DOI: 10.1002/chem.200902487

S_N2' versus S_N2 Reactivity: Control of Regioselectivity in Conversions of Baylis–Hillman Adducts

Mahiuddin Baidya, Grygoriy Y. Remennikov, Peter Mayer, and Herbert Mayr*[a]

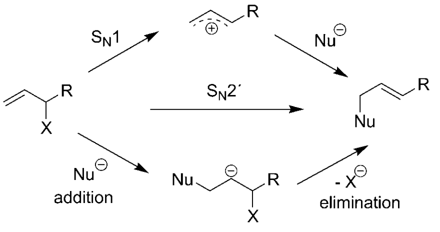
Dedicated to Dr. Klaus Römer on the occasion of his 70th birthday

Abstract: $TiCl_4$-induced Baylis–Hillman reactions of α,β-unsaturated carbonyl compounds with aldehydes yield the (*Z*)-2-(chloromethyl)vinyl carbonyl compounds **5**, which react with 1,4-diazabicyclo[2.2.2]octane (DABCO), quinuclidine, and pyridines to give the allylammonium ions **6**. Their combination with less than one equivalent of the potassium salts of stabilized carbanions (e.g. malonate) yields methylene derivatives **8** under kinetically controlled conditions (S_N2' reactions). When more than one equivalent of the carbanions is used, a second S_N2' reaction converts **8** into their thermodynamically more stable allyl isomers **9**. The second-order rate constants for the reactions of **6** with carbanions have been determined photometrically in DMSO. With these rate constants and the previously reported nucleophile-specific parameters *N* and *s* for the stabilized carbanions, the correlation log *k* (20 °C) = *s*(*N* + *E*) allowed us to calculate the electrophilicity parameters *E* for the allylammonium ions **6** ($-19 < E < -18$). The kinetic data indicate the S_N2' reactions to proceed via an addition–elimination mechanism with a rate-determining addition step.

Keywords: allylic substitution · kinetic control · linear free-energy relationships · regioselectivity · thermodynamics

Introduction

Nucleophilic substitutions of allyl derivatives often proceed with allylic rearrangements. As depicted in Scheme 1, these reactions may either proceed via allyl cations, through addition–elimination mechanisms, or via concerted S_N2' processes.[1–3] Whereas allylic substitutions through intermediate allyl cations have intensively been explored,[2] only few examples involving the addition–elimination mechanism (bottom of Scheme 1) have been reported.[3a,b] Bordwell and co-workers concluded that the concerted S_N2' mechanism may well be a myth.[3c,3d]



Scheme 1. Nucleophilic substitutions with allylic rearrangement.

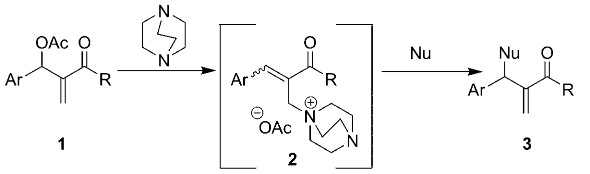
Since 1968, a large variety of allyl derivatives have become available through Baylis–Hillman reactions.[4] Because of their high functionality, these products are valuable building blocks in organic synthesis, and the regioselective conversion of these products is an important challenge for synthetic chemists. The acetoxy groups in Baylis–Hillman acetates **1** have been substituted by nitrogen, oxygen, sulfur, and carbon nucleophiles (Scheme 2).[5–9] The catalysis of these reactions by 1,4-diazabicyclo[2.2.2]octane (DABCO) has been rationalized through the intermediacy of allylammonium ions **2**, the formation of which has been proven in few cases.[5c,10]

While amine-catalyzed Baylis–Hillman reactions yield β-hydroxy-α-methylene carbonyl compounds **4**, the corresponding $TiCl_4$-induced reactions give rise to the stereoselective formation of (*Z*)-2-(chloromethyl)vinyl carbonyl

---

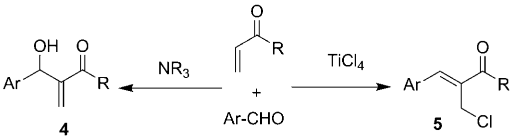
[a] M. Baidya, Dr. G. Y. Remennikov, Dr. P. Mayer, Prof. Dr. H. Mayr
Department Chemie und Biochemie
Ludwig-Maximilians-Universität München
Butenandtstrasse 5–13, 81377 München (Germany)
Fax: (+49) 89-2180-77717
E-mail: Herbert.Mayr@cup.uni-muenchen.de

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.200902487.



Scheme 2. Nucleophilic substitution reaction of Baylis–Hillman acetate in the presence of DABCO.

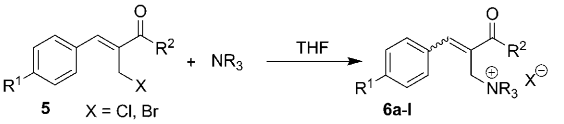
compounds **5** (Scheme 3).[11] We now report that the reactions of compounds **5** with tertiary amines and pyridines lead to the formation of isolable allylammonium salts, the alleged intermediates of the amine-catalyzed nucleophilic substitutions of Baylis–Hillman acetates (Scheme 2). By investigating products and kinetics of the reactions of these ammonium ions with various carbanions, we were able to elucidate the involved mechanisms and derive conditions for the regioselective conversions of Baylis–Hillman products.



Scheme 3. Tertiary amine and $TiCl_4$-induced Baylis–Hillman reactions.

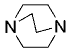
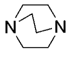
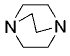
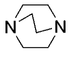
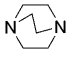
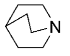
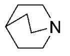
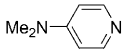
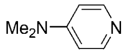
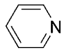
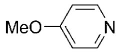
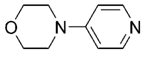
Results

Isolation of the ammonium salts 6: Treatment of the readily accessible 2-(halomethyl)vinyl ketones or esters **5**[12] with DABCO or quinuclidine in absolute THF resulted in the formation of the allylammonium halides **6a**–**g**, which precipitated as colorless powders (Scheme 4, Table 1). The substituted pyridinium salts **6h**–**l** were prepared analogously, but the isolated yields were lower (except for **6h**) because of their partial solubility in THF. The pyridinium salts **6h**–**l** are more sensitive to moisture than the corresponding DABCO and quinuclidine salts **6a**–**g**.



Scheme 4. Preparation of ammonium salts **6** from Baylis–Hillman adducts **5**.

Table 1. Reactions of tertiary amines with the Baylis–Hillman adducts **5**.

NR_3	R^1	R^2	X	Product	Yield[a] [%]	Z:E[b]
	OMe	Me	Cl	**6a**	86	93:7
	H	Me	Cl	**6b**	82	92:8
	NO_2	Me	Cl	**6c**	82	90:10
	OMe	OMe	Br	**6d**	83	30:70
	H	OMe	Br	**6e**[c]	87	40:60[c]
	OMe	Me	Cl	**6f**	87	92:8
	NO_2	Me	Cl	**6g**	95	94:6
	H	OMe	Br	**6h**	93	17:83
	OMe	Me	Cl	**6i**	73	7:93
	OMe	Me	Cl	**6j**	40	9:91
	OMe	Me	Cl	**6k**	43	7:93
	OMe	Me	Cl	**6l**	46	8:92

[a] Isolated yield. [b] Determined by ^1H NMR spectroscopy. [c] The same reaction in a 1:1 H_2O/THF solvent mixture produced **6e** with a Z/E ratio of 18:82; ref. [10b].

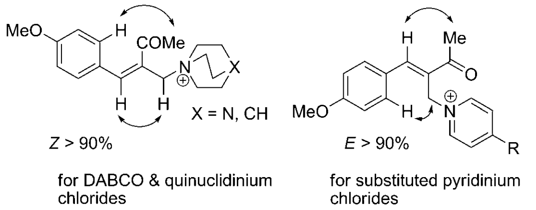
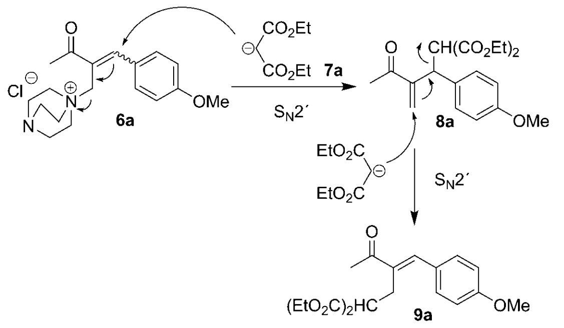


Figure 1. Configurational assignment of the ammonium salts **6a**–**l** by NOESY experiments (arrows indicate observed NOE effects).

NOESY experiments (Figure 1) showed that the ammonium chlorides **6a**–**c** and **6f**,**g** obtained with DABCO and quinuclidine were predominantly formed as Z isomers (> 90%), whereas the ammonium bromides **6d**,**e** (R^2 = OMe) were predominantly formed as E isomers (> 60%).[10b] In contrast, all pyridinium salts **6h**–**l** (X = Cl, Br) were produced with a high excess of the E isomers, and the E/Z ratio was even greater than 90:10 for compounds **6i**–**l** where X = Cl (Table 1).

Reactions of the Baylis–Hillman ammonium ions 6 with carbanions 7: Treatment of **6a** with 1.2 equivalents of potassium malonate **7a** in DMSO for 10 s or 1 min at ambient temperature gave mixtures of **8a** and **9a** in ratios of 96:4 and 92:8, respectively (Scheme 5). When the reaction time was extended to 24 h, only the styrene derivative **9a** was obtained. Because the isolated methylene derivative **8a** was also transformed into **9a** by treatment with **7a**, one can conclude that **8a** is the kinetically controlled product, whereas **9a** is the product of thermodynamic control.

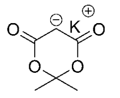
When strictly kinetically controlled conditions were established by treating the ammonium salts **6** with only 0.9 equivalents of the carbanions **7a**–**g**, the methylene derivatives **8a**–**m** were produced selectively (Table 2). Only the reac-



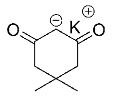
Scheme 5. Plausible reaction mechanism for the formation of **9a**.

tions of the malononitrile anion **7e** with the ammonium salts **6a**, **6f**, and **6i** gave complex product mixtures which have not been identified.

7a : $KCH(CO_2Et)_2$
7b : $KCH(CH_3)NO_2$
7c : $KCH(COMe)CO_2Et$
7d : $KCH(CN)CO_2Et$
7e : $KCH(CN)_2$
7g : $KCH(CO_2Me)_2$



7f



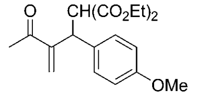
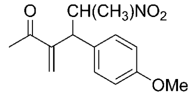
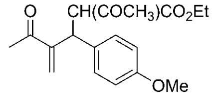
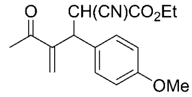
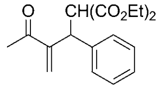
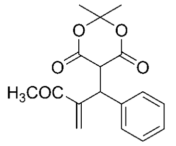
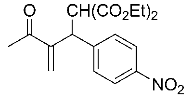
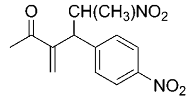
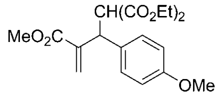
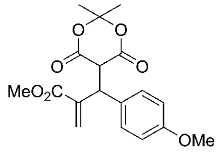
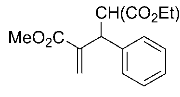
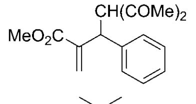
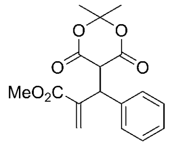
7h

The expected S_N2' product **8n** from the reaction of the dimedone carbanion **7h** with **6a** was not detectable; instead the tetrahydrochromone **10** was isolated as a 1:1 mixture of diastereomers (Scheme 6). One of the diastereomers crystallized and was characterized by X-ray analysis (Figure 2).

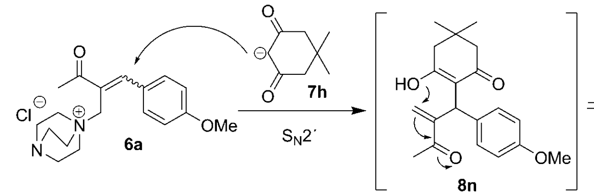
Reactions of the allyl chloride 5a with nucleophiles: Compounds **8a** and **9a**, which have been obtained from the ammonium salt **6a** (Scheme 5) can also be directly synthesized from the Baylis–Hillman chloride **5a** (Scheme 7). Combination of equimolar amounts of **5a** and K-**7a** in DMSO gave a 26:74 mixture of **8a** and **9a** (Table 3, entry 1).[13] When thermodynamic product control was realized by treating **5a** with 1.2 equivalents of K-**7a** in the presence or absence of DABCO, the arylidene derivative **9a** was formed exclusively (Table 3, entries 2, 3). The resulting 88:12 mixture of (*E*)-**9a** and (*Z*)-**9a** was separated by column chromatography. Only **8a**, the kinetically controlled product, was observed and isolated with 63 % yield, when these reagents were combined in THF/H_2O solution (Table 3, entry 4). It can be expected that compounds **8b–m** as well as the thermodynamically favored isomers **9b–m** can be synthesized analogously from the allyl chlorides **5** and the carbanions **7** without generating the corresponding ammonium ions **6** as intermediates (Scheme 5, Table 2).

Quantification of the electrophilicities of the ammonium salts 6: In numerous publications, we have demonstrated that the rates of the reactions of diarylcarbenium ions with nucleophiles follow Equation (1), in which *E* is the electro-

Table 2. Reactions of the ammonium salts **6a–l** (1.0 equiv) with substoichiometric amounts (0.90 equiv) of the potassium salts of the carbanions **7a–g** (in DMSO, at ambient temperature, 20 h).

Ammonium salt	Carbanion	Product		Yield [%]
6a	**7a**		**8a**	94
6a	**7b**		**8b**	81[c]
6a	**7c**		**8c**	[b,c]
6a	**7d**		**8d**	79[c]
6a	**7e**		[a]	
6b	**7a**		**8e**	94
6b	**7f**		**8f**	87
6c	**7a**		**8g**	85
6c	**7b**		**8h**	91
6d	**7a**		**8i**	90
6d	**7f**		**8j**	85
6e	**7a**		**8k**	95
6e	**7g**		**8l**	87
6e	**7f**		**8m**	88
6f	**7a**		**8a**	71
6f	**7e**		[a]	
6i	**7a**		**8a**	78
6i	**7d**		**8d**	75
6i	**7e**		[a]	
6j	**7a**		**8a**	85
6k	**7a**		**8a**	82

[a] Complex mixture. [b] Cyclized product was also observed (see text). [c] Small amount of S_N2 product was also observed.



Scheme 6. Reaction of the dimedone anion **7h** with the DABCO salt **6a** in DMSO.

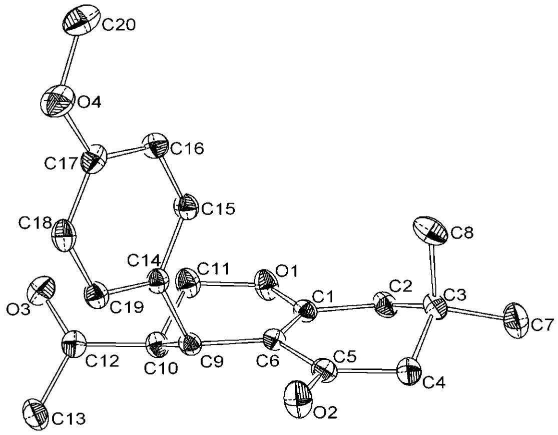
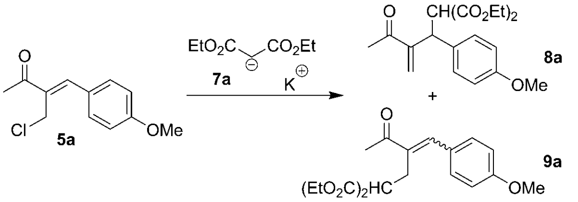


Figure 2. Crystal structure of *cis*-**10** obtained from the reaction of **6a** and K-**7h**.



Scheme 7. Reaction of **5a** with the carbanion of diethyl malonate (**7a**).

Table 3. Reaction of **5a** with **7a** under various conditions (2 h, room temperature).

Entry	**5a**:**7a**:DABCO ratio	Solvent	Yield of **8a** [%]	Yield of **9a** [%]
1	1.0:1.0:0	DMSO	24	67
2	1.0:1.2:0	DMSO	0	93
3	1.0:1.2:1.0	DMSO	0	65
4	1.0:1.2:1.0	THF/H_2O (1:1)	63	0

philicity parameter, N is the nucleophilicity parameter, and s is the nucleophile-specific slope parameter.[14] This relationship also holds for nucleophilic additions of carbanions to quinone methides,[15] which can be considered as stabilized benzhydryl cations, and to several Michael acceptors.[16]

$$\log k(20\,^\circ\mathrm{C}) = s(N + E) \qquad (1)$$

To characterize the electrophilicities of the ammonium ions **6** by Equation (1), we have studied the kinetics of their reactions with some of the carbanions **7**. Although the UV bands of the ammonium salts **6** partially overlap with those of the substitution products **8**, sufficient changes of the UV spectra allowed us to follow the reaction kinetics photometrically by using a diode array spectrometer coupled to an insertion probe described previously (see also the Supporting Information).[14k] Pseudo-first-order rate constants k_{obs} were obtained by fitting the decays of the absorbances of the styrene chromophor in the ammonium ions **6** to monoexponential functions. Because the employed allylammonium ions **6** only had a configurational purity of 90–93 %, the observed monoexponential decays indicate that the electrophilicities of the Z and E isomers do not differ significantly. Plots of k_{obs} versus the concentrations of the carbanions **7** were linear (Figure 3), and the second-order rate constants, which correspond to the slopes of these correlation lines, are listed in Table 4.

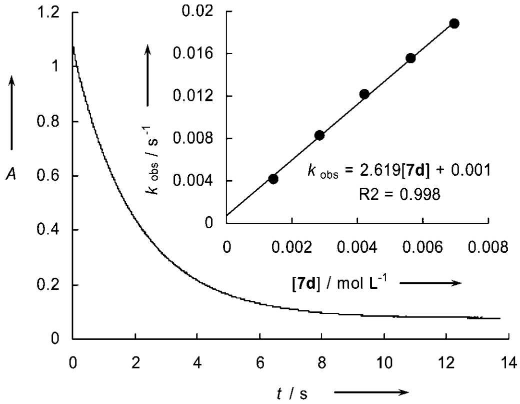


Figure 3. Exponential decay of the absorbance A of **6i** at 340 nm and linear correlation of the pseudo-first-order rate constants k_{obs} versus [**7d**] for the reaction of **6i** with **7d** in DMSO at 20 °C.

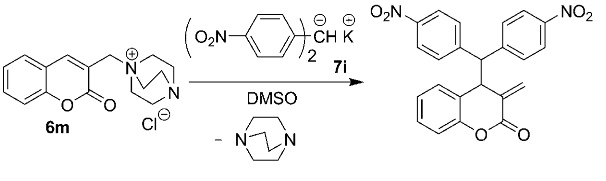
Only for the reactions of the potassium salt of diethyl malonate (**7**) with several ammonium ions **6** the k_{obs} versus [**7**] plots showed slight deviations from linearity. As specified in the Supporting Information, these deviations were small and have been neglected in the evaluations.

Because of strongly overlapping UV bands, the photometric monitoring of the reactions of the coumarin-derived ammonium ion **6m**[10a] with the carbanions **7a**–**f** is problematic. Therefore, the reaction of **6m** with the anion of Meldrum's acid (**7f**) was followed by ^{1}H NMR spectroscopy in [D_6]DMSO. The reactivity of **6m** was furthermore characterized through its reaction with the blue carbanion **7i** (potassium salt of bis(4-nitrophenyl)methyl anion),[18] which has been followed photometrically under pseudo-first-order conditions using the electrophile **6m** in high excess (Scheme 8). Details are given in the Supporting Information.

Table 4. Second-order rate constants (k) for the reactions of ammonium salts **6** with the carbanions **7** in DMSO at 20 °C and averaged E parameters for the ammonium ions **6**.

Ammonium ions (E)	Carbanions[a]	k [$\mathrm{M}^{-1}\mathrm{s}^{-1}$]	k_{calcd}[b] [$\mathrm{M}^{-1}\mathrm{s}^{-1}$]
6a (−18.6)	**7a**	4.26	11.6
6a (−18.6)	**7c**	[c]	
6a (−18.6)	**7d**	6.18	5.0
6a (−18.6)	**7e**	7.64	3.3
6f (−18.9)	**7a**	2.49	7.7
6f (−18.9)	**7c**	[c]	
6f (−18.9)	**7d**	4.21	3.2
6f (−18.9)	**7e**	5.22	2.2
6i (−19.1)	**7a**	5.59	5.6
6i (−19.1)	**7c**	0.42	0.64
6i (−19.1)	**7d**	2.62	2.3
6i (−19.1)	**7e**	2.24	1.6
6j (−17.9)	**7a**	22.1	30.8
6j (−17.9)	**7c**	3.06	4.1
6j (−17.9)	**7d**	17.1	13.6
6j (−17.9)	**7e**	13.1	9.1
6k (−18.2)	**7a**	21.0	[d]
6l (−18.9)	**7a**	7.35	[d]
6m (−17.3)	**7f**	8.78×10^{-4}[e]	1.3×10^{-3}
6m (−17.3)	**7i**	77.4	58.7

[a] N and s parameters in DMSO are from refs. [15a,17,18]: **7a**, $N=20.22$, $s=0.65$; **7c**, $N=18.82$, $s=0.69$; **7d**, $N=19.62$, $s=0.67$; **7e**, $N=19.36$, $s=0.67$; **7f**, $N=13.91$, $s=0.86$; **7i**, $N=19.92$, $s=0.67$. [b] k_{calcd} from E, N, and s using Equation (1). [c] Change of the UV spectrum was not mono-exponential. [d] $k_{\mathrm{calcd}}=k$, because only one rate constant was used for the calculation of E. [e] Determined by ^{1}H NMR kinetics.



Scheme 8. Reaction of **6m** with **7i** in DMSO.

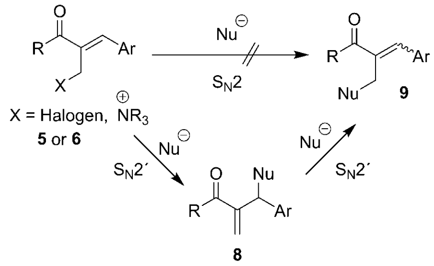
Substitution of the second-order rate constants k listed in Table 4 and the previously published N and s parameters for the carbanions **7**[15a,17,18] into Equation (1) yielded the electrophilicity parameters E for **6** which were averaged and listed in Table 4. Comparison of the experimental rate constants k and those calculated from N, s, and the averaged E values derived in this work shows agreement within a factor of 4. It has thus been demonstrated that Equation (1), which presently covers 40 orders of magnitude, can also be applied to the S_N2' substitutions studied in this work.

Discussion

The observed second-order kinetics for the reactions of the allylammonium ions **6** with the carbanions **7** exclude the S_N1 mechanism and are in line with a concerted S_N2' reaction (Scheme 1, middle) as well as with an addition–elimination mechanism (Scheme 1, bottom).

The similar reactivities of the allylammonium ions (**6**, $R^1=OMe$, $R^2=Me$) with DABCO and quinuclidine leaving groups (**6a**,**f**) and pyridine leaving groups (**6i–l**) shown in Table 4 allow us to differentiate between these alternatives. In previous work we have demonstrated that DABCO is a 10^6-fold better nucleofuge than DMAP.[19] If breaking of the C–N bond were involved in the rate-determining step, **6a** should be considerably more reactive than **6i**, because both compounds differ only in the nature of the leaving groups (DABCO vs. DMAP). The observation that both compounds show almost identical electrophilic reactivities indicates the occurrence of an addition–elimination mechanism with the addition step rate-determining.

The fact that the reactions of **5** and **6** with carbanions give the methylene compounds **8** under conditions of kinetic control, and not the thermodynamically favored isomer **9**, indicates that these compounds prefer S_N2' over S_N2 reactions which might produce compounds **9** directly. It can, therefore, be assumed that the allylammonium ions **6a–l**, formally S_N2 products of the reactions of **5** with amines, are analogously formed via two consecutive S_N2' reactions (Scheme 9).



Scheme 9. S_N2 reaction via two consecutive S_N2' reactions.

Conclusions

The mechanistic alternatives for S_N2' mechanisms depicted in Scheme 1 can be summarized in a More O'Ferrall–Jencks diagram as depicted in Figure 4.[20] Whereas the pathways via allyl cations (path *a* through the bottom-right corner) and carbanions (path *e* through the top-left corner) are well

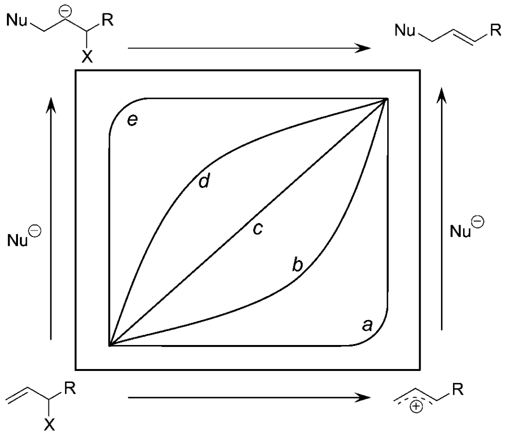
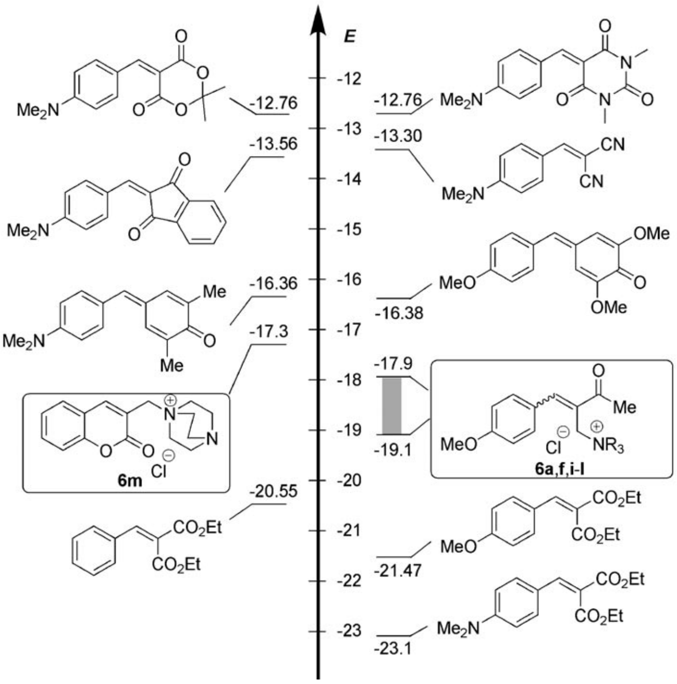


Figure 4. More O'Ferrall–Jencks diagram.

defined, many variants of the concerted S_N2' pathways are conceivable. Apart from the synchronous S_N2' mechanism along the diagonal (*c*), one can imagine a concerted mechanism in which the transition state carries partial carbocation (*b*) or partial carbanion character (*d*). In line with Bordwell's skepticism about the feasibility of bimolecular concerted mechanisms involving four or more bonds,[3] our experiments clearly show that the S_N2' reactions with the allylammonium ions studied in this work proceed via rate-determining Michael additions followed by the elimination of the amines (route (*e*) in Figure 4).

The rates of the Michael additions can be described by Equation (1), and Scheme 10 shows that the electrophilicity parameters of compounds **6a**,**f**,**i–l** range between $-19 < E < -18$, comparable to quinone methides and benzylidene malonates,[15,16] which enables us to calculate rate constants for the reactions with various nucleophiles and to predict potential reaction partners. Reviews on scope and limitations of the use of the reactivity parameters *E*, *N*, and *s* have been published.[14]



Scheme 10. Comparison of electrophilicity parameters *E* (from this work and refs. [15] and [16]; see also ref. [21]).

The fact, that the stepwise S_N2' reactions of the Baylis–Hillman products **5** and **6** are considerably faster than the corresponding S_N2 reactions, can systematically be employed in synthesis design. Because the Baylis–Hillman halides **5** as well as the Baylis–Hillman ammonium ions **6** are the thermodynamically more stable allylic isomers (internal double bonds), they are easily accessible under conditions of thermodynamic control. Since both **5** and **6** carry good leaving groups, their S_N2' reactions with strong nucleophiles (e.g. carbanions) selectively yield the thermodynamically less stable allylic isomers with terminal double bonds (e.g. **8**) under conditions of kinetic control (e.g. by using less than 1 equivalent of the nucleophiles). If stabilized carbanions are used as nucleophiles, which have a moderate nucleofugality, they can be replaced by the same or another nucleophile to yield the thermodynamically favored allylic isomers **9** with an internal double bond. Full control of regioselectivity is thus achieved.

Acknowledgements

We thank the Deutsche Forschungsgemeinschaft (Ma 673/21-2) and the Fonds der Chemischen Industrie for support of this work. Valuable suggestions by Dr. Armin R. Ofial are gratefully acknowledged.

---

[1] General reviews: a) R. H. DeWolfe, W. G. Young, *Chem. Rev.* **1956**, *56*, 753–901; b) R. M. Magid, *Tetrahedron* **1980**, *36*, 1901–1930; c) L. A. Paquette, C. J. M. Stirling, *Tetrahedron* **1992**, *48*, 7383–7423; d) J. A. Marshall, *Chem. Rev.* **1989**, *89*, 1503–1511; e) A. Alexakis, J. E. Bäckvall, O. Krause, O. Pamies, M. Dieguez, *Chem. Rev.* **2008**, *108*, 2796–2823.

[2] Reactions through allyl cations: a) W. G. Young, S. Winstein, H. L. Goering, *J. Am. Chem. Soc.* **1951**, *73*, 1958–1963; b) H. L. Goering, J. P. Blanchard, E. F. Silversmith, *J. Am. Chem. Soc.* **1954**, *76*, 5409–5418; c) H. L. Goering, E. F. Silversmith, *J. Am. Chem. Soc.* **1955**, *77*, 1129–1133; d) H. L. Goering, J. T. Doi, *J. Am. Chem. Soc.* **1960**, *82*, 5850–5854; e) H. L. Goering, G. S. Koermer, E. C. Linsay, *J. Am. Chem. Soc.* **1971**, *93*, 1230–1234; f) R. A. Sneen, *Acc. Chem. Res.* **1973**, *6*, 46–53; g) M. Speranza, A. Troiani, *J. Org. Chem.* **1998**, *63*, 1020–1026; h) A. Streitwieser, E. G. Jayasree, F. Hasanayn, S. S.-H. Leung, *J. Org. Chem.* **2008**, *73*, 9426–9434.

[3] Addition–elimination mechanisms: a) F. G. Bordwell, D. A. Schexayder, *J. Org. Chem.* **1968**, *33*, 3240–3246; b) F. G. Bordwell, T. G. Mecca, *J. Am. Chem. Soc.* **1972**, *94*, 5825–5829; c) F. G. Bordwell, *Acc. Chem. Res.* **1970**, *3*, 281–290; d) F. G. Bordwell, T. G. Mecca, *J. Am. Chem. Soc.* **1972**, *94*, 5829–5837; e) F. G. Bordwell, G. A. Pagani, *J. Am. Chem. Soc.* **1975**, *97*, 118–123.

[4] a) P. I. Dalko, *Enantioselective Organocatalysis*, Wiley-VCH, Weinheim, **2007**; b) A. Berkessel, H. Gröger, *Asymmetric Organocatalysis*, Wiley-VCH, Weinheim, **2005**; c) D. Basavaiah, A. J. Rao, T. Satyanarayana, *Chem. Rev.* **2003**, *103*, 811–891; d) V. Declerck, J. Martinez, F. Lamaty, *Chem. Rev.* **2009**, *109*, 1–48; e) P. Radha Krishna, R. Sachwani, P. S. Reddy, *Synlett* **2008**, 2897–2912; f) K. Morita, Z. Suzuki, H. Hirose, *Bull. Chem. Soc. Jpn.* **1968**, *41*, 2815; g) A. B. Baylis, M. E. D. Hillman, DE-B 215513, **1972**; [*Chem. Abstr.* **1972**, *77*, 34174q]; h) S. E. Drewes, G. H. P. Roos, *Tetrahedron* **1988**, *44*, 4653–4670; i) D. Basavaiah, K. V. Rao, R. J. Reddy, *Chem. Soc. Rev.* **2007**, *36*, 1581–1588; j) V. K. Aggarwal, S. Y. Fulford, G. C. Lloyd-Jones, *Angew. Chem.* **2005**, *117*, 1734–1736; *Angew. Chem. Int. Ed.* **2005**, *44*, 1706–1708.

[5] For nitrogen nucleophiles: a) H.-L. Cui, X. Feng, J. Peng, J. Lei, K. Jiang, Y.-C. Chen, *Angew. Chem.* **2009**, *121*, 5847–5850; *Angew. Chem. Int. Ed.* **2009**, *48*, 5737–5740; b) J. Li, X. Wang, Y. Zhang, *Tetrahedron Lett.* **2005**, *46*, 5233–5237; c) J. N. Kim, H. J. Lee, K. Y. Lee, J. H. Gong, *Synlett* **2002**, I173–I175; d) S.-H. Kwon, C.-W. Cho, *Bull. Korean Chem. Soc.* **2008**, *29*, 1835–1838; e) R. Galeazzi, G. Martelli, M. Orena, S. Rinaldi, *Synthesis* **2004**, 2560–2566; f) W. Zhong, Y. Zhao, B. Guo, P. Wu, W. Su, *Synth. Commun.* **2008**, *38*, 3291–3302; g) J. H. Gong, H. R. Kim, E. K. Ryu, J. N. Kim, *Bull. Korean Chem. Soc.* **2002**, *23*, 789–790; h) M. Ciclosi, C. Fava, R. Galeazzi, M. Orena, J. Sepulveda-Arques, *Tetrahedron Lett.* **2002**, *43*, 2199–2202; i) A. Patra, A. K. Roy, S. Batra, A. P. Badhuri, *Synlett* **2002**, 1819–1822.

[6] For oxygen nucleophiles: a) J. N. Kim, H. J. Lee, J. H. Gong, *Tetrahedron Lett.* **2002**, *43*, 9141–9146; b) Y. Du, X. Han, X. Lu, *Tetrahe-

dron Lett. **2004**, *45*, 4967–4971; c) A. Arfaoui, F. Beji, T. B. Ayed, H. Amri, *Synth. Commun.* **2008**, *38*, 3717–3725.

[7] For hydride and sulfur nucleophiles: a) Y. J. Im, J. M. Kim, J. H. Mun, J. N. Kim, *Bull. Korean Chem. Soc.* **2001**, *22*, 349–350; b) S. R. S. S. Kotti, X. Xu, G. Li, A. D. Headley, *Tetrahedron Lett.* **2004**, *45*, 1427–1431.

[8] For carbon nucleophiles: a) D. J. V. C. van Steenis, T. Marcelli, M. Lutz, A. L. Spek, J. H. V. Maarseveen, H. Hiemstra, *Adv. Synth. Catal.* **2007**, *349*, 281–286; b) L. D. S. Yadav, V. K. Rai, *Tetrahedron Lett.* **2009**, *50*, 2414–2419; c) Y. M. Chung, J. H. Gong, T. H. Kim, J. N. Kim, *Tetrahedron Lett.* **2001**, *42*, 9023–9026; d) V. Singh, G. P. Yadav, P. R. Maulik, S. Batra, *Tetrahedron* **2008**, *64*, 2979–2991.

[9] For *P*-based catalysts: a) C.-W. Cho, M. J. Krische, *Angew. Chem.* **2004**, *116*, 6857–6859; *Angew. Chem. Int. Ed.* **2004**, *43*, 6689–6691; b) C.-W. Cho, J.-R. Gong, M. J. Krische, *Org. Lett.* **2004**, *6*, 1337–1339; c) H. Park, C.-W. Cho, M. J. Krische, *J. Org. Chem.* **2006**, *71*, 7892–7894; d) T.-Z. Zhang, L.-X. Dai, L.-X. Hou, *Tetrahedron: Asymmetry* **2007**, *18*, 1990–1994; e) Y.-Q. Jiang, Y.-L. Shi, M. Shi, *J. Am. Chem. Soc.* **2008**, *130*, 7201–7203.

[10] a) S. E. Drewes, O. L. Njamela, N. D. Emslie, N. Ramesar, J. S. Field, *Synth. Commun.* **1993**, *23*, 2807–2815; b) D. Basavaiah, N. Kumaragurubaran, *Tetrahedron Lett.* **2001**, *42*, 477–479.

[11] a) M. Shi, J.-K. Jiang, S.-C. Cui, *Molecules* **2001**, *6*, 852–868; b) M. Shi, Y.-S. Feng, *J. Org. Chem.* **2001**, *66*, 406–411; c) M. Shi, J.-K. Jiang, *Tetrahedron* **2000**, *56*, 4793–4797; d) G. Li, J. Gao, H.-X. Wei, M. Enright, *Org. Lett.* **2000**, *2*, 617–620; e) Z. Han, S. Uehira, H. Shinokubo, K. Oshima, *J. Org. Chem.* **2001**, *66*, 7854–7857.

[12] a) R. Buchholz, H. M. R. Hoffmann, *Helv. Chim. Acta* **1991**, *74*, 1213–1220; b) F. Ameer, S. E. Drewes, N. D. Emslie, P. T. Kaya, R. L. Mann, *J. Chem. Soc. Perkin Trans. 1* **1983**, 2293–2295.

[13] A similar transformation was previously observed by Drewes and Emslie when synthesizing precursors for sceleranecic and integerrinecic acids: S. E. Drewes, N. D. Emslie, *J. Chem. Soc. Perkin Trans. 1* **1982**, 2079–2083.

[14] a) H. Mayr, M. Patz, *Angew. Chem.* **1994**, *106*, 990–1010; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 938–957; b) H. Mayr, M. Patz in *Frontiers of Studies on Organic Reaction Mechanisms* (Eds.: T. Okuyama, S. Tomoda, H. Yamataka), Tokyo Kagaku Dojin, Tokyo, **1995**, pp. 33–43; c) H. Mayr in *Cationic Polymerization: Mechanisms, Synthesis and Applications* (Ed.: K. Matyjaszewski), Marcel Dekker, New York, **1996**, pp. 51–136; d) H. Mayr, O. Kuhn, M. F. Gotta, M. Patz, *J. Phys. Org. Chem.* **1998**, *11*, 642–654; e) H. Mayr, T. Bug, M. F. Gotta, N. Hering, B. Irrgang, B. Janker, B. Kempf, R. Loos, A. R. Ofial, G. Remennikov, H. Schimmel, *J. Am. Chem. Soc.* **2001**, *123*, 9500–9512; f) H. Mayr, B. Kempf, A. R. Ofial, *Acc. Chem. Res.* **2003**, *36*, 66–77; g) H. Mayr, A. R. Ofial in *Carbocation Chemistry* (Eds.: G. A. Olah, G. K. S. Prakash), Wiley, Hoboken (N.J.), **2004**, Chapter 13, pp. 331–358; h) A. R. Ofial, H. Mayr, *Macromol. Symp.* **2004**, *215*, 353–367; i) H. Mayr, A. R. Ofial, *Pure Appl. Chem.* **2005**, *77*, 1807–1821; j) H. Mayr, A. R. Ofial, *Nachr. Chem.* **2008**, *56*, 871–877; k) H. Mayr, A. R. Ofial, *J. Phys. Org. Chem.* **2008**, *21*, 584–595.

[15] a) R. Lucius, R. Loos, H. Mayr, *Angew. Chem.* **2002**, *114*, 97–102; *Angew. Chem. Int. Ed.* **2002**, *41*, 91–95; b) D. Richter, N. Hampel, T. Singer, A. R. Ofial, H. Mayr, *Eur. J. Org. Chem.* **2009**, 3203–3211.

[16] a) T. Lemek, H. Mayr, *J. Org. Chem.* **2003**, *68*, 6880–6886; b) F. Seeliger, S. T. A. Berger, G. Y. Remennikov, K. Polborn, H. Mayr, *J. Org. Chem.* **2007**, *72*, 9170–9180; c) S. T. A. Berger, F. H. Seeliger, F. Hofbauer, H. Mayr, *Org. Biomol. Chem.* **2007**, *5*, 3020–3026; d) O. Kaumanns, R. Lucius, H. Mayr, *Chem. Eur. J.* **2008**, *14*, 9675–9682; e) O. Kaumanns, H. Mayr, *J. Org. Chem.* **2008**, *73*, 2738–2745.

[17] T. Bug, H. Mayr, *J. Am. Chem. Soc.* **2003**, *125*, 12980–12986.

[18] S. T. A. Berger, T. Lemek, H. Mayr, *ARKIVOC* **2008**, (*x*), 37–53.

[19] a) M. Baidya, S. Kobayashi, F. Brotzel, U. Schmidhammer, E. Riedle, H. Mayr, *Angew. Chem.* **2007**, *119*, 6288–6292; *Angew. Chem. Int. Ed.* **2007**, *46*, 6176–6179; b) F. Brotzel, B. Kempf, T. Singer, H. Zipse, H. Mayr, *Chem. Eur. J.* **2007**, *13*, 336–345.

[20] a) R. A. More O'Ferrall, *J. Chem. Soc. B* **1970**, 274–277; b) W. P. Jencks, *Chem. Rev.* **1972**, *72*, 705–718; c) W. P. Jencks, *Acc. Chem. Res.* **1980**, *13*, 161–169.

[21] For nucleophilicity and electrophilicity parameters see the database on the WWW: http://www.cup.lmu.de/oc/mayr.

Received: September 9, 2009
Revised: October 7, 2009