Tetrahedron, 1967, Vol. 23, pp. 2721 to 2733. Pergamon Press Ltd. Printed in Northern Ireland

THE STEREOCHEMISTRY AND REACTIVITY OF UNSATURATED COMPOUNDS—III

REACTIVITY OF THE DOUBLE BOND IN Δ^3-CYCLOHEXENE AND Δ^4-OCTALIN DERIVATIVES RELATIVE TO THEIR CONFORMATIONS[1,2]

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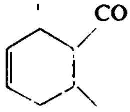
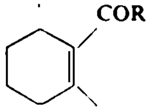
Abstract—A study of the double bond reactivity in Δ^3-cyclohexene derivatives with one polar substituent in the side chain and Me substituents in the ring has shown that the preferred conformation for these compounds, independent of their stereochemistry, has the polar group axial, giving rise to supra-annular interaction. Such interaction decreases the nucleophilicity of the ring double bond. A similar study of Δ^4-octalin-1,2-dicarboxylic acids and their esters has shown that in contrast to the reported conformational assignments[3] the preferred conformations, even for the *trans* derivatives are those with the polar substituents in diaxial position.

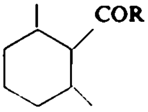
EARLIER it was shown that the CO group of carbonylic Δ^3-cyclohexene derivatives (I) is less prone to take part in nucleophilic addition reactions than the CO of the corresponding Δ^6-cyclohexene (II) and cyclohexane (III) analogs.[1,4,5]



I

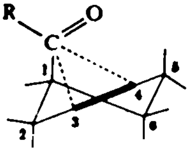


II

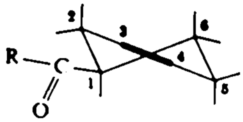


III

The underlying cause of such diminished activity of compounds I is stereochemical in origin. These compounds are preferentially in the fixed conformation IV with an axial CO close enough to the ring double bond to give rise to intramolecular interaction between the π-electrons of the latter and the electrophilic carbon of the former.[6]



IV



IVa

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[1] Part I, G. P. Kugatova-Shemyakina and Yu. A. Ovchinnikov. *Tetrahedron* **18**, 697 (1962).

[2] Part II, G. P. Kugatova-Shemyakina, V. M. Andreev and S. A. Kazaryan, *Zh. Ozg. Khim.* **2**, 2065 (1966).

[3] I. N. Nazarov, V. F. Kucherov and V. M. Andreev, *Izv. Akad. Nauk SSSR. Otdel. Khim. Nauk* 715, 817 (1956).

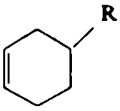
[4] G. P. Kugatova-Shemyakina, *Abstracts of congress lectures and scientific papers* (XIX-th JUPAC). *Abstracts* A.149, (1963).

[5] G. P. Kugatova-Shemyakina and G. M. Nikolaev, *International symposium on the Chemistry of Natural Products, Abstracts* E.245, Kyoto (1964).

[6] We have called the intramolecular exchange interaction we observed in Δ^3-cyclohexenic and Δ^4-octalinic systems the supra-annular effect[4] in distinction to the well known *trans*-annular[7] and field effects described by H. Kwart and L. J. Miller.[8]

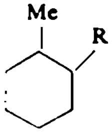
The chemical data previously obtained led to the conclusion that firstly, the supra-annular effect should be present whenever an unsaturated compound has an electrophilic center and the molecular geometry allows this center to come sufficiently close to the double bond and, secondly, the supra-annular interaction can modify the reactivity not only of the CO, but also of the ring double bond. In extension of these findings the present study is devoted to a more quantitative assessment of the effect of supra-annular interaction on the double bond reactivity.

Compounds with varying electrophilicity of the functional groups in position 1(a–e) and with varying numbers and positions of the ring methyls (V–VIII) were chosen for investigation.



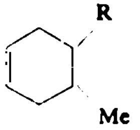
V

Va: R = CHO
Vb: R = Ac
Vc: R = COOMe
Vd: R = Me
Ve: R = CH(OMe)$_2$



VI

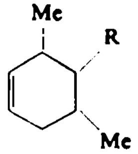
VIa: R = CHO
VIb: R = Ac
VIc: R = COOMe
VId: R = Me
VIe: R = CH(OMe)$_2$



VII

VIIa: R — CHO
VIIb: R — NO$_2$
VIIc: R — COOMe

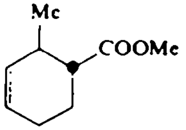
VIIIa: R — CHO



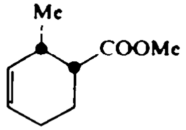
VIII

VIIIb: R — Ac
VIIIc: R — COOMe
VIIId: R — NO$_2$
VIIIe: R — CH(OMe)$_2$
VIIIf: R — Me

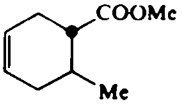
Although most of the compounds had been synthesized previously,[9–18] they were all mixtures of the *cis* and *trans* isomers[19] and therefore, the individual stereoisomers had to be isolated and then configurations determined. The separation was achieved



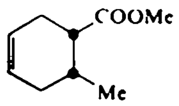
IX



X



XI



XII

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[7] A. C. Cope, M. M. Martin and M. A. McKervey, *Quart. Revs* **20**, 119 (1966).

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[9] I. N. Nazarov, G. P. Kugatova and G. A. Laumyanskas, *Zh. Obshch. Khim.* **27**, 2450 (1957).

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[12] A. A. Petrov and N. P. Sopov, *Zh. Obshch. Khim.* **22**, 591 (1952).

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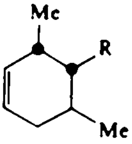
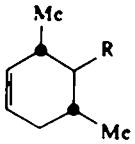
[18] A. A. Dudinskaya, G. A. Shvekhgeimer and S. S. Novikov, *Izv. Acad. Nauk SSSR. Otdel Khim. Nauk* 522, 524 (1961).

[19] An exception is the ketone VIIIb which we have synthesized for the first time. This compound is obtained in practically pure *trans-trans* form XIVb.



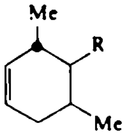
XIII

XIIIa: R = CHO
XIIIb: R = Ac
XIIIc: R = COOMe
XIIId: R = NO_2
XIIIe: R = COOH



XIV

XIVa: R = CHO
XIVb: R = Ac
XIVc: R = $COOCH_3$
XIVd: R = NO_2
XIVe: R = COOH

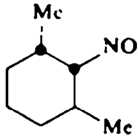


XV

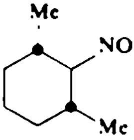
XVa: R = CHO
XVc: R = COOMe
XVe: R = COOH

by preparative GLC[20] and, in the case of the aldehydes, by fractional crystallization of their derivatives. The stereochemical purity of the substances was checked by GLC and TLC. The configurations of the isomers were determined by NMR spectra and chemically, by stereoselective synthesis to compounds of known configuration, as well as by application of the acetone rule[4,21] which, from the results of the condensation of acetone with Δ^3-cyclohexene aldehydes allows unambiguous determination of the configuration of both the latter and their reaction products (see the following communications).

It should be mentioned that the adduct VIIId obtained by condensation of piperylene and 1-nitropropylene had earlier been described as an *ortho* and *meta* isomeric mixture.[22] Actually, the condensation yields a mixture of *cis–trans*-XIIId and *trans–trans*-XIVd *ortho* adducts, where configurations were vigorously proved by NMR spectroscopy. The structures of these compounds were confirmed by catalytic hydrogenation to XVI and XVII followed by Nef transformation to the corresponding 2,6-dimethylcyclohexanones,[23] which were identified by their semicarbazones.[24,25]



XVI



XVII

The degree of the supra-annular induced double bond deactivation can be estimated by the extent of dithiocyanogen uptake, a reaction that has found wide application in quantitative determination of double bonds.[26,27]

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[20] The authors wish to express their acknowledgement to V. A. Vaver and A. N. Ushakov of the Institute for Chemistry of Natural Products, USSR Academy of Sciences for use of their chromatograph and for their aid in the isolation of the individual isomers.

[21] G. P. Shemyakina, Doctor's Theses. Institute of Organic Chemistry, USSR, Acad. Sci. Moscow (1961).

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[26] A. A. Zinov'ev, *Khimiya zhirov* (*The chemistry of Fats*) pp. 48, 234. Pishchepromizdat, M.-L. (1939).

[27] A. A. Bugorkova, L. N. Petrova and B. M. Rodionov, *Zh. Obshch. Khim.* **23**, 1808, 1813, 1822 (1953).

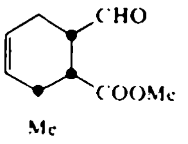
It seemed quite feasible to assume that for compounds with the alkyl group *cis* to the electrophilic substituent (X, XII, XIII, XV), the confirmed conformation would be such that the latter is axial, making possible the existence of the supra-annular effect. On the other hand, the preferred conformation for the *trans* isomers IX, XI and even more so for the *trans-trans* isomers XIVa–d, because of possible *meta* diaxial interaction, should be that of IVa rather than IV, making the supra-annular effect impossible. In view of this, we carried out the thiocyanation, first of the individual isomers and then of the mixtures.[28] Actually the preferred conformation for both *cis* and *trans* isomers turned out to be IV with axial electrophilic substituent (Table 1), so that in contrast to monocyclic compounds with two polar substituents XVIII, XIX,[2] deactivation of the double bond in monocyclic compounds with a single polar substituent VI, VII is practically independent of the stereochemistry.

TABLE 1. THIOCYANATION OF Δ^3-CYCLOHEXENIC ISOMERS

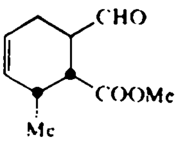
Compound	% Thiocyanation	Compound	% Thiocyanation
IX	67	XIIId	0
XI	65	XIVd	0
IX + X (2:1)	64		
XIVb	59	XIII + XIVd (1:1)	0

TABLE 1A

Compound	% Thiocyanation	Compound	% Thiocyanation
XIIIc	65	XIVc	73
XIIIc	64	XVa	32
XIVa	51	XVb	57
XIVc	76	XVc	48



XVIII



XIX

However, the double bond reactivity becomes configuration-dependent in the presence of a second *ortho* substituent on the Δ^3-cyclohexene ring (compds. XIII-XV; Table 1a). This could be due to possible *meta*-diaxial interaction of the alkyl groups, absent in *cis-trans*-XIII and *trans–cis*-XV isomers.

The thiocyanation data clearly reflect the degree of deactivation by electrophilic substituents of the Δ^3 bond in the series VIIIa–c (Table 2), showing the applicability of this reaction for evaluating the strength of the supra-annular effect.

It is noteworthy that for the same degree of electrophilicity of the 1-substituent the double bond reactivity depends on the amount and position of the alkyl groups adjacent to this substituent. For instance, the ease of thiocyanation decreases on passing from the unsubstituted ketone Vb or aldehyde Va to the disubstituted ketone

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[28] Thiocyanation was carried out with a solution of $(SCN)_2$ in a 1:2 AcOH–CCl_4 mixture at −10° for 5 min.

TABLE 2

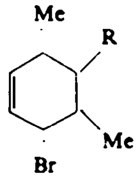
Compound	VIIIf: R = Me	VIIIc: R = COOMe	VIIIb: R = Ac	VIIIa: R = CHO	VIIId R = NO_2
Thiocyanation	92	71	59	51	0

TABLE 3. THIOCYANATION OF Δ³-CYCLOHEXENIC COMPOUNDS (V–VIII)

Compound	% Thiocyanation	Compound	% Thiocyanation
Va: R = CHO	72	Vc: R = COOMe	65
VIa: R = CHO	58	VIc: R = COOMe	64
VIIa: R = CHO	68	VIIc: R = COOMe	65
VIIIa: R = CHO	51	VIIIc: R = COOMe	71
Vb: R = Ac	81	VIIb: R = NO_2	5
VIb: R = Ac	66	VIIId: R = NO_2	0
VIIIb: R = Ac	59	VIIIf: R = Me	92

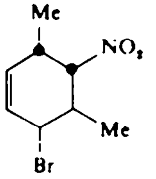
VIIIb or aldehyde VIIIa, remaining greater, however, for the ketones than for the aldehydes. Such change in thiocyanation reactivity also occurs with the nitro adducts VIIb and VIIId, but is almost absent in the esters Vc–VIIIc. The lower degree of double bond deactivation among the non-alkylated and monoalkylated adducts as compared to their dialkylated homologs is apparently due to decreased stability of type IV conformations in the former.

Another way of assessing the Δ³-bond deactivation is to determine the ability of the compounds to undergo allyl bromination[29] by bromosuccinimide and the exchange ability of the allylic bromine[30] in compounds such as XXa–e.

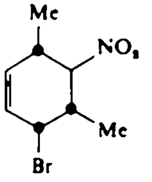


XX

XXa: R = Me
XXb: R = COOMe
XXc: R = CHO
XXd: R = $CH(OMe)_2$
XXe: R = NO_2



XXI



XXII

For instance, whereas the N-bromosuccinimide bromination of hydrocarbon VIIIf proceeds with evolution of heat and is complete in 15–20 min, bromination of the aldehyde VIIIa requires heating and of the nitro adduct VIIId in the absence of initiator occurs with considerable difficulty.

Bromosuccinimide treatment of the individual isomers XIIId and XIVd yielded the corresponding nitrobromides XXI and XXII with greatly differing mobility of the bromine atom. Thus, on treatment with potassium acetate in glacial acetic acid (100°, 4 hr) the nitrobromide XXII readily exchanges its bromine for OAc whereas in the bromide XXI such exchange does not take place even under more drastic conditions (100°, 12 hr), the latter being recovered unchanged after treatment.[31]

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[29] G. P. Kugatova-Shemyakina and V. V. Lutsenko, *Trudy Akad. Nauk Litovskoi SSR* Series B, I(21), 165 (1960).

[30] G. P. Kugatova-Shemyakina and V. V. Lutsenko, *Izv. Akad. Nauk SSSR, Otdel. Khim. Nauk* 1429 (1964).

[31] This is apparently because the nitro group in the bromide XXI is apparently axial.

The strength of the supra-annular effect may therefore also be estimated by the ease of allylic bromine acetoxy exchange. Indeed on acetolysis under the conditions indicated in Table 4, the bromide XXe, i.e. the compound with the strongest supra-annular effect either does not undergo substitution or only to the extent of 3–5%, whereas the bromide XXa with no supra-annular interaction, undergoes exchange to the extent of 40–55%.[32] As was to be expected, the rate of bromine exchange in compounds XXb–d lies between that for the bromides XXa and XXe.

TABLE 4. EXCHANGE OF BROMINE FOR OAc (IN %) IN THE Δ^3-CYCLOHEXENE DERIVATIVES (XXa–e)

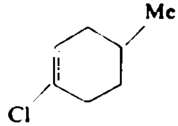
Compound / Reaction Conditions 2 M AcOK in glacial AcOH	XXa: R = Me,	XXb: R = COOMe	XXc: R = CHO	XXd: R = $CH(OMe)_2$	XXe: R = NO_2
1 hr, 40°	37	25	23	20	0
1 hr, 60°	46	37	34	33	0
1 hr, 80°	70	58	53	46	3
2·5 hr, 80°	85	79	57	56	5

The same regularity is observed in the exchange of allylic bromine for hydroxyl in the compounds XXa,c,d (Table 5), although here there is a certain levelling in the bromine reactivity. This is apparently due to the anionic reagent OH^- which may lower the stability of type IV conformations during attack on the CO carbon of aldehydes and esters.[33]

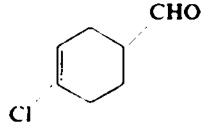
TABLE 5. EXCHANGE OF BROMINE FOR OH (IN %) IN THE Δ^3-CYCLOHEXENE DERIVATIVES XX

Compound / Reaction conditions 7% KOH in 80% CH_3OH	(XXa): R = Me	(XXc): R = CHO	(XXd): R = $CH(OMe)_2$
24 hr, 17°	55	45	42
1 hr, 60°	64	50	45
2,5 hr, 60°	71	57	50

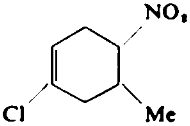
In view of the peculiar behaviour of the allylic bromine due to deactivation of the double bond, the reactivity of the vinyl halogen in the Δ^3-cyclohexene derivatives XXIII–XXV was investigated.



XXIII



XXIV



XXV

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[32] The degree of bromine exchange is determined by the amount of potassium bromide formed, which is separated and titrated with 0·1N $AgNO_3$.

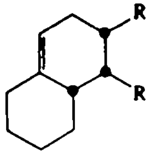
[33] The catalytic hydrogenation of the double bond, as expected, occurs with greater ease in the case of the acetal VIIIe than of the corresponding ester VIIIc or aldehyde VIIIa.[4]

It is well known that the chlorine of vinyl chloride is practically inert and does not take part in exchange reactions. In compounds manifesting the supra-annular effect, the double bond halogen acquires a certain mobility[4] (Table 6).

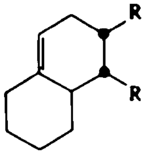
TABLE 6. EXCHANGE OF Cl FOR OAc (IN %) IN Δ^3-CYCLOHEXENIC DERIVATIVES

Compound Reaction Conditions: 2M AcOK in glacial AcOH, 80°	XXIII	XXIV	XXV
28 hrs.	0	6	29

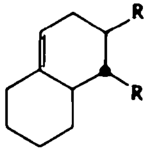
Extending these observations, the relative reactivity was determined of the individual stereoisomers of bi-functional Δ^4-octaline derivatives XXVI–XXIX because Kucherov *et al.* ascribed to the *trans*-isomers XXVII and XXIX the conformation with diequatorial substituents.[3]



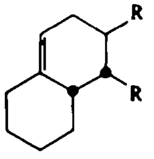
XXVI



XXVII



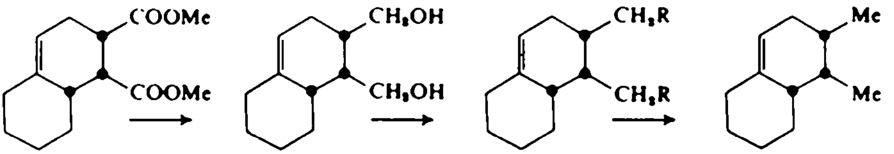
XXVIII



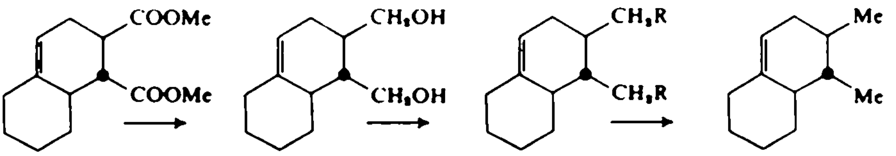
XXIX

XXVIa: R = COOMe; XXVIIa: R = COOMe; XXVIIIa: R = COOMe; XXIXa: R = COOMe;
XXVIb: R = COOH; XXVIIb: R = COOH; XXVIIIb: R = COOH; XXIXb: R = COOH
XXVIc: R = Me; XXVIIIc: R = Me;

The *syn-cis*-XXVIc and *anti-trans*-XXVIIIc 1,2-dimethyl-Δ^4-octalines were synthesized as model compounds for NMR peak assignments and also for comparative characterization of the double bond, according to the following scheme:



XXVIa XXX XXXI XXVIc



XXVIIIa XXXII XXXIII XXVIIIc

LAH reduction of the esters XXVIa and XXVIIIa yielded the corresponding glycols XXX and XXXII. Attempts to obtain their tosylates were unsuccessful: the tosylate XXXI (R = OTs) could not be isolated, whereas compound XXXIII

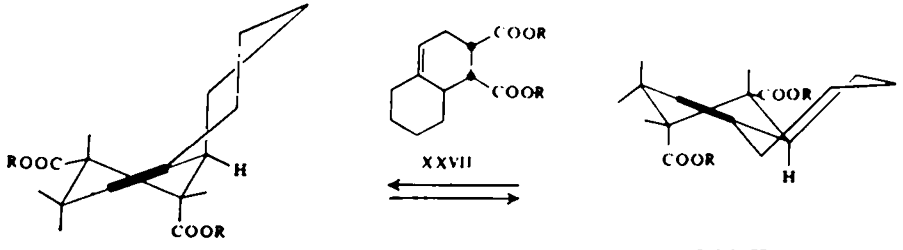
(R = OTs) was formed only in small amounts. However, good yields of the mesylates XXXI (R = OMs) and XXXIII (R = OMs) were formed by treating the glycols with methanesulfonyl chloride. LAH reduction of the mesylates then gave the hydrocarbons XXVIc and XXVIIIc.

One might expect that in the *cis* isomers XXVIa and XXVIIa (differing from each other in the stereochemistry about the C_{8a} atom) the nucleophilicity of the Δ^4 bond would decrease to about the same extent, because one of the two polar groups is always axial, regardless of the conformation (see XXXIV–XXXVII). However, the thiocyanation reactivity of the double bond of compound XXVIIa is markedly higher than that of the isomer XXVIa, approaching the reactivity of the hydrocarbon XXVIc (Table 7).

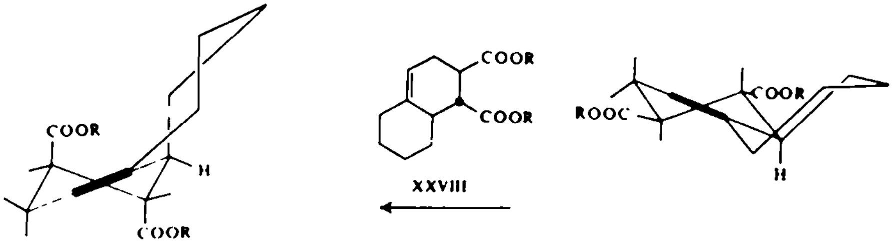
TABLE 7. THIOCYANATION OF Δ^4-OCTALINIC DERIVATIVES (XXVI–XXIX)

Compound	XXVIc	XXVIIIc	XXVIa	XXVIIa	XXVIIIa
% Thiocyanation	96	96	76	95	77
Compound	XXIXa	XXVIb	XXVIIb	XXVIIIb	XXIXb
% Thiocyanation	68	87	91	67	10

Examination of the molecular models of these compounds showed that the axial nucleophilic group cannot approach the double bond in compound XXVIIa. Similar results were obtained in the thiocyanation of the *trans* isomers XXVIIIa and XXIXa the percentage addition of dithiocyanogen in these compounds being less than in the corresponding *cis* isomers. From this it follows that for all the isomers examined the preferred conformation is probably the one with the polar substituents diaxial (see XXXVIII–XLI). The NMR data of these and a large number of other related substances indicates the complete absence of conformers with diequatorial electrophilic substituents.[34] All these data invalidate several rules derived by Kucherov *et al.* for



XXXVI* XXXVII*



XXXVIII* XXXIX*

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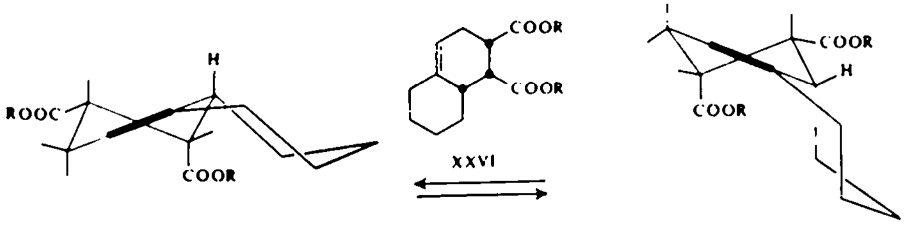
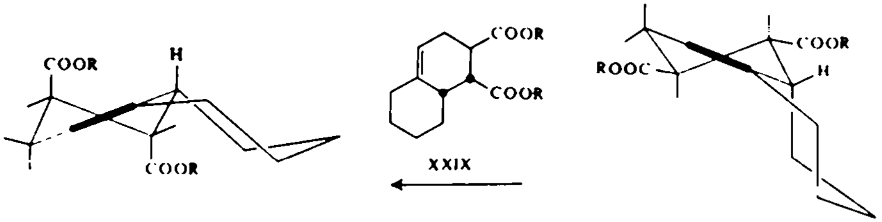
[34] G. P. Kugatova-Shemyakina, G. M. Nikolaev, V. M. Andreev, V. I. Sheichenko and V. F. Bystrov, unpublished data (see following communications).



XXXIV[a,b] XXXV



XL[a] XLI[b]

[a] The conformations as determined from NMR data.[34]

[b] The conformations as reported in the literature.[3]

compounds of this type and based on erroneous conformational assignments.[35] The same authors also assigned an incorrect conformation to the *anti-cis* isomer XXVII.

In conclusion it should be mentioned that according to preliminary results obtained in our laboratory by A. V. Bogdanova, T. M. Ushakova and A. N. Volkov, intramolecular interaction similar to that described above occurs also in linear compounds of the type CH_2= $CH(CH_2)_n$—X, the strength of the interaction depending on the electrophilicity of the substituent X.

EXPERIMENTAL

Δ³-Cyclohexene derivatives (V–VIII) were obtained by condensing the corresponding diene (1·2 mole) and dienophile (1 mole) in the presence of 0·5% hydroquinone, the mixture being heated in a steel tube at 190–200° for 3–7 hr, yield 60–80% (Table 8).

Hydrocarbons Vd, VId, VIIIf *and* XXIII were synthesized by the Wolf-Kishner reaction, a mixture of aldehyde (0·14 mole), 10 g 72% hydrazine hydrate and 100 ml diethylene glycol being refluxed for 30 min at 150°,[36] following which the reaction mixture was cooled, 8·4 g of fused KOH was added and heating at 125–130° continued for 2 hr. The product was distilled off by gradually raising the temp to 190°, yield 62–77% (Table 8).

Dimethylacetals (Ve, VIe, VIIIe) were obtained from 0·25 mole of aldehyde (Va–VIIIa), 150 ml abs MeOH and 0·5 ml conc HCl at room temp. After 72 hr, the mixture was treated with twice the volume of water and sat $NaHCO_3$aq, and dried over $MgSO_4$, yield 85–92% (Table 8).

The mixture of isomers obtained from the diene synthesis was separated by preparative GLC on a column (l = 2000 mm, d = 50 mm.) packed brick filler impregnated with polyethylene glycol succinate (10%), at 105° in a current of N, using a Gasofract PR-3000 instrument manufactured by Dr. Virus, Bonn or by fractional crystallization of the aldehyde derivs, to yield the individual isomers (Table 8).

The 5-bromo-2,6-dimethyl-Δ³-cyclohexene derivatives (XXa–e). To a soln of 0·3 mole of substance in 40 ml dry CCl_4 heated to boiling, 5·87 g N-bromosuccinimide was added so that the mixture

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[35] V. F. Kucherov and E. P. Serebryakov, *Izv. Acad. Nauk SSSR, Otdel. khim. Nauk* 1057 (1960) and all the previous papers of this series dealing with the conformations of Δ³-cyclohexene and Δ⁴-octaline series.

[36] Huang-Minlon, *J. Am. Chem. Soc.* **68**, 2487 (1946).

TABLE 8

Nos.	Compound	b.p. n_D^{20}	Found C	Found H	Calc C	Calc H	Formula
1	2	3	4	5	6	7	8
Ve	Δ^3-Cyclohexenaldehyde dimethyl acetal	67°/9 mm; 1·4568					
VIIIc	Methyl 2,6-Dimethyl-Δ^3-cyclo hexene carboxylate	79–80°/19 mm; 1·4570	71·43 71·59	9·79 9·71	71·39	9·59	$C_{10}H_{16}O_2$
VIIIf	1,2,6-Trimethyl-Δ^3-cyclohexene	147°; 1·4518	87·02 87·16	13·02 12·95	87·02	12·98	C_9H_{16}
XXIII	4-Chloro-1-methyl-Δ^3-cyclohexene	144–145°; 1·4733	64·48 64·58	8·40 8·65	64·37	8·46	$C_7H_{11}Cl^a$
XXV	4-Chloro-6-methyl-Δ^3-nitrocyclohexene	90–93°/18 mm; 1·5096	47·90 47·85	6·03 5·87	47·87	5·74	$C_7H_{10}ClNO_2{}^b$
IX	Methyl-2(β)-methyl-Δ^3-cyclohexene-1(α)-carboxylate	63–64°/6·5 mm; 1·4631	70·27 70·20	8·91 8·94	70·10	9·15	$C_9H_{14}O_2$
XI	Methyl-6(β)-methyl-Δ^3-cyclohexene-1(α)-carboxylate	79–80°/19 mm; 1·4570	69·83 70·00	9·09 9·01	70·10	9·15	$C_9H_{14}O_2$
XIIIc	Methyl 2(α),6(β)-dimethyl-Δ^3-cyclohexene-1(α)-carboxylate	86–87°/21 mm; 1·4578					
XIIIe	2(α),6(β)-Dimethyl-Δ^3-cyclohexene-1(α)-carboxylic acid	m.p. 91·5–92° (hexan)	70·05 69·91	9·05 9·28	70·10	9·15	$C_9H_{14}O_2$
XIIId	2(α),6(β)-Dimethyl-1(α)-nitro-Δ^3-cyclohexene	78°/6 mm; 1·4751	61·68 61·73	8·53 8·49	61·91	8·44	$C_8H_{13}NO_2$
XIVa	2(α),6(α)-Dimethyl-Δ^3-cyclohexene-1(β)-aldehyde	66–67°/15 mm; 1·4626	78·17 78·32	9·93 9·90	78·21	10·21	$C_9H_{14}O^c$
XIVb	2(α),6(α)-Dimethyl-1(β)-acetyl-Δ^3-cyclohexene	74–75°/9 mm; 1·4696	79·05 79·15	10·75 10·69	78·89	10·51	$C_{10}H_{16}O$
XIVc	Methyl 2(α),6(α)-dimethyl-Δ^3-cyclohexene-1(β)-carboxylate	72–73°/15 mm; 1·4540					
XIVe	2(α),6(α)-Dimethyl-Δ^3-cyclohexene-1(β)-carboxylic acid	m.p. 99–99·5° (hexan)	70·09 70·17	9·07 8·91	70·10	9·15	$C_9H_{14}O_2$
XIVd	2(α),6(α)-Dimethyl-1(β)-nitro-Δ^3-cyclohexene	72°/6 mm; 1·4665	61·91 62·07	8·30 8·23	61·91	8·44	$C_8H_{13}NO_2$
XVa	2(α),6(β)-Dimethyl-Δ^3-cyclohexene-1(β)-aldehyde	82°/26 mm; 1·4668	77·98 78·13	9·96 9·96	78·21	10·21	$C_9H_{14}O^d$
XVc	Methyl 2(α),6(β)-dimethyl-Δ^3-cyclohexene-1(β)-carboxylate	89–90°/20 mm; 1·4662					

XVe	2(α),6(β)-Dimethyl-Δ^3-cyclohexene-1(β)-carboxylic acid	126–127°/9 mm; m.p. 63–67° (hexan)	69·90 69·81	9·17 9·23	70·10	9·15	$C_9H_{14}O_2$
XVI	2(α),6(β)-Dimethyl-1(α)-nitrocyclohexane	81·5°/6 mm; 1·4636	61·43 61·30	9·69 9·72	61·12	9·62	$C_8H_{15}NO_2$
XVII	2(α),6(α)-Dimethyl-1(β)-nitrocyclohexane	75·5°/6 mm; 1·4551	61·24 61·37	9·83 9·80	61·12	9·62	$C_8H_{15}NO_2$
XXa	5-Bromo-1,2,6-trymethyl-Δ^3-cyclohexene	68–70°/9 mm; 1·5128	52·89 53·04	7·60 7·61	53·21	7·98	$C_9H_{15}Br$[e]
XXb	Methyl 5-bromo-2,6-dimethyl-Δ^3-cyclohexene carboxylate	87–89°/8 mm; 1·5137					$C_{10}H_{15}BrO_2$[f]
XXc	5-Bromo-2,6-dimethyl-Δ^3-cyclohexenaldehyde	38–40°/0·4 mm; 1·5170					$C_9H_{13}BrO$
XXd	5-Bromo-2,6-dimethyl-Δ^3-cyclohexene dimethyl acetal	85–87°/7 mm; 1·5145					$C_{11}H_{19}BrO_2$
XXe	5-Bromo-2,6-dimethyl-nitro-Δ^3-cyclohexene	75°/0·1 mm; 1·5249	41·30	5·26	41·04	5·16	$C_8H_{12}BrNO_2$[g]
XXI	5(β)-Bromo-2(α),6(β)-dimethyl-1(α)-nitro-Δ^3-cyclohexene	58–60°/0·15 mm, 1·5255	41·03 40·92	5·31 5·21	41·04	5·16	$C_8H_{12}BrNO_2$[h]
XXII	5(α)-Bromo-2(α),6(α)-dimethyl-1(β)-nitro-Δ^3-cyclohexene	68–69°/0·34; 1·5212	41·06 41·30	5·42 5·40	41·04	5·16	$C_8H_{12}BrNO_2$[i]
	5(β)-Acetoxy-2(α),6(α)-dimethyl-1(β)-nitro-Δ^3-cyclohexene	m.p. 91–92° (methanol)	56·62 56·38	7·37 7·30	56·32	7·09	$C_{10}H_{15}NO_4$
	5-Acetoxy-1,2,6-trimethyl-Δ^3-cyclohexene	80–83°/15 mm, 1·4714	72·82 72·87	9·65 9·57	72·49	9·96	$C_{11}H_{18}O_2$
	Methyl-5-acetoxy-2,6-dimethyl-Δ^3-cyclohexene carboxylate	66–69°/14 mm; 1·4707[j]					
	5-Acetoxy-2,6-dimethyl-Δ^3-cyclohexenaldehyde	69–72°/14 mm; 1·4714[j]					
	5-Acetoxy-2,6-dimethyl-Δ^3-cyclohexenaldehyde dimethyl acetal	76–78°/14 mm; 1·4736[j]					

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[a] Found: Cl, 27·12; 26·77. Calc: Cl, 27·15%.

[b] Found: Cl, 19·83; 20·01; N, 7·68; 7·73. Calc: Cl, 20,19; N 7·73%.

[c] Semicarbazone m.p. 174·5–175·5° (dil alcohol).

[d] Semicarbazone m.p. 178–178·5° (alcohol).

[e] Found: Br, 38·21; 38·13. Calc: Br, 38·80%.

[f] Found: Br, 32·43; 32·57. Calc: Br, 32·33%.

[g] Found: Br, 33·73; 33·85. Calc: Br, 34·14%.

[h] m.p. 39–39·5° (hexane), Prisms. Found: Br, 34·17; 34·06. Calc. Br, 34·14%.

[i] Found: Br, 33·90; 33·80. Calc: Br, 34·14%.

[j] The acetolysis product contains traces of bromine so that an analytically pure sample was not obtained.

boiled gently. After addition of the N-bromosuccinimide the mixture was refluxed for another 30 min after which it was cooled and the succinimide filtered off. The filtrate was washed with dil HCl, water and sat $NaHCO_3$aq, and then dried over $MgSO_4$. The unstable bromide was obtained by distillation *in vacuo*, yield 80–90% (Table 8).

2,6-*Dimethylcyclohexanone* was obtained by refluxing a mixture of 3·4 g 2,6-dimethylnitrocyclohexane (b.p. 83°/8 mm; n_D^{20} 1·4612) in 15 ml alcohol and 1·12 g KOH in 15 ml alcohol for 3 hr. The alcohol was distilled off *in vacuo*, the residue dissolved in 40 ml water and then added to 80 ml 20% H_2SO_4aq. It was then extracted with ether, washed with $NaHCO_3$aq and water and dried over $MgSO_4$. A yield, (1·5 g, 59·5%) of a mixture of *cis*- and *trans*-ketones with b.p. 54–57°/9 mm, n_D^{20} 1·4491 was obtained.[37,38] The mixture was converted to the semicarbazones and fractional crystallization gave the *trans* semicarbazone m.p. 196–197° (alcohol-hexane, 3:1),[38] and *cis* semicarbazone m.p. 182–183° (alcohol-hexane, 1:1).[38]

Addition of dithiocyanogen to the double bond of Δ^3*-cyclohexene adducts.* To a soln of dithyocyanogen in glacial AcOH prepared from lead thiocyanate,[39,40] twice the volume of dry CCl_4 was added and 60 ml of this soln was then added to a soln of 0·1–0·2 g of the reactant in AcOH cooled to −10°. The mixture was shaken and kept for 5 min at that temp, following which 20 ml KI soln was added with vigorous shaking. The excess I_2 was then titrated with 0·1N $Na_2S_2O_3$.

Acetolysis of 5-bromo-2,6-dimethyl-Δ^3*-cyclohexene derivatives* (XXa–e). To a soln of 3·92 g (0·04 M) fused AcOK in 20 ml glacial AcOH, a soln of 0·02 mole of the bromide in 10 ml glacial AcOH was added and the mixture heated with stirring for 2·5 hr at 80°. It was then cooled, the KBr filtered off, washed with glacial AcOH and dry ether and titrated with 0·1N $AgNO_3$. The filtrate was washed with water, and sat $NaHCO_3$aq and dried over $MgSO_4$. After distilling off the solvent the product was distilled *in vacuo* and chromatographed on silica gel (Table 8).

Hydrolysis of 5-bromo-2,6-dimethyl-Δ^3*-cyclohexene derivatives* (XXa,c,d). To a soln of 0·65 g KOH in 8·6 ml 80% MeOH, 2·3 g of the bromide XXa was added and the mixture stirred for 24 hr at 17°. Ether (17 ml) was then added and the KBr crystals filtered off, washed with glacial AcOH and abs ether and then titrated with 0·1N $AgNO_3$.

syn–cis-1,2-*Dihydroxymethyl-*Δ^4*-octalin* (XXX). To 60 ml of an 0·87M LAH soln in ether, 8·7 g of the dimethyl ester XXVIa in 40 ml of abs ether was added with stirring during 15 min so that the mixture continued to boil gently. It was refluxed for another hr, cooled and 50 ml of 10% H_2SO_4 (on cooling with ice) added. The ether layer was removed, washed with water and $NaHCO_3$aq and dried over Na_2SO_4. After distilling off the solvent the product was distilled *in vacuo*, yielding 5·65 g (84%) of a viscous, colorless liquid, b.p. 131–132°/0·16 mm; n_D^{19} 1·5335. (Found: C, 72·89; 73·04; H, 10·05; 10·20. Calc. for $C_{12}H_{20}O_2$: C, 73·43; H, 10·27%.)

The bis mesilate XXXI (R = OMs); m.p. 87–88° (chf); yield 50%. (Found: C, 47·72; 47·61; H, 6·97; 6·85; S, 18·38; 18·21. Calc. for $C_{14}H_{24}O_6S_2$: C, 47·70; H, 6·86; S, 18·19%.)

anti-trans-1,2-*Dihydroxymethyl-*Δ^4*-octalin* (XXXII). From 5·6 g *anti-trans*-diester XXVIIIa in 40 ml ether and 40 ml 0·87M LAH, 3·5 g (80%) of crystalline XXXII, m.p. 95–96° (heptane) was obtained. (Found: C, 73·30, 73·48; H, 10·20, 10·30. Calc. for $C_{12}H_{20}O_2$: C, 73·43; H, 10·27%.)

Bis-tosylate XXXIII (R = OTs) m.p. 130–131·5° (heptane) (Found: C, 62·23, 62·28; H, 6·35, 6·53; S, 12·46, 12·22. Calc. for $C_{26}H_{32}O_6S_2$: C, 61·88; H, 6·39; S, 12·71%.)

Bis-mesylate XXXIII (R = OMs) m.p. 99–100° (MeOH); yield 69%. (Found: C, 47·96, 47·95; H, 6·90, 6·78; S, 18·23, 18·02. Calc. for $C_{14}H_{24}O_6S_2$: C, 47·70; H, 6·86; S, 18·19%.)

syn–cis-1,2-*Dimethyl-*Δ^4*-octalin* (XXVIc). To 60 ml of a boiling soln of 1·17M LAH in abs ether, a soln of 4·7 g of XXXI (R = OMs) in 20 ml of abs THF was added with stirring during 45 min. The mixture was refluxed for another 12 hr, sat NH_4Claq (8 ml) was then carefully added, with stirring, which was continued for another hr. To this soln, 12 g anhydrous Na_2SO_4 was added and the stirring continued for 6 more hr. The ppt was filtered off, carefully washed with ether, and the filtrate concentrated, following which the product was distilled *in vacuo* over Na in a current of N, yield 1·56 g

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[37] F. E. King and T. J. King, *J. Chem. Soc.* 1373 (1954).

[38] N. S. Vul'fson and V. I. Zaretskij, *Zh. Obshch. Khim.* **28**, 369 (1958).

[39] *Handbuch der präparativen anorganischen Chemie.* G. Brauer, Ferdinand Enke Verlag, Stuttgart (1954).

[40] Houben-Weyl, *Methoden der organischen Chemie.* B.IX. E. Müller, Georg Thieme Verlag, Stuttgart (1954).

(71%) of XXVIc, b.p. 114–115°/25 mm, n_D^{20} 1·4960. (Found: C, 87·56, 87·65; H, 12·26, 12·22. Calc for $C_{12}H_{20}$: C, 87·73; H, 12·27%.)

anti-trans-1,2-*Dimethyl*-Δ^4-*octalin* (XXVIIIc). Similarly from 2·84 g XXXIII (R = OMs) in 30 ml THF and 40 ml 1·17M LAH in abs ether, 0·71 g (57%) of XXVIIIc, b.p. 109–110°/25 mm; n_D^{20} 1·4900 was obtained. (Found: C, 87·66, 87·49; H, 12·30, 12·31. Calc. for $C_{12}H_{20}$: C, 87·73; H, 12·27%.)