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ELECTROPHILE-INITIATED SELECTIVE RING TRANSFORMATIONS OF CYCLOPROPYL KETONES

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Abstract—Electrophile-mediated cyclopropane cleavage in tricyclo[3.3.0.0^{2,8}]octan-3-one (**1a**) is increasingly directed towards the maximum bond overlap site in the following order of reagents: acetyl methanesulfonate, $+Br^-$ or I^-; t-butyl-dimethylsilyl iodide; t-butyldimethylsilyl trifluoroacetate; trimethylsilyl trifluoroacetate. The latter reagent gives rise to one single regioisomer (→**6a**). Routine yields of isolated products lie between 78 and 87%. Increasing regioselectivity is governed by increasing electrophilic power and lowered nucleophilic strength of the reagents. Independent of these two factors, a C(4)-*exo* substituent in **1** directs the opening modes unidirectionally (→**2b**, **6b**). Irrespective of the substitution pattern at C(4) (**1a-d**), the cyclopropane moiety rearranges smoothly to olefinic ketones (**8a-d**) when the polymer-supported triflate analog Nafion-TMS is used in toluene at 80°. The reaction proceeds via intramolecular proton (deuterion) abstraction by the transient electron-rich enoxy double bond. This is the first fully proved case of such an intramolecular process. Aro-semibullvalenes (**18**, **22**) similarly rearrange to aro-semibarrelenes (e.g. **21**, **23**) in the presence of Nafion-TMS. The latter rearrangement also takes place at room temperature when **18** or **22** are treated with commercial tetramethylsilane (TMS) and a catalytic amount of trifluoroacetic acid. An unknown impurity in the TMS reacts with the acid to form a powerful electrophilic composition. A cheap and convenient *in situ* preparation of TMS-triflate is described by mixing trifluoromethanesulfonic acid and TMS at room temperature.

As part of a project aiming at versatile approaches towards the synthesis of condensed cyclopentanoid natural products,[1] we have studied the regioselective steering of electrophile-initiated cleavages of cyclopropyl ketones in general and those of tricyclo[3.3.0.0^{2,8}]octan-3-ones in particular. The procedures employ reagents which combine nucleophilic and electrophilic components of varying strengths, the combined action of which determines the extent of regioselectivity. Cyclopropyl carbonyl compounds can be ring-cleaved in four particular ways: (A) Geminally double-activated cyclopropyl moieties are readily attacked in a 1,4-fashion;[3-5] (B) A few monoactivated cyclopropyl derivatives are sufficiently reactive, in the absence of forced catalysis, either owing to extremely powerful nucleophiles or to the release of considerable ring strain during reaction;[4,5] (C) Cyclopropyl ketones add nucleophiles in a cooperative action with strong electrophiles such as Lewis acids,[6] acetyl,[7,9] SiR_3,[8,10] and protons;[13] (D) Alternatively, Si-induced cation formation may cause the rearrangement of cyclopropyl ketones to olefinic isomers.[10]

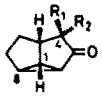
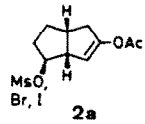
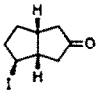
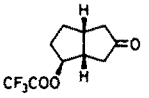
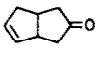
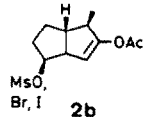
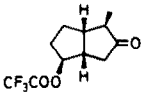
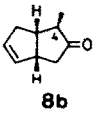
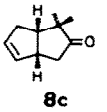
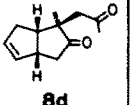
RESULTS

Addition reactions

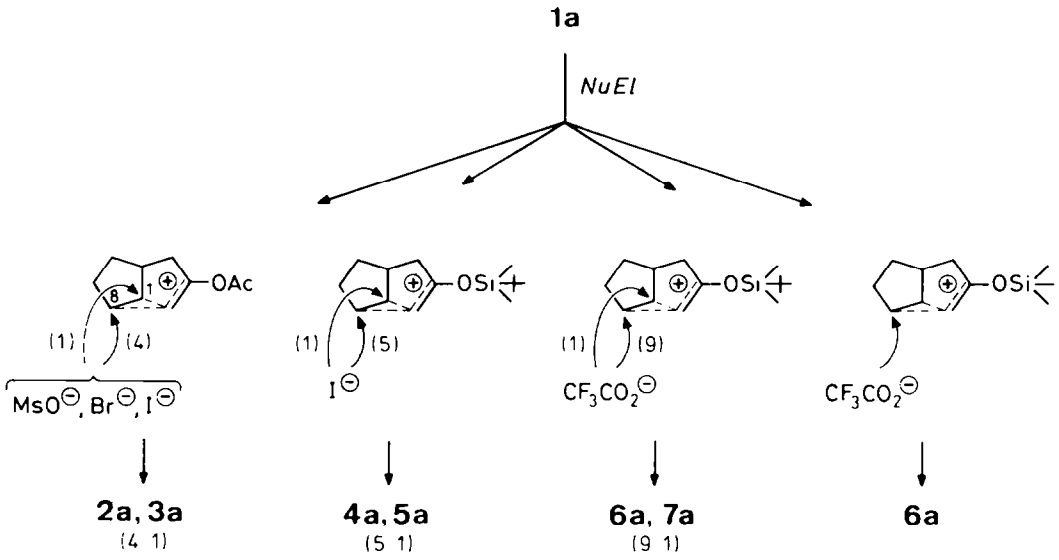
In a first set of experiments with **1a** (Table 1), we have investigated the selective action modes of reagents with and without Si. All reagents have in common the combination of a nucleophilic and an electrophilic part (NuEl). Acetyl methanesulfonate (AcOMs) has originally been used by Mazur for ether cleavages[11] and has later been employed to effect *intramolecular* addition of an olefin to a cyclopropyl ketone moiety yielding (epi-)cedrone.[7] We found the same reagent to be *intermolecularly* reactive in transferring its nucleophilic component (OMs) to **1a**, and giving rise to a 4:1 mixture of **2a** and **3a** (Table 1 and Scheme 2). Br^- and I^- were introduced[12] equally successful from their tetramethylammonium salts, affording **2a** and **3a** (Br, I) again in a 4:1 ratio.[9] These results parallel previous findings with HBr yielding the same ratio of products derived from C(1) and C(8) substitution.[13] Extensive ^1H NMR decoupling experiments demonstrated the C(8) *exo* configuration of **2a**, and evidence in favour of an overall S_N2 mechanism was presented.[9] An alternative stepwise formulation of the addition process would require the intermediacy of a delocalized cationic intermediate **10** (Scheme 1) favouring β-addition (path *i*), rather than a C(8)-localized charge as represented in **9**, which would allow for both β- and α-additions (paths *i* and *ii*). Thus, the latter alternative (**1a**→**9**) could not accommodate the high stereoselectivity observed in **1a**→**2a** (Nu = OMs). Stereoequilibration, which would satisfy the experimental result, is encountered with bromides and iodides,[14] but not with mesylates.

We have discussed in greater detail the results with reagents not containing silicon, since they can be similarly selective in the *stereochemical* steering of the opening of cyclopropyl ketones as are Si-mediated processes. With regard to *regiocontrol*, however, the Si reagents proved to be superior. When **1a** was reacted with, e.g. t-butyldimethylsilyl iodide (BDMSI), which was *in situ* generated from t-butyldimethylsilyl chloride and sodium iodide in chloroform, a 5:1 mixture of **4a** and **5a** was formed (Table 1 and Scheme 2). For the *in situ* preparation of BDMSI the known method of preparing trimethylsilyl iodide[15] had been adopted. A drastically enhanced selectivity favouring the opening at C(8) was observed when **1a** was treated with t-butyldimethylsilyl trifluoroacetate (BDMSTFA), generated from the sodium salt of trifluoroacetic acid and t-butyldimethylchlorosilane. A 9:1 ratio of **6a** and **7a** resulted. The most regioselective nucleophile addition was achieved, however, with trimethylsilyl trifluoroacetate (TMSTFA) when reacting on **1a** and affording **6a** as the sole product. Notably, in all experiments performed with Si reagents,

Table 1. Addition and rearrangement products formed from various cyclopropyl ketones

Starting Cyclopropyl Ketones [a]	Reagents	Products [a] 8-Substitution	1-Substitution	Olefin	Yield % [b]
 **1a** (R_1, R_2 = H)	$CH_3SO_2OCOCH_3$, + Br^- or I^-	 **2a**	4 : 1 **3a**	—	87(95)
	$ISi(CH_3)_2C_4H_9$-t	 **4a**	5 : 1 **5a**	—	84
	$CF_3CO_2Si(CH_3)_2C_4H_9$-t	 **6a**	9 : 1 **7a**	—	78(88)
	$CF_3CO_2Si(CH_3)_3$	**6a**	—	—	85
	$CF_3SO_2OCH_3$ $CF_3SO_2OSi(CH_3)_3$ *Nafion*-TMS	—	—	 **8a**	50 63 90
1b (R_1 = CH_3, R_2 = H)	$CH_3SO_2OCOCH_3$, + Br^- or I^-	 **2b**	—	—	72(89)
	$CF_3CO_2Si(CH_3)_3$	 **6b**	—	—	80
	Nafion-TMS	—	—	 **8b**	84
1c (R_1, R_2 = CH_3)	*Nafion*-TMS	—	—	 **8c**	87
1d (R_1 = CH_2COCH_3 R_2 = CH_3)	*Nafion*-TMS	—	—	 **8d**	60(70)

[a] Depicted structures represent *d,l*-mixtures, although we are now in a situation to carry out these transformations with >98% enantiomeric pure materials.[1,2b] [b] GLC analysis of crude reaction mixture in parentheses.



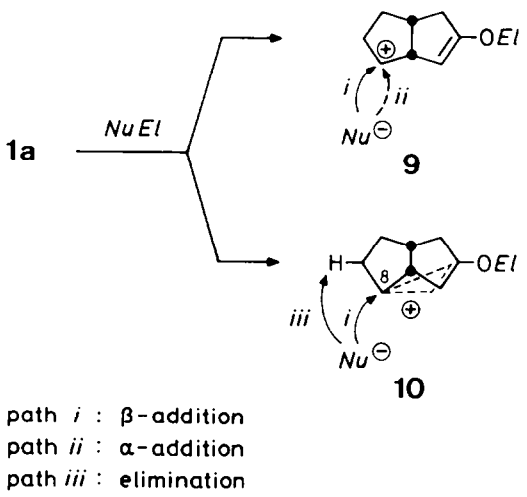
Scheme 1. Possible cationic intermediates involving C(8) upon electrophilic activation of **1a**.

the intermediate silylenol ether expected for mechanistic reasons (Scheme 2), were lost during work-up, and ketone products were isolated throughout. However, the intermediacy of enol ethers was observed (by GLC and IR, when crude samples were drawn from the mixture) for the case of **1a** → **6a**, when TMSTFA served as a reagent. The conditions used here, would have to be modified in order to isolate the silylenol ethers. In a related investigation using trimethylsilyl iodide to cleave cyclopropyl ketones, similar problems had been encountered and a partial solution only had been found.[8]

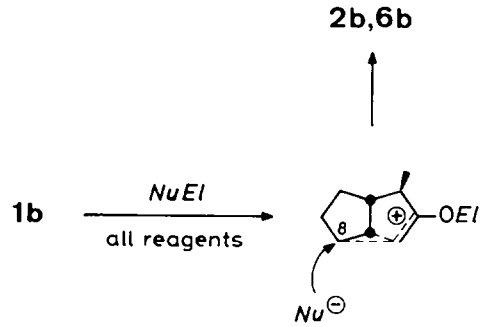
The following trend seems obvious from Scheme 2. If the electrophilic power of the reagents NuEl is increased ($Ac < Me_2Si(t\text{-}C_4H_9) < SiMe_3$) coupled with decreasing strength of the nucleophiles (MsO, Br, $I > CF_3CO_2$), addition at C(8) in **1a** becomes more important. Within the group of silyl trifluoroacetates, the trimethylsilyl group (TMSTFA) with its greater electrophilicity achieves maximum selectivity. The reaction with TMSTFA most notably reflects even more distinctly differences in C(2,8) vs C(1,2) σ overlap with the CO π-moiety in **1a** than does the reductive cleavage under Birch conditions (95:5 isomeric ratio),[13] generally accepted as an overlap measure.

The 4-*exo*-methyltricyclo[3.3.0.$0^{2,8}$]octan-3-one (**1b**) was, in contrast to the unsubstituted analog **1a**, cleaved only at C(8) with all types of reagents (AcOMs, $+Br^-$ or I^-; TMSTFA) (Scheme 3). The products isolated here were on the one hand the enol acetates **2b**, with AcOMs, $+Br^-$ or I^-, and on the other hand ketone **6b**, with the silicon reagent TSMTFA. The high regioselectivity achieved in these cases can be explained by a considerable build-up of repulsive interaction in the transition state between the H atom at C(1) and the Me group at C(4), provided that an S_N2 mechanism is operative in the ring cleavage at C(1).

In the context of the generation, as described above, of BDMSTFA from the Na salt of trifluoroacetic acid and t-butyldimethylchlorosilane, one particular observation deserves special mention. By GLC and ^1H NMR, an additional compound was detected upon mixing of the two materials (commercial grades). The formation of di-ti-butyl tetramethyldisiloxane[16] with traces of moisture seemed most likely. Indeed, this proved correct when the disiloxane was obtained also on mixing t-butyldimethyl-



Scheme 2. NuEl = $CH_3SO_2OCOCH_3$, $+Br^-$ or I^-; $ISi(CH_3)_2C_4H_9$-t; $CF_3CO_2Si(CH_3)_2C_4H_9$-t; $CF_3CO_2Si(CH_3)_3$.



Scheme 3. NuEl = $CH_3SO_2OCOCH_3$, $+Br^-$ or I^-; $CF_3CO_2Si(CH_3)_3$.

chlorosilane with sodiumiodide in aqueous acetonitrile (eqn 1), again adopting the halide exchange method known

(1) $\equiv SiCl \xrightarrow[CH_3CN\,aq]{NaI} \equiv SiOSi \equiv$

for trimethylchlorosilane.[15]

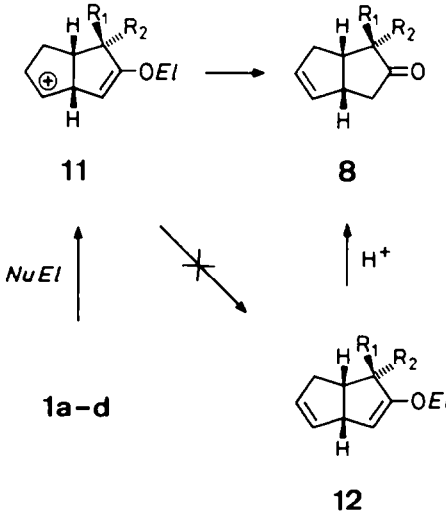
Rearrangements

Another mode of reaction, namely rearrangement of the cyclopropane part to olefins (Scheme 4), was observed with reagents NuEl embodying extremely low-power nucleophiles (methyl triflate, TMS-triflate and Nafion-TMS[17]).[10] The lowest yield of **8a** was obtained with methyl triflate (Table 1), when **1a** was allowed to react at 0° or room temperature. Considerable amounts of polymeric byproducts were formed under these conditions. Acceptable yields were achieved, however, with TMS-triflate in chloroform or toluene at room temperature, and an even better yield with the polymer-supported triflate analog Nafion-TMS, when employed in toluene at 80°. The latter conditions are most practical since Nafion-TMS is quite resistant to moisture[17] and the work-up procedure simply consists of a filtration. Routinely, 30% by weight of the polymer was taken, and it could be re-used a second time. The method was equally successful when applied to the 4-substituted tricyclo[3.3.0.$0^{2,8}$]octan-3-ones **1b, c, d**, which were smoothly rearranged to the olefinic products **8b, c, d**. The only critical point concerns the rearrangement **1b**→**8b**. Here the reaction needs to be monitored and stopped immediately after completion in order to avoid any stereoequilibration at C(4) upon extended reaction times.

The usefulness of both Nafion-TMS and TMS-triflate has been amply demonstrated in a wide range of synthetic applications.[18,19] The latter of the two reagents being more reactive, allows to lower the reaction temperature in certain cases. We have found a simple and cheap *in situ* preparation of TMS-triflate circumventing the handling problems of commercially available and readily hydrolizing material. Mixing of trifluoromethanesulfonic acid and a slight excess of tetramethylsilane at room temperature affords quantitatively TMS-triflate and methane as byproduct (eqn 2).[20] This procedure has erroneously been claimed as not

(2) $CF_3SO_3H \xrightarrow[r.t.]{TMS} CF_3SO_3Si \equiv$

working,[21] and hence other less convenient methods of preparation have come forth instead.[21,22]

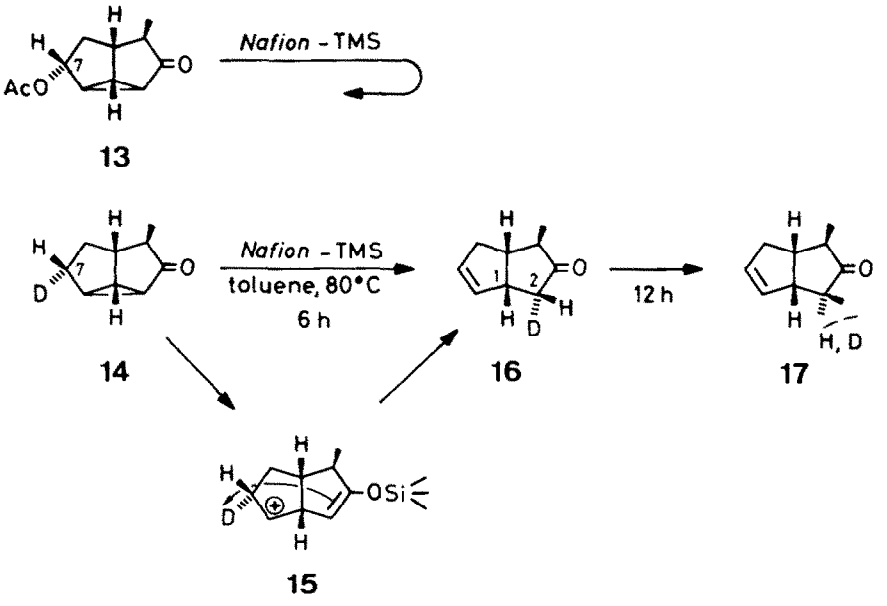


Scheme 4. NuEl = $CF_3SO_2OCH_3$; $CF_3SO_2OSi(CH_3)_3$; Nafion-TMS.

Mechanistically, the transformations **1**→**8** were at first glance highly surprising, as under quite varying experimental conditions the same ketonic products resulted. Independent of the substitution pattern at C(4) of **1** the electrophile-mediated cyclopropane cleavage should lead to the olefinic product via the cationic intermediate **11** (Scheme 4). The elimination process (Scheme 1, path *iii*) leading to **12** would then demand proton elimination by the action of, e.g. an external nucleophile. The formation of product **8** finally requires an efficient protolytic cleavage of the enoxy moiety in **12**. Two results could not be reconciled, however, with this mechanism.[23] Firstly, even upon addition of a proton scavenger such as 1,5-diazabicyclo[4.3.0]non-5-ene the intermediate **12** could not be trapped, although independent formation of **12** from, e.g. **8a** demonstrated the sufficient stability of the enolether **12** (El = $SiMe_3$; R_1, R_2 = H). Secondly, facile hydrolysis **12**→**8a** is unlikely for El = Me, which would thus protect the intermediate when methyl triflate is used for the transformation **1a**→**8a**. One is therefore tempted to postulate an intramolecular abstraction of the *endo* proton at C(7) by the electron-rich double bond of **11**. The specific geometrical arrangements of the bicyclic intermediates **11** would certainly be in favour of such a reaction course.

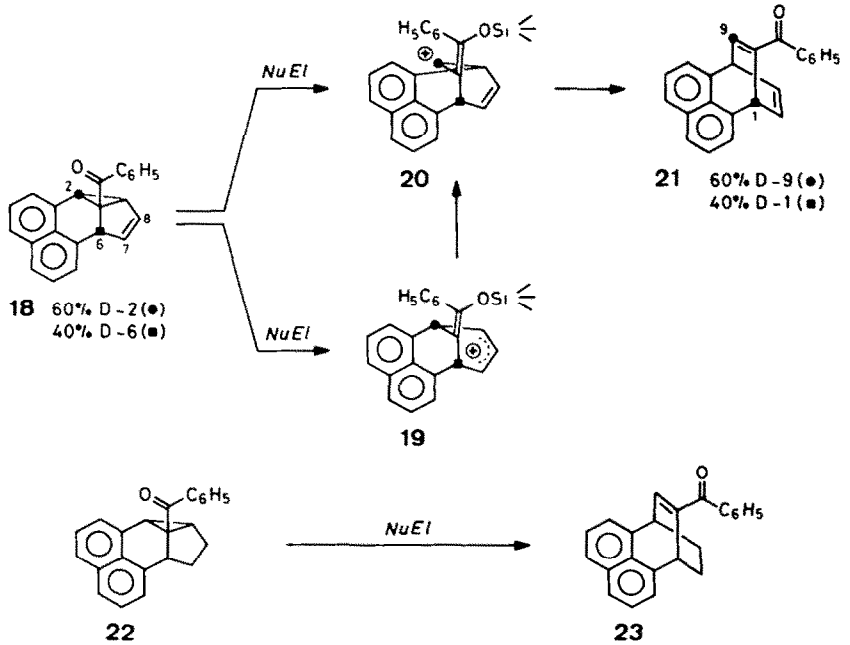
A first indication supporting an intramolecular mechanism was gained by the negative result with **13** (Scheme 5). Under conditions (Nafion-TMS, toluene ≥ 80°) which smoothly rearranged **1a–d**, the 7-*endo* acetate **13** resisted reaction. Direct conclusive evidence was obtained when the 7-*endo* deuterio analog **14** was rearranged in presence of Nafion-TMS at 80° in toluene. After 6 hr an 85% conversion was reached and an >80% *endo*-deuteriation at C(2) of **16** was determined by ^{1}H NMR difference measurements on a 270-MHz instrument comparing **16** with non-deuteriated **8b**. Extended reaction time (12 hr) led to a 1:1 stereoequilibration of deuterium at C(2) (**16**→**17**). Prior to this experiment the assignments of H(*exo*) and H(*endo*) at C(2) were made by decoupling experiments involving H-C(1) in **8b** and an NOE for H(*exo*) with H-C(1). The kinetic formation of **16** can only be explained by the intramolecular participation of the enoxy double bond effecting **15**→**16**. An alternative intermolecular mechanism would necessarily require the formation of intermediate NuD or NuH species upon deuterion and proton abstractions from C(7), with a higher probability for the latter process to occur (*exo*-abstraction, isotope effect). Preferentially exo-oriented H^+- and D^+-transfer to the double bond in **15** would terminate the sequence. Such an intermolecular variation cannot account for an >80% *endo*-deuteriation found at C(2) of **16**. The result thus constitutes for the first time full spectroscopic proof for an *intramolecular* olefin participation effecting proton (deuterion) transfer.[24]

Similarly, cyclopropyl ketones when partial structures of aro-semibullvalenes react with catalytic amounts of either of the two reagents Nafion-TMS and TMSTFA. Two representative examples are depicted in Scheme 6. The



Scheme 5. Intramolecular elimination mechanism.

method was found to be generally applicable.[10] The aro-semibullvalene structure **18** as an isotopomeric mixture (60% D-C(2), 40% D-C(6)) and the reduced form **22** (here without D labelling) are both photochemically accessible[25] and can be rearranged in high yields to the aro-barrelene-like unsaturated ketones **21** and **23**. The two latter compounds are the starting materials (neglecting the D labels) to produce **18** and **22**. The rearrangements with Nafion-TMS were conducted in toluene at room temperature affording a 99% yield for **18**→**21** and an 85% yield for **22**→**23**. The same transformations can be carried out again at room temperature with TMSTFA (90–95% yields for **18**→**21**, and 70–75% yields for **22**→**23**). We may note here that the TMSTFA brings about rearrangements as successfully as the triflate, instead of undergoing addition reactions as observed before (e.g. Scheme 2). This points either to the formation of unstable adducts (e.g. **19**→allylic adduct) or to short lived intermediates favouring intramolecular processes. With the aid of labelled **18**, a partial insight into the characteristics of the course of such a rearrangement was gained. Electrophilic activation would be expected to create first a cationic intermediate **19** with allylic character, which can rearrange to **20** and ultimately form **21**. However, this cascade should include scrambling of the deuterium label in the intermediate **19**, which was not observed. Therefore, regioselective conversion to **21** (60% D-C(9) and 40% D-C(1))[10] can only be accommodated either by a regioselective 1,2-naphthyl shift in **19** or by a concerted ring opening and naphthyl shift (**18**→**20**) circumventing **19**.



Scheme 6. NuEl = Nafion-TMS; $CF_3CO_2Si(CH_3)_3$.

Interestingly, the 7,8-unsaturation is not important as a stabilizing factor in the potential intermediates since the 7,8-dihydro aro-semibullvalene **22** does not differ in reactivity.

Catalytic steering of the rearrangements **18**→**21** and **22**→**23** was demonstrated by the following experiment. If a catalytic amount of trifluoroacetic acid was added to solutions of **18** or **22** in d_6-benzene or $CDCl_3$ containing TMS (Merck) as a standard, the reactions to **21** and **23** occurred equally facile at room temperature (eqn 3). The rates of reaction were proportional to the concentration of trifluoroacetic acid. However, if carefully redistilled TMS was used, no rearrangement could be observed (eqn 4),[10] which is in agreement with the inertness of trifluoroacetic acid towards clean TMS.[20] The acid does therefore necessarily combine with impurities

(3) **18** or **22** $\xrightarrow[CF_3CO_2H,\ r\,t]{TMS\ (commercial)}$ **21** or **23**

(4) **18** or **22** $\xrightarrow[CF_3CO_2H,\ \geq r\,t]{TMS\ (distilled)}$ no reaction

(< 0.2%) present in commercial TMS forming at least one NuEl composition of considerable electrophilic power, similar in reactivity to, e.g. Nafion-TMS and TMSTFA.

EXPERIMENTAL

General remarks. M.ps were determined on a Kofler hot microscope and are uncorrected. Mass spectra (MS) were recorded on a Varian MAT CH5 instrument at 70 eV. ^{1}H NMR spectra were measured ($CDCl_3$ unless stated otherwise) in FT mode on Bruker WP-80 and WH-270 instruments. The chemical shifts are in δ units and the coupling constants (J) in Hz. The abbreviations s, d, t, q and m refer to singlet, doublet, triplet, quartet and multiplet, respectively. The IR spectra ($CHCl_3$) were recorded on Perkin-Elmer 137 and 700 instruments and are given in cm^{-1}. GLC analyses were performed with a Varian Aerograph 1700 instrument equipped with a flame ionization detector coupled to a Spectra Physics Autolab System I computing integrator. The columns were OV 101 glass capillary columns of 20 and 35 m lengths, with nitrogen as the carrier gas. Preparative thick layer chromatography was carried out on 2 mm silica plates (Merck). The solvents were purified using standard procedures. All reactions were run under argon atmosphere. In the usual work-up the solvent was removed *in vacuo* and the residue taken up in ether and water; after shaking, the organic layer was separated and dried over $MgSO_4$.

Trimethylsilyl trifluoromethanesulfonate. 1.5 g (10 mmol) of trifluoromethanesulfonic acid and 1.1 g (12.5 mmol) tetramethylsilane (Merck) were mixed together at room temp. After standing for 1 hr, the evolution of methane (which has been identified by GLC on a 48 m glass capillary column OV 1 at 0° and by mass spectroscopy) ceased. Subsequent distillation of the mixture was performed for identification purposes only, affording trimethylsilyl trifluoromethanesulfonate in 2.2 g (99% yield) as a colorless liquid. B.p. 40°/11 torr.[21] ^{1}H NMR 0.50[22c]. MS 222 (M^+), 207, 147 (base peak), 77, 73, 69.

Di-t-butyl tetramethyldisiloxane. 2 g (13.4 mmol) of t-butyl dimethylchlorosilane were dissolved in 5 mL acetonitrile and 1 mL water. After addition of 2.25 g (15 mmol) NaI the mixture was stirred at room temp for 12 hr and during this time two layers separated. The top layer was pipetted off and distilled to afford a colorless liquid (1.3 g, 5.5 mmol), which was identified as di-t-butyl tetramethyldisiloxane (82% yield). B.p. 65°/11 torr. IR 3000, 2900, 1465, 1385, 1360, 1255, 1060, 1005, 945, 840. ^{1}H NMR 0.01 (s), 0.87 (s) in a 2:3-ratio[16] MS 246 (M^+), 231, 189, 147 (base peak), 73, 57.

Representative experiment for the transformation of **1a,b** *to* **2a,b** *with acetyl methanesulfonate and tetramethylammonium bromide or iodide.* 0.75 g (5.5 mmol) of **1b**[23] was dissolved in 15 ml acetonitrile (CH_2Cl_2 can be used instead, but the reactions will be slower). 1.2 g (8.7 mmol) acetyl methanesulfonate[11] and 1.54 g (10 mmol) tetramethylammonium bromide were added and the mixture allowed to stir for 24 hr at room temp. After filtration, the usual work-up procedure was applied and 1.28 g of crude material was isolated. Further purification was achieved on a short column of silica gel (15 g) and elution with hexane/toluene (1:4) afforded 1.02 g (3.95 mmol) of **2b** (72% yield) as a yellowish oil. IR 3070, 3010, 1760, 1670, 1645, 1490, 1455, 1375, 1340, 1225, 1200, 1145, 1095, 1040, 820. ^{1}H NMR 1.03 (d, J = 8, 3H), 1.8–2.3 (m, 7H within at 2.07 (s, 3H)), 2.41 (m, 2H), 3.51 (dd, J = 2 and 8, 1H) 4.19 (s, 1H), 5.29 (s, 1H). MS 258 (M^+), 216, 137 (base peak), 109, 79, 43.

In an exactly analogous way the reactions were conducted by adding tetramethylammonium iodide instead of the parent bromide (→iodo enolacetate **2b**) or without any addition of halides (→mesyloxy enolacetate **2b**). Equal procedures were applied for **1a**[26]→**2a**, **3a** and for the cleavage of cyclopropyl ketones in a more general scope.[9] Notably, the iodo compounds are labile materials and should be used for further transformations shortly after isolation.

Reaction of **1a** *with t-butyldimethylsilyl iodide affording* **4a** *and* **5a**. To a mixture of 0.9 g (6 mmol) of t-butyldimethylchlorosilane (Fluka) and 1.05 g (7 mmol) NaI in 10 mL $CHCl_3$, 0.4 g (3.28 mmol) of **1a**[26] were added and stirred at room temp for 20 hr. After filtration followed by the usual work-up, 0.75 g of crude **4a** and **5a** were isolated. The ratio was determined by GLC to be 5:1 (the two compounds added up to a 92% purity; 84% yield). By subsequent purification on silica (10 g) with hexane/toluene (1:1) pure oily **4a** was obtained besides material containing **5a** in 80% enriched form (20% residual **4a**). Analytical data for **4a**: IR 3000, 2910, 1740, 1445, 1400, 1360, 1160, 1125, 1000. ^{1}H NMR 1.50–2.75 (m, 8H), 2.96 (m, 2H), 3.90 (dd, J = 6 and 14, 1H). MS 250 (M^+), 123 (base peak), 95, 81, 67, 53. **5a**: IR 2990, 2900, 1710, 1385, 1260, 1100, 1010. ^{1}H NMR 1.5–2.8 (m, 10H), 3.94 (bs, 1H). MS 250 (M^+), 123 (base peak), 95, 81.

Reaction of **1a** *and* **1b** *with trimethylsilyl trifluoroacetate yielding* **6a** *and* **6b**. 2 mmol of either **1a**[26] (245 mg) or **1b**[23] (272 mg) were heated in 1 mL trimethylsilyl trifluoroacetate (Fluka or footnote 5 in lit.[10]) to 60° for a duration of 96 hr. After the usual work-up, the residual oily materials were distilled at reduced pressure affording the colorless liquids **6a** (60°, 1 torr; 403 mg; 85% yield) and **6b** (65°, 1 torr; 400 mg; 80% yield) respectively. The analytical data for both materials are already described in footnote 6 of lit.[10]

Rearrangement of **1a**→**8a** *with either methyl triflate or TMS-triflate.* 245 mg (2 mmol) of **1a**[26] were dissolved in 5 mL $CHCl_3$ (passed prior to reaction over a short column of basic alumina) and stirred after addition of either methyl triflate (0.02 mL, 0.2 mmol) or TMS-triflate (0.04 mL, 0.2 mmol) at 0° for a few min. The reaction was then allowed to proceed at room temp for 6 hr. For work-up, the mixture was washed with $NaHCO_3$aq and the organic layer dried over $MgSO_4$. The crude isolated material was purified by distillation at 65°/1 torr affording **8a**, 150 mg (50% yield) and 190 mg (63% yield), respectively. IR 3110, 3000, 1740, 1635, 1445, 1410, 1350, 1160. ^{1}H NMR 1.94 (dd, J = 4 and 18, 1H), 2.19 (m, 1H), 2.21 (m, 1H), 2.39 (d, J = 10, 1H), 2.47 (t, J = 10, 1H), 2.67 (m, 1H), 2.92 (m, 1H), 3.36 (m, 1H), 5.64 (m, 1H), 5.77 (m, 1H). MS 122 (M^+), 93, 79 (base peak), 66, 49, 39.

Representative experiment for the rearrangements **1a–d**→**8a–d** *with Nafion-TMS.* 610 mg (5 mmol) of **1a**[26] were dissolved in 10 mL toluene and heated in presence of 180 mg Nafion-TMS[17] to 80° for a duration of 12–18 hr (the efficiency of the rearrangement strongly depends on the activity of the TMS-resin, which was found to be different from batch to batch; although the yields of final product isolated were not affected). The reaction course was monitored by GLC, and after completion, work-up consisted of a filtration on 5 g silica gel. Exhaustive washing of the silica with toluene was followed by a distillation of the collected material at 65°/1 torr affording 550 mg **8a** (90% yield). For analytical data of **8a** see previous experiment.

In the same way, the reactions were run for **1b→8b** (here monitoring by GLC is crucial, since extended reaction time causes stereoequilibration at C(4)) and for **1c,d→8c,d**. For analytical data of **8b** see footnote 6 of lit.[10] and for a detailed ^{1}H NMR assignment see following experimental part (→**16**). Data of **8c,d** see.[27]

2 - endo - *Deuterio* - 4 - *exo* - *methyl* - *bicyclo*[3.3.0]*oct* - 7 - *en* - 3 - *one* (**16**) *from* 7 - *endo* - *deuterio* - 4 - *exo* - *methyl* - *tricyclo*[3.3.0.0.^{2,8}]*octan* - 3 - *one* (**14**). The sequence by which the deuteriated starting material **14** was prepared, will be given in the following short description since standard transformations are involved only. **8b** (for the preparation see previous experimental part) was acetalized (ethylene glycol; trimethyl orthoformate; *p*-toluenesulfonic acid; toluene; r.t.) and subjected to preferential *exo* epoxidation[23] (*m*-chloroperbenzoic acid; CH_2Cl; 0°). After purifying on florisil, the clean *exo*-epoxide was cleaved with lithium aluminumdeuteride in ether at −20°, yielding mainly 7-*endo*-deuterio-8-*exo*-hydroxy acetal. Hydrolysis of the acetal function (10% aq HCl; ethanol; r.t.) was followed by 8-*exo* iodination (MsCl, NEt_3, CH_2Cl_2, 0°; NaI, acetone, refl.) and cyclopropanation (DBU; ether; r.t.; →**14**). The successful 7-*endo* deuteriation in **14** (>90%D) was assigned by mass spectroscopy (137(M^+)) and by comparison with a non-deuteriated sample **1b**, which allowed positional assignments upon extensive decoupling in presence of Eu(fod)$_3$ shift reagent on a Bruker WH-270 instrument. Optimum signal separation was achieved with 10% solns of **1b** (0.5 mL) in $CDCl_3$ and 15 mg of added Eu(fod)$_3$. ^{1}H NMR assignment for **1b**: 1.10 (d, J = 7, CH_3), 1.53 (dt, J = 7 and 14, H_{endo}-C(7)), 1.56 (dd, J = 7 and 10, H_{exo}-C(7)), 1.72 (q, J = 7, H-C(4)), 1.91 (q, J = 5, H-C(2)), 1.96–2.10 (m, $H_{exo,endo}$-C(6), H-C(8)), 2.43 (t, J = 5, H-C(5)), 2.65 (q, J = 5, H-C(1)).

Compound **14** was equally rearranged as described in the previous experimental part for **1b→8b**. The reaction reached after 6 hr a conversion of 85%. Mass spectroscopy (137(M^+)) together with a ^{1}H NMR analysis (Bruker WH-270) revealed 80% *endo* deuteriation at C(2) (**16**). The NMR assignment is based on the comparison with a non-deuteriated sample **8b**, which was extensively decoupled in presence of Eu(fod)$_3$ shift reagent (0.5 mL 10% solns of **8b** in $CDCl_3$ with 20 mg Eu(fod)$_3$). ^{1}H NMR assignment for **8b**: 1.02 (d, J = 7, CH_3) 1.90 (q, J = 7, H.C(4)), 2.24 (dd, J = 8 and 16, H_{endo}-C(6)), 2.26 (dd, J = 3 and 19, H_{endo}-C(2)), 2.39 (q, J = 8, H-C(5)), 2.42 (dd, J = 10 and 19, H_{exo}-C(2)), 2.64 (dd, J = 8 and 16, H_{exo}-C(6)), 3.26 (m, J = 3,8 and 10, H-C(1)), 5.64 (bs, H-C(7)), 5.72 (bs, H-C(8)). Additionally, an NOE was measured for H_{exo}-C(2) with H-C(1). If the reaction was allowed to proceed in total for 12 hr, 1:1 scrambling of deuterium resulted at C(2).

Rearrangements of **18** *and* **22** *to* **21** *and* **23**. The experimental details of the rearrangement **18→21** at room temp (in benzene or toluene) with Nafion-TMS (99% yield), TMSTFA (2 mol-equiv or catalytic, 90–95% yield) and with TMS (Merck) + trifluoroacetic acid (catalytic) have already been published.[10] The rearrangement **22→23** was performed in analogous way. The yields of isolated **23** were 85% with Nafion-TMS and 70–75% with the TMSTFA procedure. For analytical data, including deuterium analysis, of all materials see Ref. 25.

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