and *trans*-cyclopentanols obtained from methylmagnesium bromide and 2-methylcyclopentanone.[7] The cis and trans isomers of 1,2-dimethylcyclopentanol differ in the NMR absorptions of their methyl groups.[9] The cis isomer (5) shows a doublet at δ 0.86 and a singlet at δ 1.10. The corresponding absorptions of the trans isomer are at δ 0.90 and 1.20.

To confirm the structure of the cathodically obtained 6-hepten-2-ol, it was independently prepared from 4 by reduction with sodium borohydride.[8]

Acknowledgment. We are grateful to the National Science Foundation for support of this work.

Photochemically Induced Allylic Hydrogen Abstraction from 1-X-1,2-Dialkylethylenes: Experimental Data and Theoretical Calculations

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Results are presented for the first time concerning the influence of a substituent in directing the allylic hydrogen abstraction. The observed regioselectivity must be attributed only to electronic factors, either mesomeric or inductive, induced by the substituent. A bent transition state, asymmetrically bridging the double bond, is postulated to rationalize the experimental data.

Allylic hydrogen abstractions have been known for a long time and have been reported for a number of abstracting agents. The abstraction of an allylic hydrogen is easier than an alkyl one due to the stabilization by resonance of an allylic radical.[1] However, while this reaction has been reported for terminal or alkyl-substituted alkenes,[2] there is a complete lack of selectivity data and correlated quantitative results if different substituents are located on the double bond. In fact, until now no species useful for such a study was available because of concurrent reactions that usually take place and, in some cases, prevail.[3]

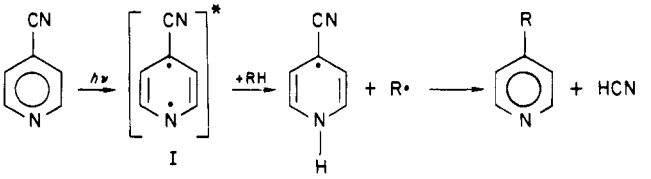
We have already reported[4] that photochemically excited heterocyclic bases may abstract a hydrogen atom from a suitable donor and then cross-dimerization with the radicals thus generated occurs without side reactions (see Scheme I). In particular we have shown that this reaction is especially effective for allylic hydrogen abstraction.[4]

Therefore, in this paper we report the results obtained from reacting photochemically excited 4-cyanopyridine as abstracting species with 1-X-1,2-dialkylethylenes. The vinylic substituent X exerts its influence on the π electrons (see Scheme II) so that the allylic positions α or β are bound to carbon atoms with different partial charges and consequently their hydrogens will be abstracted by an electrophilic radical with different selectivities.

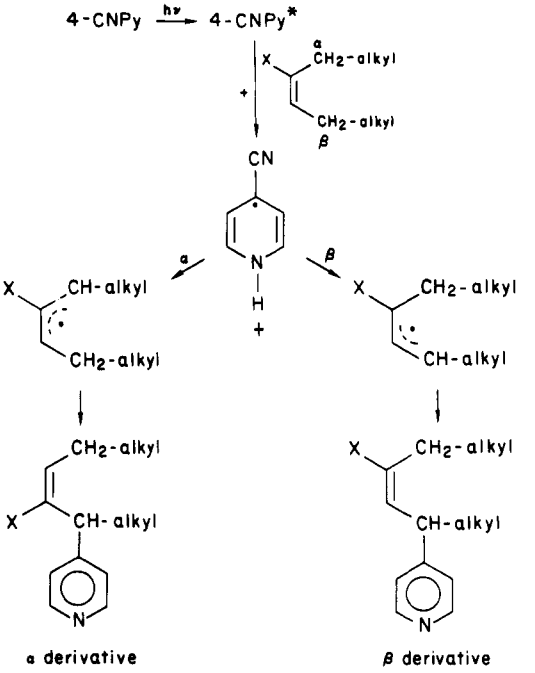
Two different experimental conditions were used in our study: (a) irradiation of solutions of 4-cyanopyridine in presence of an alkene to determine the influence of the substituent on allylic hydrogen abstraction and (b) competitive experiments in which solutions of 4-cyanopyridine were irradiated in the presence of two different alkenes to establish a general pattern of reactivity between the different series of alkenes employed.

The results are best interpreted in terms of a bent transition state asymmetrically bridging the double bond, and the selectivities may be correlated with the electronic effects induced by the substituents.

Scheme I



Scheme II



Results and Discussion

General Reactivities. The results for the reactions carried out under competitive conditions are summarized in Table I. First of all, to understand the nature of the abstracting radical, we can make a comparison with the relative reactivity and the selectivity for the allylic hy-

† Centro per lo Studio della Sostanze Naturali.
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(1) (a) Pryor, W. A. "Free Radicals"; McGraw-Hill: New York, 1966. (b) Kochi, J. K. "Free Radicals"; Wiley: New York, 1973; Vol. 2, p 692. (c) Tedder, J. M.; Walton, J. C. "Advances in Free Radical Chemistry"; Heyden: London, 1980; Vol. 6, p 155.
(2) (a) Horner, L.; Winkelmann, F. H. *Neuere Methoden Prep. Org. Chem.* **1961**, *3*, 58. (b) Nechvatal, A. "Advances in Free Radical Chemistry"; Logos Press: London, 1972; Vol. 4, p 175. (c) Skell, P. S.; Day, J. C. *Acc. Chem. Res.* **1978**, *11*, 381.

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Table I. Competitive Reactions[a]

A	B	A/B[b]
cyclohexene	cycloheptene	1.80
cyclohexene	2-pentene	2.05
cycloheptene	2-pentene	1.09
1-methoxycyclohexene	cyclohexene	2.00
1-[(trimethylsilyl)oxy]cyclohexene	cyclohexene	1.60
1-acetoxycyclohexene	cyclohexene	0.36
1-[(trimethylsilyl)oxy]cycloheptene	cycloheptene	1.50
3-[(trimethylsilyl)oxy]-2-pentene	2-pentene	1.07
1-[(trimethylsilyl)oxy]cyclohexene	1-[(trimethylsilyl)oxy]cycloheptene	2.50
1-[(trimethylsilyl)oxy]cyclohexene	3-[(trimethylsilyl)oxy]-2-pentene	2.74
1-[(trimethylsilyl)oxy]cycloheptene	3-[(trimethylsilyl)oxy]-2-pentene	1.16

[a] 1 mmole of 4-cyanopyridine, 2.5 mmole of A, and 2.5 mmole of B in 15 mL of anhydrous acetonitrile. Irradiation time at 254 nm, 1 h; T, 40 °C. All values are ±0.05. [b] A/B ratio per hydrogen atom.

Table II. Allylic Chlorination with *tert*-Butyl Hypochlorite[a]

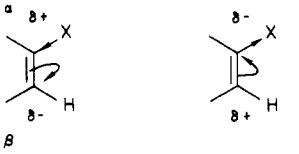
t-BuOCl + RH → t-BuOH + RCl

	relative reactivity[b]	
cyclohexene	368	
trans-2-pentene	94.4	
cis-2-pentene	92.1	
	% composition of allylic chlorides	
	4-chloro-2-pentene	1-chloro-2-pentene and 3-chloro-1-pentene
trans-2-pentene	76	24
cis-2-pentene	76.4	23.6

[a] Reference 5; T = 40 °C. [b] Per hydrogen, relative to *n*-butene.

drogen abstraction from simple alkenes obtained by using as abstracting species the electrophilic *tert*-butoxy radical[5] reported in Table II. The analogy in trend of this data led us to conclude that the nitrogen atom of the excited pyridine (I) (see Scheme I) is electrophilic in nature too. Another conclusion may be drawn from the data in Table I: 1-substituted cyclohexenes show a greater reactivity than the corresponding cycloheptenes and these in turn a greater reactivity than noncyclic alkenes, a result which has been already reported for other abstracting radicals.[5] To understand this trend in reactivity, we first note that the bond-dissociation energies implied for the abstraction of the hydrogen from an allylic CH_2 are virtually the same for molecules bearing the same substituent: entropy then is the controlling factor. Now the allylic radical can be stabilized by resonance only if all the atoms bonded to it lie in its plane, and this results in an entropy loss for the radical with respect to the original molecule. This loss is low in a rigid system such as the cyclohexene, is higher in a more loose system such as the cycloheptene, and is even higher in a noncyclic system. In the latter case energetics may add some problem because in 2-pentenes a carbon atom is primary, while in the cyclic systems they are all secondary. Bond-dissociation energy plays then an important role in the hydrogen abstraction, and we will discuss this point later. The same trend in reactivity was found when a substituent is located on the double bond. The reactivity of the substituted alkenes reflects the overall electron-donating (or -withdrawing) character of the substituent, hence the π-electron density, and is in keeping with the electrophilicity of our abstracting species: the higher the electron density on the double bond induced by the substituent, the higher the reactivity.

Scheme III



To have an estimate of these π-electron densities, semiempirical quantum-mechanical calculations have been carried out on some cyclohexene derivatives using the programs CNDO/2[6] and MINDO/3.[7]

The MO corresponding essentially to the π bond of the alkene has been calculated to be in general the HOMO (this is not the case for acetylcyclohexene where a lone pair on the carbonylic oxygen actually forms the HOMO, as reported experimentally for analogous compounds[8]). For this MO we then compared the coefficients of the p_z AO's of the two double bonded carbon atoms between different compounds. The larger these contributions are, the higher the π-electron density is. It may be seen from the values reported in Table III that these coefficients can be used to predict the observed trend in reactivity if we neglect the entries corresponding to X = Cl for MINDO/3 and X = CN for CNDO/2. In fact, a possible shortcoming of these methods must be borne in mind: it is known that the programs tend to back-donate an excess of electrons on very electronegative groups, and this may be particularly effective if some conjugation is possible.

We should also mention that other computed quantities such as the bond orders[9] or the bond indexes[10a] would be preferable, being also closer to the chemical intuition. However, as could be anticipated, no clear trend was discernible for our compounds, some of which may exhibit some charge separation: in fact, these quantities refer only to covalently bonding electrons, i.e., electrons "in the bonds" as distinguished from those "on the atoms".[10b] This turns out to be particularly relevant for methoxycyclohexene, which would be predicted to be the least reactive compound on the basis only of the above mentioned quantities.

Selectivity of Abstraction. In Table IV we report the quantities of the only isomer(s) that is (are) obtained by irradiating the 4-cyanopyridine in the presence of an alkene (see Scheme II). The data show that the allylic position α to the carbon carrying the substituent (see Scheme III) becomes less reactive than the β position with increasing the electron-donating character of the substituent. On the contrary, the relative reactivity of the two positions shows the opposite trend with an increasing electron-withdrawing substituent, until the α position may be the only reactive site left.

(3) Korth, H.-G.; Sustmann, R. *Tetrahedron Lett.* **1985**, *21*, 2551.
(4) Bernardi, R.; Caronna, T.; Morrocchi, S.; Traldi, P.; Vittimberga, B. M. *J. Chem. Soc., Perkin Trans 1* **1981**, 1607 and references cited therein.
(5) Walling C.; Thaler, W. *J. Am. Chem. Soc.* **1961**, *83*, 3877.
(6) Pople, J. A.; Beveridge, D. L. "Approximate Molecular Orbital Theory"; McGraw-Hill: New York, 1970.
(7) Bingham, R. C.; Dewar, M. J. S.; Lo, D. H. *J. Am. Chem. Soc.* **1975**, *97*, 1285, 1294, 1302, 1307.
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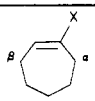
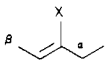
(9) Mulliken, R. S. *J. Chem. Phys.* **1955**, *23*, 1833.
(10) (a) Wiberg, K. *Tetrahedron* **1968**, *24*, 1083. (b) Armstrong, D. R.; Perkins, P. G.; Stewart, J. J. P. *J. Chem. Soc., Dalton Trans.* **1973**, 838.

Table III. HOMO Energy,[a] Coefficients in the HOMO,[a] and Total Electron Density due to All Occupied MO's for the p_z AO's on the Double Bonded Atoms C_1 and C_2 for Selected Cyclohexene Derivatives[b]

			coefficients				electron density			
	HOMO energy, eV		MINDO/3		CNDO/2		MINDO/3		CNDO/2	
X	MINDO/3	CNDO/2	C_1	C_2	C_1	C_2	C_1	C_2	C_1	C_2
H	-9.47	-12.86	0.6083	0.6083	0.5354	0.5354	1.005	1.005	1.015	1.015
OCH_3	-8.69	-11.57	0.4620	0.6774	0.4159	0.5863	0.889	1.199	0.962	1.142
$COCH_3$	-9.73	-12.59	0.6023	0.5743	0.4882	0.4996	1.050	0.929	1.032	0.972
CH_2CN	-9.37	-12.44	0.5741	0.5936	0.5082	0.5461	1.018	0.996	1.014	1.026
Cl	-9.33	-12.47	0.5265	0.6189	0.4224	0.4866	0.966	1.069	1.020	0.993
CN	-9.27	-12.48	0.5444	0.5763	0.5021	0.5375	1.022	0.978	1.025	0.993

[a] If X = $COCH_3$ these values refer to the MO following in energy the HOMO (see text). [b] C_1 is the atom carrying the substituents.

Table IV. Selectivity in Allylic Hydrogen Abstraction by Excited 4-Cyanopyridine and Chemical Shifts for the Vinylic Proton (δ)

													
X	β^a	α^a	β/α	δ^b	β^a	α^a	β/α	δ^b	β^a	α^a	β/α	β/α corr[c]	δ^b
OCH_3	16.60	4.70	3.54	4.60	11.50	2.15	5.34	4.70	9.90	2.89	3.41	2.27	4.35
$OSi(CH_3)_3$	29.97	9.55	3.14	4.67	17.92	4.77	3.76	5.05	23.01	19.90	2.46	1.64	4.50
Ph	5.36	2.09	2.74	6.08									
$OCOCH_3$	8.40	4.80	1.74	5.32	6.35	2.60	2.45	5.45	4.08	5.52	0.74	0.49	5.08
H	7.90[c]		1	5.60	3.30[c]		1	5.77	5.45	11.35	0.48	0.32	5.40
CH_2CN	5.50	7.60	0.71	5.80									
Cl[d]			0.67	5.71									
$COOCH_3$		6.34		6.98									
$COCH_3$		1.20		6.85									
CN		0.80		6.65		0.12		6.73		0.14			6.20

[a] Yield % of isomer obtained irradiating 1 mmol of 4-cyanopyridine and 5 mmol of alkene in 15 mL of anhydrous CH_3CN for 1 h; all values are ±0.05. [b] Chemical shifts are in ppm from Me_4Si as internal standard; solvent $CDCl_3$; all values are ±0.02. [c] Statistically corrected. [d] Ratio determined by NMR. See ref 19.

To rationalize this behavior, we must take into consideration the inductive and/or mesomeric effect of the substituents which influence both the overall π-electron density at the double bond (hence the general reactivity, as already said) and its distribution over the two carbon atoms. As a consequence, an electron-donating group (e.g., OCH_3) favors the abstraction from the β position but permits also, though to a lesser extent, that from the α position. On the other hand, electron-withdrawing substituents (e.g., Cl) deactivate the α position less than the β position and in extreme cases (e.g., CN) the latter is completely inactive.

The influence of the substituents on the π-electron density may be quantified through NMR by noting that the above-mentioned unsymmetrical electron density over the unsaturated carbon atoms will affect in a different way the vinylic proton whose chemical shift will be correspondingly influenced for a homogeneous class of molecules. If the shift of this hydrogen is found at higher field (which is the case of an electron-donor substituent), then the β position will be close to an electron-rich carbon atom, and its hydrogen will be abstracted preferentially by an electrophilic radical. The opposite is true in the presence of an electron-withdrawing substituent. For this reason we sought a correlation between the observed selectivities and the vinylic hydrogen chemical shifts. The results are shown in Figure 1 together with the best fit least-squares lines.

In some cases the anisotropy of the substituent may shift the vinylic proton downfield (e.g., $COCH_3$, Ph). Theoretical calculations permit a rough evaluation of this effect.[11] For X = $COCH_3$, assuming a geometry with C=O in the same plane of the double bond, this effect may be estimated to a maximum of δ 0.4; this brings the vinylic hydrogen shift to a limiting value of δ ~6.5, but the change does not affect the reported correlation. As for phenyl, assuming again that the aromatic ring and the double bond lie in the same plane, the anisotropic shift may be estimated in δ ~0.7; the corrected shift becomes δ ~5.4, consistent with the presence of both isomers. It is to be noted that in this case the corrected point just approaches the best fit line and does not lie "on" it, but we bring to mind that theoretical methods are reported to underestimate the anisotropic effect.[11]

A discussion of the experimental selectivities as predicted by quantum-mechanical methods is deferred to a later section after some considerations about the proposed mechanism of reaction.

In almost all the allylic hydrogen abstractions by other radicals a transition state involving an interaction between the π electrons of the double bond and the abstracting species was postulated.[12] Since our reacting species, i.e., the pyridinic nitrogen radical, behaves similarly to the other electrophilic radicals (see what is reported above), we would like to suggest a similar mechanism of reaction in the present case (see Figure 2).

If the π electrons are not equally distributed over the vinylic carbons the complex that should be formed between I and the different alkenes is a nonsymmetrical one, and I will be able to abstract the allylic hydrogen that will be closer. The geometry of this complex should require an angle of ~90° between the singly occupied nitrogen orbital and the C–H of the reactive hydrogen, in agreement, e.g., with the geometry required for the allylic hydroperoxydation of alkenes with singlet oxygen.[13] Because for

(11) Jackman, L. M.; Sternhell, S. "Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry"; Pergamon Press: New York, 1969; p 88.

(12) Huyser, E. S. "Advances in Free Radical Chemistry"; Logos Press: London, 1966; Vol. 1, p 77. See in particular pp 91 and 110.

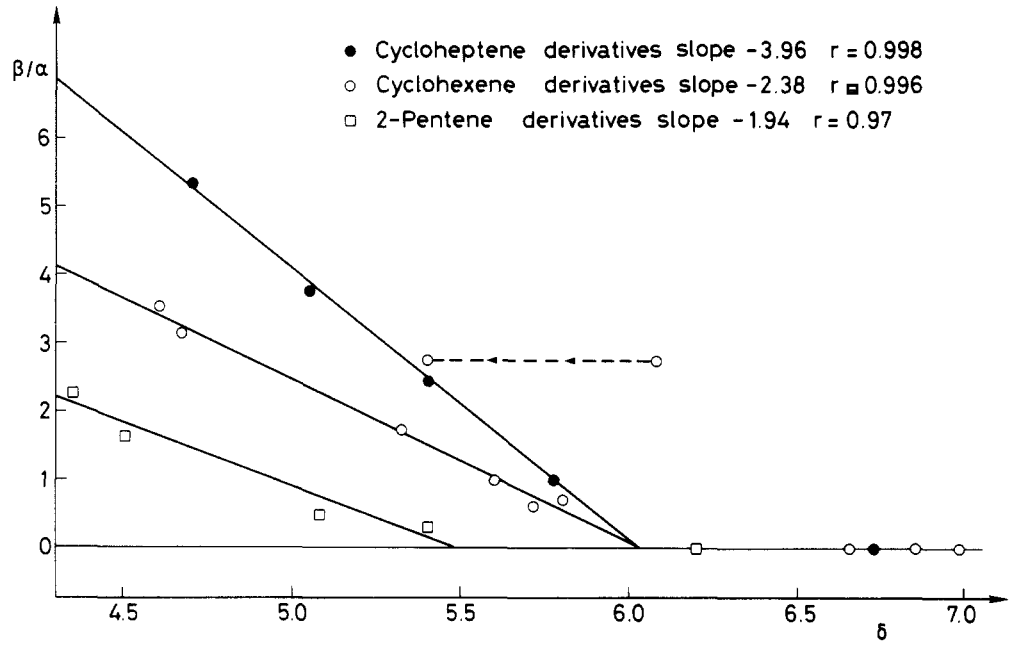


Figure 1. Correlation between the selectivities in the allylic hydrogen abstraction by photoexcited 4-cyanopyridine and the vinylic hydrogen chemical shift.

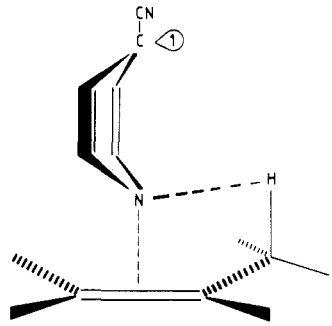


Figure 2. Complex between the photoexcited 4-cyanopyridine and the alkene.

the two rings the energetics implied are virtually the same, the different selectivities observed with the same substituent may be ascribed to the entropy variation discussed in a previous section.

The case of 2-pentenes deserves other considerations. The selectivity of abstraction of the allylic hydrogen from 2-pentene is different from that of the cyclic systems, as may be seen in Tables II and IV. This is due to the fact that the bond-dissociation energy for a primary C–H is higher than that of a secondary C–H, and this difference in energy explains the observed lower selectivity.

On the basis of this mechanism, we may now find the calculated parameters describing the observed selectivity. In fact, no correlation was found with computed net atomic charges nor with the coefficients of the p_z AO's of the MO corresponding to the double bond. The experimental selectivity may be reproduced only if we compare the number of electrons in the p_z AO's forming the π bond between the two olefinic carbon atoms, or, otherwise said, the contribution of this AO to the net atomic charge of the corresponding atom (see Table III). We note that this choice is in keeping with the postulated complex formed through donation of the double bond π electrons to the nitrogen of the abstracting radical. The electrophilic species will be found near to the atom having the highest electron density in the p_z AO and thus will abstract preferentially the closer allylic hydrogen. Again, we see that MINDO/3 predicts an excess of back-donation if the substituent is Cl, but we should also mention that if X = CH_2CN (see Table III) CNDO/2 predicts a slight increase in electron density at the unsubstituted olefinic carbon atom. We have no simple explanation for this somewhat puzzling effect. The values of the charge residues on the two axial hydrogens that may actually undergo the abstraction via the postulated nonsymmetrical complex are reported in Table V. (Only MINDO/3 values are given, as CNDO/2 gives very small and somewhat random values.) The trend correlates well with the global reactivities and reflects somehow the donating or withdrawing effect of the substituent over the π electrons of the double bond.

Table V. Computed Charge Residue on the Axial Hydrogen Undergoing Abstraction[a]

X	charge residue on axial hydrogen	X	charge residue on axial hydrogen
OCH_3	−0.046	CN	−0.029
H	−0.036	$COCH_3$	−0.025
CH_2CN	−0.031	Cl	−0.016

[a] Only MINDO/3 values are reported.

Experimental Section

Theoretical Studies. Quantum-mechanical calculations were carried out at the semiempirical level on selected cyclohexene derivatives using standard versions of the programs CNDO/2[6] and MINDO/3.[7] The geometry was refined with MINDO/3 for the substituted allylic moiety, while the remaining part was kept fixed to that of cyclohexene (previously fully optimized under the constraint of C_2 symmetry). The refined geometries were used as input for CNDO/2.

The HOMO of all the compounds but one is formed mainly by the π bond of the alkene with small contributions from the nonconjugated π- or n-electrons of the substituent. The exception is acetylcyclohexene, whose HOMO is formed mainly by the oxygen lone pair (which is not reactive in the present conditions) as reported for other carbonyl compounds.[8]

Starting Materials. 4-Cyanopyridine, cyclohexene, cycloheptene, *trans*-2-pentene, 1-(carboxymethyl)cyclohexene, 1-cyclohexenyl trimethylsilyl ether, 1-acetylcyclohexene, and 1-(cyanomethyl)-1-cyclohexene are commerical products. The other

(13) Stephenson, L. M.; Grdina, M. J.; Orfanopoulos, M. *Acc. Chem. Res.* **1980**, *13*, 419.

Table VI. Mass Fragmentation and NMR Spectroscopic Data

compd[a]	m^+/e	^{1}H NMR,[b] δ
1-α	198, 197, 158, 130, 117, 91, 78	8.5 (dd, H_a and H_b, $J_{ac} = J_{bd} = 4.5$ Hz, $J_{ab} = 1.8$ Hz), 7.2 (dd, H_c and H_d, $J_{ca} = J_{db} = 4.5$ Hz, $J_{cd} = 1.8$ Hz), 6.2 (m, CX=C*H*CH_2), 3.43 (br s, 1 H, CHPyCX=), 2.85 (s, 2 H, CH_2CN), 2.12–1.5 (br s, 6 H, $(CH_2)_3$)
1-β	198, 158, 130, 117, 79	8.5 (dd, H_a and H_b), 7.2 (dd, H_c and H_d), 5.8 (m, 1 H, CX=C*H*CHPy), 3.40 (br s, 1 H, C*H*PyCH=), 3.1 (s, 2 H, CH_2CN), 2.12–1.5 (br s, 6 H, $(CH_2)_3$)
2-α	235, 206, 129, 116, 91, 77	8.35 (dd, H_a and H_b), 6.4 (t, 1 H CX=C*H*CH_2, $J_{CH-CH_2} = 4$ Hz), 3.95 (br s, 1 H, C*H*PyCX=), 7.5–7 (br s, 7 H, Ph and H_c and H_d), 2.1–1.4 (br s, 6 H, $(CH_2)_3$)
2-β	235, 129, 114, 91, 77	8.5 (dd, H_a and H_b), 6.05 (d, 1 H, CX=C*H*CHPy, $J_{CH-CH} = 2$ Hz), 3.5 (br s, 1 H, C*H*PyCH=), 7.5–7 (br s, 7 H, Ph and H_c and H_d), 2.1–1.4 (br s, 6 H, $(CH_2)_3$)
3-α	217, 185, 158, 130, 104, 78	8.5 (dd, H_a and H_b), 7.12 (dd, H_c and H_d), 7.32 (t, 1 H, CX=C*H*CH_2, $J_{CH-CH_2} = 4$ Hz), 3.75 (br s, 1 H, CHPyCX=), 3.6 (s, 3 H, $COOCH_3$), 2.5–1.4 (br s, 6 H, $(CH_2)_3$)
4-α	189, 161, 133, 107, 84, 78	8.53 (dd, H_a and H_b), 7.12 (dd, H_c and H_d), 3.75 (m, 1 H, COC*H*PyCH$_2$), 2.6 (m, 2 H, $COCH_2$), 2.1–1.2 (m, 8 H, $(CH_2)_4$)
4-β	189, 145, 133, 119, 107, 93	8.50 (dd, H_a and H_b), 7.18 (dd, H_c and H_d), 3.1–2.5 (m, 5 H, CHPyCH$_2$COCH$_2$), 2.2–1.5 (br s, 6 H, $(CH_2)_3$)
5-α	198, 197, 171, 157, 144, 132	8.55 (dd, H_a and H_b), 7.5 (dd, H_c and H_d), 7.1 (t, 1 H, CX=C*H*CH_2, $J_{CH-CH_2} = 5$ Hz), 3.7 (br s, 1 H, CHPyCX=), 2.5–1.2 (br s, 8 H, $(CH_2)_4$)
6-β	163, 149, 134, 107, 95, 79	8.5 (dd, H_a and H_b), 7.12 (dd, H_c and H_d), 2.8 (m, 4 H, $COCH_2CH_2Py$), 2.4 (q, 2 H, $COCH_2CH_3$, $J_{CH_2-CH_3} = 7.5$ Hz), 1.0 (t, 3 H, CH_3CH_2, $J_{CH_3-CH_2} = 7.5$ Hz)
7-α	147, 146, 132, 117, 91, 78	8.5 (dd, H_a and H_b), 7.15 (dd, H_c and H_d), 5.5 (m, 2 H, CH=CH), 3.6 (m, 1 H, CH_3C*H*PyCH=), 1.7 (d, 3 H, CH_3CH=, $J_{CH_3-CH} = 3.5$ Hz), 1.3 (d, 3 H, CH_3CHPy, $J_{CH_3-CHPy} = 7.5$ Hz)
7-β	147, 132, 118, 117, 93, 91	8.5 (dd, H_a and H_b), 7.12 (dd, H_c and H_d), 5.5 (m, 2 H, CH=CH), 3.3 (d, 2 H, CH_2PyCH=, $J_{CH_2Py-CH} = 6$ Hz), 2.1 (m, 2 H, CH_3CH_2CH=, $J_{CH_2-CH_3} = 7.5$), 0.85 (t, 3 H, CH_3CH_2, $J_{CH_3CH_2} = 7.5$ Hz)
7-β′	147, 132, 118, 105, 91, 78	8.5 (dd, H_a and H_b), 7.12 (dd, H_c and H_d), 6.12–5.68 (m, 1 H, CH=CH_2, $J_{CH=CH_2} = 7.5$ Hz), 5.12 and 4.98 (s and d, 2 H, CH=CH_2, $J_{CH_2=CH} = 7.5$ Hz), 3.2 (m, 1 H, C*H*PyCH=), 1.75 (m, 2 H, CH_3CH_2CHPy, $J_{CH_2-CH_3} = 7.5$ Hz), 0.85 (t, 3 H, CH_3CH_2, $J_{CH_3-CH_2} = 7.5$ Hz)
8-α	172, 171, 158, 142, 94, 79	8.55 (dd, H_a and H_b), 7.15 (dd, H_c and H_d), 6.5 [6.3] (q, 1 H, CX=C*H*CH_3, $J_{CH-CH_3} = 7$ Hz), 3.9 [3.65] (q, 1 H, CH_3C*H*PyCX=, $J_{CH-CH_3} = 7.5$), 1.86 [2.0] (d, 3 H, CH_3CH=, $J_{CH_3-CH} = 7$ Hz), 1.51 [1.49] (d, 3 H, CH_3CHPy, $J_{CH_3-CH} = 7.5$ Hz)

[a] All products are oils. Numbers refer to starting materials (alkene or ketone). The derivatives are identified as α or β with respect to the convention used in this paper. Satisfactory analytical data (±0.4% for C, H, N) were obtained for all new compounds. [b] For solutions in $CDCl_3$. H_a, H_b, H_c, and H_d refer respectively to the hydrogen atoms at the positions 2, 6, 3, and 5 of the pyridine ring. J_{ac}, J_{bd}, J_{ab}, and J_{cd} values are reported only for the first product; in all the other cases the values are the same and are no further reported. In the case of *E* and *Z* isomers (8-α) the NMR values are reported for one isomer with those of the other isomer in brackets; no attempt was made to identify the isomers.

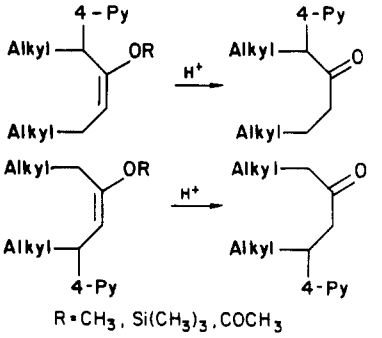
compounds were synthesized from the corresponding ketones (3-pentanone, cyclohexanone, and cycloheptanone) by using the following methods. (a) Methoxy derivatives: MeOH elimination, catalyzed via *p*-toluenesulfonic acid, from the corresponding dimethyl ketals.[14] (b) Trimethylsilyl ethers: by treatment with trimethylsilyl chloride in Et_3N.[15] (c) Acetoxy derivatives: boiling with acetic anhydride in presence of sodium acetate or *p*-toluenesulfonic acid.[16] (d) Nitriles: H_2O elimination from the corresponding cyanohydrines using $SOCl_2$.[17]

NMR spectra were recorded on a Varian EM 390 90-MHz spectrometer and chemical shifts are reported as ppm (δ) relative to internal Me_4Si. Mass spectra were recorded with a Hitachi-Perkin-Elmer RMU 6D single focusing spectrometer. Gas chromatographic analyses were performed on a Dani 3800 gas chromatograph using a 2-m glass column (i.d. 2 mm) packed with 5% SP-1000 on 100/120 Supelcoport and temperature programming from 80 to 220 °C (4 °C min^{-1} after the first minute) or a 2-m glass column (i.d. 2 mm) packed with 10% Carbowax 20 M and temperature programming from 110 to 180 °C (4 °C min^{-1} after 4 min).

Photochemical Reactions. All the photochemical reactions were run in quartz vessels in a RPR-100 Rayonet photochemical reactor.

(1) Preparative Reactions. 4-Cyanopyridine (5 mmol), dissolved in 40 mL of CH_3CN, was added with a threefold excess of an alkene and the resulting solution irradiated for 20 h. The reaction mixture was concentrated, and the products were isolated via chromatography over silica gel, using as eluent hexane–ethyl acetate.

Scheme IV



In the case of methoxy, acetoxy, and trimethylsilyl ether derivatives, the irradiated solution was concentrated, treated with diluted HCl, and, after 2 h, basified with diluted NH_3, extracted with CH_2Cl_2, and dried over anhydrous sodium sulfate, and the corresponding ketones (see Scheme IV) were isolated as reported above.

Spectral data for the new compounds are reported in Table VI. The derivatives are identified as α or β with respect to the convention used in this paper; the alkene is identified by the following code: 1-(cyanomethyl)-1-cyclohexene (**1**), 1-phenylcyclohexene (**2**), 1-(carboxymethyl)cyclohexene (**3**), cycloheptanone (**4**), 1-cyanocycloheptene (**5**), 3-pentanone (**6**), 2-pentene (**7**) (β refers to 1-substituted 2-pentene, β′ refers to 3-substituted 1-pentene), 3-cyano 2-pentene (**8**). The others were already reported in the literature.[18]

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(19) 1-Chlorocyclohexene is unstable. No quantitative determination of the two allylic derivatives was made. The β/α ratio was determined via NMR.

(2) Determination of Positional Selectivity. 4-Cyanopyridine (10 mL of a 0.1 M solution) in anhydrous acetonitrile was combined with 5 mmol of alkene (the molar ratio of 4-cyanopyridine–alkene was 1:5) and 5 mL of anhydrous acetonitrile. The solution was irradiated for 1 h. At the end of the irradiation, it was concentrated or in the case of the methoxy, acetoxy and trimethylsilyl ether derivatives treated as mentioned before and analyzed by GC. No variation was found in the isomer ratio with respect to the preparative reactions whose values are reported in Table IV.

(3) Competitive Reactions. 4-Cyanopyridine (10 mL of a 0.1 M solution) in anhydrous acetonitrile was combined with an equimolar quantity of two different alkenes and 5 mL of anhydrous acetonitrile (the molar ratio of 4-cyanopyridine–alkene 1–alkene 2 was 1:2.5:2.5). The resulting solution was irradiated for 1 h and then treated as reported before. The relative reactivities are reported in Table I. Some experiments were run with different alkenes ratio, but no difference in the relative reactivities was found after correction for the different molar ratios. In any case, no difference was found in the isomer ratio.

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Registry No. 1, 6975-71-9; 1-α, 89344-81-0; 1-β, 100190-68-9; 2, 771-98-2; 2-α, 100190-69-0; 2-β, 100190-70-3; 3, 61401-14-7; 3-α, 100190-71-4; 5, 20343-19-5; 7, 109-68-2; 7-α, 100190-72-5; 7-β, 100190-73-6; 7-β', 100190-74-7; 8, 89580-25-6; 8-α, 100190-75-8; $CH_3CH_2C(OSiMe_3)$=$CHCH_3$, 17510-47-3; CH_3CH=$C(OMe)$-CH_2CH_3, 41623-41-0; CH_3CH=$C(OAc)CH_2CH_3$, 13893-75-9; H_2, 1333-74-0; 1-acetylcyclohexene, 932-66-1; 4-cyanopyridine, 100-48-1; cyclohexene, 110-83-8; 1-methoxycyclohexene, 931-57-7; 1-chlorocyclohexene, 930-66-5; cycloheptene, 628-92-2; 1-[(trimethylsilyl)oxy]cyclohexene, 6651-36-1; 1-acetoxycyclohexene, 1424-22-2; 1-[(trimethylsilyl)oxy]cycloheptene, 22081-48-7; methyl 1-cyclohexenecarboxylate, 18448-47-0; 1-methoxycycloheptene, 50438-50-1; 1-phenylcycloheptene, 25308-75-2; 1-acetoxycycloheptene, 14477-74-8.

Total Synthesis of (4*R*)- and (4*S*)-5,6-Dihydro-1-β-D-ribofuranosyl-4*H*-pyrazolo[3,4-*d*][1,3]diazepin-4-ol and (8*R*)- and (8*S*)-7,8-Dihydro-3-β-D-ribofuranosyl-6*H*-*v*-triazolo[4,5-*d*][1,3]diazepin-8-ol: Two Heterocyclic Analogues of the Nucleoside Antibiotic Coformycin

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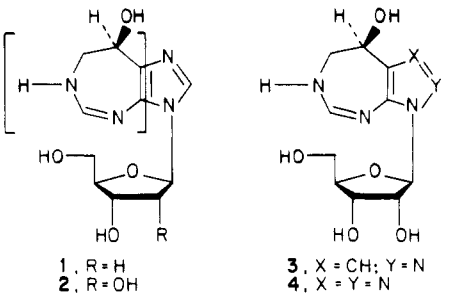
The reaction of 5-amino-1-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)pyrazole-4-carboxaldehyde (**10**) with *N*,*N*-dimethylformamide dimethyl acetal (DMFDMA) has provided 5-[((dimethylamino)methylene)amino]-1-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)pyrazole-4-carboxaldehyde (**11**). Subsequent reaction of the protected aldehyde **11** with trimethylsilyl cyanide (Me_3SiCN) afforded the protected trimethylsilyl cyanohydrins **12**. A reduction of the nitrile group of **12** in neutral media using cobalt boride catalyst yielded an aminomethyl intermediate which initiated an in situ annulation. Subsequent deprotection of the β-D-ribofuranosyl moiety of the product gave a mixture of the (4*R*)- and (4*S*)-5,6-dihydro-1-β-D-ribofuranosyl-4*H*-pyrazolo[3,4-*d*][1,3]diazepin-4-ol (compounds **3** and **15**). A similar series of reactions, starting with 5-amino-3-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-*v*-triazole-4-carboxaldehyde, has furnished a mixture of (8*R*)- and (8*S*)-7,8-dihydro-3-β-D-ribofuranosyl-6*H*-*v*-triazolo[4,5-*d*][1,3]diazepin-8-ol (**4** and **26**). The chromatographic separation of **4** and **26** followed by a spectroscopic characterization of each compound is described herein.

We have recently witnessed a burgeoning interest in the synthesis[1,2,6] of strong inhibitors of the ubiquitous enzyme adenosine deaminase[4] (these synthetic efforts have involved both chemical and fermentation methods). A recent chemical synthesis of the very potent adenosine deaminase inhibitor (8*R*)-3-(2-deoxy-β-D-*erythro*-pentofuranosyl)-3,6,7,8-tetrahydroimidazo[4,5-*d*][1,3]diazepin-8-ol[2,3] (**1**, 2′-deoxycoformycin, pentostatin) has prompted us to report on our research efforts which have been directed toward the chemical synthesis of some heterocyclic analogs of coformycin (**2**), the 2′-hydroxy analogue of the nucleoside antibiotic pentostatin. Our efforts were prompted in part by the finding[5] that, as an antileukemic agent, pen-

Chart I



1, R = H
2, R = OH
3, X = CH; Y = N
4, X = Y = N

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