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# ALLYLIC SUBSTITUTION BY CARBON NUCLEOPHILES ON 4-BROMO-4-METHYL-2-PENTENOATE : ANTI-MICHAEL REGIOSELECTIVITY.

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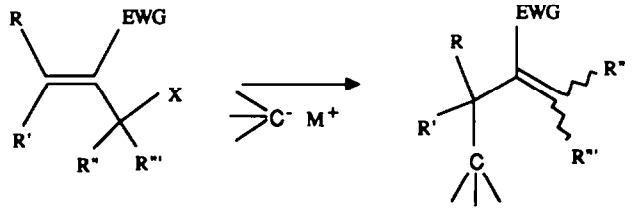
Abstract

The reaction of carbanions α-to nitriles with tertiary bromoester **1** does not give cyclopropanes, whatever the reaction conditions, while Li enolate of methyl phenylacetate does, in THF or THF-$Et_2O$. From lithiated aminonitriles **5**, in THF-HMPA, the reaction leads to a mixture of $S_N$ and $S_N'$ products in equal amounts via a radical process. From arylaceto- and propionitriles **4** whatever the conditions, and from methyl phenylacetate enolate **16**, either associated to Li in THF-HMPA or to K in THF, $S_N'$ anti-Michaël products are predominantly formed via a concerted inner sphere process, showing thus the possibility of a polar-SET mechanistic spectrum from a single electrophilic reagent.

Allylic substitution with double bond migration ($S_N'$) promoted by carbon nucleophiles without transition metal or copper catalysis is not frequent in the literature [1], unless the double bond is activated by a properly located electron withdrawing substituent [2].

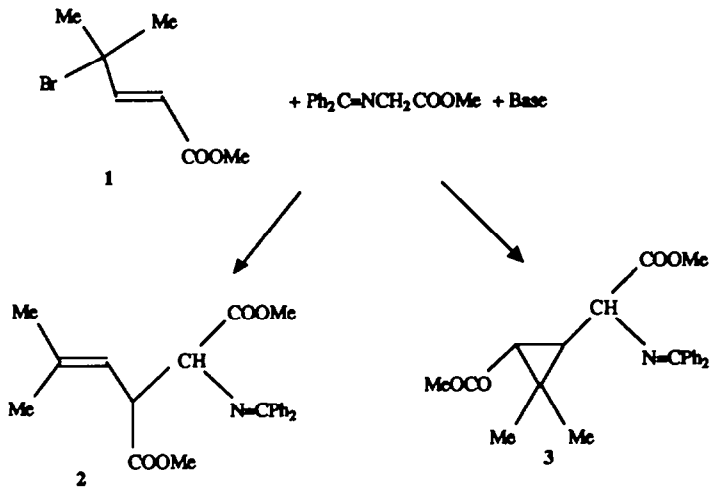
Scheme 1




However, when the nucleophilic reagent bears a heteroatom, apparent $S_N'$ substitution can take place via a $S_N2$ process at the heteroatom followed by a 2.3 sigmatropic rearrangement of a subsequently generated ylid [3].

Recently, BORDWELL and coll. [4] and LISSELL [3d] showed that some carbanions reacted with secondary and tertiary allylic halides leading to $S_N'$ products, occasionnally accompanied by untransposed $S_N$ products. Furthermore, JOUCLA and coll. [5] observed that the reaction of tertiary 4-bromo-pentenoate **1** with $Ph_2C{=}NCH_2COOMe$ in the presence of base in a dipolar aprotic solvent produced the anti-Michael $S_N'$ product **2**, while, in THF, Michaël addition-Ring closure (MIRC) took

place, leading to cyclopropanes 3.




These observations raise two interesting possibilities : 1) it it possible to generalize such a $S_N'$ reaction to other carbon nucleophiles ? ; 2) because tertiary bromides are not prone to $S_N2$ substitution and because $S_N1$ reactions are not likely in dipolar aprotic solvents, one might wonder whether such reactions take place via Single Electron Transfer (SET). This possibility was in line with the recent approaches of nucleophilic substitutions [6] and with BORDWELL'S latest interpretations [7].

In such an eventuality, carbanions α to nitriles should be good candidates as nucleophiles because some of them are prone to SET processes in dipolar aprotic media [8].

In the present paper, we examine the reactions of bromoester 1 with several carbanions α to nitriles formed from 4 a-d, as well as carbanions from aminonitriles 5a,b,e which are prone to favor SET processes [9a] due to the captodative character of the corresponding radicals [9b,c]. Moreover, since our preliminary results [10] showed that no MIRC could be observed in the reaction of bromoester 1 with these carbanions, we also investigate the reaction of 1 with the Li and K enolates of methylphenylacetate 6, the ester related to 4.

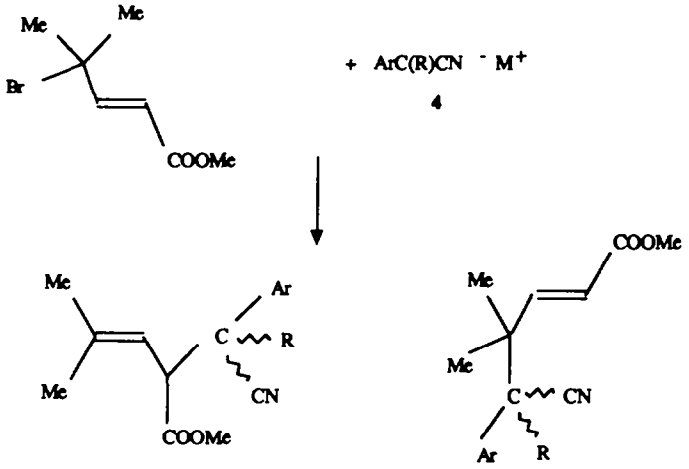
| $ArCH(R)CN$ | $ArCH(CN)NMe_2$ | $PhCH_2COOMe$ |
|---|---|---|
| 4 | 5 | 6 |
| a) Ar = Ph, R=H | a) Ar = Ph | |
| b) Ar = p.$MeOC_6H_4$, R = H | b) Ar = p.$MeOC_6H_4$ | |
| c) Ar = m.$ClC_6H_4$, R = H | e) Ar = p.$ClC_6H_4$ | |
| d) Ar = Ph, R = Me | | |

Results

The carbanionic reagents were generated at low temperature by action of n.BuLi, LHMDS, KHMDS or KOt.Bu on the related carbon acids. The reactions were run at room temperature using a slight excess of carbanionic reagent relative to the bromoester in $Et_2O$, THF, THF-HMPA, toluene or DMSO. In a few cases, $BF_3.Et_2O$ was also added. After aqueous $NH_4Cl$ treatment, the different compounds formed were separated by column chromatography or crystallization and identified by IR, NMR, MS and elemental analysis.

When the reaction was run from carbanions α to nitriles generated from **4a-d** and **5a,b,e** two series of products were be identified : $S_N'$ products **6, 7, 8** resulting from substitution with double bond migration and $S_N$ ones **9, 10, 11**. The ratios of these products depended upon the reagents and the conditions. Cyclopropanes resulting from MIRC reaction were never detected (scheme II).

Scheme II

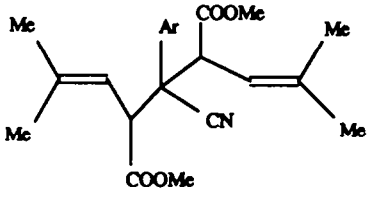



**6** (R = H)
**7** (R = Me)
**8** (R = $NMe_2$)

**9** (R = H)
**10** (R = Me)
**11** (R = $NMe_2$)

a) Ar = Ph ; b) Ar = p.$MeOC_6H_4$ ; c) Ar = m.$ClC_6H_4$ ; e) Ar = p.$ClC_6H_4$

In addition, a bis alkylated $S_N'$ product **12** was isolated when the reaction with **4a-c** and bromoester **1** was performed in THF-HMPA .

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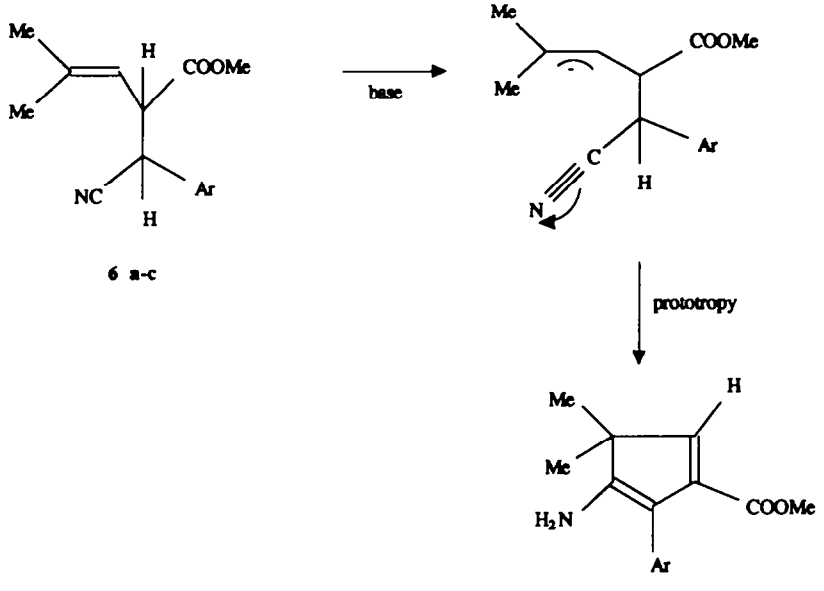
Moreover, when the reaction was run with arylacetonitriles **4a-c** in the presence of lithiated bases in THF, $Et_2O$ or toluene cyclic derivatives **13a-c** were obtained in amounts depending on the reaction conditions. From their IR, $^1H$ and $^{13}C$ NMR spectra, MS and elemental analysis, as well as by base treatment of purified **6a-c**, it appears that the formation of **13** resulted from base catalyzed cyclisation of the related $S_N'$ products followed by prototropy (Scheme III).

Scheme III




**6 a-c**

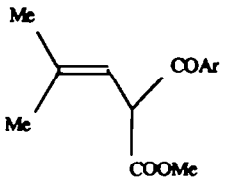
**13 a-c**

Therefore starting from arylacetonitriles **4a-c**, the $S_N'$ process can lead to three different compounds : **6**, **12** and **13**. By altering to the reaction conditions, each of them can be obtained predominantly : with KHMDS as a base in THF or toluene, **6** is the major product (Table 1, entries 7,8,11,12), while with LHMDS in toluene or $Et_2O$, the amount of cyclopentadiene **13** greatly increases (Table 1, entries 4,6,10) due to the associating medium as well as to electrophilic assistance by $Li^+$ to CN attack. In contrast, in poorly associating conditions (THF-HMPA) and at room temperature, bis substituted compounds **12** are formed (Table 1, entries 5,13). The

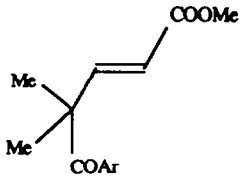
substitution of the aromatic ring of **4** does not bring any noticeable difference in the nature of the products obtained.

Compounds **6, 7** and **9, 10** were usually 60:40 mixtures of diastereoisomers, except when the reaction was run with propionitrile **4d** and bromoester **1** in DMSO or THF-HMPA : one stereoisomer was highly predominating and its configuration is to be assigned by X-ray determination (Table 1, entry 15).

When the reaction was run with aminonitriles **5a,b,e**, the products were identified after unmasking of the latent keto groups as related keto esters **14** and **15**.

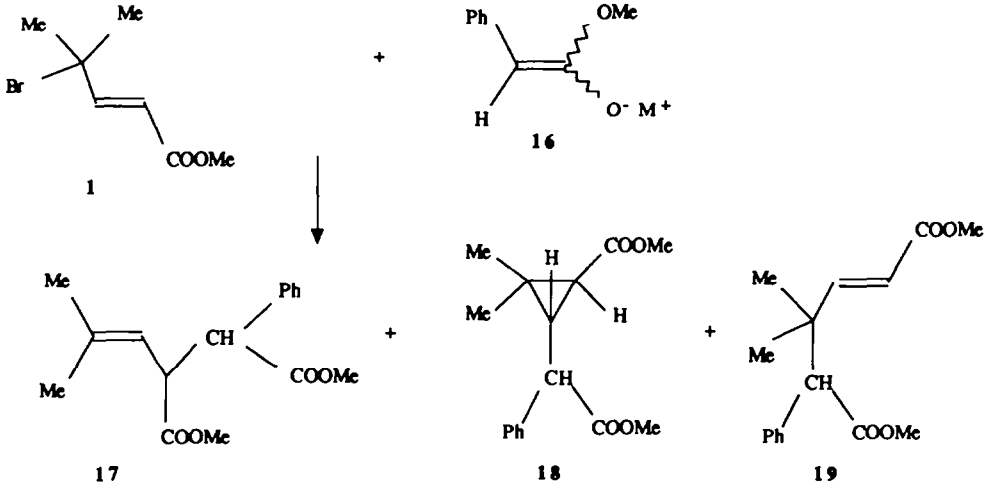



**14a,b,e**




**15a,b,e**

Finally, the reaction of ester enolate **16** with bromoester **1** led to a mixture of $S_N'$ products **17** and E diastereoisomeric cyclopropanes **18** in amounts depending on the reaction conditions, next to small amounts of $S_N$ one **19**.




All the results are in Tables I and II. The various determinations were made by capillary GPC with internal standard or by $^1H$ NMR ($CH_2Cl_2$ as internal standard). Yields are given related to **1** ; when an excess of nucleophile was used, the corresponding amount of carbon acid was recovered unchanged after work-up.

**Table 1**

Reactions of carbanions α to nitriles with ester **1** at room temperature.
(Yields determined by GLC with internal standard)

| Entry | Carbon acid (4 or 5/1 molar ratio) | Base | Solvent (reaction time) | Yields % in $S_N'$ | $S_N$ | MIRC |
|---|---|---|---|---|---|---|
| 1 | **4a** (2) | LHMDS or nBuLi | THF (15 mn) | **6a**:54 **13a**:39 | **9a**:3 | <1 |
| 2 | **4a** (1.5)[a] | LHMDS | THF (15 mn) | **6a**:69 **13a**:29 | **9a**:2 | <1 |
| 3 | **4a** (2)[b] | LHMDS | THF (15 mn) | **6a**:56 **13a**:8 | **9a**:7 | <1 |
| 4 | **4a** (1.5) | LHMDS | $Et_2O$ (15 mn) | **6a**:48 **13a**:48 | **9a**:2 | <1 |
| 5 | **4a** (1) | LHMDS | THF-HMPA (15 mn) | **6a**:55 **12a**:26 **13a**:2 | **9a**:7 | <1 |
| 6 | **4a** (2) | LHMDS | Toluene (15 mn) | **6a**:22 **13a**:41 | <1 | <1 |
| 7 | **4a** (1) | KHMDS | THF (15 mn) | **6a**:86 **13a**:5 | <1 | <1 |
| 8 | **4a** (1) | KHMDS | Toluene (15 mn) | **6a**:77 **13a**:7 | **9a**:2 | <1 |
| 9 | **4b** (1)[c] | LHMDS | THF (15 mn) | **6b**:62 **13b**:2 | **9b**:4 | <1 |
| 10 | **4b** (1) | LHMDS | Toluene (15 mn) | **6b**:20 **13b**:54 | <1 | <1 |
| 11 | **4b** (1) | KHMDS | Toluene (15 mn) | **6b**:75 **13b**:6 | **9b**:4 | <1 |
| 12 | **4c** (1) | KHMDS | THF (15 mn) | **6c**:50 **13c**:2 | <1 | <1 |
| 13 | **4c** (2) | LHMDS | THF-HMPA (30 mn) | **6c**:51 **12c**:22 | <1 | <1 |
| 14 | **4d** (1) | nBuLi | THF | **7a**:65[d] | <1 | <1 |
| 15 | **4d** (1) | tBuOK or nBuLi | DMSO [h] THF-HMPA (10 mn) | **7a**:95[e] | <1 | <1 |
| 16 | **5a** (1) | nBuLi (4 hrs) | THF-HMPA | **14a**:32 | **15a**:32 | <1 |
| 17 | **5b** (1) | nBuLi (4 hrs) | THF-HMPA | **14b**:28 | **15b**:33 | <1 |
| 18 | **5b** (1)[f,g] | nBuLi (4 hrs) | THF-HMPA | **14b**:5 | **15b**:10 | <1 |
| 19 | **5e** (1) | nBuLi (4 hrs) | THF-HMPA | **14c**:36 | **15c**:34 | <1 |
| 20 | **5e** (1)[f] | nBuLi (4 hrs) | THF-HMPA | **14c**:13 | **15c**:14 | <1 |

a) In the presence of 1 eq. LiBr, the starting materials are recovered

b) Reaction run in the presence of 1 eq. $BF_3.Et_2O$ ; ratio of **6a** stereoisomers : 33/67

c) Reaction run at -15°C

d) Mixture of 2 stereoisomers 45/55

e) Mixture of 2 stereoisomers 95/5

f) Reaction run in the presence of tetramethyl-4,4,6,6 piperidinenitroxide

g) Similar result in the presence of m.dinitrobenzene

h) No decrease in yield in the presence of m.dinitrobenzene or tetramethyl-4,4,6,6 piperidine nitroxide

**Table 2**

Reactions of methyl phenylacetate enolate with ester **1** at room temperature. (Yields determined by GLC with internal standard)

| Entry | Base | Solvent (reaction time) | Yields % in $S_N'$ **17**[a] | $S_N$ **19** | MIRC **18**[b] |
|---|---|---|---|---|---|
| 21 | LHMDS | THF (2 hrs) | 16 | 2 | 56 |
| 22 | LHMDS | THF-$Et_2O$ (2 hrs) | 15 | 1 | 59 |
| 23 | LHMDS | THF-HMPA[c] (30 mn) | 67 | 8 | <1 |
| 24 | KHMDS | THF (2 hrs) | 60 | 15 | <1 |

a) Stereoisomers in 70/30 ratio

b) Stereoisomers in 60/40 ratio

c) 4 molar eq. HMPA ; if 2 molar eq. HMPA are used, the yields are the same but within 2 hrs.

The main features of our results are the following :

a) The $S_N'$ process takes place from tertiary bromide **1** with all the carbon nucleophiles studied. From arylacetonitriles **4a-d**, it occurs whatever the reaction conditions (base, solvent) (Table 1, entries 1 - 15) ; from aminonitriles **5a,b,e** or ester enolate **16**, it requires THF-HMPA when the associated cation is $Li^+$ (entries 16, 17, 19, 23). However, $K^+$ ester enolate **16**, in THF, also leads to $S_N'$ products **17** (entry 24).

b) The regioselectivity of the reaction is different when arylacetonitriles **4a-d** derivatives and ester enolate **16** on one hand or aminonitriles **5a,b,e** on the other hand are used. In the former case, only small amounts of $S_N$ products **9** and **10** are obtained next to $S_N'$ ones (entries 1 - 15, 23) while in the latter, nearly equal amounts of both, **8** and **11**, are formed (entries 16, 17, 19).

c) MIRC reaction, leading to cyclopropanes, previously observed by JOUCLA [5] with an ester enolate, takes place solely with lithiated ester enolate **16**, $M^+ = Li^+$ in THF or THF-$Et_2O$ (entries 21, 22).

Further experiments were done in order to interpret these results :

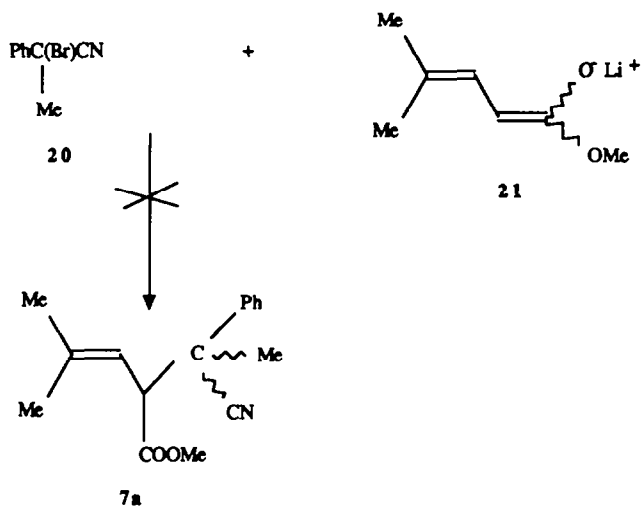
- The reaction of bromoester **1** with the carbanion formed from **4d** was run in DMSO in the dark or in the presence of radical traps (m.dinitrobenzene and 4,4,6,6-tetramethylpiperidine N-oxide) : no decrease in the yield of **1a** was noticed after the same reaction time (entry 15).

When the same experiments were run with aminonitriles **5a,b**, the yields in **8** and **11** were significantly reduced (entries18, 20).

- The reaction of aminonitrile **5a** with bromoester **1** was run in DMSO in the presence of $K_2CO_3$, conditions in which STELLA [3a-d, 11] observed N-quaternarization followed by ylid formation and 2.3 sigmatropic rearrangement, on the way to $S_N'$ products : under such conditions, the starting materials remained unchanged. Therefore, the $S_N'$ reaction does not involve such a two-step process in the present case.

MEISLICH and JASNE [12a] have already observed attack of $I^-$ in DMSO on the allylically substituted bromine of 4-bromoisophorone : such a process could also take place in our systems.

We therefore tried the reaction of bromo-2 phenyl-2 propionitrile **20** with methyl 4-methyl-penten-2-oate enolate **21** formed by action of LDA on the corresponding ester in THF ; it did not generate any $S_N'$ product **7a** after 15 mn at room temperature, conditions in which **7a** was obtained from **4d** and **1**. Only starting materials were recovered after aqueous work up, next to small amounts of dimers PhC(Me)-C(Me)Ph (CN, CN).




This experiment rules out the possibility of a $S_N'$ reaction involving attack on positive bromine by the soft carbanionic species .

Discussion

Two aspects of our results deserve comment :

- The lack of cyclopropane formation when the reaction was run with lithiated carbanion α to nitriles and bromoester **1** in THF.
- The mechanism of the allylic substitution.

a) MIRC reaction

These is ample precedent in the literature for reactions of lithiated carbanions [13] or of ester enolates [5,14] with bromocrotonates, leading to cyclopropanes by a MIRC process in THF or to $S_{N2}$ products in dissociating solvents.

When the reaction is run from bromide **1** in THF, conjugate addition is to be expected, although it is known to be sensitive to steric hindrance [15]. For instance, it has been shown that, without Lewis acid catalysis, conjugate addition of lithiated aminonitriles on β,β disubstituted α-

enones does not take place [15b]. Such an effect certainly explains why no reaction is seen from lithiated aminonitriles **5** and bromoester **1** in THF.

However, lithiated ester enolate **16** behaves as expected, leading to cyclopropanes **18** in THF, although next to some $S_N'$ product. From lithiated arylacetonitriles **4a-d**, which promote conjugate addition to α,β-unsaturated esters [16] as well as to α-enones, but which are sensitive to the electrophile steric hindrance [15c], no cyclopropanes are obtained. Moreover, $S_N'$ products are rapidly formed as the reaction goes to completion within 15 min from **4a-d** in THF, while it lasts for 4 hrs from **16**, $M^+ = Li^+$. This difference in reactivity between $Li^+$ enolate **16** and lithiated phenylacetonitrile is certainly inherent to the structure of both lithiated anionic species in THF [17]. This point is under active investigation [18].

b) Allylic substitution

From tertiary bromide **1**, allylic substitution takes place in two ways, either without any regioselectivity or via predominant $S_N'$ anti Michael process.

The non-regioselective pathway is observed from aminonitriles **5a,b,e** in THF-HMPA. Radical traps lower the yield of the reaction [19,20], implicating therefore an outer-sphere S.E.T. [6], followed by a radical process, which is likely a $S_{RN}1$ one as no duplication product was obtained ; the chains are probably short, as the reaction is not totally inhibited by these traps [20]. Loose ion pairing of the carbanionic species with the counterion is necessary for the primary electron transfer to occur, as the HOMO energy of the electron donor is raised related to that of a tight ion pair. A similar interpretation has been recently given by SAWYER and ROBERTS [6g], to explain the different behavior of hydroxide ion in dipolar aprotic solvent and in water (lowering of the HOMO level by solvation).

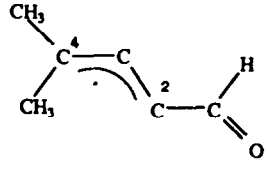
The poor regioselectivity of the reaction is not entirely unexpected as radical recombinations usually occur with no barrier. They are thus under diffusion control and do not exhibit any sensitivity to steric hindrance [6c]. However, MO UHF calculations have been performed on **22** as a model with the 3-21G basis set [21]. In an UHF study of radical recombination, two important stabilizing frontier interactions are to be considered : one occurs between the HO of the substrate and the LUMO of the reagent (α spin orbitals), the other implies the LU of the substrate and the HOMO of the reagent (β spin orbitals). Selectivity depends upon coefficients in both orbitals on a given partner. Calculations performed on **22** give the following results :

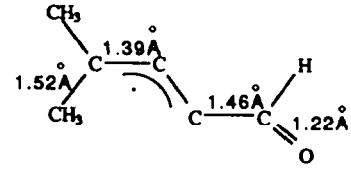
HOMO (α spin) : atom $C_4$ : 0.380 ($2p_z$) + 0.507 ($2p'_z$)

atom $C_2$ : -0.272 ($2p_z$) - 0.374 ($2p'_z$)

LUMO (β spin) : atom $C_4$ : -0.217 ($2p_z$) - 0.393 ($2p'_z$)

atom $C_2$ : 0.260 ($2p_z$) + 0.517 ($2p'_z$)



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From the figures, it appears that while reaction at $C_4$ is slightly favored in the first interaction, it is the reverse in the second one, the global result being in line with the experimental lack of discrimination.

SET from aminonitrile anions has precedent [8a,22a]. Such a behaviour is also observed in the reaction of lithiated 1,1 bis phenylthioethane with bromoester **1** in THF-HMPA : equal amounts of $S_N$ and $S_N'$ products are obtained, next to dimer $(PhS)_2C(CH_3)-C(CH_3)(SPh)_2$, indicative of a SET process [22b].

The predominating $S_N'$ process, whose regioselectivity is anti-Michaël, is observed for reactions of carbanions formed from arylaceto- and propionitriles **4a-d** whatever the associated cation and the solvent and from enolate **16**, either with $M^+ = Li^+$ in THF-HMPA or $M^+ = K^+$ in THF. From **4d** in DMSO, the reaction does not involve a radical-chain process, as radical traps do not slow it down. It seems reasonable to extend this observation to the other reagents.

This reaction could be envisioned to take place via a heterolytic process, involving a C-Br bond breaking as the determining step as proposed by BORDWELL in a few cases [4]. Such a mechanism seems unlikely in the present case as tertiary bromide **1** remains unchanged in the solvents used, either in the absence of nucleophile, or after some time, when the reaction is slow. Moreover, the rate of the reaction depends upon the concentration in anionic reagent [23].

As nucleophilic bromine attack, as a preliminary step, has been ruled out, it appears that the $S_N'$ process might be a concerted one, even from easily oxidable carbanions, having a HOMO level high in energy. Concertedness of the $S_N'$ process was also concluded by MEISLICH and JASNE [12b] who examined the reaction of pivalic acid salts with 4-bromoisophorone in aprotic solvents. In the latter case, the reaction was slower and the relative amount of $S_N$ products higher, due to the structure of the reagents. In the present case, the concerted inner sphere electron shift should be easy due to the narrow HOMO-LUMO gap between the partners which, according to PROSS and SHAIK [6a,b], favors the $DA\text{-}D^+A^-$ interaction, lowering the transition state energy. Polar pathways being sensitive to steric hindrance, coupling takes place at the least hindered site i.e. $\alpha$ to the ester group instead of on the quaternary carbon.

Therefore, according to the nature of the nucleophile, the allylic substitution implies either a SET or a concerted polar pathway showing thus, from a single electrophile, the existence of a "polar-SET mechanistic spectrum" [6a].

## Conclusion

The reaction of allylic tertiary bromoester **1** with charge delocalised reagents $\alpha$ to nitriles or with the enolate of methyl phenylacetate can lead, in suitable reaction conditions, to products resulting from allylic substitution. According to the substituents of the carbanion, this process might involve a concerted inner sphere electron transfer giving mainly the $S_N'$ anti-Michaël product, or take place via a two step outer sphere single electron transfer, leading to a mixture of $S_N$ and $S_N'$ products in equal amounts. From our results, it appears that the steric hindrance of the nucleophile as well as its ability to stabilize radicals [9] favors the SET pathway which is

observed with carbanions formed from aminonitriles (captodative systems) or from $CH_3CH(SPh)_2$, α to sulfur.

Experimental section

Bromoester **1**, bromonitrile **20** and aminonitriles **5** were prepared by literature methods [24]. The other nitriles were commercial and used without further purification.

Diethyl ether and toluene were R.P. Normapur spectroscopic grade solvents : they were kept over $MgSO_4$ under argon. THF was distilled over benzophenone ketyl or LAH before use. DMSO was distilled over KOH and HMPA over $CaH_2$.

LHMDS 1M in THF (Jansen), KHMDS 0.5M in toluene (Aldrich) and n.BuLi in hexane ( 1.6M, determined by titration with diphenylacetic acid) or solid dried KOt.Bu (Fluka) were used as bases.

IR spectra were recorded with a Perkin-Elmer 1310 infrared spectrometer ; they are given as υ max. in $cm^{-1}$. $^1H$ and $^{13}C$ NMR spectra were run on a Brücker AM 250 equipment ($^1H$ : 250 MHz, TMS internal standard ; $^{13}C$ : 62 MHz, $CDCl_3$ internal standard) on a Perkin-Elmer R32 (90 MHz) or on a Brücker AC200 ($^1H$ 200 MHz). Chemical shifts are given in δ ppm related to TMS. Mass spectra were performed on a Nermag 10-10 mass spectrometer. Microanalyses were done by the Service de Microanalyse du C.N.R.S.

The various compounds were purified by TLC or by Flash Chromatography on silica gel (230-400 mesh). Determinations by GLC were run on a 5160 MEGA Carlo Erba equiment using diethyl phtalate as internal standard (OV1 capillary column, 15 m, vector gas He (0.5 bar), temperature programmation from 70 to 180 or to 220°C, 10°C/mn).

General procedure

All the reactions were run under argon atmosphere.

- a) with lithiated bases : 3 or 5 mmoles of neutral precursor (**4** or **5**) were dissolved into 25 mL THF, 25 mL of a THF-HMPA mixture (4:1 v/v) or, when LHMDS was used as a base into 22 mL THF in a four necked vessel equipped with an argon entry, inner thermometer, mechanical stirring and a rubber septum. The vessel was cooled to -70°C and one molar equivalent of base (n.BuLi 1.6M in hexane or LHMDS in THF) was added slowly via a syringe. After 30 mn stirring, the temperature was raised to -50°C and 3 or 5 mmoles **1** were added via a syringe. The mixture was then raised to room temperature, stirred for 15 mn (from **4**) or 4 hrs (from **5**). The mixture was cooled again to -70°C and quenched by addition of an aqueous saturated solution of $NH_4Cl$. The organic phase was extracted by $Et_2O$ (from **4**) or ethyl acetate (from **5**), washed by water, dried over $MgSO_4$. The solvents were distilled under reduced pressure and the residue analyzed and purified.

From methyl phenylacetate **6**, the reaction was run in a similar fashion, unless the enolate was generated by addition of the ester to a slight excess of LHMDS in $Et_2O$-THF, THF or THF-HMPA (5 mmoles **6** in 1 mL solvent).

- b) with potassium bases. When using KHMDS in toluene as a base the reaction was run as previously on a 3 mmolar scale : the solvent was 12 mL THF + 6 mL toluene originating from the KHMDS solution.

In DMSO, KOt.Bu (400 mg) was dissolved into 10 mL DMSO ; 3 mmoles nitrile was added and stirring was maintained for 15 mn before the introduction of **1**. The reaction was run for 15 further mn, quenched at room temperature as before and extracted by EtOAc.

When the reactions were run with aminonitriles **5** on a 3 mmolar scale, the reaction mixture, after evaporation of the solvents, was dissolved into 18 mL of $Et_2O$-THF (1:2 v/v) and treated by 4 mL aqueous $AgNO_3$ 1M. After 2 hrs 30 mn stirring and filtration of AgCN, the organic

phase was separated, the aqueous phase extracted several times by EtOAc. The organic phases were set together, washed with brine and dried over $MgSO_4$ and treated as previously.

Reaction of bromonitrile **20** with enolate **21**

. LDA (3 mmoles) was prepared by action of n.BuLi (1.8 mL of 1.6M solution in hexane) on diisopropylamine (0.8 mL) in 1.2 mL THF. After evaporation of the solvents under argon, it was dissolved into 4 mL THF at -70°C. 2.5 mmoles methyl 4-methyl-2-pentenoate (320 mg) were added and the mixture was stirred at -70°C under argon for 30 mn. 2.5 mmoles bromonitrile **20** (530 mg) were added via a syringe and the temperature of the mixture was raised to 20°C, then stirred for 15 mn. After aqueous $NH_4Cl$ treatment and $Et_2O$ extraction, the crude mixture was analyzed by $^1H$ NMR and GPC : only bromonitrile **20**, starting ester and a small amount of PhC(CN)-C(CN)Ph could be characterized. ($CH_3$ $CH_3$)

3-Methoxycarbonyl-5-methyl-2-phenyl-hex-4-ene nitrile **6a**

Isolated by Flash column chromatography (pentane : $Et_2O$ 99:1 v/v)

*Isomer 1* m.p. 73.5° (hexane) ; Retention time 11.8 mn.

$^1H$ NMR (200 MHz, $CDCl_3$) : 1.5 (d, J = 1 Hz,.3H) ; 1.82 (d., J = 1 Hz, 3H) ; 3.57 (s., 3H) ; 3.65 (broad t., 1H) ; 4.26 (d., J = 9 Hz, 1H) ; 5.28 (d., J = 10 Hz, 1H) ; 7.35 (broad s., 5H).

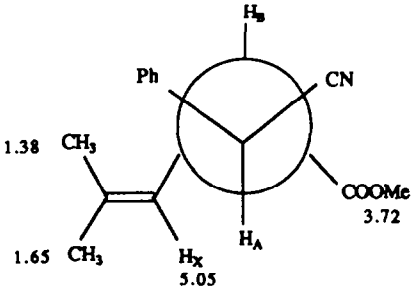
Analysis : $C_{15}H_{17}NO_2$ = 243. Calc % C = 74.04 ; H = 7.04 ; N = 5.76 ; found % C = 73.59 ; H = 6.97 ; N = 5.89.

M.S. (ionization) : 127 (25) ; 244 (8) ; 261 (100) ($M+NH_4^+$).

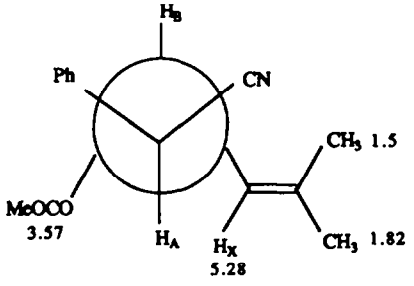
*Isomer 2* (deduced from the mixture) ; Retention time 12.1 mn.

$^1H$ NMR (200 MHz, $CDCl_3$) : 1.38 (d, J = 1 Hz,., 3H) ; 1.65 (d., J = 1 Hz, 3H) ; 3.72 (s., 3H) ; 3.62 (broad t., 1H) ; 4.05 (d., J = 9 Hz, 1H) ; 5.05 (dq., J = 10 Hz and 1 Hz, 1H) ; 7.35 (broad s., 5H).

Comparison of the $^1H$ NMR spectra allows the following configuration assignments.




Isomer 2




Isomer 1

M.S. (ionization) : 127 (20) ; 244 (8) ; 261 (100) ($M+NH_4^+$).

3-Methoxycarbonyl-5-methyl-2-(4-methoxyphenyl)-hex-4-ene nitrile **6b**

Purified by flash column chromatography (pentane : $Et_2O$ 99:1 v/v).

*Isomer 1* (70% of the mixture). m.p. 105° (hexane) ; Retention time 15.5 mn.

$^1H$ NMR (90 MHz, $CDCl_3$) : 1.60 (d., J = 1 Hz), 3H) ; 1.80 (d., J = 1 Hz, 3H) ; 3.6 (s., 3H) ; 3.83 (s., 3H) ; 3.6 - 3.8 (massif, 1H) ; 4.2 (d., J = 8.5 Hz, 1H) ; 5.37 (dq, J = 10 and 1 Hz, 1H) ; 6.9 - 7.40 (syst. AA'BB', 4H).

M.S. 67 (23) ; 95 (42) ; 127 (39) ; 146 (100) ; 147 (72) ; 273 (11) ($M^+$).

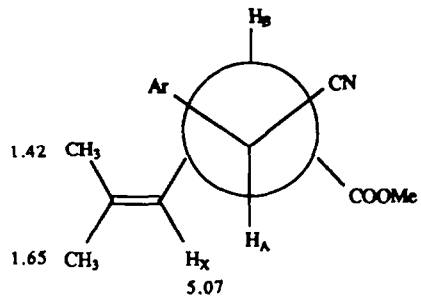
Analysis : $C_{16}H_{19}NO_3$ = 273. Calc % C = 70.31 ; H = 7.01 ; N = 5.12 ; found % C = 69.62 ; H = 6.99 ; N = 5.29.

*Isomer 2* : Retention time 15.8 mn.

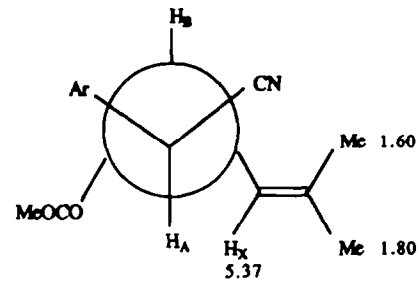
$^1H$ NMR (250 MHz, $CDCl_3$, deduced from the 70/30 mixture) : 1.42 (d., J = 1 Hz, 3H) ; 1.65 (d., J = 1 Hz, 3H) ; 3.68 (s., 3H) ; 3.74 (s., 3H) ; 3.6 - 3.8 (massif, 1H) ; 4.01 (d., J = 8.5 Hz, 1H) ; 5.07 (dq., J = 10 and 1 Hz, 1H) ; 6.80 - 6.95 (m., 2H) ; 7.12 - 7.28 (m., 2H).

M.S. : 67 (28) ; 95 (40) ; 127 (36) ; 146 (100) ; 147 (67) ; 214 (10) ; 273 (8.5) ($M^+$).

Comparison of the $^1H$ NMR spectra allows the following configuration assignments.




Isomer 2




Isomer 1

3-Methoxycarbonyl-5-methyl-2-(3-chlorophenyl)-hex-4-ene nitrile 6c

Purified by flash column chromatography (pentane : $Et_2O$ 99:1 v/v).

*Isomer 1* : oil ; Retention time 13.6 mn.

$^1H$ NMR (90 MHz, $CDCl_3$) : 1.58 (d., J = 1 Hz, 3H) ; 1.82 (d., J = 1 Hz, 3H) ; 3.62 (s., 3H) ; 3.70 (t., J = 8 Hz, 1H) ; 4.30 (d., J = 8 Hz, 1H) ; 5.30 (dq, J = 8 and 1 Hz, 1H) ; 7.20 - 7.45 (m., 4H).

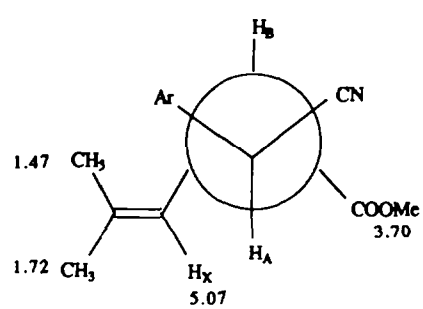
M.S. : 41 (20) ; 67 (39) ; 95 (56) ; 99 (15) ; 127 (100) ; 218 (4) ($M^+$).

*Isomer 2* : oil ; Retention time : 13.8 mn.

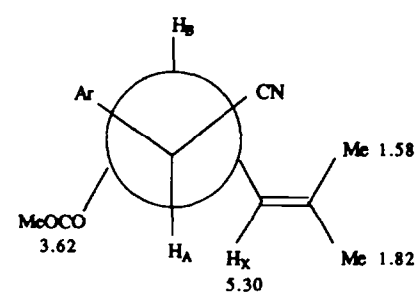
$^1H$ NMR (250 MHz, $CDCl_3$) : 1.47 (d., J = 1 Hz) ; 1.72 (d., J = 1 Hz, 3H) ; 3.68 (t., J = 8 Hz, 1H) ; 3.70 (s., 3H) ; 4.08 (d., J = 8 Hz, 1H) ; 5.07 (dq., J = 8 and 1 Hz, 1H) ; 7.20 - 7.45 (m., 4H).

M.S. : 41 (25) ; 67 (44) ; 95 (58) ; 99 (17) ; 127 (100) ; 218 (1.5) ($M^+$)

Comparison of the $^1H$ NMR spectra allows the following configuration assignments.




Isomer 2




Isomer 1

3-Methoxycarbonyl-2,5dimethyl-2-phenyl-hex-4-ene nitrile7a

*Isomer 1* : m.p. 103-106°C (pentane) ; Retention time 12.3 mn.

$^1H$ NMR (90 MHz, $CDCl_3$) : 1.60 (s., 3H) ; 1.69 (broad s., 3H) ; 1,82 (broad s, 3H) ; 3.40 (s., 3H) ; 3.58 (d., J = 11 Hz, 1H) ; 5.52 (dq, J = 11 and 1 Hz, 1H) ; 7.10 - 7.30 (m., 3H) ; 7.45 - 7.65 (m, 2H).

$^{13}C$ NMR ($CDCl_3$) : 18.4 (q.) ; 25.9 (q.) ; 45.0 (s.) ; 51.7 (q.) ; 54.2 (d.) ; 117.5 (d.) ; 121.5 (s.) ; 125.7 (d.) ; 128.0 (d.) ; 128.7 (d.) ; 138.4 (s.) ; 140.2 (s.) ; 170.6 (s.).

MS : 41 (11) ; 67 (33) ; 95 (36) ; 127 (100) ; 128 (13) ; 131 (23) ; 257 (2) ($M^+$).

Analysis $C_{16}H_{19}NO_2$ = 257 : calc. % C = 74.7 ; H = 7.4 ; N = 5.45 ; found % : C =74.70 ; H = 7.43 ; N = 5.42.

*Isomer 2* : Retention time 10.1 mn.

$^1H$ NMR (200 MHz, $CDCl_3$ deduced from the 1/1 mixture) : 1.28 (s., 3H) ; 1.65 (broad s., 3H) ; 1,82 (broad s, 3H) ; 3.62 (s., 3H) ; 3.70 (d., J = 11 Hz, 1H) ; 5.30 (dq, J = 11 and 1 Hz, 1H) ; 7.2 - 7.5 (m., 5H).

Trans methyl 5-cyano-5-(4-methoxyphenyl)-4,4 dimethyl-pent-2-enoate **9b**

m.p. 98 - 101°C.

Purified by flash column chromatography (pentane:$Et_2O$ 99:1 v/v).

$^1H$ NMR (90 MHz, $CDCl_3$) : 1.20 (s., 6H) ; 3.68 (s., 1H) ; 3.75 (s., 3H) ; 3.82 (s., 3H) ; 5.72 (d., J = 16 Hz, 1H) ; 6.82 - 7.0 (m., 3H) ; 7.15 - 7.30 (m., 2H).

5-Cyano-4,6-dimethoxycarbonyl-2,8-dimethyl-5-phenyl-nona-2,7 diene **12a**

Isolated by flash column chromatography (pentane:$Et_2O$ 95:5 v/v).

m.p. 105-8° (pentane) ; Retention time 23.6 mn.

$^1H$ NMR (250 MHz, $CDCl_3$) : 1.8 (d., J = 1 Hz, 6H) ; 1.84 (d., = 1 Hz, 6H) ; 3.40 (s., 6H) ; 4.15 (d., J = 10 Hz, 2H) ; 5.40 (dq, J = 10 and1 Hz, 2H) ; 7.30 - 7.5 (massif, 5H).

$^{13}C$ NMR ($CDCl_3$) : 18.9 (q.) ; 26.3 (q.) ; 50.7 (d.) ; 59.2 (q.) ; 117.3 (d.) ; 118.7 (s.) ; 125.7 (d.) ; 127.7 (d.) ; 128.9 (d.) ; 129.7 (d.) ; 134.6 (s.) ; 140.7 (s.) ; 170.2 (s.).

MS (ionization) : 127 (22) ; 128 (11) ; 129 (16) ; 144 (7) ; 146 (11) ; 261(1) ; 262 (11) ; 370 (12) ; 386 (35) ; 387 (100) ($M^+ + NH_4$) ; 388 (34).

Analysis : $C_{22}H_{27}NO_4$ = 369. Calc % C = 71.52 ; H = 7.37 ; N = 3.79 ; O = 17.32 ; found % C = 71.79 ; H = 7.11 ; N = 3.75 ; O = 17.28.

5-Cyano-4,6-dimethoxycarbonyl-2,8-dimethyl-5--(4-methoxyphenyl)-nona-2,7-diene **12b**

m.p. = 119-121°C (hexane). Purified by flash column chromatography (pentane/$Et_2O$ 99:1 v/v); Retention time 24.1 mn.

$^1H$ NMR (90 MHz, $CDCl_3$) : 1.80 (broad s., 12H) ; 3.45 (s., 6H) ; 3.75 (s, 3H) ; 4.10 (d., J = 10Hz, 1H) ; 5.47 (broad d., J = 10 Hz, 1H) ; 6.70 - 6.95 (m, 2H) ; 7.35 - 7.55 (m., 2H)

MS : 41 (21) ; 59 (15) ; 67 (39) ; 69 (21) ; 77 (10) ; 95 (33) ; 127 (27) ; 128 (20) ; 146 (34) ; 147 (25) ; 197 (10) ; 198 (24) ; 212 (100) ; 213 (41) ; 272 (45) ; 273 (18) ; 399 (17) ($M^+$).

Analysis : $C_{23}H_{29}NO_5$ = 399. Calc % C = 69.15 ; H = 7.32 ; N = 3.51 ; found % C = 69.20 ; H = 7.35 ; N = 3.69.

5-Cyano-4,6-dimethoxycarbonyl-2,8-dimethyl-5-(3-chlorophenyl)-nona-2,7-diene **12c**

m.p. 100 - 102.5°C (hexane) ; Retention time 22.1 mn.

$^1H$ NMR (90 MHz, $CDCl_3$) : 1.80 (broad s., 12H) ; 3.45 (s., 6H) ; 4.12 (d., J = 10Hz, 2H) ; 5.38 (dq., J = 10 and 1 Hz, 2H) ; 7.25 - 7.55 (m., 4H)

MS : 41 (17) ; 59 (11) ; 67 (31) ; 95 (47) ; 127 (100) ; 128 (19) ; 218 (8) ; 403 (3.2) ($M^+$).

Analysis : $C_{22}H_{26}ClNO_4$ = 403.5. Calc % C = 65.43 ; H = 6.44 ; N = 3.47 ; Cl = 8.80 ; found % : C = 65.63 ; H = 6.53 ; N = 3.38 ; Cl = 8.88.

4-Amino-5,5-dimethyl-2-methoxycarbonyl-3-phenyl-cyclopenta-1,3-diene **13a**

m.p. : 82-5° (pentane). Purified by flash column chromatography (pentane/$Et_2O$ 99:1 v/v) ; Retention time 14.2 mn.

$^1H$ NMR (250 MHz, $CDCl_3$) : 1.30 (s., 6H) ; 3.7 (s., 3H) ; 5.5 - 6.2 (broad m., 2H) ; 6.40 (s, 1H) ; 7.3 (broad s., 5H).

$^{13}C$ NMR ($CDCl_3$) : 23.2 (q.) ; 47.8 (s.) ; 49.5 (q.) ; 106.3 (s.) ; 127.7 (d.) ; 128.1 (d.) ; 129 (d.) ; 133.4 (s.) ; 137.1 (s.) ; 153.1 (d.) ; 157 (s.) ; 166 (s.).

MS : 167 (2) ; 184 (7) ; 196 (4) ; 212 (10) ; 243 (66) ($M^+$) ; 244 (100) ($M^+ + 1$).

Analysis : $C_{15}H_{17}NO_2$ = 243. Calc % C = 74.04 ; H = 7.07 ; N = 5.76 ; found % C = 72.50 ; H = 6.92 ; N = 5.84.

4-Amino-5,5-dimethyl-2-methoxycarbonyl-3-(4-methoxyphenyl)-cyclopenta-1,3-diene **13b**

m.p. : 89-91° (pentane). Purified by flash column chromatography (pentane/$Et_2O$ 99:1 v/v) ; Retention time 19.9 mn.

$^1H$ NMR (90 MHz, $CDCl_3$) : 1.35 (s., 3H) ; 3.8 (s., 3H) ; 3.85 (s., 3H) ; 5.65 - 5.90 (massif, 2H) ; 6.37 (S., 1H) ; 6.85 - 7.35 (AA'BB' system, 4H).

$^{13}C$ NMR ($CDCl_3$) : 23.2 (q.) ; 48.1 (s.) ; 50.1 (q.) ; 55.5 (q.) ; 106 (s.) ; 114.6 (d.) ; 126.1 (s.) ; 129.2 (d.) ; 136.9 (s.) ; 152.2 (d.) ; 158.7 (s.) ; 159.8 (s.) ; 167.2 (s.).
MS : 183 (9) ; 198 (15) ; 214 (100) ; 215 (17) ; 226 (47) ; 241 (11) ; 273 (75) ($M^+$) ; 274 (14) ($M^+$ +1).
Analysis : $C_{16}H_{19}NO_3$ = 273. Calc % C = 70.31 ; H = 7.01 ; N = 5.12 ; found % C = 70.68 ; H = 7.0 ; N = 5.35.

4-Amino-5,5-dimethyl-2-methoxycarbonyl-3-(3-chlorophenyl)-cyclopenta-1,3-diene **13c**

m.p. : 110-112° (pentane). Purified by flash column chromatography (pentane/$Et_2O$ 99:1 v/v) ; Retention time 18.4 mn.
$^1H$ NMR (250 MHz, $CDCl_3$) : 1.35 (s., 6H) ; 3.78 (s., 3H) ; 5.6 - 6.0 (broad m., 2H) ; 6.48 (s., 1H) ; 7.2 - 7.4 (massif, 4H).
MS : 83 (19) ; 84 (19) ; 139 (12) ; 166 (17) ; 167 (37) ; 168 (14) ; 182 (14) ; 183 (10) ; 195 (19) ; 218 (100) ; 219 (17) ; 220 (32) ; 230 (40) ; 232 (15) ; 277 (87) ($M^+$) ; 278 (15) ; 279 (31) ($M^+$).
Analysis : $C_{15}H_{16}ClNO_2$ = 277.5. Calc % C = 64.9 ; H = 5.81 ; found % C = 64.9 ; H = 5.82

Methyl-2-benzoyl-4-methyl-pent-3-enoate **14a**

Oil. Purified by flash colum chromatography (hexane/EtO 99:1 v/v) ; Retention time 13.3 mn.
$^1H$ NMR (250 MHz, $CDCl_3$) : 1.75 (d., J = 0.7 Hz, 3H) ; 1.79 (d., J = 0.7 Hz, 3H) ; 3.7 (s., 3H) ; 5.15 (d , J = 10 Hz., 1H) ; 5.60 (dq, J = 10, 0.7 Hz, 1H) ; 7.4 - 7.6 (m., 3H) ; 7.9 - 8.05 (m., 2H).
$^{13}C$ NMR ($CDCl_3$) : 18.8 (q.) ; 25.9 (q.) ; 52.5 (q.) ; 54.6 (d.) ; 116.9 (d.) ; 128.7 (d.) ; 129.6 (d.) ; 133.5.(d.) ; 135.8 (s.) ; 138.1 (s.) ; 169 8 (s.); 193.9 (s.).
MS : 43 (43) ; 55 (21) ; 77 (47) ; 83 (43) ; 105 (100) ; 122 (21) ; 232 (13) ($M^+$).

Methyl-2-(4-methoxybenzoyl)-4-methyl-pent-3-enoate **14b**

Purified by flash chromatography as a mixture with **15b** (30/70).; Retention time 16 mn.
$^1H$ NMR (250 MHz, $CDCl_3$) : 1.75 (d., J = 0.7 Hz, 3H) ; 1.80 (d., J = 0.7 Hz, 3H) ; 3.7 (s., 3H) ; 3.88 (s., 3H) ; 5.08 (d , J = 10 Hz., 1H) ; 5.60 (dq, J = 10 and 0.7 Hz, 1H) ; 6.92 (dt., J = 10 and 1 Hz, 2H) ; 7.95 (dt., J = 10 and 1 Hz, 2H).
MS : 77 (13) ; 92 (6) ; 134 (16) ; 135 (100) ; 136 (9).

Methyl-2-(4-chlorobenzoyl)-4-methyl-pent-3-enoate **14c**

Oil Purified by flash chromatography (pentane/$Et_2O$ 99.4:0.6 v/v).; Retention time 14.1 mn.
$^1H$ NMR (250 MHz, $CDCl_3$) : 1.75 (broad s., 3H) ; 1.8 (broad s., 3H) ; 3.7 (s., 3H) ; 5.1 (d, J = 8.5 Hz, 1H) ; 5.6 (broad d., J = 8.5 Hz, 1H) ; 7.55 - 8.0 (AA'BB system, 4H).
$^{13}C$ NMR ($CDCl_3$) : 18.9 (q.) ; 26.05 (q.) ; 52.8 (q.) ; 54.9 (d.) ; 116.9 (d.) ; 128.2 ; 128.4 ; 128.6 ; 129.3 (d.) ; 130.4 (s.) ; 138.6 (s.) ; 160.9 (s.) ; 193.1 (s).

Methyl 4-benzoyl-4-methyl-pent-2-enoate **15a**

Oil. Purified by flash column chromatography (hexane/$Et_2O$ 99:1 v/v) ; Retention time 11.7 mn.
$^1H$ NMR (250 MHz, $CDCl_3$) : 1.48 (s., 6H) ; 3.76 (s., 3H) ; 5.97 (d., J = 16 Hz, 1H) ; 7.32 (d., J = 16 Hz, 1H) ; 7.35 - 7.5 (m., 3H) ; 7.75 - 7.85 (m., 2H).
$^{13}C$ NMR ($CDCl_3$) : 25.8 (q.) ; 49.5 (s.) ; 52.5 (q.) ; 119 (d.) ; 127.6 (d.) ; 128.6 (d.) ; 132 (d.) ; 135 (s.) ; 153 (d.) ; 166.7 (s.) ; 212.1 (s.).
MS : 51 (7) ; 77 (33) ; 96 (7) ; 104 (15) ; 105 (100).

Methyl 4-(4-methoxybenzoyl)-4-methyl-pent-2-enoate **15b**

Oil. Purified by flash chromatography as a mixture with **14b** (70/30) ; Retention time 15.7 mn.
$^1H$ NMR (250 MHz, $CDCl_3$) : 1.48 (s., 6H) ; 3.75 (s., 3H) ; 4.82 (s., 3H) ; 5.96 (d., J = 16 Hz, 1H) ; 6.98 (dt., J = 10 and 1 Hz, 2H) ; 7.30 (d., J = 16 Hz, 1H) ; 7.85 (dt., J = 10 and 1 Hz, 2H).
MS : 77 (12) ; 92 (5) ; 134 (15) ; 135 (100) ; 136 (9) ; 262 (1) ($M^+$).

Methyl 4-(4-chlorobenzoyl)-4-methyl-pent-2-enoate 15e

Oil. Purified by flash chromatography (pentane/$Et_2O$ 99.4:0.6 v/v) ; Retention time 13.85 mn.

$^1H$ NMR (250 MHz, $CDCl_3$) : 1.45 (s., 6H) ; 3.75 (s., 3H) ; 5.9 (d., J = 16 Hz, 1H) ; 7.4 (d, J = 16 Hz, 1H) ; 7.3 - 7.8 (AA'BB' system, 4H).

$^{13}C$ NMR ($CDCl_3$) : 26.6 ; 50 ; 52.5 ; 120.6 ; 129 ; 131.9 ; 135 ; 139.4 ; 153.8 ; 167.5 ; 201.2.

IR : 1720 (s) ; 1680 (s) ; 1675(s) ; 600 - 800 (s).

Methyl 2-phenyl-3-methoxycarbonyl-5-methyl-hex-4-enoate 17

2 diastereoisomers separated by flash chromatography (pentane/$Et_2O$ 99.8:0.2 v/v).

*Isomer 1* : oil ; Retention time 11.9 mn.

$^1H$ NMR (250 MHz, $CDCl_3$) : 1.35 (s., 3H) ; 1.5 (s., 3H) ; 3.65 (s., 3H) ; 3.7 (s., 3H) ; 3.9 - 4.05 (AB part of ABX system, $^3J_{AB}$ = 12.5 Hz, 2H) ; 4.82 (d,1H, $H_X$) ; 7.15 - 7.35 (massif, 5H).

IR : 1735 (s), 1670 (s).

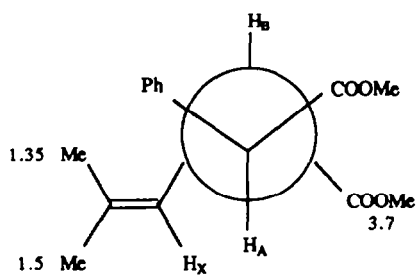
MS : 67 (15) ; 95 (33) ; 118 (27) ; 127 (58) ; 150 (100) ; 157 (19) ; 276 (4) ($M^+$).

*Isomer 2* : m.p. : 120°C ; Retention time 11.8 mn.

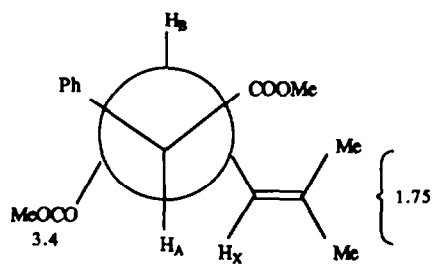
$^1H$ NMR (250 MHz, $CDCl_3$) : 1.75 (broad s., 6H) ; 3.4 (s., 3H) ; 3.62 (s., 3H) ; 3.9 - 4.1 (AB part of ABX system, $^3J_{AB}$ = 11 Hz, 2H) ; 5.15 (d,1H, $H_X$) ; 7.2 - 7.4 (massif, 5H).

Same IR and MS as isomer 1.

Comparison of $^1H$ NMR spectra allows the following configuration assignments :



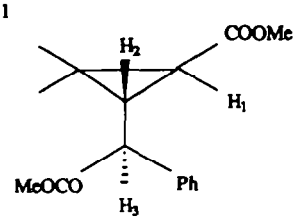

Isomer 1



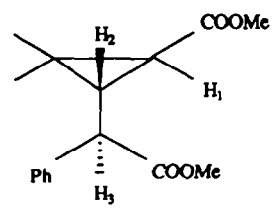

Isomer 2

E-Methyl 2-(phenylcarboxymethyl)methyl-3-dimethylcyclopropanecarboxylates 18a,b

Isomer 1




Isomer 2




*Isomer 1* : m.p. : 88 - 90.5° ; Retention time 12.2 mn.

$^1H$ NMR (250 MHz, $CDCl_3$) : 1.25 (s., 3H) ; 1.27 (d., J = 5.2 Hz, $H_1$) ; 1.3 (s., 3H) ; 2.15 (dd., J = 5.2 and 11.2 Hz, $H_2$) ; 3.3 (d., J = 11.2 Hz, $H_3$) ; 3.6 (s, 3H) ; 3.7 (s., 3H) ; 7.2 - 7.4 (massif, 5H).

IR : 1735 (s).

MS : 59 (6) ; 77 (5) ; 91 (7) ; 95 (30) ; 115 (7) ; 118 (9) ; 127 (100) ; 128 (13) ; 150 (13) ; 157 (12).

*Isomer 2* : Retention time 12.5 mn.

$^1H$ NMR (250 MHz, $CDCl_3$) : 1.07 (s., 3H) ; 1.2 (s., 3H) ; 1.52 (d., J = 5.2 Hz, $H_1$) ; 2.2 (dd., J = 5.2 and 11.2 Hz, $H_2$) ; 3.35 (d., J = 11.2 Hz, $H_3$) ; 3.7 (s., 3H) ; 3.75 (s., 3H) ; 7.2 - 7.4 (massif, 5H).
Same IR and MS as isomer 1.

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