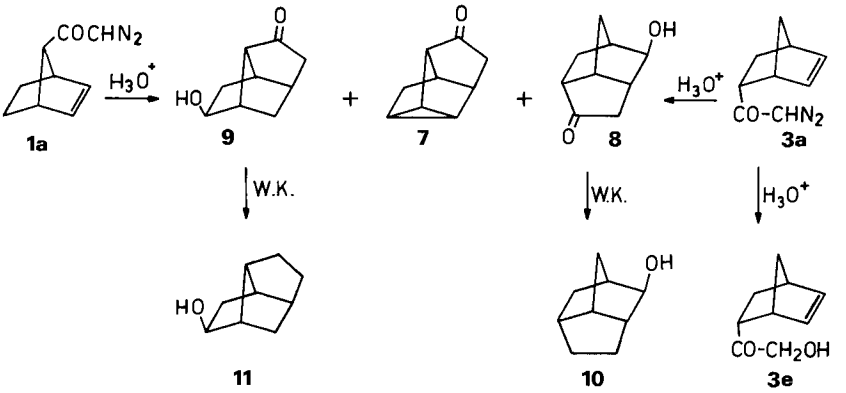
The 7-*syn*-diazoketone **1a** gives a mixture of tri- and tetracyclic products, consisting of 25% of tetracyclo[4.3.0.$0^{2,4}$.$0^{3,7}$]nonan-8-one (8-deltacyclanone, **7**) [20], 28% of 9-*exo*-hydroxy-tricyclo[4.2.1.$0^{3,7}$]nonan-4-one (9-*exo*-hydroxy-brendan-4-one[3]), **8**) and 47% of 4-*exo*-hydroxy-tricyclo[4.3.0.$0^{3,7}$]nonan-8-one (4-*exo*-hydroxybrexan-8-one[3]), **9**) *(Scheme 1)*. In contrast, carbenic cyclization of **1a** had been found to give 85% of 5-deltacyclanone [6], an isomer of **7** which we did not find among the products of acid-catalysed cyclization.

The hydrolysis of the 5-*endo* compound **3a** yields 73% of the hydroxy-ketone **3e**, and 27% of the same cyclization products as formed by the cyclization of **1a**: 1% of 8-deltacyclanone (**7**), 23% of hydroxy-brendanone **8** and 3% of hydroxy-brexanone **9** *(Scheme 1)*. – Carbenic cyclization of **3a** yielded an iso-deltacyclanone [10] not found in the acid hydrolysis mixture.

[2]) The value for **1a** fits the correlation of rates with entropies of activation indicated by *Matesich* [19] for *A-S_E2* reactions: calc. – 7.8 e.u.

[3]) The names were proposed by *Nickon et al.* [10]: brexane for a skeleton with a bridge in the *exo* position of the norbornyl system, brendane for one in the *endo* position.

Scheme 1



To identify the hydrolysis products, authentic samples were prepared; 8-deltacyclanone **7** was known [20]. 5-*endo*-Hydroxyacetyl-2-norbornene (**3e**) was isolated by column chromatography; the analytical and spectral data fit the indicated structure. **8** and **9**, very difficult to isolate in the small quantities available after diazoketone hydrolysis, were identified by comparison with samples obtained from **7** by acetolysis followed by hydrolysis *(vide infra)*.

By prolonged heating of 8-deltacyclanone (**7**) [20] at 70° with a solution of $HClO_4$ in acetic acid [21] to open the cyclopropane ring, we obtained a mixture of two isomeric acetates $C_{11}H_{14}O_3$, which were separated by analytical GC. and by very careful, repeated column chromatography. The more easily eluted acetate, m.p. 51° upon alkaline hydrolysis, always yielded a mixture of two isomeric alcohols (**8**+**9**). The second acetate, m.p. 65°, was easily hydrolysed to the corresponding keto-alcohol, m.p. 154–157°. The fragmentation pattern in the MS. and the NMR. spectra at 270 MHz of this alcohol and its acetate are consistent with the structures of 9-*exo*-hydroxy-brendan-4-one (**8**) and its acetate. The assignement of the protons in NMR., using a shift reagent, agrees satisfactorily with that of norbornane [22] and tricyclo[3.3.0.$0^{2,7}$]octane derivatives [23]. The spectrum of the **8**-acetate was identical with that recently mentioned by *Nickon et al.* [24].

The semicarbazone of **8** was reduced by the *Wolff-Kishner* method; we obtained the known tricyclo[4.2.1.$0^{3,7}$]nonan-2-*exo*-ol (2-*exo*-brendanol, **10**) [10] [17][4]).

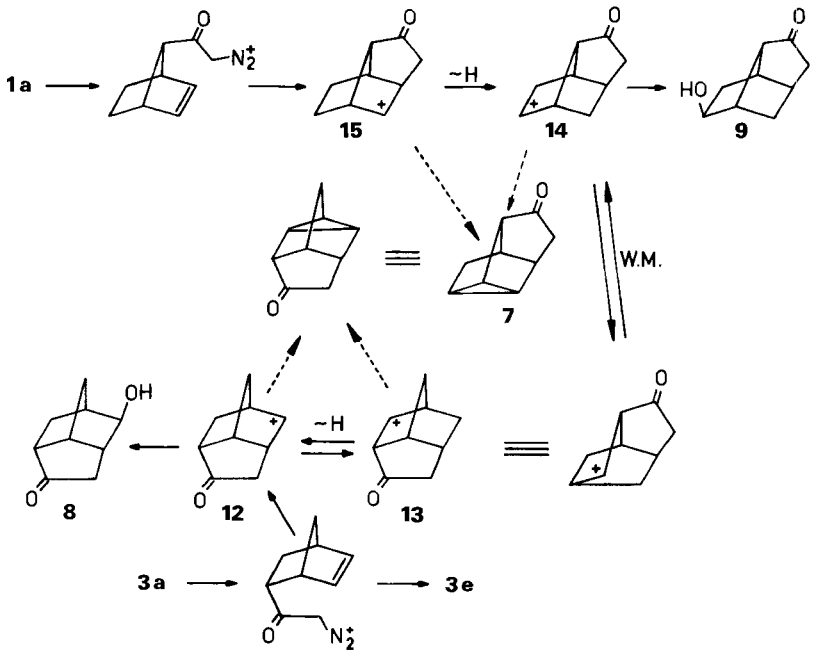
In order to obtain the isomeric keto-alcohol **9**, separation of the acetates and subsequent alcaline hydrolysis was not practicable because of isomerization; we therefore hydrolysed the above-mentioned mixture of acetates and separated the keto-alcohols by repeated column chromatography (monitored by GC.-MS.). The first eluted keto-alcohol, m.p. 68–69° corresponds to the acetate of m.p. 51° (the second product was **8**). The NMR. spectra at 270 MHz and MS. of the alcohol and its acetate are consistent with the structures of 4-*exo*-hydroxy-brexan-8-one (**9**) and its acetate. The semicarbazone of **9** was reduced by the *Wolff-Kishner* method yielding the known tricyclo[4.3.0.$0^{3,7}$]nonan-4-*exo*-ol (4-*exo*-brexanol, **11**) [10] [17][4]).

[4]) We thank Prof. *A. Nickon* for samples of **10** and **11**.

Discussion. – The results of products analysis agree with those of kinetics; **1a** presents strong anchimeric acceleration ($\geqslant$835-fold) and 100% cyclization, whereas in **3a** participation is weak (acceleration ~2-fold and 27% cyclization). A similar difference of participation between the position 7-*syn* and 5-*endo* of 2-norbornene was found in the acetolysis of brosylates $R-CH_2-CH_2-OBs$: *Bly et al.* [17] found 140,000-fold acceleration and 100% cyclization when the brosyloxyethyl group was in the position 7-*syn* of 2-norbornene, whereas *Allred & Maricich* [25] found only 15-fold acceleration and *ca.* 95% cyclization for the 5-*endo* position. The π-electrons exert a greater effect on the brosylate solvolysis than on the diazoketone hydrolysis: this might be attributed to the fact that the diazonium group is a better leaving group, making it less discriminating towards nucleophiles.

Cyclization in 7-*syn* attacks the double bond from the *exo* side of the norbornene system, in 5-*endo* from the *endo* side; as the rates of the two reactions are different, we are in the presence of an *exo: endo* rate ratio of $\geqslant 10^3$ in our case and $\sim 10^4$ in that of the brosylate solvolysis (which makes a reasonable agreement). This rather high value cannot be attributed to simple steric reasons: the distances between the two groups and their arrangement are not very different[5]), and there is no steric hindrance by hydrogen atoms in 7-*syn* or 5-*endo*. We see two reasons for the *exo-endo* ratio of about $10^4 : 1$) *Bartlett* [27] and *Bly* [28] have postulated a symmetrical transition state for solvolytic cyclization of the brosylates in the cyclo-

Scheme 2



[5]) On molecular models we estimate that C(9) can approach the center of the double bond of **1a** up to 2,3 Å.

pentenyl-ethyl and 7-*syn*-norbornenyl-ethyl systems[6]); we were led to the same assumption for the cyclization of diazoacetyl-cyclopentenes [5]. In the norbornene system, however, only the 7-*syn*, but not 5-*endo* position is symmetrical with respect to the double bond; 2) *Fukui et al.* [29] have recently calculated that the highest occupied molecular orbital (HOMO) of norbornene extends preferentially to the *exo* direction, which makes the electron density higher in the *exo* lobe[7]).

Formation of the cyclized products, the same from **1a** and **3a**, can be explained in the following way *(Scheme 2):* the diazonium ion formed by protonation of the 5-*endo* diazoketone **3a** gives, by cyclization, the brendanonyl type carbenium ion **12**, which can either capture a molecule of water furnishing the alcohol **8** (main cyclized product), or can be transformed by a 1,3 hydride shift (→ **13**) followed by a *Wagner-Meerwein* rearrangement to the brexanonyl type ion **14**, before fixing the nucleophile, giving the alcohol **9**. On the other hand the diazonium ion formed by protonation of **1a** gives the brexanonyl type ion **15**; as attack on the carbenium carbon would on both sides be *endo* (with respect to one or the other of the two norbornane systems which make up the brexane skeleton), **15** can be stabilized only after rearrangement. After a 1,3 hydride shift forming **14**, the system is accessible to attack by a nucleophile (→ **9**). Alternatively **14** can undergo a *Wagner-Meerwein* rearrangement forming the brendanonyl skeleton (**13**), followed by a 1,3 hydride shift and reaction of **12** to form **8**. 8-Deltacyclanone **7**, found in both reactions, can in principle be formed from any of the intermediate ions; it is not possible to specify the immediate precursor. Under the conditions of acid hydrolysis **7** is not transformed into **8** or **9**. On acetolysis at 60°, however, **7** yields the acetates of **8** and **9**, probably *via* the ions **12**–**15**. As the ratio **8**-acetate/**9**-acetate varies with reaction time, and as the ratio **7**/**8**/**9** is different starting from **1a** and from **3a**, we conclude that the equilibrium between ions **12**–**14** is not attained, at least not for all ions (or ion-pairs).

It is of course possible to design other reaction pathways to explain the formation of the products[8]); we have formulated the majority of the transformation steps in the direction of increasing stability of the intermediate ions. These are probably influenced by the carbonyl group: the site of the carbenium ion has a tendency to move away from the carbonyl group, and not to be in the axis of the dipole C=O. Nevertheless this influence cannot be very important; this can be seen in the comparison of our result with those obtained by *Bly et al.* [17]: the *β*-(*syn*-7-norbornenyl)ethyl brosylate cyclization forms, in the absence of a carbonyl group, 42% of 2-*exo*-brendyl acetate, 36% of 4-*exo*-brexyl acetate and 22% of deltacyclane; this product distribution is comparable with our result: 28% of brendyl, 47% of brexyl and 25% of deltacyclanyl derivatives, **8**, **9**, and **7**.

In the foregoing discussion we have formulated rearrangements using classical ions; clearly they could be written with delocalized non-classical ions or ion pairs [30].

[6]) This could be formulated as a non-classical *H*-cycloproponium type transition state.

[7]) The torsional effect postulated by *Schleyer* [26] would subsist, and one might equally imagine conformation differences.

[8]) P.e. the transformation **15** → **12** might pass by the sequence ~ WM. + ~ H + ~ WM.

We thank Prof. *C. A. Bunton* for stimulating discussions, Mrs. *Pari Malherbe-Davanloo* for the NMR. spectra at 270 MHz, Mrs. *Ingrid Noppel-Fuss* for technical assistance and the *Swiss National Science Foundation* for financial support.

Experimental Part

General: [5]. – NMR. spectra at 270 MHz (**8**, **9** and acetates): *Bruker* HX 270; GC.-MS.: *Hewlett-Packard* 5980 A.-Microanalyses: Mr. *E. Thommen*, Organisch-chemisches Institut, Basel.

Syntheses. – 7-syn- *and* 7-anti-*methoxycarbonyl-2-norbornene* (**1d**, **2d**) [7]. The mixture of acids **1b**+**2b**, obtained in 42% yield as described [7], was esterified with an excess of diazomethane at RT. NMR. spectrum indicates *syn: anti* = 1:3. The mixture, (4.0 g) was separated on a column of SiO_2 pretreated with $AgNO_3$ [8], eluted with ether/petrol ether 1:2. Pure **2d** (2.23 g) and pure **1d** (0.84 g) (GC.) were isolated. The products were identified by comparison of spectroscopic data with those of the literature [7].

*2-Norbornene-7-*syn-*carboxylic acid* (**1b**). **1d** (1.0 g) was hydrolysed at 20° in aqueous methanol (10 ml) containing KOH (0.5 g). The acid **1b** was isolated and sublimed: 0.72 g (79%), m.p. 90–95° ([7]: 91–96°).

*2-Norbornene-7-*anti-*carboxylic acid* (**2b**). Hydrolysis (as above) of ester **2d** (1.0 g) followed by sublimation gave **2b**, 0.59 g (61%), m.p. 69–73° ([7]: 70–73°).

*7-*syn-*Diazoacetyl-norbornene-2* (**1a**) [6]. **1b** (0.71 g) reacted at RT. in benzene (50 ml) with oxalyl chloride (1.3 g). After 3 h the excess of reagent and solvent were evaporated. The acid chloride **1c**, dissolved in 10 ml of dry ether, was added dropwise at 0° to a stirred ethereal solution of diazomethane (prepared from 3 g of *N*-methyl-nitroso-urea). After 4 h the solvent was evaporated in vacuo.

1a was purified by chromatography on a cooled column (30 cm × 1.5 cm; 10°) of silica gel (0.2–0.5 mm) with CH_2Cl_2: 0.35 g (43%), yelloworange oil. It is difficult to avoid partial decomposition on the column. UV. (dioxane/water 60/40 *v/v*): λ_{sh} = 272 (3.91); λ_{max} = 251 (4.02). – IR. (CH_2Cl_2): 2100 (N=N); 1630 (C=O). – NMR. (CCl_4): 5.95 (*t*, *J* = 1.9, 2 H); 5.28 (*s*, 1 H); 3.1 (*m*, 2 H); 2.3 (*t*, *J* = 1.5, 1 H); 2.0–0.8 (*m*, 4 H).

*7-*anti-*diazoacetyl-norbornene-2* (**2a**). Subjecting the acid **2b** (0.71 g) to the procedure described for **1a**, yielded the diazoketone **2b** as a unstable yellow oil, 0.64 g (88%). – UV. (dioxane/water 60:40 *v/v*): λ_{sh} = 273 (4.05); λ_{max} = 250 (4.10). – IR. (CH_2Cl_2): 2095 (N=N); 1630 (C=O). – NMR. (CCl_4): 6.0 (*t*, *J* = 2.0, 2 H); 5.16 (*s*, 1 H); 3.0 (*m*, 2 H); 2.3 (*m*, *J* = 1.5, 1 H); 2.0–0.8 (*m*, 4 H).

Norbornane-7-carboxylic acid (**5d**). In the catalytic hydrogenation of **2b** (0.55 g, 4.0 mmol) in abs. EtOH (20 ml) in the presence of Pd-C 10% (0.10 g) *ca.* 5 mmol of H_2 were absorbed. After sublimation **5b**, 0.41 g (73%), m.p. 75–77° was obtained ([8]: 77.5–78.5°).

*5-*endo-*Diazoacetyl-norbornene-2* (**3a**) [10]. Proceeding with **3b** [11] (1.42 g) as described for **1a**, we obtained **3a**, 1.40 g (85%), as a rather unstable orange oil. – UV. (EtOH): λ_{sh} = 273 (4.04); λ_{max} = 251 (4.06). – IR. (CH_2Cl_2): 2100 (N=N); 1633. – NMR. (CCl_4): 6.08 (*m*, 2 H); 5.35 (*s*, 1 H); 3.3–2.8 (*m*, 3 H); 2.1–0.9 (*m*, 4 H).

*5-*exo-*Diazoacetyl-norbornene-2* (**4a**). Proceeding as described for the preparation of **1a**, **4b** [11] (1.42 g) yielded **4a**, 1.20 g (73%), unstable yellow oil. – UV. (EtOH): λ_{sh} = 272 (4.08); λ_{max} = 250 (4.12). – IR. (CH_2Cl_2): 2095 (N=N); 1630 (C=O). – NMR. (CCl_4): 6.10 (*m*, 2 H); 5.22 (*s*, 1 H); 2.08 (*m*, 2 H); 2.3–1.1 (*m*, 5 H).

*2-*endo-*Diazoacetyl-norbornane* (**6b**). **6b** [13] (1.44 g) (prepared by catalytic hydrogenation of **3b** in the presence of Pd-C in EtOH; m.p. 64–65°), treated as described for the preparation of **1a**, yielded **6a**, 1.05 g (65%), yellow oil, not very stable. – UV. (EtOH): λ_{sh} = 272 (4.23); λ_{max} = 249 (4.30). – IR. (CCl_4): 2100 (N=N); 1640 (C=O). – NMR. (CCl_4): 5.20 (*s*, 1 H); 2.70 (*m*, 1 H); 2.40 (*m*, 2 H); 2.0–0.9 (complex *m*, 8 H).

Acetolysis of 8-deltacyclanone (**7**). **7** (4.3 g, 32 mmol) [20] in CH_3COOH (37.4 ml) and 70% aq. $HClO_4$ (1.5 ml) was heated at 70°. After 16 h one half of the mixture was poured on to crushed ice; 40% NaOH (20 ml) was added, the neutralization was completed by adding solid Na_2CO_3. The aqueous phase was extracted 4 times with CH_2Cl_2 (50 ml), the combined extracts were washed with 5% aqueous $NaHCO_3$ and dried over $MgSO_4$. After evaporation of the solvent an oil (1.3 g) was isolated (= *extract A*).

The second half of the acetolysis mixture was heated 120 h at 70°, then treated as the first half. A dark oil, 1.7 g, was isolated (= *extract B*).

Extracts A and B were analysed by analytical GC. (5% Carbowax, 190°). The same two main products were found in both: from extract A 43% of **8**-acetate (retention time 3.2 min.) and 57% of **9**-acetate (retention time 3.8 min.); from extract B 65% of **8**-acetate and 35% of **9**-acetate (retention times as above).

9-exo-Acetoxy-brendan-4-one (**8**-*acetate*). By slow column chromatography of extract B on SiO_2, eluting during 2 days with petrol ether, fractions rich in **9**-acetate were removed from the column; the separation was followed by GC. of samples. By slow elution with 25% ether/petrol ether **8**-acetate, 1.05 g, was obtained; after recrystallization from hexane and sublimation: 0.50 g, m.p. 65°. – IR. (CCl_4): 1735 (C=O). – NMR. (270 MHz, $CDCl_3$) (**16a**): 4.23 (*s*, 1 H, C*H*–O); 2.76 (*s*, 1 H, H–C(7)); 2.39 (*m*, 5 H); 1.99 (*m*, 2 H); 2.05 (*s*, 3 H, CH_3CO); 1.57 (*d*, $J = 11$, 1 H, H–C(8*a*)); 1.31 (*d*, $J = 14$, 1 H, H–C(2*n*)).

In the presence of variable amounts of Eu(fod)$_3$ [31], the following relative slopes of $\Delta\delta$ over [Eu(fod)$_3$]/[**8**-acetate] have been observed: H–C(9): (1.00); H–C(5*n*): 0.91; H–C(5*x*): 0.60; H–C(2*n*): 0.48; H–C(2*x*): 0.23; H–C(8*s*): 0.32; H–C(8*a*): 0.24. – MS.: 194 (M^+, 5.7%).

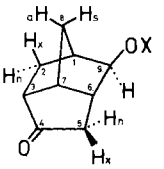
$C_{11}H_{14}O_3$ (194.2) Calc. C 68.02 H 7.27% Found C 68.21 H 7.27%

Semicarbazone of **8**-acetate: recrystallized 3 times from EtOH, m.p. 192–193°.

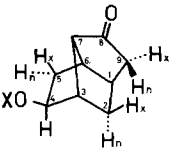
$C_{12}H_{17}N_3O_3$ (251.3) Calc. C 57.35 H 6.82 N 16.72% Found C 57.29 H 7.00 N 16.82%

9-exo-Hydroxy-brendan-4-one (**8**). **8**-Acetate (0.30 g) was stirred for 2 h at RT. with K_2CO_3 (0.11 g) in water (3 ml) and methanol (5 ml). The methanol was evaporated, the aqueous phase extracted 3 times with ether; the united extracts were washed with $NaHCO_3$ solution and water and dried over $MgSO_4$. After evaporation of the solvent and column chromatography (70% ether/30% petrol ether), **8**, 0.235 g (100%) was isolated and recrystallized from $CHCl_3$/hexane; m.p. 154–157°[9]). – IR. (CCl_4): 3420 (bonded OH), 1740 (C=O). – NMR. (270 MHz, $CDCl_3$) (**16b**): 3.41 (*s*, 1 H, H–C(9)); 2.73 (br. *s*, $J_{6,7} = 2$, H–C(7)); 2.48 (*s*, OH); 2.33–2.25 (*m*, 5 H); 2.09 (*d*, $J_{gem} = 11$, $J_{8s,2n} = 1$, H–C(8*s*)); 1.93 (*m*, $J_{gem} = 14$, $J_{2x,3} = 11$, $J_{2x,1} = 4$, 1 H, H–C(2*x*)); 1.52 (*d*, $J_{gem} = 11$, $J_{8a,9} = 1$, 1 H, H–C(8*a*)); 1.17 (*d*, $J_{gem} = 14$, $J_{2n,8s} = 1$, 1 H, H–C(2*n*)). – MS.: 152 (M^+, 13), 124 (10), 91 (9), 83 (100%).

$C_9H_{12}O_2$ (152.2) Calc. C 71.02 H 7.95% Found C 70.84 H 7.86%



16a (X = Ac)
b (X = H)



17a (X = Ac)
b (X = H)

Semicarbazone of **8**: recrystallized from EtOH/H_2O, m.p. 176–177°.

$C_{10}H_{15}N_3O_2$ (209.2) Calc. C 57.40 H 7.23 N 20.08% Found C 57.43 H 7.31 N 20.27%

2-exo-Brendanol (**10**). **8**-Semicarbazone (32 mg) was heated in a small Kugelrohr with powdered KOH (100 mg) for 2 h at 300°. The product was sublimed at 100°/12 Torr: m.p. 127–128°, 12 mg, identical with an authentic sample of **10** [10] [17][4]) (m.p. 129°; mixture 127–128°). – IR. (CCl_4): 2960, 2870. – NMR. (CCl_4): 3.15 (*s*, 1 H); 2.8 (br. 1 H, OH); 2.3–0.5 (*m*, 12 H). – MS.: 138 (M^+, 14), 120 (60), 92 (68), 91 (52), 79 (100%).

4-exo-Acetoxy-brexan-8-one (**9**-*acetate*). Extract A was chromatographed on a SiO_2 column with 5–15% ether/petrol ether: control by GC. allowed to follow the enrichment of **9**-acetate. To isolate pure

[9]) During hydrolysis of **8**-acetate, no isomerization to **9** was observed: under identical conditions, however, **9**-acetate always formed mixtures of **8** + **9**.

9-acetate, the enriched fractions were chromatographed 4 times. White hygroscopic crystals, 0.40 g, were isolated; recrystallized from hexane and sublimed, m.p. 51°. – IR. (CH_2Cl_2): 1740 (C=O). – MS.: 194 (M^+, 3.7%). – NMR. (270 MHz; $CDCl_3$) (**17a**): 4.76 (*d*, J = 6.6, H–C(4)); 2.70 (*s*, 1 H); 2.34 (*m*, 3 H); 2.22 (*s*, 2 H); 1.92 (*m*, 1 H); 2.05 (*s*, 3 H, CH_3CO–); 1.73 (*d*×*d*, J_{gem} = 14.7, J' = 5.2, 1 H, H–C(5*x*)); 1.51 (*d*×*d*, J_{gem} = 14.5, J' = 6, 1 H, H–C(2*x*)); 1.31 (*d*×*d*, J_{gem} = 14.5, J' = 6, 1 H, H–C(2*n*)).

$C_{11}H_{14}O_3$ (194.2) Calc. C 68.08 H 7.27% Found C 68.17 H 7.27%

Semicarbazone of **9**-acetate. After recrystallization from EtOH: m.p. 205–206°.

$C_{12}H_{17}N_3O_3$ (251.3) Calc. C 57.35 H 6.82 N 16.72% Found C 57.08 H 6.99 N 16.47%

4-exo-*Hydroxy-brexan-8-one* (**9**)[9]. Extract A (formed by acetolysis of 7, 3.0 g) was hydrolysed with K_2CO_3 (1.1 g) in methanol (50 ml) and water (30 ml). After 2 h at 20°, the methanol was evaporated *in vacuo* and the aq. solution extracted with ether, which was washed with water, dried over $MgSO_4$ and evaporated: a viscous oil, 2.0 g, was obtained, which was chromatographed on a silica gel column with ether/petrol ether 3:10 until 7:10. The fractions were 3–5 times rechromatographed until pure products were obtained. The success of separation was confirmed by GC.-MS. (3% Silar 5CP, 190°), judging by the presence or absence of the typical peaks at m/e = 124 (**8**) and 108 (**9**).

The fraction first eluted by 30–40% ether/petrol ether consisted of **9**, white hygroscopic crystals, m.p. 68–69° (recrystallized from hexane). – IR. (CCl_4): 3420 (bonded OH), 1740 (C=O). – NMR. (270 MHz, $CDCl_3$) (**17b**): 3.97 (*d*, $J_{4,5n}$ = 5.2, H–C(4)); 2.78 (*s*, H–C(7)); 2.60 (*s*, –OH); 2.50 (overlapped *d*×*d*, $J_{6,5x}$ = 5, $J_{6,3}$ = 1, H–C(6)); 2.27 (*d*, $J_{1,2x}$ = 5, H–C(1))[10]; 2.27 (*m*, $J_{3,2n}$ = 5, $J_{3,6}$ = 1, H–C(3)[10]); 2.19 (*d*×*d*, J_{gem} = 17, $J_{9x,2n}$ = 1.5, H–C(9*x*)); 1.93 (*d*×*d*, J_{gem} = 14, $J_{5n,4}$ = 5.2, H–C(5*n*)[10]; 1.93 (*d*, J_{gem} = 17, H–C(9*n*)[10])); 1.57 (*d*×*d*, J_{gem} = 14, $J_{5x,6}$ = 5, H–C(5*x*)); 1.14 (*d*×*d*, J_{gem} = 13, $J_{2x,1}$ = 5, $J_{2x,9n}$ = 1.5, H–C(2*x*)); 1.06 (*d*×*d*, J_{gem} = 13, $J_{2n,3}$ = 5, H–C(2*n*)). – MS.: 152 (M^+, 35), 108 (43), 91 (13), 83 (16), 80 (49), 79 (44), 66 (100%).

$C_9H_{12}O_2$ (152.2) Calc. C 71.02 H 7.95% Found C 70.78 H 8.05%

The second fraction eluted from the SiO_2 column (60% ether/petrol ether) consisted of **8**, identical with the product obtained by hydrolysis of **8**-acetate.

Semicarbazone of **9**: recrystallized from EtOH/H_2O, m.p. 152–154°.

$C_{10}H_{15}N_3O_2$ (209.2) Calc. C 57.40 H 7.23 N 20.08% Found C 56.87 H 7.48 N 19.56%

4-exo-*Brexanol* (**11**). **9**-Semicarbazone (21 mg) was heated in a small Kugelrohr with pulverized KOH (100 mg) for 2 h at 300°. The product was sublimed at 100°/12 Torr: **11**, 7 mg, m.p. 52–54°, identical with an authentic sample [10] [17][4]) (m.p. 52–55°; mixture 52–54°). – IR. (CCl_4): 2940, 2870, 1450, 1330. – MS.: 138 (M^+, 18), 120 (29), 91 (23), 79 (52), 66 (100%).

Hydrolyses. – *Hydrolysis of* 7-syn-*diazoacetyl-norbornene* (**1a**). A solution of **1a** (0.30 g), in acetone/1N H_2SO_4 (1:4 *v*/*v*, 10 ml) was kept at RT. until the evolution of N_2 ceased. The mixture was neutralized and extracted as described [5], the oil (> 95% volatile) was analysed by GC. (Carbowax 5% on WAW 80–100; 150 cm × 0.4 cm; 8 min at 130°, rise to 180° in 2 min, 16 min at 180°); 3 peaks with the following retention times and relative areas (internal standard: *n*-decanol) were found: 8-delta-cyclanone (7): 3.2 min, 25%; hydroxy-brendanone (**8**): 16.7 min, 28%; hydroxy-brexanone (**9**): 18.2 min, 47%; 7, **8** and **9** were identified by retention times of authentic compounds (see above).

Hydrolysis of 5-endo-*diazoacetyl-norbornene* (**3a**). A solution of **3a** (2.0 g) in acetone/1N H_2SO_4 (1:4 *v*/*v*, 62 ml) was kept at RT. until the end of the N_2 evolution, then extracted as described before [5]: the oil, 1.5 g, > 95% volatile was analysed by GC. (Carbowax 5%; 8 min at 160°, heated in 1 min to 190°, 8 min at 190°); 4 peaks with the following retention times and relative areas were found: **8**-deltacyclanone (7): 1.86 min, 1%; hydroxyketone **3e**: 4.2 min, 73%; hydroxy-brendanone (**8**): 12.8 min, 23%; hydroxy-brexanone (**9**): 15.7 min (3%). **7**, **8** and **9** were identified by injection of authentic compounds; purity control was effected by GC.

5-endo-*Hydroxyacetyl-norbornene-2* (**3e**). The crude oil isolated after hydrolysis of **3a** was chromatographed on a column of silica gel, with 1–10% ether/petrol ether. **3e**, 0.7 g, (58%) of purity > 99% (GC.) was obtained; after recrystallization from hexane m.p. 29–30°. – IR. (CCl_4): 3480, 1710. – NMR.

[10]) By decoupling.

(CCl_4): 6.02 (*m*, 2 H); 4.15 (*s*, 2 H, $-CH_2O-$); 3.31–2.83 (*m*, 4 H); 2.06–1.16 (*m*, 4 H). – MS.: 152 (M^+, 2.9), 134 (2.3), 117 (26), 91 (19), 67 (78), 56 (100%).

$C_9H_{12}O_2$ (152.2) Calc. C 71.02 H 7.95% Found C 71.23 H 8.13%

α-Naphtylurethane, recrystallized 3 times from EtOH, m.p. 121°.

$C_{20}H_{19}NO_3$ (321.4) Calc. C 74.74 H 5.96 N 4.35% Found C 74.51 H 6.12 N 4.49%

Kinetics. – The UV. spectrometric method and the preparation of the solutions have been described [5].

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