formamid versetzte man mit 0,8 g 78-proz. NaH und nach einer Stunde mit 2,5 ml Äthyljodid. Man rührte eine weitere Stunde bei 50°, verdampfte das Lösungsmittel und schüttelte den Rückstand zwischen Wasser und Methylenchlorid aus. Das aus der organischen Phase gewonnene Rohprodukt lieferte beim Kristallisieren aus Essigester/Äther 1,73 g **3**. Durch Chromatographie der Mutterlauge an Kieselgel wurden mit Toluol/Essigester 1:1 0,9 g **4** und hierauf mit reinem Essigester weitere 0,47 g **3** eluiert. Eigenschaften von **3** und **4** siehe Tabelle 2.

3. *10,11-Diäthyl-4,6,7,8-tetrahydro-10a,6a-iminopropano-indolo[3,3a,4-gh]chinolin-9(10H),12-dion* (**6**) und trans-*10-Äthyl-9-oxo-4,6,6a,7,8,9,10,10a-octahydro-indolo[3,3a,4-gh]chinolin-6a-(propionsäureäthylamid)* (**5**). Eine Lösung von 15,5 g **3** in 300 ml flüssigem Ammoniak versetzte man mit soviel (4,0 g) Natrium, bis die Lösung blau blieb. Bei der Chromatographie des rohen Reaktionsgemisches an einer Kieselgelsäule wurden mit Chloroform + 5% Methanol zuerst 40% **6** und dann mit dem gleichen Elutionsmittel 19% **5** ins Filtrat gewaschen. Eigenschaften von **5** und **6** siehe Tabelle 3.

4. *11-Äthyl-4-benzyl-9-methylamino-4,6,7,8-tetrahydro-10a,6a-iminopropano-indolo[3,3a,4-gh]chinolin-12-on* (**8**). Eine Lösung von 1,1 g **4** in 25 ml 2-Propanol wurde mit 1,2 ml 2N Salzsäure in wasserfreiem 2-Propanol und 15 ml Methylamin 15 Std. im Autoklaven auf 100° erwärmt. Nach dem Eindampfen lieferte Kristallisation des Rückstandes aus 2-Propanol/Petroläther 0,55 g *Hydrochlorid von* **8**, Smp. 177–180°. IR.-Spektrum in Nujol: breite Bande bei 1644–1660 cm^{-1}. Charakteristische Signale des NMR.-Spektrums der Base ($CDCl_3$): 4,25 δ (NH, breit), 3,6 δ ($-CH_2-CH_3$, breites *m*), 2,7 δ ($N-CH_3$, *s*), 0,5 δ (CH_2CH_3, *t*). $C_{27}H_{30}N_4O$ (426,5).

5. trans-*9-Oxo-4,6,6a,7,8,9,10,10a-octahydro-indolo[3,3a,4-gh]chinolin-6a-(propionsäureäthylamid)* (**9**). Man versetzte eine Lösung von 3,85 g **4** in 60 ml flüssigem Ammoniak und 30 ml absolutem Äther mit 1,15 g Natrium und verdampfte das Ammoniak nach 2 Std. Den Rückstand schüttelte man zwischen Chloroform und Salzsäure aus und chromatographierte das aus der organischen Phase gewonnene Rohprodukt an einer Kieselgelsäule. **9** wurde mit Chloroform + 10–15% Methanol ins Filtrat gewaschen. Smp. 229–231°. IR.-Spektrum in Nujol: 3275 cm^{-1} (NH), 1642 cm^{-1} (CO). $C_{19}H_{23}N_3O_2$ (325,4).

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214. Rates of Chromium(VI)-Oxidation of Benzocyclenols

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(12. VII. 71)

Summary. The oxidation rate of benzocyclobutenol (**6**) and of the homologous alcohols up to 1-benzocyclo-octenol (**7**) with chromium(VI) has been determined in 90% acetic acid. The rate profile for the oxidation reaction is similar to that obtained for the solvolysis of the corresponding chlorides, and clearly shows a low reactivity for the benzocyclobutenyl skeleton, for reactions in which the hybridization changes from sp^3 to sp^2. On the other hand, semicarbazone formation occurs faster with benzocyclobutenone (**6a**) than with the homologous ketones. The implication of these results for the oxidation mechanism is discussed.

In a previous communication [1] the rate of oxidation of 4,6-dimethylbenzocyclobutenol (**1**) with chromium(VI) was reported to be lower then that for 1-indanol

(**2**) and for 1-tetralol (**3**). This difference in reactivity was interpreted as due to angle strain in the highly strained oxidation product 4,6-dimethylbenzo-cyclobutenone (**1a**). In this interpretation however, it was assumed that each of the methyl groups in **1** had the same rate accelerating effect as that in 1-(4-methylphenyl)-ethanol (**4**) which is more reactive, by a factor of 1.75, than 1-phenylethanol (**5**), justification being based on the similarity of the *Hammett* ϱ-values for the pK_{R+} of di- and of tri-phenyl-methanols [2] with those of 1-phenyl-3,5,6-trimethyl-benzocyclobutenols [3].

In view of the mechanistic interest in the oxidation of alcohols leading to strained ketones [4] the kinetic measurements were extended to a series of benzocyclenols from benzocyclobutenol (**6**) to 1-benzocyclo-octenol (**7**) and to various other model compounds. The results of these measurements are in full agreement with the assumptions originally made. The rate constants obtained are summarized in Table I where the data for the benzocyclenols are first listed. Relative to the rate of oxidation of 1-phenylethanol (**5**) that of benzocyclobutenol (**6**) is 1.7, in very good agreement with the value 1.8, predicted from that of **1**, previously shown to be 5.5 [1]. Additional methyl substitution of the benzene ring increases the rate in the same order as has

Table I. *Rate of oxidation of alcohols with chromium(VI)*
At 25° in 90% acetic acid, containing 0.01 M potassium acetate

No	Alcohol	k_2 (M^{-1},min^{-1})	k_{rel}
6		1.34	1.7
2		7.28[a]	9.3
3		11.5	14.7
9		2.26	2.9
7		0.49	0.63
1		4.28[a]	5.5
8		11.6	15
5		0.784	1.0
10		0.30	0.38
4		1.37[a]	1.75
11		0.56[a]	0.7
12		3.37[a]	4.3

[a]) Ref. [1].

been observed for **1** [1]. Thus, 3,4,5,6-tetramethylbenzo-cyclobutenol (**8**) reacts about 2.7 times faster than **1**, which in turn is 3.2 times more reactive than benzocyclobutenol (**6**).

The rate profile for the oxidation of the unsubstituted benzocyclenols is shown in Fig. I. The lowest reactivities in the series are found at the extreme end of the profile,

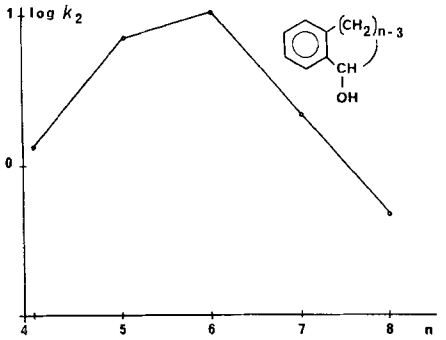


Fig. 1. *Rate profile for the chromium(VI)-oxidation of benzocyclenols*

namely for benzocyclobutenol (**6**) and 5-benzocyclo-octenol (**7**), whereas the other bicyclic alcohols **2**, **3** and **9** are accelerated not only with respect to **6** and **7**, but also to the acyclic model compound 1-(4-methylphenyl)-ethanol (**4**). The lower rate of **7** in comparison to that of **4** can be ascribed to steric inhibition of resonance between the phenyl ring and the developing carbonyl in the transition state. The same effect is also operative in the oxidation of 5-benzocycloheptenol (**9**). In both **7** and **9** the carbonyl groups cannot achieve coplanarity with the adjacent aromatic system, as is evidenced by the low extinction coefficient for the carbonyl chromophore in their UV. spectra [5]. Assuming that the transition state for the oxidation has ketonic character to some degree, the importance of resonance in transition state stabilization becomes obvious. The carbonyl character of the transition state has been clearly demonstrated by *Wilcox* [6] and other investigators [7] [8]. For example, it was found that in the oxidation of norbornanol, the ratio of the rate constants for the *exo*- and *endo*-alcohols reflects the ground state energy difference between these alcohols.

A correlation between the *exo-endo* ratio of the oxidation rate constants and the stability of the corresponding epimeric alcohols can only be found if the transition states for both alcohols have very similar or identical energies. From the slope of plots of log k_{exo}/k_{endo} against $\Delta G°$, it was deduced that 60 to 90% of the non-bonded interactions are eliminated by change to the activated complex. Calculations have shown that this energy loss is achieved by a relatively small conformational change of the C–O bond. The latter is believed to be rotated by only 12° with respect to the adjacent methylene group in the activated complex, whereas transformation to the carbonyl product requires a corresponding rotation of 55° [6] [8]. So it was suggested that the transition state should resemble the alcohol rather than the ketone [9]. But this hypothesis in no way agrees with the energetic situation. Rate diminution in alcohol oxidation due to steric inhibition of resonance, as observed for benzocyclo-

octenol (**7**) and 1-(2-methylphenyl)-ethanol (**10**) [10], provides additional support for the carbonyl character of the transition state in alcohol oxidations.

In [1] the rate of 1-tetralol (**3**) oxidation was reported to be lower than that for 1-indanol (**2**), the rate constant for the former having been extrapolated from data in [10]. Under the conditions here used however, it has been found that **3** is more reactive than **2**, the rate constant reported for **3** in Table I representing the average of *ca.* 15 runs using samples differing by their methods of purification. The higher reactivity of **3** with respect to that of **2** is in contradiction with the solvolysis rates of the corresponding chlorides [5], see Fig. II which shows 1-chloro-indane to be the most reactive of the benzocyclenyl chlorides. The difference in reactivity between **2** and **3** in oxidation, however, is not considerable and is probably not of major importance.

Attempts have been made to correlate rates of reactions involving hybridization changes from sp^3 to sp^2, with the IR. stretching frequencies of the corresponding carbonyl groups [12] by considering torsional and steric interactions in the ground state [13]. This *Foote-Schleyer* correlation was of considerable value in estimating non-assisted solvolysis rates and the treatment was later replaced by complete computer calculations based on classical energy functions [14]. In the original form, the *Foote-Schleyer* correlation only considers bond hybridization or angle strain, as expressed by the position of the carbonyl band for the ketones, in the evaluation of the stability of

Table II. *Relative rates of oxidation of alcohols and of their corresponding chloride solvolysis, and IR. carbonyl stretching frequencies of the corresponding ketones*

No	Alcohol	k_{rel} Oxidation	k_{rel} Solvolysis		$\nu_{(C=O)}$
6	Benzocyclobutenol	1.71		0.01 [b]	1765 1785
2	1-Indanol	9.27 [d]	1560 [a]		1720
3	1-Tetralol	14.7	420 [a]		1690
9	5-Benzocycloheptenol	2.89	12.1 [a]	9.2 [c]	1685
7	5-Benzocyclo-octenol	0.63	1.5 [a]		1672
1	1-Phenylethanol	1.00	ca. 1 [a]	1.0 [c]	1690
10	1-(2-Methylphenyl)-ethanol	0.30		22 [c]	1690
4	1-(4-Methylphenyl)-ethanol	1.75 [d]	—		1685
11	1-(2,4-Dimethylphenyl)-ethanol	0.71 [d]			1685
12	1-(2,4,6-Trimethylphenyl)-ethanol	4.30	—	1690 [c]	1705

[a] In ethanol, 40°, from [5].
[b] See expl.
[c] In ethanol, 25°, from [11].
[d] From [1].

the transition state, which is obviously only a first approximation. Nevertheless, the arguments can be applied qualitatively to the rate profile for benzocyclenol oxidation. These relative rates and the IR. stretching frequency of the corresponding ketones, as well as the chloride solvolysis rates are summarized in Table II. Taking the position of the carbonyl band of 1-tetralone at 1690 (the same position as for acetophenone) as a reference point for an unstrained ketone, one finds that shift to higher wave-numbers corresponds to decrease in reactivity. Thus for 1-indanol (**2**) and benzo-

cyclobutenol (**6**) the oxidation rates reflect the angle strain in the ketone. Similarly a widening of the bond angle, which also produces a shift to lower wavenumbers, as exemplified by **7** and **9**, leads to a decrease in reactivity. As mentioned above, however, the low rate of oxidation for **7** and **9** is considered to arise from resonance inhibition rather than from angle strain in the ketones. The spectral data in Table II demonstrate that, in the series of methyl substituted 1-phenylethanols, resonance inhibition in the ketone has very little, if any, effect on the position of the carbonyl band, whereas the effect on oxidation and solvolysis rates is considerable. In consequence it must be assumed that the agreement between carbonyl-absorption and reactivity for 5-benzocycloheptenol (**9**) and for 5-benzocyclo-octenol (**7**) is purely coincidental.

The arguments in favour of steric rate-retardation, resulting from angle strain, as explanation of low rate of oxidation of benzocyclobutenol (**6**) by chromium(VI) have been presented elsewhere [1]. The low oxidation-rate of **6** is mirrored by an even more striking resistance to solvolysis of the corresponding 1-chloro-benzocyclobutene, which was found to be completely stable in ethanol at 40° over a period of 2 months, its maximum rate constant being 10^{-8} s^{-1} (deduced on the basis of the limit for detection of reaction products by NMR. spectra). The resistance of the analogous 1-bromo- and 1,2-dibromo-compounds towards S_N1 and S_N2 reactions is already documented qualitatively [15]. The rate profile for solvolysis of the 1-chloro-benzocyclenes, based on data by other investigators, is shown in Fig. 2. The rate profiles for oxidation (Fig. 1) and chloride solvolysis (Fig. 2) are similar, but as mentioned earlier, 1-tetralol

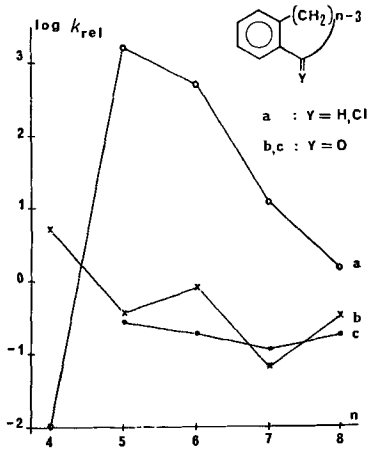


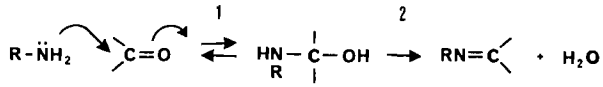
Fig. 2. *Solvolysis of 1-chloro-benzocyclenes* [a] *and semicarbazone formation of 1-benzocyclenones* [b] [c]

[a] Data from Table II; rates relative to that of 1-phenylethyl chloride.
[b] See [17] and experimental; rates relative to acetophenone.
[c] See [5] [11]; rates relative to acetophenone.

(**3**) is the most reactive towards oxidation, whereas 1-chloro-indane has the highest solvolysis rate; moreover the rate variations for solvolysis are, as usual, much more impressive than those for oxidation [16].

Although there is some mechanistic analogy between solvolysis and chromium(VI)-oxidation, for example both cases involve a hybridization change from sp^3 to sp^2 at the reacting carbon atom, complete agreement between the respective reaction rates cannot be expected. The steric requirements for an empty p-orbital in a carbonium ion and in a carbonyl group are not the same, and both the development of charge and its stabilization are quite different in the two cases.

In reactions involving hydribization changes from sp^2 to sp^3, the benzocyclobutenyl skeleton may be expected to be more reactive than the homologous five- and six-ring compounds; this is indeed observed. Preliminary results indicate that in the formation of semicarbazones, as compared with 1-indanone (**2a**), benzocyclobutenone (**6a**) is accelerated by factors of 2–10, depending on the pH; a typical rate profile for this reaction is included in Fig. 2 [17]. The low reactivities of the seven- and eight-ring ketones are unexpected, but are in agreement with published results (curve c) [5] [11]. They may be due to a change in the rate-limiting step from nucleophilic attack on the ketone to elimination of water from the tetrahedral intermediate, occuring in the series of substrates at constant pH. Analogous anomalies are well known



from *Jencks'* work on substituted benzaldehydes [18]. It is interesting to note that, in contrast to their rates of semicarbazone formation, that for reduction of benzocycloheptenone (**9a**) with aluminium isopropoxide is higher than that of 1-tetralone (**3a**) [11]. Unfortunately, for benzocyclobutenones, owing to their instability under the basic conditions used [19] [20], the corresponding reduction rates cannot be obtained.

Although the interpretation of the rate profiles for the benzocyclene derivatives in oxidation, solvolysis, and semicarbazone formation is not straightforward, the benzocyclobutenyl skeleton shows, in all these reactions, the reactivity expected from stereochemical considerations, *i.e.*: with respect to the homologous members of the series, reaction rates diminish when reaction involves change of hybridization from sp^3 to sp^2, and grow when change is from sp^2 to sp^3. In the absence of other significant accelerating or retarding effects, see [1], this reactivity is best explained by bond hybridization (or angle) strain in the sp^2-hybridized benzocyclobutenyl system, namely in the ketone and the carbonium ion. The rate-diminuation observed in the oxidation of benzo-cyclobutenol (**6**) is in agreement with a transition state resembling the ketone, and supplies a missing link for the argument in favour of the generally recognized mechanism for alcohol oxidation.

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Experimental. – *Alcohols.* Benzocyclobutenol (**6**) was obtained either by the addition of benzyne to vinyl acetate [21] and subsequent hydrolysis of the ester formed, or by reaction of chloro-benzocyclobutene [22] with silver trifluoroacetate in benzene followed by acid catalyzed *trans*-esterification analogous to the procedure described for the bromo-analogue [19]. For preparation of 4,6-dimethylbenzo-cyclobutenol (**1**) and 3,4,5,6-tetramethylbenzo-cyclobutenol (**8**), see [20]. The other alcohols, either commercially available products or obtained by sodium boro-

hydride reduction of the ketones, were purified by conventional methods and purity checked by NMR. spectroscopy.

IR. spectra were obtained in carbon tetrachloride solution with a *Perkin Elmer* 257 instrument.

Kinetic measurements. The previously reported method [1] was used for the oxidation reaction. Rates of formation of semicarbazones were determined by monitoring the absorption change in a UV.-cell, thermostatted at 25° with buffered (pH 3.7) 0.02 M semicarbazide hydrochloride solutions. Stock solutions of substrates were 0.01 M in dry acetonitrile. The substrate solutions introduced into the cell by means of a λ-pipet, were such that the final solution contained *ca.* 10^{-4} moles of ketone and 0.6–1% of acetonitrile. No corrections were made to the observed pseudofirst order rate constants.

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