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Nucleophilic β-Oniovinylation: Concept, Mechanism, Scope, and Applications

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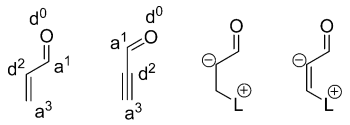
Abstract: Insertion of an electron-deficient alkyne A−C≡C−A (A = CO_2Me) into the C−L^+ bond of an acyl-onio salt R−C(O)−L^+ (R = Ar, OAlk; L = 4-dimethylaminopyridine, PPh_3) has for the first time been achieved in the presence of catalytic amounts of the nucleophile L. For R = OMe, a second insertion of the alkyne was observed. X-ray structures were obtained for a number of such β-oniovinylation products. Depending on reaction conditions, preferentially *E*- or *Z*-stereochemistry was observed, the *Z*-isomer being the thermodynamically more stable. A mechanism for this novel insertion reaction is presented which accounts for the topology of the products and rationalizes the observed stereochemistry. The β-onio-activated Michael systems thus generated represent a virtually unexplored class of compounds. The onio substituent in such compounds can be selectively replaced by a number of nucleophiles. Thus a series of Michael systems with donor functions in the β-position is easily synthesized. These compounds represent a source for useful further transformations, for example, cyclizations to quinolones, thiochromones, and pyrazoles.

Introduction

α,β-Unsaturated carbonyl compounds **1** and **2** count among the most important substrates in organic synthesis. Their d^0-, a^1-, and a^3-reactivities[1] belong to the classical repertoire of organic synthesis. However, d^2-reactivity at the α-position (cf. **1**, **2**; Chart 1) of these carbonyl compounds is completely underdeveloped and usually remains dormant. In their pioneering work, Morita et al.,[2] Baylis and Hillman,[3] and Rauhut and Carrier[4] as well as many subsequent workers[5] have demonstrated that d^2-reactivity can be brought to the fore in these (and electronically related) compounds by addition of catalytic amounts of nucleophiles L (normally tertiary amines and phosphines). E1cb-type intermediates **3** and **4** act as d^2-reagents in subsequent reactions with electrophiles. The vast majority of such reactions have been performed with systems **1**; comparatively few have been performed with systems **2**.

Without exception, all products thus obtained derive from addition reactions[6] of intermediates of type **3** or **4**. α-Hydroxyalkylation products are thus obtained with aldehydes and ketones as standard electrophiles. To the best of our knowledge, no substitution reactions on appropriate electrophilic centers have been performed with d^2-reagents of type **3** and **4**. The most obvious problem with this latter reaction category is the danger of rapid irreversible consumption of L by substitution reactions involving L and the substitutable electrophilic center in question, before d^2-nucleophiles such as **3** and **4** are formed to any reasonable amount in equilibrium concentrations. Thus a conventional attempt to acylate intermediates **3** and **4** by using acid halides as electrophiles is problematic, since the latter are much stronger electrophiles than Michael systems and will successfully compete for L under formation of acyl-onio salts. We envisaged that this difficulty might be overcome by reacting stoichiometric amounts of presynthesized acyl-onio salts[7] with

Chart 1. Structural Examples for Systems **1** and **2**, Which Can Be Activated with Regard to Their d^2-Reactivity by Nucleophiles L (**3**, **4**)



1 **2** **3** **4**

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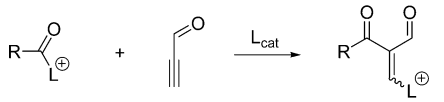
(1) Seebach, D. *Angew. Chem.* **1979**, *91* (4), 259−278.
(2) Morita, K.; Suzuki, Z.; Hirose, H. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 2815.
(3) Baylis, A. B.; Hillman, M. E. D. German Patent 2155113, 1972; *Chem. Abstr.* **1972**, *77*, 34174q.
(4) Rauhut, M.; Currier, H. U.S. Patent 3074999, 1963; *Chem. Abstr.* **1963**, *58*, 11224a.
(5) Basavaiah, D.; Rao, A. J.; Satyanarayana, T. *Chem. Rev.* **2003**, *103*, 811−891.
(6) (a) Winterfeldt, E. *Chem. Ber.* **1965**, *98*, 1581−1587. (b) Winterfeldt, E. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 423−434. (c) Nozaki, K.; Sato, N.; Ikeda, K.; Takaya, H. *J. Org. Chem.* **1996**, *61*, 4516−4519. (d) Johnson, A. W.; Tebby, J. C. *J. Chem. Soc.* **1961**, 2126−2130. (e) Nair, V.; Rajesh, C.; Vinod, A. U.; Bindu, S.; Sreekanth, A. R.; Mathen, J. S.; Balagopal, L. *Acc. Chem. Res.* **2003**, *36*, 899−907. (f) Nair, V.; Menon, R. S.; Sreekanth, A. R.; Abhilash, N.; Biju, A. T. *Acc. Chem. Res.* **2006**, *39*, 520−530.
(7) Steglich, W.; Hoefle, G. *Angew. Chem., Int. Ed. Engl.* **1969**, *8* (12), 981.

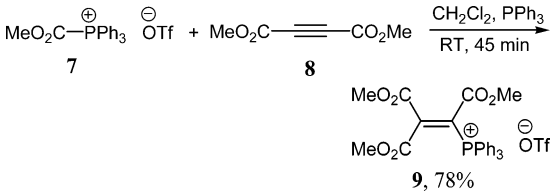
10.1021/ja071316a CCC: $40.75

Scheme 1. General Reaction Scheme for Catalytic Insertion of an Electron-Deficient Alkyne **2** into an Onio-Activated Acyl Compound **5** by Employing a^3- and d^2-Reactivity of a Michael System



5 **2** **6**

Scheme 2. Formation of **9**



7 **8** **9**, 78%

Michael systems in the presence of catalytic amounts of L according to Scheme 1.

This reaction mode would maintain a stationary concentration of the nucleophilic catalyst L, as its attack on the strong electrophile **5** would regenerate L in a self-exchange reaction. Consequently, a unique situation arises in that L serves the double purpose of simultaneously increasing the a^1-reactivity of the acylating agent[7] and the d^2-reactivity of the Michael system. Furthermore, this type of reaction would be both stoichiometric and catalytic in L.

Formation of **6** amounts to an insertion of an electron-deficient alkyne into the $C-L^+$ bond of an electron-deficient acyl-onio component. To the best of our knowledge, this type of reaction has so far never been reported. The presumed product **6** is of considerable interest in itself since it represents a vinylogous acyl-onio compound, a virtually unexplored type of electrostatically activated Michael acceptors.

We have addressed this problem by reaction of structurally defined acyl-onio salts as substitutable electrophiles with representatives of d^2-nucleophiles of type **4** (generated in situ from the corresponding electron-deficient alkyne **2**) in prototypical model reactions. Subsequently we report on results and insights obtained in the course of these investigations.

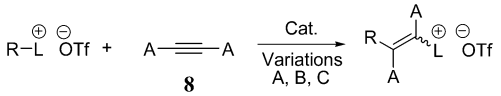
Results and Discussion

As a first model investigation for the insertion reaction considered in Scheme 1, we synthesized the (methoxycarbonyl)-triphenylphosphonium triflate **7** according to the SASAPOS protocol[8] and reacted it with dimethyl acetylenedicarboxylate **8** (DMAD) in the presence of a catalytic amount (2%) of PPh_3. Under mild conditions (CH_2Cl_2, room temperature, <1 h) the desired insertion reaction could indeed be observed, the β-onio-substituted Michael system **9** being the sole reaction product (Scheme 2). In the absence of PPh_3, the product did not form.

Even though the cation of compound **9** has been made before by Shaw et al.,[9] this new synthetic method is a progressive path, as no delicate methylation process involving highly toxic reactants is needed anymore. The reaction product **9** was fully characterized (cf. Experimental Section), including an X-ray structural analysis (Figure S1, Supporting Information).

(8) Weiss, R.; Pühlhofer, F. *Angew. Chem., Int. Ed.* **2002**, *41* (20), 3815−3817.
(9) Shaw, M. A.; Tebby, J. C.; Ronayne, J.; Williams, D. H. *J. Chem. Soc. C* **1967**, *10*, 944−947.

Scheme 3. General Reaction Equation for the Formation of Vinylonio Compounds[a]



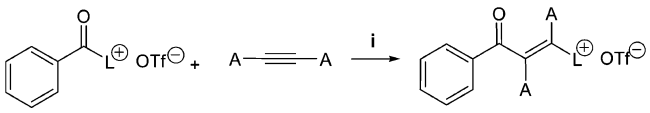
8

[a] A = CO_2Me; OTf^- (triflate) = $CF_3SO_3^-$; L = PPh_3, 4-dimethylaminopyridine (DMAP).

Table 1. Different Combinations of Reagents in the NOV Reaction Shown in Scheme 3

variations	L	catalyst
type A	PPh_3	PPh_3
type B	DMAP	PPh_3
type C	DMAP	DMAP

Scheme 4. Formation of **10Z**[a]



8 **10Z**

[a] L = DMAP, A = CO_2Me. (i) CH_2Cl_2, PPh_3 (cat.), room temperature, 16 h, 84%.

The reaction shown in Scheme 2 is considered proof of principle for a novel synthetically useful type of nucleophilic substitution that amounts to an insertion of an electron-deficient alkyne into the C−L bond of a highly electrophilic $R-C(O)-L^+$ system under the mediating influence of nucleophile L. To the best of our knowledge, this reaction type is without precedence in the literature. We have termed it nucleophilic (β)-oniovinylation (NOV).

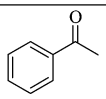
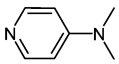
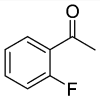
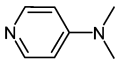
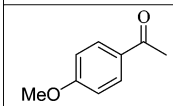
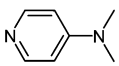
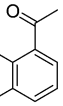
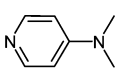
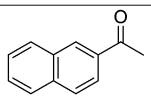
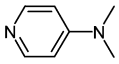
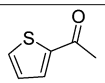
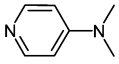
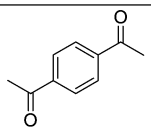
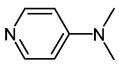
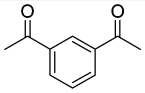
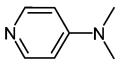
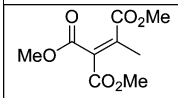
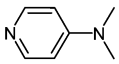
As there are obviously no stereoisomers in the example presented above, it is not possible at this point to discuss stereochemical aspects (syn vs anti addition to the triple bond) of this novel reaction. These and other mechanistic aspects of this reaction are addressed below.

The NOV protocol was successfully applied to a number of other onio-activated electrophiles. A general reaction equation is shown in Scheme 3. Three types of general reaction procedures can be distinguished, depending on substrate and catalyst (Table 1). One example for type B is formation of the β-oniovinylation product **10Z** from benzoyl(4-dimethylaminopyridinio) triflate (Scheme 4; Figure S2, Supporting Information). This reaction is useful for a first view on the addition pattern (to the acetylene) being applied during the NOV reaction, as in **10Z** the substituents at the initial d^2-position of the acetylene can be distinguished.

As can be seen from the structural plot, the stereochemistry of **10Z** indicates anti addition to the acetylene. NMR data prove that the reaction product consists of only one isomer. In this case stereochemistry is clearly specified as the result of an anti addition to DMAD. The two ester groups are almost coplanar with the ethylene unit (twisted only by 2° and 14°), but bond lengths for the DMAD backbone are almost the same as in **9**. The torsional angle between the π-systems of ethylene and benzoyl is 86°. The exocyclic $C-NMe_2$ bond indicates a high degree of double-bond character (1.333 Å), at the expense of the aromaticity of the pyridinium substituent.

A number of further substrates could be shown to react in the same way (cf. Table 2). Some of the products mentioned

Table 2. Summary of Successful NOV Reactions (see Scheme 3)

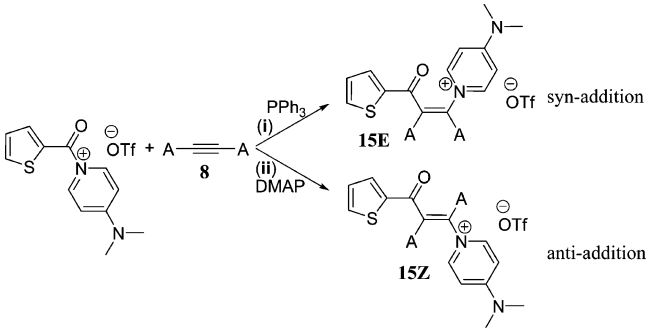
R –	L	Product	Method cf. table **1**	Stereochemistry	Yield %	X-Ray
		**10Z** **10E**	B B	Z mixture	84 79	+ + (E)
		**11**	C	Z	39	+
		**12**	B	Z	73	+
		**13Z** **13E**	C B	Z E / (mixture)	80 25 / (73)	– +
		**14**	B	Z	79	+
		**15Z** **15E**	C B	Z E / (mixture)	68 21 / (77)	+ +
		**16**	C	Z, Z	77	+
		**17**	C		40	–
	PPh_3	**9**	A	–	78	+
		**18**	B	Z	79	+
	PPh_3	**19**	A	Z	55	(–)

are useful for a closer look at the reaction characteristics of NOV.

For some products of the β-oniovinylation, ^{13}C NMR and X-ray analysis proved the exclusive formation of one of the two configurational isomers. To a certain extent these results classify the β-oniovinylation as a stereospecific anti addition with respect to DMAD **8**. However, there are results contradicting this simple proposition: In some cases mixtures of syn (*E*) and anti (*Z*) addition product and even pure compounds of the syn addition pattern were obtained. *N*-[2-(2-thienylcarbonyl)-1,2-di(methoxycarbonyl)ethenyl]-4-dimethylaminopyridinio triflate could be isolated as a pure *E* (**15E**) or *Z* compound (**15Z**) by simple variation of the catalyst (PPh_3 yielding *E* vs DMAP yielding *Z*; Scheme 5). Compounds **15E** and **15Z** have been fully characterized, including X-ray analysis.

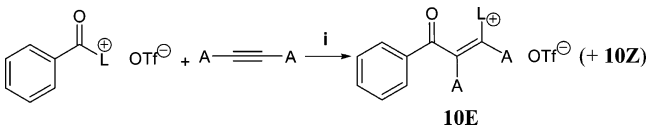
Experimental results suggest that short reaction times and PPh_3-catalysis are the key for the formation of anti addition products. By application of this method to benzoyl(4-dimethylaminopyridinio) triflate, the *E*-compound **10E** could be obtained (Scheme 6; Figure S3, Supporting Information) and fully characterized. However, it was mixed with the corresponding *Z*-compound **10Z.**

Scheme 5. Selective Formation of Two Stereochemically Alternative Vinylonio Products from the Same Substrate[a]



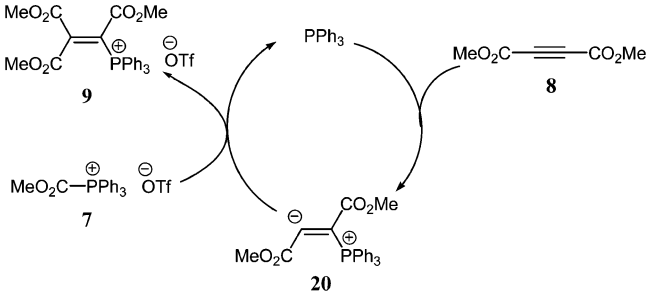
[a] Reactions were carried out in CH_3CN at room temperature. (i) PPh_3 (2.3 mol %), 2 h, 21%; (ii) DMAP (8.8 mol %), 3 days, 68%. A = CO_2Me.

Scheme 6. Formation of **10E**[a]



[a] L = DMAP, A = CO_2Me. (i) CH_2Cl_2, PPh_3 (cat.), room temperature, 10 min, 84%. The short reaction time allows us to obtain the major part as the *E*-product **10E** (*E*/*Z* = 3:1). Overall yield is 79%.

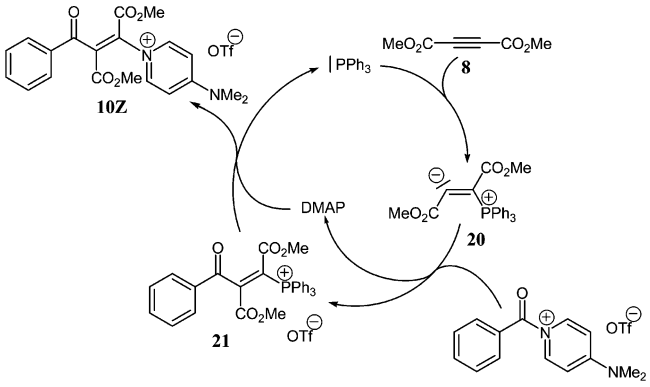
Scheme 7. Proposed Catalytic Cycle for Formation of **9**



Mechanistic Considerations. First we refer to the most simple NOV reaction (type A) shown in Scheme 2. For this reaction we propose the reaction mechanism given in Scheme 7. The initial step is the attack of the primary nucleophile PPh_3 on the acetylene **8**, generating **20** and activating d^2-reactivity of the acetylene. The intermediate **20** reacts fast, attacking the electrophilic carbonyl center of the acyl-phosphonio precursor **7**. In a proposed addition−elimination process, the product **9** is formed and the catalyst PPh_3 is liberated. (The liberated PPh_3 molecule is not identical to the one that initiated the reaction!) This reaction is significantly faster than the possible side reaction of **20** with another PPh_3 molecule forming a stable 2:1 compound of PPh_3 and DMAD previously described by Shaw et al.[9]

A different proposition has to be made for the reaction sequence and especially the role of the catalyst PPh_3 in the case of DMAP as onio ligand (type B). The reaction sequence is similar to type A, up to the formation of a vinylphosphonio intermediate **21** and liberation of the initial onio ligand DMAP. At least one more reaction step has to be explained as the primary nucleophile (catalyst PPh_3) cannot keep its position after the NOV reaction and is replaced by the liberated pyridine: The C−N bond is lower in energy compared to the C−P bond, thus the substitution fits expectations. Consequently, the final product is **10Z** instead of **21**. The catalyst is regenerated for further catalytic cycles (Scheme 8).

Scheme 8. Catalytic Cycle for Formation of **10Z**



There is some evidence that the initial product from the catalytic cycle in Scheme **8** is the syn addition product **10E**. This could be due to a S_N2-type phosphine/pyridine exchange reaction (instead of addition−elimination). Studies by Rappoport[10] suggest that such substitutions at a Michael position are very fast and thus S_N2-like. For that reason, inversion at the reaction center has to be expected.

In self-exchange experiments it could be shown that the anti addition product is the thermodynamic product. It is very likely that the occurrence of the anti addition product is due to some free DMAP in the reaction mixture because of impurity of the precursor. This is how both appearance and disappearance of *E*-products like **15E** and **10E** can be explained.

Bifunctional and Repetitive NOV. The described NOV reaction pattern has also been applied both to bifunctional aroylonio compounds and to products of NOV (cf. Table 2). Some compounds could be obtained that showed two vinylonio functions or proved repetitive NOV reaction. One of them is *Z*,*Z*-1,4-phenylenebis[[2-(4-dimethylaminopyridinio)-1,2-di-(methoxycarbonyl)ethenyl]carbonyl] bistriflate **16**. It can be obtained from 1,4-phenylenebis[(4-dimethylaminopyridinio)-carbonyl] bistriflate **22**, applying reaction conditions of type C (Scheme 9). The bis(vinylonio) product **16** was fully characterized, including X-ray analysis.

Compound **23** is unique, as it is the only electrophile for NOV with a non-acylic reaction center (cf. Scheme 1 vs Scheme 3). Related research by Nair et al.[11] shows that carbonyl groups, not Michael positions, are the appropriate reaction partners for composite nucleophiles like **20**. The reactivity of **23** is probably due to the deactivation of the carbonyl function in the ester groups combined with the high electron deficit of the ethene. Compound **23** is thus the only compound so far to which the vinylonio reaction could be applied one more time, forming the product **18** (Scheme 10). This reaction can be considered as similar to the nucleophilic (e.g., anionic) induced polymerization of acetylenes. However, **18** (Figure S4, Supporting Information) does not react with DMAD anymore. No product with three (or more) DMAD units can be found. This is quite remarkable, as intuition suggests that further insertions should be even easier the longer the chain gets: the conjugated π-system should attract reactions because of its reduced lowest unoccupied molecular

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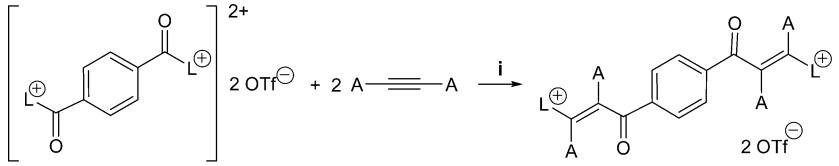
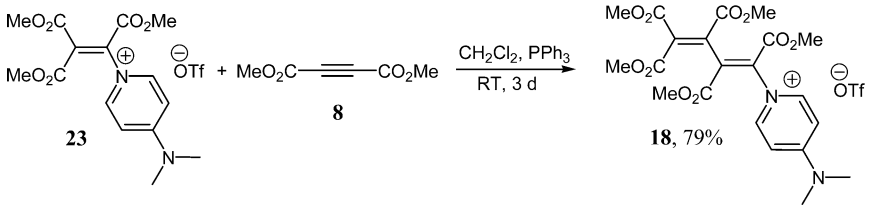
Scheme 9. Repetitive (Bifunctional) β-Oniovinylation[a]

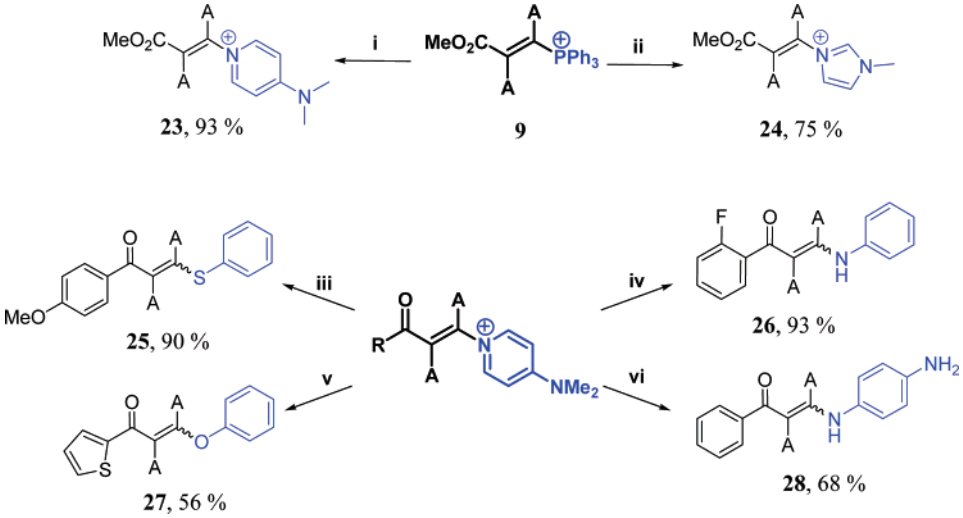


[a] A = CO_2Me, L = DMAP. (i) CH_3CN, DMAP (cat.), room temperature, 4 days, 77%.

Scheme 10. Repetitive β-Oniovinylation by Insertion of DMAD into an Already Existing Vinylonio Function



Scheme 11. Characteristic Nucleophilic Substitution Reactions in Some Vinylonio Compounds[a]



[a] A = CO_2Me. (i) DMAP, 16 h; (ii) *N*-methylimidazole, 30 min; (iii) R = 4-methoxyphenyl or thiophenol, 1 h, −DMAPH$^+$; (iv) R = 2-fluorophenyl or aniline, 12 h, −DMAPH$^+$; (v) R = 2-thienyl or phenol, DBU, 3 days, − DMAPH$^+$; (vi) R = phenyl or p-phenylenediamine, 12 h, −DMAPH$^+$. All reactions were carried out at room temperature. Anion: $CF_3SO_3^-$.

orbital (LUMO). But this assumption is invalid in case of **18**, as π-conjugation is very poor (cf. Figure S4). Additionally, the steric situation of the desired reaction center does not offer a trajectory for the bulky composite nucleophile.

Applications/Simple Derivatizations. Due to the β-vinylonio compounds being highly functionalized, a variety of subsequent reactions can be envisaged, bringing new derivatives of Michael systems into reach. A first impression of compounds accessible by nucleophilic substitution of the onio substituent at the Michael position is given by the examples in Scheme 11. Two types of such derivatizations can be distinguished: (a) onio exchange and (b) substitution with protic nucleophiles.

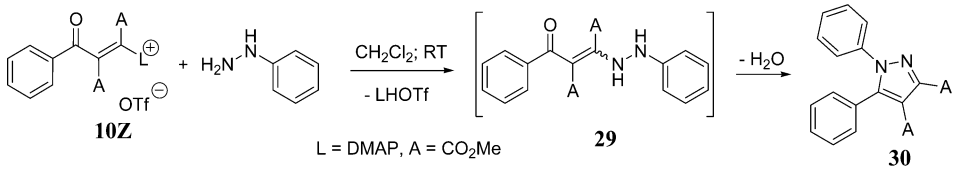
(a) Onio exchange (i and ii in Scheme 11): The phosphonio substituent in the vinylphosphonio compound **9** can be exchanged against other nucleophiles like DMAP and *N*-methylimidazole. This has already been implied to explain the catalytic function of PPh_3 in the formation of vinylpyridinio compounds according to Scheme 8. Thus compounds **23** and **24** are accessible. They have been fully characterized, including X-ray analysis.

(b) Reaction of vinyl-DMAP-onio compounds with nucleophiles of type H-Nu (O-, S-, and N-based nucleophiles; iii−vi in Scheme 11). The vinylonio systems are transformed into neutral push−pull derivatives. As a byproduct, DMAPH$^+$OTf$^-$ is formed. These reactions yield a mixture of *E* and *Z* products. This can be shown by doubled signal sets in all the NMR spectra.

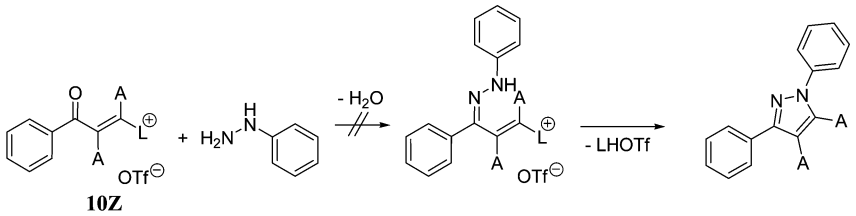
More Complex Derivatizations. In some cases the substitution of L$^+$ described above is followed by a intramolecular reaction. We thus could obtain N- and S-heterocyclic compounds (pyrazoles, quinolones, and a thiochromone).

New Pyrazole Synthesis. 1-Phenylpyrazoles can be obtained from vinylonio compounds **10Z** and **16** by treatment with phenylhydrazine. Compound **10Z** gave a dimethyl diphenylpyrazoledicarboxylate **30** (Scheme 12). The hydrazine substitutes the onio ligand L followed by deprotonation and an intramolecular condensation reaction of the intermediate **29**, giving dimethyl 1,5-diphenylpyrazole-3,4-dicarboxylate **30**. NMR spectra and X-ray analysis show that only one regioisomer is formed (Figure S5, Supporting Information). This gives evidence that the nucleophilic substitution of the onio ligand is significantly faster than a conceivable formation of the corresponding hydrazone. This mechanistic pathway is discredited because it

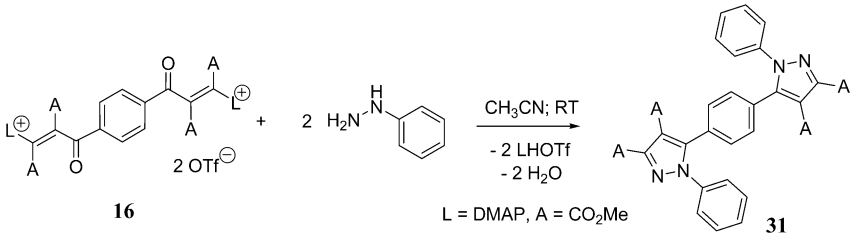
Scheme 12. Reaction of **10Z** with Phenylhydrazine



Scheme 13. Alternative Reaction Pathway of **10Z** with Phenylhydrazine, Showing That the Isolated Product **30** Excludes This Mechanism Because of Its Regiochemistry



Scheme 14. Reaction of **16** with Phenylhydrazine



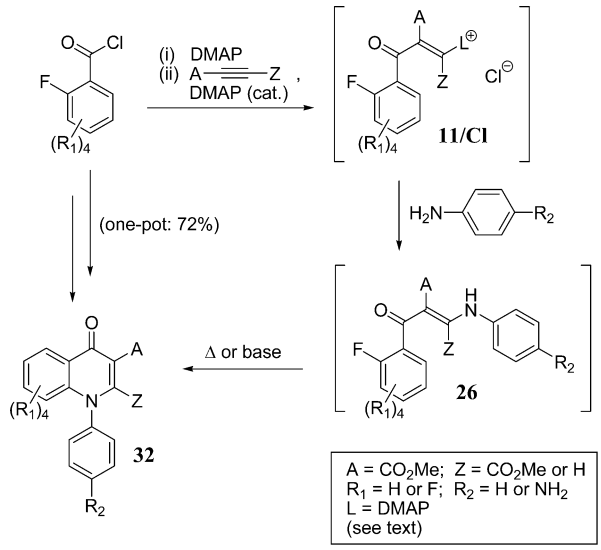
would give dimethyl 1,3-diphenylpyrazole-4,5-dicarboxylate rather than the actual product, **30** (Scheme 13).

The new protocol for pyrazole synthesis in Scheme 12 can also be applied multiple times within the same molecule (Scheme 14). After column chromatography (SiO_2), only one regioisomer (**31**) was detected. The position of the phenyl groups was determined by ^{1}H nuclear Overhauser effect (NOE) NMR (500 MHz). Together with the crystallographic data provided above, it proves the regioselectivity of this new pyrazole synthesis. Due to the high reactivity of the vinylonio intermediates, pyrazole formation can be achieved under mild conditions. Thus this new synthetic approach is likely to be useful for the synthesis of substituted pyrazoles with delicate functional groups.

New Quinolone and Thiochromone Synthesis. Further reactions on NOV products were carried out with aniline or its derivatives as nucleophiles. For instance, starting from the 2-fluorobenzoylvinylonio system **11**/OTf, the corresponding neutral product **26** could be obtained as an *E*/*Z* mixture in a 2:1 ratio (yield 82%, white solid). Refluxing of **26** in acetonitrile for 2 days or its treatment with base (*n*-butyllithium) led to the formation of quinolone **32** in high yields (reflux 92%, base 69%) via nucleophilic aromatic substitution of the fluoride by the amine group (cf. Scheme 15).

On the basis of these findings, we were able to derive a novel one-pot quinolone synthesis. Starting from 2-fluorobenzoyl chloride, the intermediate vinylonio species **11**/Cl was generated in situ by addition of (i) DMAP and (ii, after 1 h) DMAD with a catalytic amount of DMAP. Further addition of aniline (or one of its derivatives) and treatment with *n*-butyllithium gave the quinolone product **32** (Z = CO_2Me) (yield 72%; isolation via column chromatography). It was completely characterized,

Scheme 15. Quinolone Synthesis

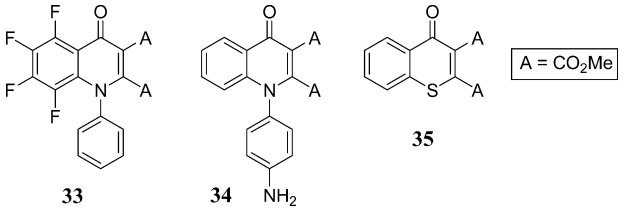


including an X-ray analysis (cf. Figure S6, Supporting Information).

Using this procedure (albeit partly via isolating some of the intermediate products), we also synthesized products **33**−**35** (cf. Chart 2) by variation of the starting electrophile (**33**, overall yield 33%) or the substituting nucleophile (**34**, yield 60%; **35**, yield 25%). Thiochromone **35** was also characterized by X-ray analysis.

When methyl propiolate was used as the acetylene component (Z = H), only moderate to low yields were obtained (one-pot quinolone synthesis, 35%), compared to DMAD as electrophilic substituent. This is probably due to the deprotonation of the acidic acetylene proton by the intermediately formed composite

Chart 2. Quinolones **33** and **34** and Thiochromone **35**



nucleophile. Unfortunately, methyl 3-(trimethylsilyl)propiolate (Z = TMS) did not undergo any vinylonio reaction.

Yet, as the decarboxylation of quinolones of type **32** at C2 is known from the literature to be simple and highly effective,[12] the above-mentioned method provides a novel synthetic approach to modern fluoroquinolone antibiotics (which bear a hydrogen substituent at C2 as well as a carboxy group at C3). These constitute the most important class of antiobiotics used today, curing a wide variety of diseases.[13] In comparison to the currently used syntheses for fluoroquinolones, namely, the Gould−Jacobs[14] and especially the Grohe[15] method, the synthetic route introduced above features some distinctive advantages: in addition to the mild reaction conditions, the one-pot approach, and the favorable "atom economy", it should be possible to introduce very weakly nucleophilic amines at **11**/Cl, due to the strong electrostatic activation by the onio ligand (which is also a much better leaving group compared to alkoxy or dimethylamino substituents employed by the established Grohe method[15]). Hence, in addition to the advantages, our method has the potential to increase the range of accessible fluoroquinolones (especially those with weakly nucleophilic amines introduced at N1 and those bearing a substituent at C2 that can be derived from a carboxymethyl group), thus enabling the development and testing of prospective structures for novel antibiotics.

Conclusion

Nucleophilic β-oniovinylation (NOV), as presented in this paper, constitutes a novel synthetic method for the preparation of (formerly almost unknown) β-onio-activated Michael systems. The products are obtained under mild conditions from onio derivatives of carboxylic acids, DMAD, and catalytic amounts of either DMAP or PPh_3, making use of the alkyne's implicit d^2-reactivity. As the products are highly functionalized, they are themselves the starting points for further subsequent reactions and syntheses. A few first examples were presented in this paper, namely, the synthesis of pyrazoles and quinolones, and a wide array of heterocycles may be accessible via this route.

During our investigations we also came upon some limitations of NOV. With regard to aliphatic carboxylic acid derivatives as substrates, acetic acid chloride (as well as trichloroacetic acid chloride) proved to be incompatible with NOV, as a proton (or chloro substituent) at the α carbon was attacked by the composite nucleophile (methoxyacetic acid was compatible, though). With respect to aromatic carboxylic acid derivatives, nucleophilic heteroatoms (like N) within the aromatic could lead to unwanted intramolecular reactions. In addition, strongly electron-donating groups or strongly electron-withdrawing substituents at the aromatic should be avoided, as they might lead to Friedel−Crafts-like reactions with DMAD or might create further centers for nucleophilic attack (respectively). An NOV-like reactivity of alkenes **1** instead of DMAD could not be provoked.

Further investigations into NOV will very likely reveal more applications of this method and will equally likely develop a more precise idea of its limitations.

Experimental Section

Unless otherwise stated, all manipulations were performed under an inert atmosphere of nitrogen via standard Schlenk techniques. Dry solvents were employed throughout.

1,2,2-Tri(methoxycarbonyl)ethenyltriphenylphosphonio triflate (9). The employed compound **7** was prepared in situ by addition of 1.404 g (5.35 mmol) triphenylphosphine to a solution of 0.39 mL (5.07 mmol) of methyl chloroformate and 0.92 mL (5.09 mmol) (trimethylsilyl)trifluoromethanesulfonate in CH_2Cl_2 at room temperature. On addition of 0.62 mL (5.07 mmol) of dimethyl acetylenedicarboxylate, the color of the solution turns to orange and considerable heat develops. The product **9** precipitates on addition of Et_2O. It is filtered and washed with a mixture of CH_2Cl_2 and Et_2O 1:1. Yield: 2.330 g (75%) colorless powder. *M* ($C_{27}H_{24}F_3O_9PS$) = 612.52. FAB-MS: 463 (**9** − OTf^-). IR (KBr): 2959 (w), 1742 (s), 1439 (m), 1265 (br, vs), 1170 (w), 1104 (m), 1030 (m), 1011 (w), 900 (w), 863 (w), 755 (w), 723 (w), 691 (w), 637 (m), 572 (w), 517 (m). ^{1}H NMR ($CDCl_3$): 7.72 (m, 15H), 3.85 (s, 3H, O*Me*), 3.37 (s, 3H, O*Me*), 3.08 (s, 3H, O*Me*). ^{13}C NMR ($CDCl_3$): 161.77 (d, *C*O), 160.85 (d, *C*O), 160.28 (d, *C*O), 144.20, 136.12, 134.09, 131.79, 130.44, 120.72 [q, ^1J(C−F) = −321 Hz, *C*$F_3SO_3^-$], 114.84, 54.49 (s, O*Me*), 54.11 (s, O*Me*), 53.78 (s, O*Me*). Anal. $C_{27}H_{24}F_3O_9PS$: calcd C 52.95, H 3.95, S 5.23; found C 52.60, H 4.36, S 5.19.

Dimethyl 1,5-Diphenylpyrazole-3,4-dicarboxylate (30). A solution of 639 mg (1.23 mmol) of (*Z*)-*N*-[2-benzoyl-1,2-di(methoxycarbonyl)-ethenyl]-4-dimethylaminopyridinio triflate **10Z** in 15 mL of CH_2Cl_2 is treated with 0.12 mL (1.21 mmol) of phenylhydrazine at room temperature. After 15 h the solvent was removed and the product was isolated by column chromatography (mobile phase, hexane/ethyl acetate 1:1). Yield: 204 mg (49%) yellow crystals. *M* ($C_{19}H_{16}N_2O_4$) = 336.34. FAB-MS: 337 (**30** + H^+), 305 (**30** − MeO^-). IR (KBr): 1723 (m), 1500 (w), 1401 (br, vs), 1330 (w), 1317 (w), 1261 (w), 1225 (m), 1079 (m), 969 (w), 792 (w), 762 (w), 696 (w). ^{1}H NMR ($CDCl_3$): 7.34 (m, br, 10H, *Ar*), 3.93 (s, 3H, O*Me*), 3.72 (s, 3H, O*Me*). ^{13}C NMR ($CDCl_3$): 163.32, 162.14, 144.68, 143.00, 138.41, 129.87, 129.37, 128.82, 128.47, 128.22, 127.61, 125.45, 115.38, 52.48, 52.10. Anal. $C_{19}H_{16}N_2O_4$: calcd C 67.85, H 4.79, N 8.33; found C 67.51, H 4.78, N 8.17.

Dimethyl 4-Oxo-1-phenyl-1,4-dihydroquinoline-2,3-dicarboxylate (32; $R_1 = R_2 = H$, $Z = CO_2Me$). (a) From **26** ($R_1 = R_2 = H$, $Z = CO_2Me$), by use of base (*n*-BuLi): A solution of 533 mg (1.49 mmol) of **26** in 20 mL of CH_2Cl_2 was cooled to −78 °C and treated with 1.05 mL of a 1.6 M solution of *n*-butyllithium in hexanes (corresponding to 1.68 mmol of butyllithium). After being stirred for 60 min, the solution was warmed to room temperature and stirred for another 15 min. The solution was treated with 40 mL of H_2O, and the layers were separated. The organic layer was washed another three times with 40 mL of H_2O and dried over $MgSO_4$. After removal of the solvent, the product was isolated by column chromatography (mobile phase hexane/ethyl acetate 2:1, slowly more polar). Yield: 348 mg (69%), white powder. M ($C_{19}H_{15}NO_5$) = 337.33. FAB-MS: 338 (**32** + H^+). IR (KBr): 3052 (w), 2954 (w), 1744 (s), 1714 (s), 1631 (s), 1604 (s), 1536 (m), 1492 (m), 1468 (s), 1436 (m), 1330 (m), 1297 (s), 1275 (m), 1225 (s), 1174

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(w), 1158 (w), 1136 (m), 1076 (w), 1042 (m), 972 (m), 952 (w), 935 (w), 910 (w), 876 (w), 841 (w), 808 (w), 767 (s), 742 (m), 726 (w), 704 (m), 644 (w), 600 (m), 503 (w). ^{1}H NMR ($CDCl_3$): 8.50 [dd, ^3J(H−H) = 8.1 Hz, ^4J(H−H) = 1.6 Hz, 1H, C5-*H*), 7.59 (m, 3H, C3′-*H*/C4′-*H*), 7.50 [ddd, ^3J(H−H) = 7.1 Hz, ^3J(H−H) = 7.1 Hz, ^4J(H−H) = 1.6 Hz, 1H, C7-*H*], 7.40 (m, 3 H, C6-*H*/*C*2′-*H*), 6.76 [d, ^3J(H−H) = 8.1 Hz, 1H, C8-*H*], 3.92 (s, 3H, CO_2*Me*), 3.52 (s, 3H, CO_2*Me*). ^{13}C NMR ($CDCl_3$): 174.3 (*C*4), 166.0 (*C*O_2Me), 162.6 (*C*O_2Me), 149.4 (*C*2), 141.0 (*C*8a), 137.2 (*C*1′), 132.9 (*C*7), 130.5 (*C*4′), 129.9 (*C*3′), 129.4 (*C*2′), 127.4 (*C*4a), 127.1 (*C*5), 125.5 (*C*6), 118.1 (*C*8), 110.7 (*C*3), 52.9 (CO_2*Me*), 52.6 (CO_2*Me*).

(b) From **26** ($R_1 = R_2 =$ H, $Z = CO_2$Me), by use of heat: A yellow solution of 139 mg (0.39 mmol) of **26** in 15 mL of CH_3CN was heated to reflux for 2 days. After removal of the solvent, the residue was chromatographed on SiO_2 (mobile phase hexane/ethyl acetate 1:1; R_f ca. 0.15). Yield: 122 mg (93%), white powder. Analytical data as above.

(c) One-pot synthesis from 2-fluorobenzoyl chloride: A solution of 0.8 mL (6.70 mmol) of 2-fluorobenzoyl chloride in 50 mL of CH_2Cl_2 was treated with 845 mg (6.92 mmol) of DMAP, resulting in a white suspension. After the reaction mixture was stirred for 3 h, a solution of 0.84 mL (6.83 mmol) of DMAD in 20 mL of CH_2Cl_2 was slowly added dropwise, yielding a clear, red solution. After this solution was stirred for 21 h, 0.92 mL (10.1 mmol) of aniline was added dropwise. The resulting orange solution was again stirred for 2 days and cooled to −78 °C, and 5.5 mL of a 1.6 M solution of *n*-butyllithium in hexanes was added (corresponding to 8.8 mmol of *n*-butyllithium). After being stirred for 30 min, the solution was warmed to room temperature and stirred for another 22 h. The precipitate was filtered off, and after addition of 130 mL CH_2Cl_2 to the filtrate, it was treated with 80 mL of water. After separation of the layers, the organic phase was washed twice with 50 mL of water and dried over $MgSO_4$, and the solvent was evaporated. The resulting residue was chromatographed on SiO_2 (mobile phase hexane/ethyl acetate 3:2, slowly more polar until pure ethyl acetate was reached; R_f ca. 0.05). Yield: 1.61 g (71% referring to 2-fluorobenzoyl chloride), white powder. Analytical data as above. Table 3 contains the CCDC numbers for all structures mentioned in the text, sorted by the corresponding compound (as mentioned in the text).The supplementary crystallographic data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Table 3.

compd	CCDC number
9	637381
10Z	637387
10E	637378
11	637390
12	637377
13E	637385
14	637379
15Z	637386
15E	637384
16	637380
18	637383
23	637394
24	637382
25	637388
30	637393
32	637389
35	637391

Acknowledgment. S.M.H. thanks the Studienstiftung des Deutschen Volkes and the State of Bavaria (BayBFG) for scholarships. We also thank Prof. W. Bauer for the ^{1}H NOE NMR measurements and several fruitful discussions. This work is dedicated to the memory of Werner Reinhart.

Supporting Information Available: Further experimental procedures and characterization of the products, crystallographic files in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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