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FACTORS CONTROLLING THE REGIOSELECTIVITY OF ADDITIONS TO α-ENONES—VI

REACTIONS OF ACETONITRILE AND PHENYLACETONITRILE ANIONS

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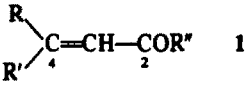
Abstract—Reaction of α-enones **1a–g** with acetonitrile anion **5**, in THF at −80° gives, irreversibly, alcohols **7** or **11**, resulting from carbonyl carbon attack, whatever the associated cation is (K^+ or Li^+). The reaction is considered to be under charge control. In THF, lithiated phenylacetonitrile **6** gives the alcohols **8** and **12** under kinetic control with benzalacetone **1b**, 2-cyclohexenone **1d** and 3-methyl 2-cyclohexenone **1e**. Lithium alcoholate formation is reversible and ketones **10b**, **14a** and **14b** formation, resulting from carbon 4 attack, is thermodynamically controlled. The other α-enones studied lead, under the same reaction conditions, to ketones **10a**, **10c**, **14c** and **14d** only. In a THF–HMPA mixture, reagent **6** only gives the starting α-enone, ketones **10** and **14**. The lower lying the α-enone LUMO level, the faster the reaction, which indicates, in the present case, that the transition state for carbon carbon double bond attack occurs relatively early in the reaction path.

α-Enones **1** are ambident electrophiles, the two reactive sites being carbons 2 and 4:



1

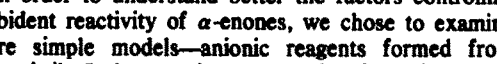
Generalized perturbation theory[1] gives an interpretation of their reactivity vs nucleophiles.[2] Charge localized reagents are thought to attack carbon 2, the positive charge of which being larger (charge control), charge delocalized ones carbon 4, the atomic coefficient of which being larger in the LUMO (frontier control). This interpretation is in accordance with some results.

We previously observed that charge localized species, **2** and **3** (R‴ = H), attack benzalacetone **1b** (R = Ph, R′ = H, R″ = CH_3) at the carbonyl carbon, though charge delocalized ones, **2** and **3** (R‴ = Ph), attack this α-enone and chalcone **1a** (R = R″ = Ph, R′ = H) at carbon 4.[3] However, this did not allow us to interpret the reactivity order of aromatic, aliphatic and alicyclic α-enones vs reagent **4**.[4] We suggested that in the transition state, deconjugation factors in the case of R = Ph, or steric ones when R and R′ are not H, are predominant over orbital interactions.

2 **3**

4

In order to understand better the factors controlling ambident reactivity of α-enones, we chose to examine more simple models—anionic reagents formed from acetonitrile **5**, the negative charge of which being rather localized,[5] and from phenylacetonitrile **6**, the negative charge of which being highly delocalized.[5,6] We studied their reaction with the α-enones we previously examined compounds **1a–g**[4] (see Table 1).



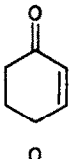
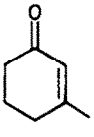
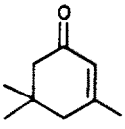
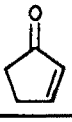
5 **6**

This work has two aims:

(a) Determining whether the reaction is charge-controlled or frontier controlled.

(b) In the case of orbital control, determining whether nucleophile HOMO and electrophile LUMO interaction will be the predominating factor in interpreting the α-enones reactivity order.

Table 1.

	LUMO Hückel[4]
PhCH=CHCOPh **1a**	−0.132
PhCH=CHCOCH$_3$ **1b**	−0.226
CH$_3$CH=CHCOPh **1c**	−0.238
 **1d**	−0.400
 **1e**	−0.490
 **1f**	−0.490
 **1g**	−0.400

Recently, a more sophisticated interpretation of ambident reactivity of α-enones has been proposed.[7] It has been underlined that complexation of a hard cation, such as Li^+ by the α-enone, inverts the relative atomic coefficients of C_2 and C_4 in the LUMO. When there is no complexation, $c_2^2 < c_4^2$, though when there is complexation, or when the α-enone is protonated,[8] $c_2^2 > c_4^2$; the

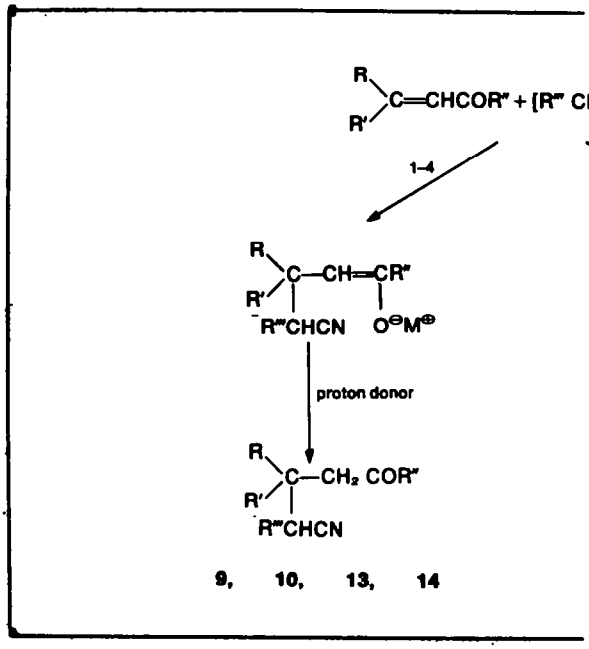
implication is a change of the reactive site of the α-enone by a given nucleophile, so that attack of carbonyl carbon can either result from charge control[1,2] or from frontier control on an α-enone which is complexing with a cation.[7] Evidently, such a complexation can take place only in a poorly dissociating and basic solvent; its efficiency will be higher, the better Lewis acid the cation is ($Li^+ > Na^+ > K^+$).

Therefore, we must consider the eventuality of such an interaction. For this reason we shall examine the reaction of the α-enones with reagent **5**, $M^+ = Li^+$ and K^+ in THF[a] and with reagent **6**, $M^+ = Li^+$ in THF and in a THF 80–HMPA 20 mixture, the latter solvent being highly basic will be more prone to solvate Li^+ than the α-enone.

Choice of experimental conditions—identification of products

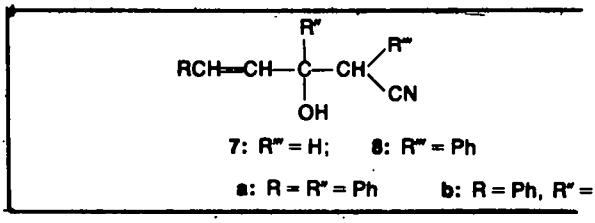
Lithiated acetonitrile not being stable above −60°C,[9] the reactions were run at low temperature. Reagents **5** and **6** were formed by action of one equivalent of *n*-butyllithium or potassium trimethylsilylamide on the corresponding nitrile at −80°C.

The reaction scheme is as follows:



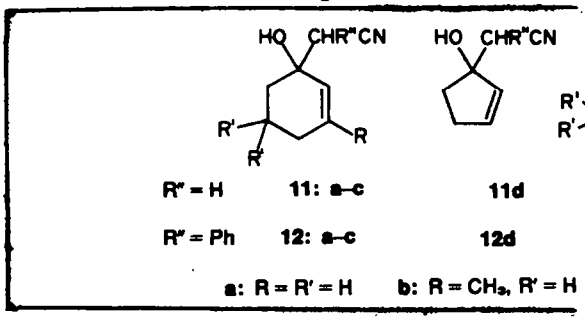
After hydrolysis, the expected products are the following:

From linear α-enones **1a–c**, alcohols **7** and **8a–c** resulting from carbonyl attack and ketones **9a–c** and **10a–c** resulting from carbon 4 attack.



Alcohol **7a** and ketones **10a** and **10b** are already known[10,11] but they were obtained under different experimental conditions. Alcohols **7b**, **7c**, **8b** and ketone **10c** have been isolated, purified and identified by analysis, IR and NMR.

From cyclic α-enones, alcohols **11a–d** and **12a–d** resulting from carbonyl attack and ketones **13a–d** and **14a–d** resulting from carbon 4 attack.



[a] Acetonitrile anion is known to give duplication in the presence of dipolar aprotic solvent.[8a,9]

To our knowledge, none of these compounds have been described. The products have been isolated, purified and identified as above.

RESULTS

The results are listed in Tables 2, 3 and 4. The yields and determinations have been done by NMR with internal standard, unless otherwise indicated. The reaction mixture contains only the indicated products and starting materials. If the reactions are run long enough, the total yields are at least 90%.

Table 2 shows that the acetonitrile anion gives only alcohols **7** or **11**, whatever the associated cation is; they result from α-enone carbonyl attack. We have verified that the corresponding alcoholate formation is irreversible: treatment of **7** or **11** by one molar equivalent of *n*-BuLi or $(Me_3Si)_2NK$ in THF, followed by hydrolysis, leaves them unchanged.

Table 2. Reaction of α-enones and acetonitrile anion **5** in THF at −80°C (reactants concentrations 0.2 M)

Exp. No.	α-Enone	M^+	Product[a]
1	**1a**	Li	**7a**
2	**1a**	K	**7a**
3	**1b**	Li	**7b**
4	**1b**	K	**7b**
5	**1c**	Li	**7c**
6	**1c**	K	**7c**
7	**1d**	Li	**11a**
8	**1e**	Li	**11b**
9	**1f**	Li	**11c**
10	**1g**	Li	**11d**

[a]Whatever the reaction time is, these are the only products formed. For a given reaction time, the yields are better when $M^+ = Li^+$.

Table 3. Reaction of α-enones and lithiated phenylacetonitrile **6** in THF (reactants concentrations 0.2 M)

Exp. No.	α-Enone	T°C	Reaction time (min)	Yield %	Products
11	**1a**	−90	2	90	**10a**[a]
12	**1b**	−70	1	70	**8b**[b] + **10b**[b] 78:22[c]
13	**1b**	−70	15	85	**8b** + **10b**[b] 28:72[c]
14	**1b**	−60	120	90	**10b**[b]
15	**1c**	−90	2	85	**10c**[b]
16	**1d**	−70	1	65	**12a**[b] + **14a**[b] 45:55
17	**1d**	−70	15	70	**12a** + **14a** 30:70
18	**1d**	−60	180	90	**14a**[b]
19	**1e**	−90	2	70	**12b**[b] + **14b**[b] 65:35
20	**1e**	−70	15	75	**12b** + **14b** 30:70
21	**1e**	−60	120	95	**14b**[b]
22	**1f**	−70	1	45	**14c**[b]
23	**1f**	−70	15	95	**14c**[b]
24	**1g**	−90	2	85	**14d**[a]
25	**1g**	−70	10	90	**14d**[a]

[a]Only one stereoisomer is formed. [b]Mixture of two stereoisomers. [c]Determination by weighing after TLC on silicagel.

[b]According to various cases, one or two stereoisomers are formed: we have not determined their configuration nor if their formation is kinetically or thermodynamically controlled.

Table 4. Reaction of α-enones and lithiated phenylacetonitrile **6** in the THF 80–HMPA 20 at −70°C 1 min

Exp. No.	α-Enone	Reactants (concentration)	Yield (%)	Products
26	**1a**	0.02 M	80	**10a**[a]
27	**1b**	0.02 M	40	**10b**[b]
28	**1c**	0.02 M	40	**10c**[b]
29	**1d**	0.02 M	20	**14a**[b]
30	**1d**	0.2 M	90	**14a**[b]
31	**1e**	0.2 M	70	**14b**[b]
32	**1f**	0.2 M	10	**14c**[b]
33	**1g**	0.02 M	70	**14d**[a]

[a]Only one stereoisomer is formed. [b]Mixture of two stereoisomers.

From Table 3, we can see two series of results in THF, when starting from lithiated phenylacetonitrile **6**. Some α-enones **1a**, **1c**, **1f**, **1g** give only ketones **10** or **14** resulting from carbon 4 attack[b] (exp. No. 11, 15, 22, 23, 24, 25), whatever the temperature and reaction time are. Other α-enones, compounds **1b**, **1d** and **1e**, give a mixture of alcohols **8** or **12**, resulting from carbonyl attack, and ketones **10** or **14**, resulting from carbon 4 attack. The longer the reaction time (exp. 12, 13, 14, 16, 17, 18, 19, 20, 21) the greater the amount of ketone in the reaction mixture. Consequently, lithium alcoholate formation is reversible; the product ratio, under kinetic control, is probably close to that obtained after 1 min. The ketone, **10** or **14**, precursor (enolate or carbanion α to CN) is thermodynamically more stable than the alcoholates. Schultz and Yee[12] have recently obtained similar results when reacting 2-cyclohexenone **1d** with organolithium reagents α to esters, in THF. We have also run the reaction of **6**, $M^+ = Li^+$ and benzalacetone **1b** in diethylether at −70°C: after 1 min, **8b** + **10b** are formed in the ratio 75:25; equilibration to **10b** is slower than in THF as after 5 h at −60°C, the **8b**/**10b** ratio is still 38:62.

Table 4 shows that, in THF 80–HMPA 20, only ketones **10** or **14** are formed. However, if HMPA is added to the reaction mixture obtained in THF from α enones **1b** or **1d**, no alcohol **8b** or **12a** can be characterized after immediate hydrolysis, showing that the corresponding alcoholate formation is highly reversible when HMPA is present.

In this medium, yields of ketones at a given reaction time, according to the reagents concentration, allow us to classify the α-enones reactivities towards lithiated phenylacetonitrile **6** as follows: **1a** > **1g** > **1b** = **1c** > **1d** > **1e** ≫ **1f**.

DISCUSSION

Reaction control

(a) Acetonitrile anion **5** leads only to products resulting from carbonyl carbon attack whatever the α-enone and associated cation are. Consequently, the reaction has a good chance of being under charge control.

(b) Lithiated phenylacetonitrile **6** leads only to products resulting from carbon 4 attack with α-enones **1a**, **1c**, **1f** and **1g**, whatever the solvent is. From compounds **1b**, **1d** and **1e** both carbonyl attack and

carbon 4 attack are observed in THF, though carbon 4 attack is only seen in THF–HMPA. In the latter case, it is not possible to conclude that no attack of carbonyl carbon takes place under kinetic control, due to the instability of the corresponding lithium alcoholates in this medium. These results are, however, in accordance with a frontier control of this reaction, as carbonyl complexation in this case cannot be envisaged as being due to the high basicity of HMPA.

These results can be compared to some other literature data:

—chalcone **1a** and crotonophenone **1c** always give more carbon 4 attack than benzalacetone **1b** with $NaBH_4$[13] or lithiated anion **4'**.[14]

$$[(EtO)_2P(O)CHCN]^{\ominus}Li^{\oplus} \quad 4'$$

—2-cyclopentenone **1g** always give more carbon 4 attack than 2-cyclohexenone **1d**.[14–18]

However, isophorone **1f** behaviour seems peculiar as hydrides reduce its carbonyl group,[19] though sodium cyanoborohydride in acidic medium gives carbon 4 attack.[20] The problem of isophorone reactivity will be studied further in our laboratory.

A possible interpretation of the different results, is as follows: in THF the reaction of **1a**, **1c** and **1g** would only take place with free α-enone, therefore only carbon 4 attack could be seen. Reaction of **1b**, **1d** and **1e** would take place both with free and Li-complexed α-enone, attack of both sites could therefore occur.[c] The differences observed could be due to easier complexation of Li^+ by α-enones **1b**, **1d** and **1e**. In fact, it has been shown that the benzalacetone **1b** carbonyl oxygen is more basic than that of chalcone **1a**.[21] We have tried to obtain evidence for this phenomenon by ^{13}C NMR study, but we were unable to find mechanistically significant results.[4,22] Such an interpretation would also imply that Li complexation, lowering the LUMO level,[7] would induce electrophilic assistance as well as a change of regioselectivity: it has been shown previously[17] that if this is the case for 2-cyclohexenone **1d** reduction, it is not for 2-cyclopentenone **1g** as this latter compound mainly reacts at C_4, as we have observed with **6**. Furthermore, comparison of exps. 22 and 32 (Tables 3 and 4) shows the isophorone **1f** carbon 4 attack by lithiated phenylacetonitrile **6** is faster when Li^+ is not solvated by HMPA. Consequently, carbon 4 attack may also take place for some α-enones when they complex the lithium cation, depending upon their structure. Therefore, the calculations performed with acrolein cannot be generalized to all $\alpha\beta$-unsatured carbonyl compounds.[7]

Predominating interactions in case of orbital control

In the mixture THF–HMPA, we could determine the carbon 4 reactivity order of α-enones **1a–1g** vs nucleophile **6**. In all cases, but one **1g**, the lower the energy level of the α-enone LUMO, the faster the reaction. Compounds **1a**, **1b** and **1c**, which are phenyl substituted, are more reactive than alicyclic ones; benzalacetone **1b** and crotonophenone **1c**, the LUMO levels of which being very close, react at the same rate. On the other hand, with reagent **4**, we observed[4] that for α-enones **1a** and **1b** reaction at position 4 was slower than the reaction of **1c** and even of **1d**.

Therefore, in the present case, frontier orbital interaction may be considered as the predominating factor. Reagent **6** has a highly delocalized negative charge at least in the presence of a dipolar aprotic solvent—as ^1H NMR determinations in DMSO or HMPA with the sodium derivative[6b] have shown. Furthermore, its HOMO energy level is certainly very high as it is phenyl conjugated.[e]

Frontier control also implies that the transition state occurs relatively early in the reaction path: in fact, factors such as loss of conjugation energy when carbon 4 geometry changes from trigonal to tetrahedral do not intervene. This latter factor was taken into account for α-enones reactions with phosphorylated reagent **4**.[4] Steric factors also predominate when the transition state occurs later in the reaction path, as we previously noticed,[4] and must be less important when it occurs earlier. When comparing reaction rates of **4** and **6** (in THF–HMPA) either with 2-cyclohexenone **1d** or 3-methyl 2-cyclohexenone **1e**, we see that in the former case, carbon 4 attack of **1e** is far slower than with **1d**[4] though, in the later, both reactions have nearly the same rate.

Consequently, as has been done for cycloadditions,[25] it is possible to deduce from the reactivity of the activated double bonds of α-enones, under orbital control, good evidence for the relative position of the transition state in the reaction path, according to the nature of the nucleophile.

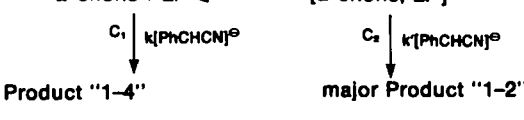
CONCLUSION

Reaction of acetonitrile anion **5** with α-enones only gives carbonyl carbon attack, whatever the associated cation is; it is probably under charge control. Lithiated phenylacetonitrile **6** reaction is under orbital control. In THF–HMPA, where associated cation complexation by α-enone is improbable, the reaction is frontier controlled; the lower lying the α-enone LUMO level, the faster the reaction. The transition state occurs relatively early in the reaction path compared to reactions of other nucleophiles such as phosphorylated anions **4**, for which the predominating factors are deconjugation in the transition state and steric effects.

EXPERIMENTAL

Reactions were run in a four necked flask, with a mechanical stirrer, dropping funnel, thermometer and under dry N_2. THF

[c] The kinetic scheme for both processes is as follows:



This implies that $k[C_1]$ and $k'[C_2]$ are of the same order of magnitude.

[d] Spectra of **1a**, **1b**, **1d** and **1g** have been run in THF with and without added $LiClO_4$. In all cases carbonyl carbon lowfield shifts have been noticed in the presence of Li^+, but the differences were not high; they were of the same magnitude (2–4 ppm) as those observed recently by House and Chu[23] with similar compounds.

[e] Perturbation energy calculations have been performed with arbitrarily varying HOMO energy level nucleophiles and various α-enones, taking into account all the vacant α-enone orbitals. They show that for low lying HOMO species, a leveling of perturbation energy is observed. For intermediate ones, perturbation energy order does not correspond to LUMO α-enones levels. Only with high lying HOMO nucleophiles do the perturbation energy orders follow LUMO α-enones levels.[24]

was distilled over KOH then LAH. HMPT was fractionated under reduced pressure over CaH_2. IR spectra were run on a Perkin-Elmer 157 spectrophotometer; NMR spectra on T 60 Varian (solvent CCl_4 or $CDCl_3$, internal TMS as standard). For determinations, internal standard was orthonitrobenzaldehyde or benzylalcohol. Where a correct microanalysis has been obtained, it is quoted: analysis.

General procedure. *n*-BuLi (10^{-2} mol, 2 N) in hexane was added within 1 min to 10^{-2} mole nitrile in 50 cm³ solvent at −70°C. After 30 min stirring, the solution was cooled to the required temperature. The α-enone (10^{-2} mole) dissolved in 5 cm³ THF was rapidly added, while the temperature was maintained. After variable reaction time, 20 cm³ HCl N or AcOH 2N were added. The reaction mixture was then allowed to warm up to room temp. After ether addition, the organic layer was washed with $NaHCO_3$ solution, saturated NaCl solution until neutral and dried over Na_2SO_4. Solvents were evaporated under reduced pressure, and the residue analyzed by NMR.

Description of products (all syntheses were run in THF). All alcohols showed OH and CN at 3400 and 2250 cm⁻¹ in the IR.

3,5 - *Diphenyl* - 3 - *hydroxy* - 4 - *pentennitrile* **7a** ($C_{17}H_{15}NO$). F = 151°.[10] NMR ($CDCl_3$): 2.93 s (2H: CH_2CN); 6.57 AB system $^3J_{AB}$ = 16 Hz; $\Delta\nu_{AB}$ = 0.13 (2H: ethylenic protons), 7.3 m (10H: aromatic protons).

3 - *Hydroxy* - 3 - *methyl* - 5 - *phenyl* - 4 - *pentennitrile* **7b** ($C_{12}H_{13}NO$ oil). Isolated by CCM on silicagel (Hexane 70:ether 30). NMR (CCl_4): 1.4 s (3H: CH_3); 2.43 s (2H: CH_2CN); 6.24: AB system $^3J_{AB}$ = 16 Hz; $\Delta\nu_{AB}$: 0.42 (2H: ethylenic protons); 7.05 broad s (5H: aromatic protons).

3 - *Hydroxy* - 5 - *methyl* - 3 - *phenyl* - 4 - *pentennitrile* **7c** ($C_{12}H_{13}NO$ oil). Isolated by CCM on silicagel (Hexane 80:ether 20). NMR (CCl_4): 1.63 (ill defined quartet, 3H: CH_3); 2.65 s (2H: CH_2CN); 5.55 (broad singlet: 2H olefinic protons); 7.08 broad signal (5H: aromatic protons).

1' - *Hydroxy* - 2' - *cyclohexenylacetonitrile* **11a** ($C_8H_{11}NO$ oil). Isolated by GLC (SE 30 lm, 140°C, retention time 8 min). NMR (CCl_4): 2.5 s (2H: CH_2CN); 5.97 broad signal (2H: olefinic protons).

1' - *Hydroxy* - 3',5',5' - *trimethyl* - 2' - *cyclohexenylacetonitrile* **11c** ($C_{11}H_{17}NO$ oil). Isolated by GLC (Apiezon lm, 110°C, retention time 8 min). NMR (CCl_4): 1.0 broad s (6H: CH_3); 1.75 s (3H: CH_3); 2.40 s (2H: CH_2CN); 5.40 broad s (1H: olefinic H).

1' - *Hydroxy* - 2' - *cyclopentenylacetonitrile* **11d** (C_7H_9NO oil). Isolated by GLC (Apiezon lm, 80°C, retention time 7 min). NMR (CCl_4): 2.56 s (CH_2CN); 5.8 broad signal (2H: olefinic protons).

4 - *Benzoyl* - 2,3 - *diphenylbutanenitrile* **10a** ($C_{23}H_{19}NO$). After 2 min reaction at −90°C, the residue crystallizes. F = 117°C (Et_2O), single isomer.[11a] Analysis. NMR (CCl_4) 250 MHz: 3.6 ABC system (3H); 4.4 d $^3J_{HH}$ = 5 Hz (1H: CHCN); 7–8 broad signal (15H: aromatic protons).

2,3 - *Diphenyl* - 5 - *oxo hexanenitrile* **10b** ($C_{18}H_{17}NO$). After 2 h reaction at −60°C, 1.6 g raw residue is treated by 10 cm³ ether. At −20°C, one obtains a 2:1 mixture of erythro/threo compounds. NMR identical to literature.[11c]

2,5 - *Diphenyl* - 3 - *hydroxy* - 3 - *methyl* - 4 - *pentennitrile* **8b** ($C_{18}H_{17}NO$). After 1 min at −70°C, 1 g raw material is crystallized in 6 cm³ ether 1:cyclohexane 1 at −20°C. A single isomer is obtained F = 89°C. Analysis. NMR (CCl_4): 1.4 s (3H: CH_3); 2.5 s (1H: OH); 3.9 s (1H: CHCN); 6.35 AB syst. $^3J_{HH}$: 16 Hz (2H: ethylenic protons); 7.2 m (10H: aromatic protons).

4 - *Benzoyl* - 3 - *methyl* - 2 - *phenyl butanenitrile* **10c** ($C_8H_{17}NO$). After 1 h at −70°C, 2 g raw material crystallize in 10 cm³, ether at −20°C. Major isomer is isolated F = 55°C (ether). Analysis. IR ν_{CN}: 2250; ν_{CO}: 1680. NMR (CCl_4): 1.05 d $^3J_{HH}$: 7 Hz (3H: CH_3); 2.6 to 2.9 m (1H: $CHCH_3$); 3.1 to 3.3 m (2H: CH_2); 4.25 d $^3J_{HH}$: 4 Hz (1H: CHCN); 7.5–8 m (10H: aromatic protons). Minor isomer: NMR (from the mixture): 1.15 d $^3J_{HH}$: 7 Hz (3H: CH_3); 4.0 d $^3J_{HH}$: 5 Hz (1H: CHCN).

2 - [3' - *Oxocyclohexyl*] 2 - *phenylacetonitrile* **14a** ($C_{14}H_{15}NO$). After 3 h at −60°C, the residue crystallizes. By dissolving 1 g material into 10 cm³ ether, one isomer is isolated F = 119°C (ether). Analysis. IR ν_{CN}: 2250; ν_{CO}: 1710. NMR (CCl_4): 1.6–2.5 m (9H, cyclic protons); 3.9 m (1H, CHCN); 7.3 s (5H: aromatic protons).

2 - [1' - *Hydroxy* - 2' - *cyclohexenyl*] 2 - *phenylacetonitrile* **12a** ($C_{14}H_{15}NO$). After 2 min reaction at −90°C, the residue is chromatographed on silicagel thin layer (elution ether 30:hexane 70). After ten migrations, a mixture of stereoisomers is obtained. Analysis. NMR (CCl_4): 3.85 and 3.87 s (ratio 2:1:CHCN of both isomers);7.4 s (5H: aromatic protons).

2 - [1' - *Methyl* - 3' - *oxocyclohexyl*] 2 - *phenylacetonitrile* **14b** ($C_{15}H_{17}NO$). After 2 h reaction at −60°C, the residue is chromatographed on silicagel thin layer (elution ether 30:hexane 70). After four migrations a mixture of stereoisomers is obtained. Analysis. IR ν_{CN}: 2250; ν_{CO}: 1710. NMR (CCl_4): 3.7 and 3.75 s (ratio 3:2 CHCN of both isomers); 1.0 s (3H: CH_3); 7.3 s (5H: aromatic protons).

2 - [1' - *Hydroxy* - 3' - *methyl* - 2' - *cyclohexenyl*] 2 - *phenyl* - *acetonitrile* **12b** ($C_{15}H_{17}NO$). After 2 min reaction at −90°C, the residue is chromatographed on silicagel thin layer (elution:ether 1:hexane 1). After five migrations a mixture of stereoisomers is obtained. Another TLC on silicagel (elution ether 30:hexane 70) gives the major isomer F = 116°C. Analysis. NMR (CCl_4): 1.5–2.0 m (10H); 3.8 s (1H: CHCN); 5.5 m (1H: ethylenic proton); 7.3 s (5H: aromatic protons). Minor isomer: NMR (from the mixture): 3.85 s (1H: CHCN); 5.3 m (1H: ethylenic proton).

2 - [3' - *Oxo* - 1',5',5' - *trimethylcyclohexyl*] 2 - *phenyl* - *acetonitrile* **14c** ($C_{17}H_{21}NO$). After 15 min reaction at −70°C, 2 g raw material is crystallized into 10 cm³ ether. The two formed isomers could not be separated. Analysis. IR ν_{CN}: 2250; ν_{CO}: 1710. NMR (CCl_4): 1.1 (9H: three very close singlets); 3.7 s and 3.8 s (1H: CHCN of both isomers); 7.3 s (5H: aromatic protons).

2 - [3' - *Oxocyclopentyl*] 2 - *phenylacetonitrile* **14d** ($C_{13}H_{13}NO$). After 1 h reaction at −70°C, the residue crystallizes. A single isomer is obtained. F = 88°C (ether). Analysis. IR: ν_{CN}: 2250; ν_{CO}: 1740. NMR (CCl_4): 1.7–2.8 m (7H: cyclic protons); 3.85 d $^3J_{HH}$: 6 Hz (1H: CHCN); 7.4 s (5H: aromatic protons).

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