# 1,2- *versus* 1,4-Addition to α-donor-cyclopenten-1-ones; a comparison of calculated and experimental data †

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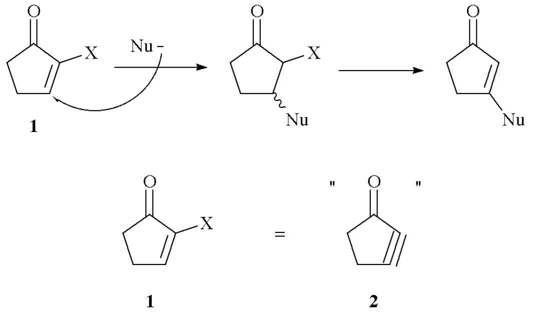
A series of α-donor-cyclopenten-1-ones, **1** (α-donor; X = H, Cl, Br, OMe, pyrrolidin-1-yl, SPh and SePh) were treated with methyllithium, lithium dimethylcuprate and cyanomethyllithium in tetrahydrofuran at −78 °C. The reactions between **1** and methyllithium gave 1,2-adducts in 28–75% yield. No trace of the corresponding 1,4-adduct was observed. By treatment of **1** with lithium dimethylcuprate only 1,4-addition was obtained in 51–76% yield, except for X = OMe or pyrrolidin-1-yl, which gave no reaction at all. In the reactions between **1** and cyanomethyllithium the 1,2-adducts were the main products (43–60%), but varying amounts of 1,4-adducts (8–30%) were also formed. The products formed have been fully characterized. Net atomic charges obtained by density functional theory (DFT) calculations of the lithiated cations of **1** with X = H, Cl, Br or OMe showed very small differences between the substituted and unsubstituted systems for all X, except for X = OMe. In this case the $C^2$ position was positive rather than negative. The $C^3$ position was found to be significantly more negative. The calculated relative energies of the methylated and cyanomethylated 1,2- and 1,4-adducts with X = H, Cl, Br and OMe indicated that the 1,4-adducts were thermodynamically favoured by 8 to 12 kcal $mol^{-1}$ for all but one case. In the cyanomethylation of **1** with X = OMe the 1,2-adduct was predicted to be favoured by 12 kcal $mol^{-1}$. Thus, the predominance of 1,2-attack in the reactions involving methyllithium and cyanomethyllithium cannot be explained by the relative thermodynamic stabilities of the products.

## Introduction

As part of a larger project on the synthetic use of α-donor-α,β-unsaturated ketones, cyclopentenones have been of particular interest as potentially useful synthetic intermediates. Especially, nucleophilic conjugate addition to such substrates would be a useful reaction.[1] The presence of an electron donating substituent in the α-position of the cyclopentenone as shown in Scheme 1 would make it possible to regenerate the initial double bond.



**Scheme 1** α-Donor-cyclopentenones as electrophiles in conjugate addition reactions.

The product formed could then be used in a second conjugate addition. Thus, **1** would constitute a synthetic equivalent for the unknown 2-oxocyclopent-1-yne, **2**, illustrated in Scheme 1.

There are only a few examples in the literature where cyclic α-donor-α,β-unsaturated ketones have been used in conjugated addition reactions. Kowalski *et al.*[2a] have reported selective 1,4-addition to 2-bromocyclopent-2-en-1-one, **1c**. They isolated the 1,4-adduct as the corresponding acetate in 73% yield. Other cyclic α-bromo-α,β-unsaturated ketones have also been reported to undergo selective 1,4-addition of allyllithium, allylmagnesium bromide and lithium dialkylcuprates.[2b,c] The yields obtained were generally good, ≥74%. In a paper by Fang[3a] 2-phenylthiocyclopent-2-en-1-one, **1f**, was treated with 2-methylmalonic methyl and ethyl esters and ethyl propionate to give selective 1,4-addition. In the latter case addition of HMPA to the enolate was required to suppress the competing 1,2-addition reaction. The isolated yields varied from 45 to 95%. Monteiro[3b] has applied 1,4-addition of $Me_2CuLi$ to **1f** as a key step in the synthesis of (±)-methyl dehydrojasmonate. Liotta and coworkers[4] have subjected various cyclic α-phenylselenyl enones (*e.g.* **1g**) to several organocuprates and obtained excellent 1,4-selectivities and yields. Addition reactions between cyclic α-ketoenamines (*e.g.* pyrrolidin-2-ylcyclopent-2-en-1-one, **1e**) and diazenes have been reported by Felluga *et al.*[5] to take place at the β-position. These reactions may, however, be regarded as analogues to the Diels–Alder reactions. Finally, selective 1,4-addition of organocuprates to (*S*)-2-(*p*-tolylsulfinyl)cycloalk-2-en-1-ones has been reported by Posner *et al.*[6] Although the sulfinyl group is generally regarded as electron accepting, it may also function as a donor of its lone pair electrons.

Even though the above mentioned reports of successful conjugate addition to cyclic α-donor-α,β-unsaturated ketones have been available for quite some time, the application of this group of compounds is rather scarce. In order to shed some light on the scope and limitations of these compounds as electrophiles in conjugate addition reactions, we have treated a series of α-donor-cyclopenten-1-ones, **1**, with various substituents X [X = H, Cl, Br, OMe, pyrrolidin-1-yl (Pyl), SPh and SePh] with

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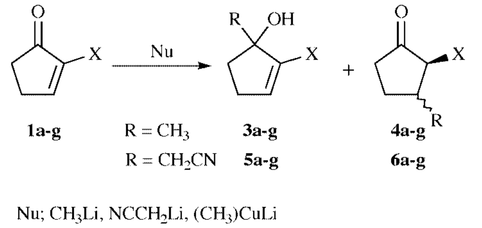
† Spectroscopic data and optimized geometries for a selection of compounds are available as supplementary data. For direct electronic access see http://www.rsc.org/suppdata/p2/1999/1835, otherwise available from BLDSC (SUPPL. NO. 57606, pp. 28) or the RSC Library. See Instructions for authors available *via* the RSC web page (http://www.rsc.org/authors).

**Table 1** Absolute energies (*E*/hartree) and relative energies ($\Delta E$/kcal mol$^{-1}$) estimated from Mulliken population analysis. $\Delta E$ for **9a–d** has been defined as the reaction energy for **1a–d** + $Li^+$→**9a–d**. $\Delta E$ for **10 (11) a–d** has been defined as the reaction energy for **1a–d** + **7**→**10 (11) a–d**. $\Delta E$ for **12 (13) a–d** has been defined as the reaction energy for **1a–d** + **8**→**12 (13) a–d**

| Species | $-E^a$ | $-E^b$ | $-\Delta E^a$ | $-\Delta E^b$ | ZPE $^b$ | $-\Delta G$(solv.)$^b$ |
|---|---|---|---|---|---|---|
| $Li^+$ | 7.28491 | 7.28494 | | | | |
| $:CH_3$ | 39.82371 | 39.80385 | | | | |
| $[:CH_2CN]$ | 132.16970 | 132.11228 | | | | |
| **1a** | 269.41370 | 269.30939 | | | 61.8 | 4.1 |
| **b** | 729.03540 | 283.64702 | | | 55.8 | 3.7 |
| **c** | 2842.9566 | 281.86305 | | | 55.4 | 3.9 |
| **d** | 383.96250 | 383.81389 | | | 82.0 | 3.0 |
| **7** | 47.41397 | 47.39779 | | | | 6.0 |
| **8** | | 139.64702 | | | 21.5 | 9.7 |
| **9a** | 276.78792 | 276.68843 | 56.1 | 59.0 | 63.3 | 46.0 |
| **b** | 736.40830 | 291.01801 | 55.2 | 56.6 | 57.0 | 43.0 |
| **c** | 2850.3320 | 3289.23930 | 56.8 | 57.3 | 56.6 | 43.1 |
| **d** | 391.35593 | 391.21073 | 68.1 | 70.2 | 84.1 | 42.8 |
| **10a** | 316.89439 | 316.78435 | 41.9 | 56.1 | 87.5 | 8.1 |
| **b** | 776.52727 | 331.12990 | 48.9 | 55.9 | 81.3 | 6.7 |
| **c** | 2890.44943 | 329.34882 | 49.4 | 55.2 | 81.0 | 6.6 |
| **d** | 431.45900 | 431.30515 | 51.8 | 58.7 | 108.0 | 8.2 |
| **11a** | 316.91054 | 316.78434 | 52.1 | 48.4 | 87.5 | 10.9 |
| **b** | 776.55357 | 331.15138 | 65.4 | 69.4 | 82.4 | 7.1 |
| **c** | 2890.47615 | 329.37009 | 66.2 | 68.6 | 82.1 | 7.0 |
| **d** | 431.47602 | 431.31860 | 62.5 | 67.0 | 108.4 | 6.8 |
| **12a** | | 409.01291 | | 35.5 | 86.4 | 6.7 |
| **b** | | 423.35603 | | 41.5 | 80.3 | 8.0 |
| **c** | | 421.57486 | | 40.7 | 80.0 | 5.7 |
| **d** | | 523.53305 | | 45.3 | 107.0 | 7.6 |
| **13a** | | 409.01668 | | 37.8 | 87.2 | 12.2 |
| **b** | | 423.36895 | | 49.6 | 81.2 | 8.6 |
| **c** | | 421.58793 | | 48.8 | 81.0 | 8.8 |
| **d** | | 523.51868 | | 36.2 | 107.3 | 11.8 |

[a] Calculation level B3LYP/6-311G*. [b] Calculation level B3LYP/LanL2DZ.

three different nucleophiles (MeLi, $Me_2CuLi$ and $LiCH_2CN$). In these reactions both 1,2- and 1,4-additions were anticipated as depicted in Scheme 2.

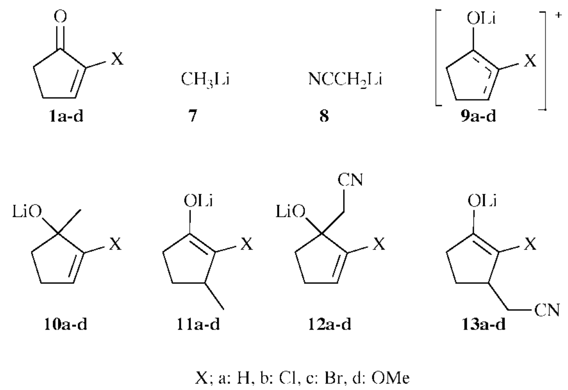


**Scheme 2** Nucleophilic addition to α-donor-cyclopentenones **1a–g**.

The results obtained were evaluated in the light of theoretical calculations of the net charge distributions and frontier orbitals for **1** with X = H, Cl, Br and OMe, and the relative energies of the lithiated 1,2- and 1,4-adducts obtained by reaction of **1a–d** with MeLi and $NCCH_2Li$. The theoretical calculations were carried out to shed some light on the structures and relative stabilities of the starting materials and products. A more thorough study of reaction pathways is beyond the scope of the present work.

## Computational studies

The compounds included in the computational studies are shown in Scheme 3. The absolute and relative energies for all the species included in our study are given in Table 1, where also zero-point energy values and solvent effects using the LanL2DZ basis are included. Numbering of the different species is given in Scheme 3.



**Scheme 3** Compounds included in the DFT calculations.

The optimized geometries of a selection of the molecules are available as supplementary data.† We have chosen to present the molecules for which X = H and OMe as these display the largest differences in geometries. Only the key geometrical parameters showing the general shape of the molecules, are included.

In this study we have tacitly assumed that the additions of MeLi and $NCCH_2Li$ to the cyclopentenones occur as two-step reactions in which the $Li^+$ first adds, creating a cation which is susceptible to a nucleophilic attack by the methyl and cyanomethyl anions, respectively.

The relative energies of the cations **9a–d** obtained by the two basis sets show that the addition of $Li^+$ to the cyclopentenones is strongly exothermic, as expected. Furthermore, the predicted exothermicity is found to be largely independent of the substituent X, except for the OMe group which gives a larger reaction energy. This is easily explained as being due to a favourable position of the positively charged Li atom in the attractive field of two oxygen atoms. This increased stability of the cation is clearly demonstrated by the optimized structures of **9a** and **9d**. In the former the $C^1$–O–Li arrangement is linear with an O–Li bond of 1.73 Å, whereas in the latter there is a large deviation from linearity, and a lengthening of this bond to 1.89 Å with an

**Table 2** Net atomic charges for the cations **9a–d** estimated from Mulliken population analysis based on B3LYP/LanL2DZ

| **9** | $qO$ | $qC^1$ | $qC^2$ | $qC^3$ |
|---|---|---|---|---|
| **a** | −0.60 | 0.37 | −0.28 | −0.09 |
| **b** | −0.50 | 0.14 | −0.18 | −0.10 |
| **c** | −0.49 | 0.49 | −0.29 | −0.07 |
| **d** | −0.40 | 0.26 | 0.30 | −0.23 |

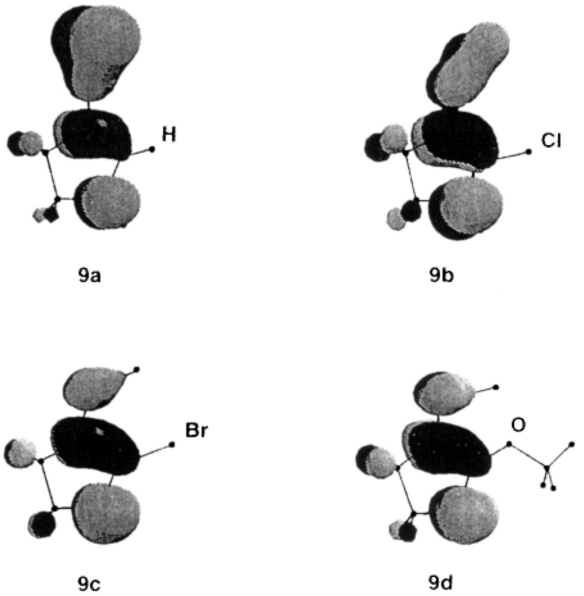


**Fig. 1** LUMO + 1 orbitals in the cations **5a–d** from RHF/3-21G* calculations.

**Table 3** Treatment of **1a–g** with methyllithium in THF, at −78 °C

| **1** | X | **1**:**3**:**4** (GLC of reaction, 1 h) | Crude (%) | Isol. prod. (%) |
|---|---|---|---|---|
| **a** | H | 3.1:96.6:0 | — | —[a] |
| **b** | Cl | 23.1:76.9:0 | 82.5 | 28.0 |
| **c** | Br | 17.2:82.0:0 | 75.9 | 35.8 |
| **d** | OMe | 13.5:86.5:0 | 67.5 | —[b] |
| **e** | Pyl | 67.4:20.5:0 | — | —[b] |
| **f** | SPh | 13.2:86.7:0 | 94.4 | 75.6 |
| **g** | SePh | 20.5:63.6:0 | 83.2 | 59.7 |

[a] Compound **3a** was identified by GLC-MS of the reaction mixture. [b] Compounds **4e–d** were identified by GLC-MS of the reaction mixture, but were hydrolysed to 2-hydroxy-2-methylcyclopentanone (**14**) during work-up.

additional bonding interaction to the methoxy group resulting in an O–Li distance of 1.98 Å.

The calculated atomic net charges in the cations **9a–d** based on a Mulliken population analysis are shown in Table 2. The data reveal a charge distribution leading to a pronounced positive charge on the carbon atom ($C^1$) adjacent to the oxygen, a significant negative charge on $C^2$, except for in **9d** where this atom has a positive charge due to the proximity of the methoxy oxygen. The atom $C^3$ has a negative, but very small net charge in **9a–c**. In **9d** the negative charge is rather significant. These charges indicate that the most susceptible site for a nucleophilic attack on the cations **9** would be $C^1$.

Fig. 1 depicts a picture of the second lowest unoccupied (LUMO + 1) orbitals obtained for the geometry optimized cations **9** by SCF calculations using a 3-21G* basis set.[7] The reason for this choice of orbitals is that the LUMO in the cations is for obvious reasons strictly located on the Li atom from which the nucleophilic anions have escaped.

Using frontier orbitals rather than net charges the shape and extension of the second lowest unoccupied orbital (LUMO + 1) in the cations, **9a–d**, would be expected to give information on the most favoured region for a nucleophilic attack. As shown in Fig. 1 these orbitals, which are independent of the substituent X, are dominated by the π-orbital confined to the carbonyl oxygen atom and the virtually planar unsaturated part of the ring. These orbitals have a node between oxygen and $C^1$, and another one between $C^2$ and $C^3$. The middle region of the orbital, located between $C^1$ and $C^2$ is oriented more towards $C^1$ than $C^2$, thus making this site a likely one for nucleophilic attack. The figure also shows a dominant part of the orbital centred around $C^3$, making this centre competitive with $C^1$ for addition of an anion.

Comparison of the relative energies (uncorrected for ΔZPE) for the isomer pairs **10a–d** and **11a–d** (Nu: MeLi), and **12a–d** and **13a–d** (Nu: $NCCH_2Li$), shows a significant preference for the latter member of the pairs, that is the 1,4-adducts. This is independent of whether the nucleophile is MeLi or $NCCH_2Li$, with the notable exception of **12d**, which has a lower energy than the isomer **13d**. In the case of MeLi the energy differences between the two isomeric forms of the reaction product were estimated to be around 10–12 kcal $mol^{-1}$ in favour of the 1,4-adducts, irrespective of the nature of the substituent at $C^2$. For $NCCH_2Li$ the corresponding differences for the substituted compounds were found to be around 8 kcal $mol^{-1}$ in favour of the 1,4-adducts, except for the methoxy derivative where this difference was around 9 kcal $mol^{-1}$ in favour of the 1,2-adduct. So, regarding the thermodynamic stability of the reaction products alone would suggest that addition to $C^3$ would be favoured as compared to addition to $C^1$. An exception was found for the addition of $NCCH_2Li$ to the methoxy derivative **9d**, which gives a product **12d** having a very favourable attractive interaction involving Li, the two oxygen atoms and the nitrile nitrogen. The solvent effects estimated as described above are found to be roughly equal for the 1,2- and 1,4-adducts and a given substituent. This implies that the conclusions reached above on the basis of the theoretical calculations would be valid also in a THF solution.

## Experimental studies

The α-donor substituted cyclopentenones **1b** and **1d–g** were prepared according to literature procedures.[2a,3b,4,8,9] Compound **1c** was prepared by direct chlorination of cyclopent-2-en-1-one in 37% yield. These model substrates were treated with methyllithium, lithium dimethylcuprate and cyanomethyllithium in THF at −78 °C as depicted in Scheme 2. The product composition of the reaction mixtures was analysed by GLC after 1 h, and the reactions worked up after 1.5 h. The results of treatment of **1a–g** with MeLi are given in Table 3.

As expected, only 1,2-adducts (**3a–g**) were obtained. No traces of 1,4-adducts (**4a–g**) were observed by GLC analysis of the reaction mixtures or of the crude products. For **1d** the 1,2-adduct **3d** was isolated as a crude product and identified by $^1H$ NMR and GLC-MS. However, **3d** was hydrolysed after 5–10 min at room temperature to 2-methyl-2-hydroxycyclopentanone, **14**, which quickly was dehydrated to give 2-methylcyclopent-2-en-1-one, **15**, which was identified by GC co-chromatography with an authentic sample, $^1H$ NMR, $^{13}C$ NMR and GLC-MS. The final product **15** was, however not isolated due to its volatility. Similarly, **3e** was identified as the only product from **1e** by GLC-MS of the reaction mixture. The enamine function was hydrolysed within minutes at room temperature to give 2-hydroxy-2-methylcyclopentanone, **14**.

With the exception of **1a**, relatively large amounts of starting material remained unreacted, even after prolonged reaction times (12 h). GLC analysis of experiments performed in the presence of an internal standard showed a "loss of mass" up to 40%. This indicated that MeLi also reacted as a base, abstracting an α-proton as a side reaction. The low isolated yields for

**Table 4** Treatment of **1a**–**g** with lithium dimethylcuprate in THF, at −78 °C

| **1** | X | **1**:**3**:**4** (GLC of reaction, 1 h) | Crude (%) | Isol. prod. (%) | *cis*:*trans* ($^1$H NMR) |
|---|---|---|---|---|---|
| **a** | H | 0:0:100 | <60 | —[a] | — |
| **b** | Cl | 0:0:100 | 87.6 | 53.6 | 3.9:1 |
| **c** | Br | 0:0:100 | 87.3 | 53.3 | 3.2:1 |
| **d** | OMe | 100:0:0 | — | — | — |
| **e** | Pyl | 100:0:0 | — | — | — |
| **f** | SPh | 0:0:100 | 80.4 | 51.3 | 7.8:1 |
| **g** | SePh | 0:0:100 | 81.8 | 76.1 | 8.3:1 |

[a] Compound **4a** was identified by GLC-MS of the reaction mixture and GLC co-chromatography with an authentic sample.

**Table 5** Treatment of **1a**–**g** with cyanomethyllithium in THF, at −78 °C

| **1** | X | **1**:**5**:**6** (GLC of reaction, 1 h) | Crude (%) | Isol. prod. (%) | *cis*:*trans* ($^1$H NMR) |
|---|---|---|---|---|---|
| **a** | H | 0:67.8:32.2 | 80 | **5a**; 43.3 | — |
| | | | | **6a**; 30.0 | — |
| **b** | Cl | 0:92.1:8.9 | 84.0 | **5b**; 47.5 | — |
| | | | | **6b**; 8.9 | 2.9:1 |
| **c** | Br | 0:98.5:1.5 | 70.5 | **5c**; 46.0 | — |
| | | | | **6c**; 0 | — |
| **d** | OMe | 0:100:0 | 90.7 | **6d**; 60.1 | — |
| **e** | Pyl | 5.2:94.8:0 | 79.7 | **16**; 74.8[a] | — |
| **f** | SPh | 1.3:80.3:18.0 | 79.9 | **5f**; 57.1 | — |
| | | | | **6f**; 16.2 | 6.1:1 |
| **g** | SePh | 4.7:68.2:16.4 | 78.5 | **5g**; 48.0 | — |
| | | | | **6g**; 14.1 | 5.6:1 |

[a] Compound **5e** hydrolysed to 2-cyanomethyl-2-hydroxycyclopentanone (**16**) upon work-up.

**3b**, **c** and **g** may be caused by reactions on the silica gel used for purification.

The calculated relative energies for the lithiated products **10a**–**d** and **11a**–**d** indicated that the 1,4-adducts would be the thermodynamically most stable product. However, in the reactions of **1a**–**g** with MeLi only 1,2-adducts were obtained. This indicates that the products are formed under kinetic control. A thorough understanding of the experimentally obtained data would, however, require estimation of all activation energies for the possible steps involved in the total reaction sequence from starting material to products. If the barrier to dissociation of MeLi in the field of the dissolved cyclopentenones is larger than the barrier to a concerted addition in the carbonyl region of the molecules, the reaction products from 1,2-addition, **3a**–**g**, would be favoured. If, on the other hand, the dissociation barrier of MeLi is low, the methyl anion would be able to orient itself in the field of the cations in a second step of the reaction, making 1,4-addition possible.

The results obtained by treatment of **1a**–**g** with $Me_2CuLi$ are given in Table 4. Only 1,4-adducts were obtained, with the exception of **1d** and **1e**, which were found to be unreactive towards $Me_2CuLi$. The crude yields were fairly good and the purities above 90% by $^1$H NMR. However, the yields after flash chromatography were only moderate.

The mechanism for the addition of dialkyl cuprates to conjugated carbonyl compounds has been investigated by several authors.[10] The generally accepted mechanism today involves the following steps: first lithium coordinates to the carbonyl oxygen, copper coordinates to the double bond. Copper then adds as copper(III) to the $C^3$ position and thereby directs one methyl group into this position, rather than the more electrophilic $C^1$ position. When the electron donating group, X, was OMe or Pyl, **1d**–**e**, no reaction took place. We interpret these findings as a result of the increased negative charge in the $C^3$ position of the starting materials, thus disfavouring the transfer of the methyl group. It may also be that the donor group X competes with the double bond in the coordination to copper.

The ratio of *cis*:*trans* 1,4-adducts were in all cases in favour of the *cis* isomer. A tentative way to rationalize these observations is to involve steric effects. Clarification of this issue would, however, require extensive computational studies reaching far beyond the scope of this project.

The reactions between **1a**–**g** and $NCCH_2Li$ also gave predominantly 1,2-adducts, but various amounts of 1,4-adducts, **6a**–**c**, **6f**–**g** were also obtained, as shown in Table 5. In the cases where X was OMe and Pyl, **1d** and **1e**, only 1,2-addition was obtained. For the reaction with **1e**, the isolated product was 2-cyanomethyl-2-hydroxycyclopentanone, **16**, formed by hydrolysis of the enamine during work-up. GLC of reaction mixtures run with internal standard did not indicate any major "loss of mass", except for the reaction involving **1g**.

The crude yields were acceptable, but the yields of the purified products were somewhat lower than expected. Also in these reactions, the *cis* isomer was the favoured 1,4-adduct. The amount of 1,4-adduct, **6a**–**g**, formed in the reactions decreased in the following order of X: H (32%) > SPh, SePh (18–15%) > Cl (9%) > Br (2%) > OMe, pyrrolidinyl (0%). The net charge distribution of the cation **9d** (X = OMe) also showed a clear negative charge on the $C^3$ atom. The relative energies for **12d** and **13d** showed that the 1,2-adduct **12d** was the thermodynamically favoured one. Both of these factors strongly disfavour 1,4-addition. If we assume that the lone pair electrons of the pyrrolidinyl substituent are in conjugation with the double bond system of the cyclopentenone ring, the influence of the lone pair electrons may be expected to be very similar to the influence of the OMe group on the charge distributions of **9e** and the relative energies of **12e** and **13e**. In the cases where X was Cl and Br very little 1,4-addition was obtained. For these compounds the net charge distributions did not differ much from the unsubstituted system. The relative energies showed that the 1,4-adducts were thermodynamically preferred. The reason for the low share of 1,4-addition might therefore be ascribed to an increase in the ability of X to coordinate to the nucleophile as X becomes more electronegative and polarizable. Such a coordination might influence the direction of the attack in favour of 1,2-addition.

## Conclusion

By treatment of **1a**–**g** with methyllithium the 1,2-adducts **3a**–**g** were formed in 28–75% yield. No traces of the corresponding 1,4-adducts **4a**–**g** were observed, indicating that the products were formed under kinetic control. The reactions between **1a**–**g** and lithium dimethylcuprate gave only the 1,4-adducts **4a**–**c** and **4f**–**g** in 51–76% yield. No reaction was observed for **1d** and **1e** (X = OMe and pyrrolidin-1-yl). Treatment of **1a**–**g** with cyanomethyllithium predominantly gave the 1,2-adducts **12a**–**g** (43–60% yield). However, formation of the corresponding 1,4-adducts **13a**–**c** and **13f**–**g** (8–30% yield) was also observed with the amount of 1,4-addition decreasing in the following order: H (32%) > SPh, SePh (18–15%) > Cl (9%) > Br (2%) > OMe, pyrrolidinyl (0%).

The calculated net atomic charges of **9a**–**d** obtained by DFT calculations showed only minor differences for the α-donor-substituted systems **9b** and **9c** (X = Cl and Br) compared to the unsubstituted compound, **9a**. Compound **9d** (X = OMe) differed, however, in the $C^2$ position, which was found to be positively charged rather than negatively as for the others. The $C^3$ position in **9d** was found to be significantly negative relative to the three other cyclopentenones **9a**–**c**. The relative energies estimated for the 1,2- and the 1,4-adducts from addition of methyllithium or cyanomethyllithium pointed out the 1,4-adduct as thermodynamically favoured. An exception was found for the addition of cyanomethyllithium to **1d** (X = OMe), where the 1,2-adduct, **12d**, was the thermodynamically most stable one.

For synthetic purposes conjugate 1,4-addition is the most desirable reaction. The estimated relative energy calculations showed that the 1,4-adducts were thermodynamically most stable. This points to a future development of the experimental procedures favouring the 1,4-addition. A possible lead may be to explore electrophilic catalysis in reaction with nucleophiles giving mixtures of 1,2- and 1,4-addition, such as cyanomethyllithium.

## Experimental

All reactions were carried out under a nitrogen atmosphere. The chemicals were commercial products of *p.a.* quality and used directly as delivered unless otherwise stated. Copper iodide was purified by treatment with potassium iodide as described by Taylor.[10b] All solvents were dried by published procedures.[19] Melting points were determined on a Büchi 535 apparatus and are uncorrected. TLC was performed on Merck 5554 Fertigplatten, DC-Alufolien, Kieselgel $60_{254}$, using UV light at 254 nm and 5% alcoholic molybdophosphoric acid for detection. Flash chromatography was carried out using Merck's Kieselgel 60 (230–400 mesh). GLC analyses were performed on a Varian 3300 chromatograph equipped with split injector, FID detector and a Varian 4400 integrator. Two capillary columns were applied; Chrompack CP sil 8 CB (25 m) and Supelco SPB-20 (30 m). The elemental analyses were performed by the Institute of Chemical Technology in Prague, Czech Republic. Exact mass measurements were carried out on an AEI MS-902 double focusing mass spectrometer (Nier-Johnson geometry) and a Fisons Instrument VG Prospec mass spectrometer, by peak matching with perfluorokerosene as standard for mass references. IR spectra were recorded on a 470 IR Shimadzu spectrometer and are reported as wave number, *ν*. $^1$H and $^{13}$C NMR spectra were recorded on a JEOL JNM-EX 400 FT NMR SYSTEM, using $CDCl_3$ as solvent and reference. Chemical shifts are given in ppm and *J* values in Hz. Mass spectra were registered on a Hewlett Packard 5890 Series II GC spectrometer equipped with a Chrompack CP sil 5 CB capillary column (25 m), followed by a VG Quattro mass spectrometer. The spectra were obtained at 220 °C and 70 eV. Signals of intensity <5% have been omitted.

### Preparation of α-donor-cyclopenten-1-ones

**2-Bromocyclopent-2-en-1-one[2a] (1b), 2-methoxycyclopent-2-en-1-one[16] (1d), 2-(pyrrolidin-1-yl)cyclopent-2-en-1-one[17] (1e), 2-phenylthiocyclopent-2-en-1-one[3b] (1f) and 2-phenylselenocyclopent-2-en-1-one[4] (1g).** These were prepared according to literature procedures.

**2-Chlorocyclopent-2-en-1-one (1c).** A solution of cyclopent-2-en-1-one (2.00 ml, 64.56 mmol) in dry $CH_2Cl_2$ (50 ml) was cooled to −78 °C and $Cl_2$ was bubbled through until the reaction turned yellow (2–3 min). The reaction was stirred at −78 °C until it became colour free (5 min) and then $Cl_2$ was bubbled through until the yellow colour reappeared (1–2 min). After stirring at −78 °C for another 30 min to the reaction was added aqueous NaOH (30%, 30 ml) and diethyl ether (30 ml). The mixture was stirred vigorously at room temperature for 1 h. The phases were separated and the aqueous layer extracted with diethyl ether (2 × 30 ml). The combined organic layers were washed with aqueous $Na_2CO_3$ (3 × 50 ml), water (2 × 50 ml) and sat. NaCl solution (50 ml). Drying ($MgSO_4$) and evaporation of the solvent under reduced pressure afforded **1c** (1.08 g, 37% yield, purity > 99% by GLC) as a light yellow oil. HRMS Found *M* 116.0025. Calc. for $C_5H_5ClO$: 116.0029; IR $\nu_{max}$ (neat) 3410w, 3070w, 2920m, 1715s, 1595s, 1435m, 1400m, 1290s, 1235m, 1165m, 1015m, 995m, 950s, 915w, 780m, 750m cm$^{-1}$; $^1$H NMR *δ* 2.52–2.54 (2H, m), 2.67–2.70 (2H, m), 7.58 (1H, t, *J* 2.93); $^{13}$C NMR *δ* 25.9, 33.0, 136.3, 157.3, 201.1; MS *m*/*z* 118 (*M* + 2, 4%), 116 (*M*, 12), 88 (8), 73 (8), 62 (9), 61 (9), 60 (21), 53 (49), 52 (9), 51 (26), 50 (29), 49 (18), 48 (10), 47 (24).

### General procedure for treatment of α-donor-cyclopent-2-en-1-ones with methyllithium

A solution of MeLi (1.65 M in diethyl ether, 1.0 equiv.) in THF (2 ml) was cooled to −78 °C. To this mixture was added a cold (−78 °C) solution of **1a**–**g** (0.5 mmol) in THF (3 ml) *via* cannula. The reaction was stirred at −78 °C for 1 h. At this time, a sample (10 µl) for GC analysis was withdrawn. After 1.5 h total reaction time the mixture was lifted out of the cooling bath and water added (3 ml) immediately. The mixture was stirred at room temperature for 10 min and then extracted with $CH_2Cl_2$ (3 × 5 ml). The combined organic layers were washed with sat. NaCl solution (4 ml) and dried ($MgSO_4$). Evaporation of the solvent under reduced pressure gave a crude product which was analysed by GLC and $^1$H NMR, and subsequently purified by flash chromatography.

The product composition and yields obtained by treatment of **1a**–**g** with MeLi are given in Table 3. Full spectroscopic documentation of the isolated products are available as supplementary data.†

### General procedure for treatment of α-donor-cyclopent-2-en-1-ones with lithium dimethylcuprate

A suspension of CuI (2 equiv.) in THF (6 ml) was cooled to −15 °C and a solution of MeLi in diethyl ether (1.71 M, 4 equiv.) was added. The mixture was stirred at −15 °C until all the yellow, solid material was dissolved. The resulting clear, colour free cuprate solution was cooled to −78 °C and added to a cold (−78 °C) solution of **1a**–**g** (0.6 mmol) in THF (3 ml) *via* cannula. The reaction was stirred at −78 °C for 1 h, at which time a sample (10 µl) was withdrawn for GLC analysis. After a total reaction time of 1.5 h, the reaction was lifted out of the cooling bath and aqueous $NH_3$ (2 M, 3 ml), aqueous $NH_4Cl$ (10 weight%, 3 ml) and diethyl ether (10 ml) were added. The mixture was stirred vigorously in air at room temperature until all precipitated material had dissolved. The phases were separated and the deep blue aqueous layer was extracted with diethyl ether (2 × 10 ml). The combined organic layers were washed with sat. NaCl solution (10 ml) and dried ($MgSO_4$). Evaporation of the solvent under reduced pressure afforded a crude product which was analysed by GLC and $^1$H NMR prior to purification by flash chromatography.

The product composition and yields obtained by treatment of **1a**–**g** with lithium dimethylcuprate are given in Table 4. Full spectroscopic documentation of the isolated products are available as supplementary data.†

### General procedure for treatment of α-donor-cyclopent-2-en-1-ones with cyanomethyllithium

A solution of acetonitrile (1 equiv.) in THF (2 ml) was cooled to −78 °C and a solution of methyllithium in diethyl ether (1.65 M, 1 equiv.) was added. The mixture was stirred for 15 min. A precooled solution (−78 °C) of **1** (0.5 mmol) in THF (3 ml) was then transferred into the cyanomethyllithium solution *via* cannula. The reaction was kept stirring at −78 °C and monitored by GLC after 1 h. After 1.5 h the reaction was lifted out of the cooling bath, aqueous ammonium chloride (sat., 1 ml) was added and the mixture was stirred vigorously for 15 min. The organic solvent was evaporated before the residue was treated with more aqueous ammonium chloride (sat., 3 ml) and extracted with ethyl acetate (3 × 5 ml). The combined organic layers were washed with sat. NaCl solution (4 ml) and dried ($MgSO_4$). Removal of the solvent under reduced pressure gave a crude product which was analysed by GC and $^1$H NMR before it was purified by flash chromatography.

The product composition and yields obtained by treatment of **1a**–**g** with cyanomethyllithium are given in Table 5. Full spectroscopic documentation of the isolated products is available as supplementary data.†

### Computational method

The species included in the computational studies were all fully optimized by density functional theory (DFT) calculations,[11] using Becke's 3-parameter hybrid exchange functional[12] and the non-local correlation functional of Lee, Yang and Parr (LYP). Calculations using the triple zeta basis 6-311G*[13] and a smaller one comprising a Dunning double-zeta[14] for all first row atoms, and the Los Alamos ECP plus double zeta for the heavier atoms[15] (LanL2DZ) showed rather small differences in predicted geometries, vibrational frequencies and relative energies for some of the species chosen as test compounds. Accordingly, we adopted the less expensive LanL2DZ basis consistently throughout the calculations. Solvent effects simulating THF as solvent were estimated using the polarized continuum model of Tomasi.[16,17] The program package Gaussian 94[18] was used throughout all the calculations.

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