JOC Article

# Synthesis and Reactivity of a Novel Class of Long-Lived Ammonium Ylides: Derivatives of Benzo[*b*]pyrrolo[2,1-*f*][1.6]naphthyridine

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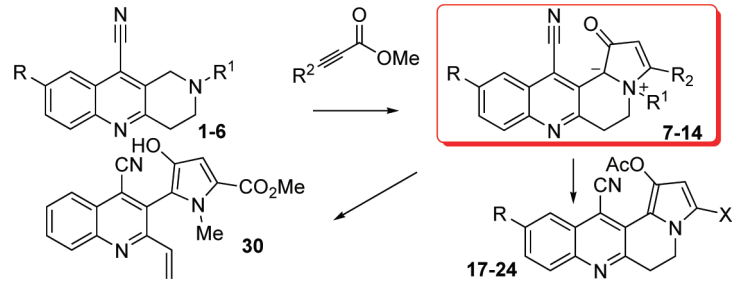


Reaction of 10-cyanotetrahydrobenzo[*b*][1,6]naphthyridines (**1**−**6**) with activated alkynes affords stable benzo[*b*]pyrrolo[2,1-*f*][1,6]naphthyridine-4-ium ylides (**7**−**14**) in moderate yields. A proposed mechanism for their formation consists of a new tandem multistage process.

## Introduction

Tandem reactions provide an opportunity for linking the synthetic power of two or more transformations in a single operation.[1,2] These reactions are among the most powerful building tools available because they rapidly increase the complexity of a substrate starting from relatively simple precursors.[3,4] Michael addition is one of the most common reaction steps in different tandem transformations.[5,6]

As a consequence of our continuing interest in the development of tandem transformations of heteroannulated tetrahydropyridines under the action of activated alkynes,[7] we studied the reaction of tetrahydrobenzonaphthyridines **1**−**6** with methyl propiolate and dimethylacetylene dicarboxylate (DMAD). We have previously reported [8]on the transformations of compounds **1** and **2** under the action of DMAD in methanol at room temperature. It was demonstrated that they undergo addition of the DMAD molecule, followed by Stevens rearrangement of the intermediate ylide, yielding methyl dioates **A**. The alternative transformation sequence starts with the migration of dimethyl butene dioate anion to the carbon of CN group, followed by the addition of 1 mol of water, thus providing succinates **B** (Scheme 1). We have also registered (in the case of **1**) the formation of a small amount of a deeply red colored byproduct, to which we were unable to assign a structure. Later on we elucidated the structure of this byproduct, a representative of a new class of long-lived ammonium ylides, and optimized the reaction conditions for its synthesis.

In this Article, we would like to report effective syntheses of benzo[*b*]pyrrolo[2,1-*f*][1,6] naphthyridine-4-ium ylides by the tandem reaction of methyl propiolate and DMAD with easily accessible 10-cyanotetrahydrobenzo[*b*][1,6]naphthyridines. Investigation of some chemical properties of these ylides is also described.

(1) Ho, T. L. In *Tandem Organic Reactions*; Wiley-Interscience: New York, 1992.
(2) Tietze, L. F.; Beifuss, U. *Angew. Chem., Int. Ed.* **1993**, *32*, 31.
(3) Ziegler, F. E. In *Comprehensive Organic Synthesis*; Paquette, L. A. Ed.; Pergamon Press: Oxford, 1991; Vol. 5, Chapter 7, p 3.
(4) (a) Tsuge, O.; Kanemasa, S.; Takenaka, S. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 2073. (b) Tsuge, O.; Kanemasa, S.; Takenaka, S. *Chem. Lett.* **1983**, 519. (c) Curran, D. P. *Synlett* **1991**, 63.
(5) For selected papers on tandem reactions involving Michael addition see: (a) Shigeta, Y.; Node, M.; Nishide, K.; Shiraki, H.; Obata, K. J. *J. Am. Chem. Soc.* **2000**, *9*, 1927. (b) Bunce, R. A.; Herron, D. M.; Ackerman, M. L. *J. Org. Chem.* **2000**, *9*, 2847. (c) Trost, B.; Yang, M.; Wuitschik, H. G. *Org. Lett.* **2005**, *21*, 4761. (d) Zu, L.; Wang, J.; Li, H.; Xie, H.; Jiang, W.; Wang, W. *J. Am. Chem. Soc.* **2007**, *5*, 1036. (e) Jauch, J. *J. Org. Chem.* **2001**, *2*, 609. (g) Stelmakh, A.; Stellfeld, T.; Kalesse, M. *Org. Lett.* **2006**, *16*, 3485.
(6) For selected reviews on tandem reactions, see: (a) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 1, 115. (b) Winkler, J. D. *Chem. Rev.* **1996**, *1*, 167.
(7) (a) Voskressensky, L. G.; Borisova, T. N.; Kulikova, L. N.; Varlamov, A. V.; Catto, M.; Altomare, C.; Carotti, A. *Eur. J. Org. Chem.* **2004**, 3128. (b) Voskressensky, L. G.; Borisova, T. N.; Kostenev, I. S.; Kulikova, L. N.; Varlamov, A. V. *Tetrahedron Lett.* **2006**, *47*, 999.
(8) Voskressensky, L. G.; Borisova, T. N.; Kostenev, I. S.; Vorobiev, I. V.; Varlamov, A. V. *Tetrahedron Lett.* **2005**, *46*, 1975.



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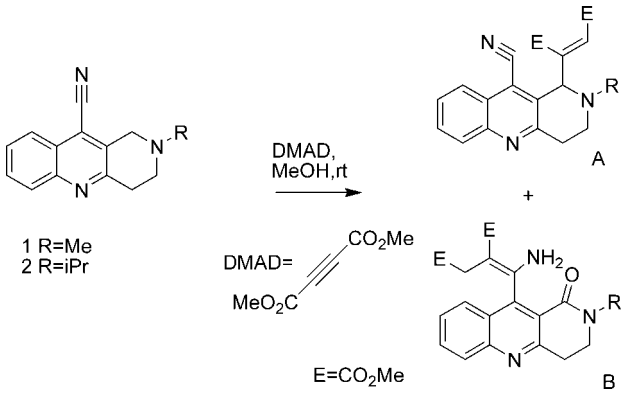
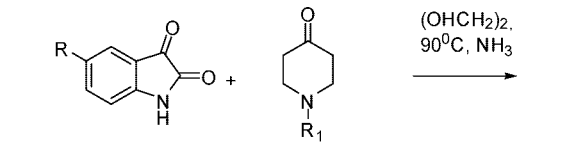
**SCHEME 1. Transformations of Tetrahydrobenzonaphthyridines 1 and 2 under the Action of DMAD**




**SCHEME 2. Synthesis of the starting materials**




**1-6**

| | R | $R^1$ | Mp ($^0$C) | Yield(%) |
|---|---|---|---|---|
| 1 | H | Me | 153-155 | 44 |
| 2 | H | *i*Pr | 110-112 | 82 |
| 3 | Br | Me | 168-170 | 32 |
| 4 | F | Me | 127-129 | 65 |
| 5 | F | *i*Pr | 93-95 | 60 |
| 6 | $NO_2$ | *i*Pr | 168-170 | 55 |

## Results and Discussion

**Synthesis of the Ylides.** The cyano-substituted tetrahydrobenzonaphthyridines (**1**−**6**), requisite for the present study, were synthesized according to the protocol previously described by condensation of isatines with $\gamma$-piperidones in the presence of gaseous ammonia (Pfitzinger reaction), followed by the dehydration reaction of the resulting 10-carbamoyl derivative[8,9] (Scheme 2).

The reaction of derivatives **1**−**6** with methyl propiolate or DMAD (1.2 molar excess) in boiling methanol for 2 h led to the formation of intensively colored (usually red or brown) powders, which were filtered off, washed with ethyl acetate, and dried on air. Our attempts to recrystallize them failed, due to the very low solubility of these compounds in common organic solvents (except for DMSO or DMF). We were also unable to elucidate their structures, based on common spectral ($^1$H, $^{13}$C NMR, mass spectra, IR) and microanalysis data. One structure was assigned unambiguously by the X-ray analysis

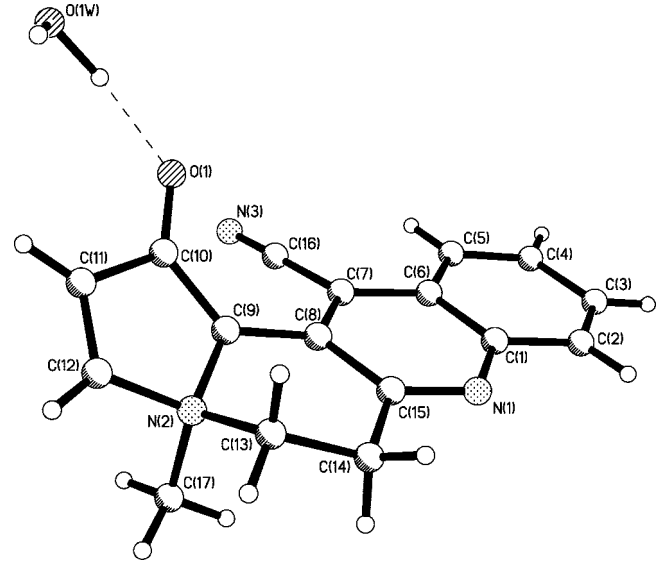



**FIGURE 1.** X-ray crystal structure of the ylide (hydrate form) **7**.

of the suitable monocrystal of the compound **7**, obtained by slow evaporation of its diluted methanolic solution (Figure 1).

The pyrroline fragment of the molecule is planar. The $N^+(2)-C(12b)$ and $N^+(2)-C(3)$ (atom numbering according to the X-ray structure in Figure 1) bond lengths (0.1480 and 0.1476 nm, respectively) are analogous to the $N^+-C$ in quaternary ammonium salts. The C═O (0.1250 nm) bond is longer than the average corresponding bond in O═C−C═C fragment (0.1215 nm) denoting its participation in the negative charge delocalization. We presume that the reaction starts with the formation of the zwitterionic intermediate **A**, the anionic part of which than cleaves one proton from the $C_1$ methelene group, thus producing ylide **B**, which can undergo two alternative transformations, Stevens rearrangement[10,11] (pathway a) or the intramolecular $S_N$ reaction (pathway b), accompanying by the elimination of the methoxide anion and pyrroline cycle formation (this process predominates under more forcing reaction conditions). We presume that the configuration of the double bond in the enamine fragment of **B** defines the reaction pathway: the *E*-configuration favors the Stevens rearrangement, while *Z*-configuration makes possible the nucleophilic attack and formation of ylides **7**−**14** (Scheme 3).

The elemental analysis of compounds **7**−**14** (see Supporting Information) shows that they did not form hydrates under the usual reaction conditions; the formation of a crystalline hydrate in the case of the ylide **7** is most likely attributed to the use of water-containing methanol for recrystallization. We failed to isolate ylide **9** in its pure form; under the reaction/separation conditions it underwent the rearrangement to give 1-hydroxy derivative **9a**, which was isolated in 63% yield. However, the formation of the ylide **9** was demonstrated by means of the NMR analysis of the reaction mixture. Later on we managed to obtain a monocrystal of water-free ylide **8,** which was analyzed by the X-ray diffraction method.

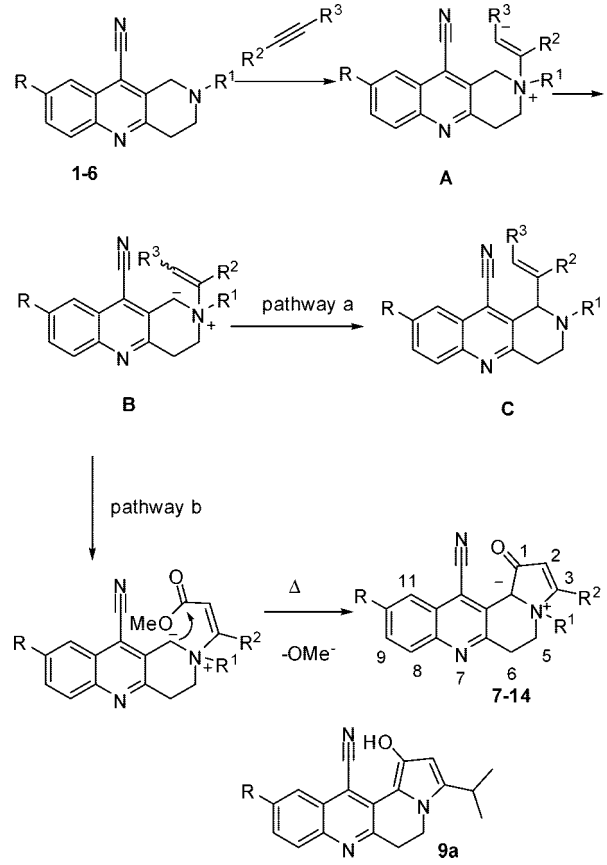
In the $^1$H NMR spectra of compounds **7**−**14**, the protons of $CH_2$-5 and $CH_2$-6 (see Scheme 3 for numbering) resonate in

(9) Gatto, F.; del-Giudice, M. R.; Mustazza, C. *J. Heterocycl. Chem.* **1996**, *33*, 1807.

(10) For selected papers on Stevens rearrangement, see: (a) Brewster, J. H.; Kline, M. M. *J. Am. Chem. Soc.* **1953**, *74*, 5179. (b) Jenney, E. F.; Druey, J. *Angew. Chem., Int. Ed.* **1962**, *1*, 155. (c) Blid, J.; Somfai, P. *Tetrahedron Lett.* **2003**, *44*, 3159.

(11) For a recent review on Stevens rearrangement, see: Vanecko, J. A.; Wan H.; West, F. G. *Tetrahedron* **2006**, *62*, 1043.

**SCHEME 3. Proposed Mechanism for the Formation of Ylides 7−14**




| | R | $R^1$ | $R^2$ | Yield % |
|---|---|---|---|---|
| 7 | H | Me | H | 27 |
| 8 | H | Me | COOMe | 45 |
| 9a | H | *i*-Pr | H | 63 |
| 10 | Br | Me | H | 21 |
| 11 | Br | Me | COOMe | 40 |
| 12 | F | Me | COOMe | 47 |
| 13 | F | *i*-Pr | H | 32 |
| 14 | $NO_2$ | *i*-Pr | H | 25 |

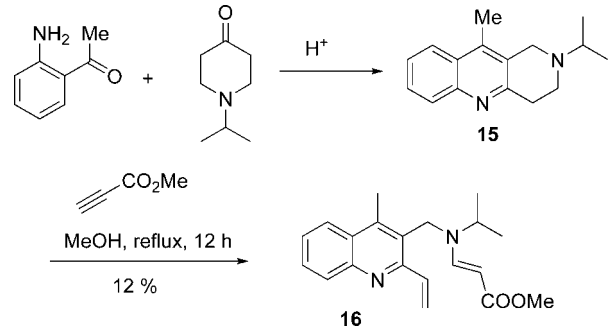
the field of 3−4.5 ppm, one of the CH-5 protons being observed as a dd signal around $\delta$ 4−4.5 ppm. $^{13}$C NMR spectra of ylides **7−14** showed the signal of C-1 carbon atom around 170 ppm, some 20 ppm lower, than the usual signals of the carbonyl carbons, once again denoting the participation of the unsaturated ketone in the negative charge delocalization. The signal of the ylidic carbon (C-12b) was registered at around 100 ppm, and this value is analogous to those reported for the quinolizinium ylides. [12]

We presumed that the presence of a strong electron-withdrawing group in position 10 of the starting tetrahydrobenzonaphthyridines is a must for this tetracyclic ylides formation. In order to confirm or disprove this presumption, we synthesized 10-methyl[13] substituted congener **15** and examined its reaction with DMAD and methyl propiolate under similar reaction conditions. Compound **15** was inert toward DMAD (only small amounts of tarring products were formed after 12 h of refluxing in dry methanol) but reacted with methyl propiolate, producing 2-vinylquinoline **16** in 12% yield (Scheme 4).

The formation of 2-vinyl quinoline derivative **16** may be explained by the alternative cleavage of the most acidic proton (C-4 methylene group) in the intermediate **D** by the in situ formed methoxide anion, provoking a Hoffman-like elimination reaction that led to the tetrahydropyridine ring cleavage (Scheme 5).

The reactivity of heterocyclic ammonium ylides has not been exhaustively studied,[14] basically due to the absence of preparative protocols for their synthesis. In this regard we were interested in examining some reactions of ylides **7−14**.

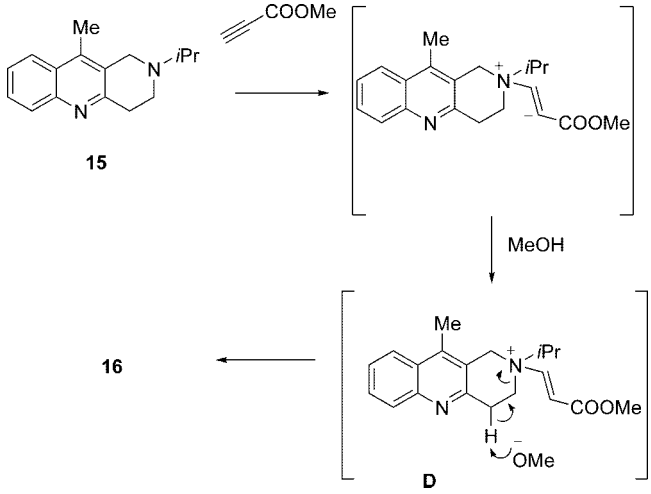
**SCHEME 4. Synthesis of 10-Methylbenzonaphthyridine 15 and Its Reaction with Methyl Propiolate**



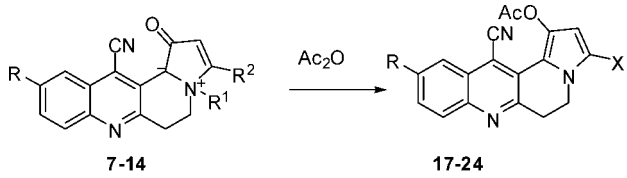

It was demonstrated that carbonyl-stabilized ammonium ylides, depending on the reaction conditions, undergo either C- or O-acylation.[15] We studied the acetylation reaction of the ylides **7−14** under the action of acetic anhydride. In all cases the O-acetylation took place, accompanied by the elimination of the *N*-Alk radical and subsequent aromatization of the pyrroline fragment, yielding 1-acetoxypyrrolo[2,1-*f*]naphthyridines **17−24** (Scheme 6). The structure of this new heterocyclic system was confirmed by the X-ray analysis of the compound **18**, obtained by recrystallization from hexanes−ethyl acetate mixture.

(12) Kostik, E. I.; Abiko, A.; Oku, A. *J. Org. Chem.* **2001**, *66*, 1638.
(13) Oka, H.; Iida, M.; Sato, J.; Hondd, M. U.S. Patent 6.294.547B.1., 2001.
(14) For selected papers on heterocyclic ammonium ylides reactivity, see: (a) Aggarwal, V. K.; Fang, G. Y.; Jonathan, P.; Charmant, H.; Graham, M. *Org. Lett.* **2003**, *5*, 1757. (b) Audrey, A.; Larmanjat, B.; Marrot, J.; Couty, F.; David, O. *Chem. Commun.* **2007**, 2500. (c) Robiette, R.; Conza, M.; Aggarwal, V. K. *Org. Biomol. Chem.* **2006**, *4*, 621.
(15) Chopard, P. A.; Searle, R. J. D.; Devitt, F. H. *J. Org. Chem.* **1965**, *30*, 1015.

**SCHEME 5. Mechanism of 2-Vinylquinoline 16 Formation.**




**SCHEME 6. Acetylation of Compounds 7−14**




| | R | X | Yield (%) |
|---|---|---|---|
| **17** | H | H | 86 |
| **18** | H | COOMe | 82 |
| **19** | H | *i*Pr | 65 |
| **20** | Br | H | 78 |
| **21** | Br | COOMe | 73 |
| **22** | F | COOMe | 75 |
| **23** | F | *i*Pr | 92 |
| **24** | $NO_2$ | *i*Pr | 61 |

The quinoline and pyrrole fragments of the tetracycle **18** are planar, the torsion angle between these planes having the value of 27°.

The acetylation of *N*-*i*Pr ylides **9**, **13**, and **14** was accompanied by the migration of the isopropyl radical to the α-position of the pyrrole ring, presumably through the formation of the quaternary salt **E** (Scheme 7).

The reactions of the ylides **7** and **8** with acid chlorides proceeded analogously, providing the tetracyclic derivatives **25**−**28** (Scheme 8).

It was reported that ammonium ylides generated in situ undergo an aldol-type reaction with aromatic aldehydes affording highly substituted amino acid frameworks in a convergent, three-component reaction.[16] A more recent paper describes the epoxidation reaction of aryl-stabilized ammonium ylides under the action of aromatic aldehydes.[17] Applying these protocols to our tetracyclic ammonium ylides could provoke the $C_{12b}$-N bond cleavage, leading to formation of the nine-membered ring (Scheme 9).

Having this idea in mind, we studied the reaction of ylides **7**, **8**, and **12** with freshly distilled benzaldehyde. In both cases the reactions required heating and took around 6 h to finish. The only products isolated were the corresponding 2-vinyl-3-pyrrolylquinolines **29**−**31**. We presume that compounds **7**, **8**, and **12** reacted in their alcoholate form **F**, accepting a proton from a molecule of benzoic acid (which resulted from the oxidation of benzaldehyde), thus forming quarternary ammonium salt **G**. The latter underwent Hoffman elimination under the action of benzoate anion, yielding 2-vinyl quinolines **29**−**31**. The control reaction of the compounds **7**, **8**, and **12** with benzoic acid led to the formation of **29**−**31** as well.

Inspection of the crystal packing of the compound **29** (suitable monocrystal was obtained by recrystallization from ethyl acetate) revealed that it consists of two crystallographically independent types of molecules, differing mainly by the bonds lengths in the pyrrole fragment. 3-Hydroxypyrrole moiety exists in its oxy-form, being stabilized by hydrogen [$OH\cdots N_{(quinoline)}$] bonding. The planes of the quinoline and pyrrole rings are almost perpendicular.

We decided to investigate the reactivity of the ammonium ylides under more forcing (classic Hoffman elimination reaction) conditions; as expected under the action of a strong base, ylide **8** underwent six-membered ring opening, providing the corresponding 2-vinyl quinoline **30** in good yields. (Scheme 10)

In conclusion, a variety of stable benzo[*b*]pyrrolo[2,1-*f*][1,6]naphthyridine-4-ium ylides, representatives of a new heterocyclic system, were synthesized in good to high yields by the reaction of acetylenic esters with easy obtainable tetrahydrobenzonaphthyridines. The plausible mechanism of this one-pot reaction includes the tandem Michael addition−Stevens rearrangement−intramolecular $S_N$ reactions sequence. The reactivity of the resulting ylides is mainly characterized by two types of transformations: (1) cleavage of the alkyl radical from the ylide nitrogen atom with concurrent addition of an electrophile to the oxygen atom, and (2) Hoffmann elimination reaction, leading to the formation of 2-vinyl quinolines with simultaneous aromatization of the pyrrolene moiety.

## Experimental Section

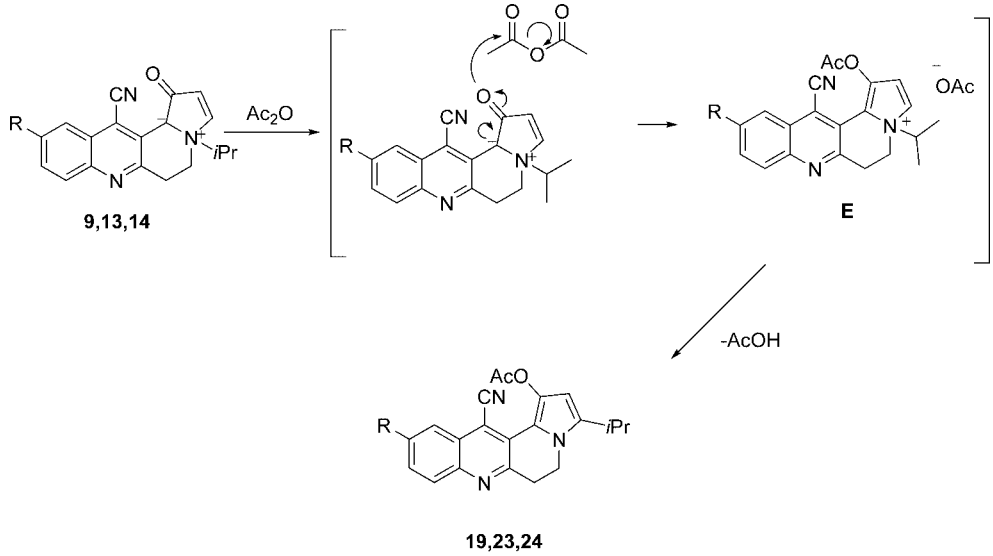
The starting 10-cyanobenzonaphthyridines **1**−**6** were synthesized according to the protocol previously described. [8,18]

**General Procedure for Synthesis of Ylides 7−14.** To the solution of the corresponding 10-cyanobenzonaphthyridine **1**−**6** (2.24 mmol) in 40 mL of methanol was added 0.48 g (3.36 mmol) of DMAD or 0.28 g (3.36 mmol) of methyl propiolate in one portion, and the reaction mixture was refluxed for 2−3 h (TLC monitoring, ethyl acetate). After the completion of the reaction, the precipitate formed was collected by filtration and dried in air .

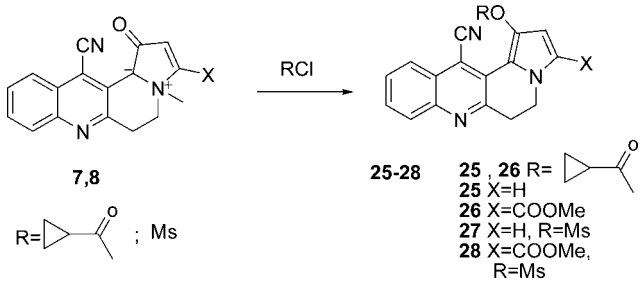
**10-Methyl-2-isopropyl-1,2,3,4-tetrahydrobenzo[*b*][1.6]naphthyridine (15).** The mixture of *N*-isopropylpiperidon-**4** (5.00 g, 35.46 mmol) and 2-aminoacetophenone (5.27 g, 39.01 mmol) in 100 mL of absolute ethanol was stirred for 5 h at 70 °C, while bubbling dry HCl gas through the reaction mixture. After the completion of the reaction (TLC monitoring, ethyl acetate), the reaction mixture was cooled, and the precipitate formed was collected by filtration and dissolved in 100 mL of 20% NaOH . The resulting solution was extracted with dichloromethane (3 ×

(16) Wang, Y.; Chen, Z.; Mi, A.; Hu, W. *Chem. Commun.* **2004**, 2486.
(17) Papageorgiou, C. D.; Cubillo de Dios, M. A.; Ley, S. V.; Gaunt, M. J. *Angew. Chem., Int. Ed.* **2004**, *35*, 4641.
(18) Voskressensky, L. G.; Borisova, T. N.; Listratova, A. V.; Vorobiev, I. V.; Alexandrov, G. G.; Varlamov, A. V. *J. Heterocycl. Chem.* **2005**, *42*, 1207.

**SCHEME 7. Acetylation of Compounds 9, 13, and 14 Accompanied by Migration of the *i*Pr Radical**




**SCHEME 8. Reaction of Compounds 7 and 8 with Acid Chlorides**




100 mL). The organic extract was dried over $MgSO_4$ followed by the evaporation of the solvent under reduced pressure to give a crystalline residue, which was recrystallized from ethyl acetate/hexane mixture to yield 3.76 g (50%) of **15** as white solid, mp 100−102 °C. $^1$H NMR (400 MHz, $CDCl_3$): 1.21 (d, 6H, $J$ = 6.5); 2.54 (s, 3H); 2.91 (T, 2H, $J$ = 5.7); 3.07 (spt, 1H, $J$ = 6.5); 3.22 (t, 2H, $J$ = 5.7); 3.92 (s, 2H); 7.49 (t, 1H, $J$ = 8.1); 7.61 (t, 1H, $J$ = 8.1); 7.97 (dd, 2H, $J$ = 4.0, 8.7). $^{13}$C NMR (100 MHz, DMSO): $\delta$ 13.0, 18.3 (2 × C), 34.5, 45.1, 49.5, 53.9, 124.1, 125.8, 126.6, 127.6, 128.6, 129.0, 139.8, 146.2, 156.5 ESI MS: 241($M^+$ + 1). Anal. Calcd for $C_{16}H_{20}N_2$: C 80.00; H 8.33; N 11.67. Found: C 79.88; H 8.57; N 11.50.

**12-Cyano-4-methyl-1-oxo-1,5,6,12b-tetrahydrobenzo[*b*]-pyrrolo[2,1-*f*]-1,6-naphthyridine-4-ium Ylide (7).** Orange solid 0.36 g (yield 27%). $^1$H NMR (400 MHz, DMSO): 3.32 (s, 3H), 3.71 (m, 2H), 4.32 (dd,2H, $J$ = 4.9,10.7), 6.68 (bs, 1H), 7.60 (m, 2H), 7.74(bs,1H), 7.88 (t, 2H, $J$ = 6.8). $^{13}$C NMR (100 MHz, DMSO): $\delta$ 28.2, 49.9, 58.2, 99.5, 110.3, 116.8, 122.6, 126.3, 126.6, 126.8, 128.3, 128.7, 130.9, 141.9, 146.8, 150.0, 168.0. EI MS *m*/*z*, (I %) 275($M^+$, 82); 260(40); 246(37); 232 (36); 222(39); 205(37); 191(21); 164(18); 152(21); 138(28); 126(55); 102(15); 84(30); 76(18); 57(30); 42(100). Anal. Calcd for $C_{17}H_{13}N_3O$: C 74.18; H 4.73; N 15.27. Found: C 74.39; H 4.67; N 15.40.

**(*E*)-Methyl-3-(isopropyl((4-methyl-2-vinylquinolin-3-yl)amino)acrylate (16).** The mixture of **15** (0.50 g, 2.36 mmol) and methyl propiolate (0.28 g, 2.83 mmol) in 30 mL of absolute methanol was refluxed for 12 h. The solvent was evaporated under reduced pressure, the resulted yellow oil was purified by column chromatography (column size 2 × 20 cm, eluent ethyl acetate/hexane 1:10 mixture) to give 80 mg (12%) of **16** as colorless prisms with mp 118−120 °C. $^1$H NMR (400 MHz, $CDCl_3$): 1.05 (d, 6H, $J$ = 6.7), 2.60 (s, 3H), 3.06(m,1H), 3.70 (s, 3H), 4.41 (s, 2H), 4.97 (d, 1H, $J$ = 12.7), 5.57 (dd, 1H, $J$ = 2.0, 10.6), 6.46 (dd, 1H, $J$ = 2.0,16.7), 6.94 (dd, 1H, $J$ = 10.6, 16.7), 7.45 (t,1H, $J$ = 7.4), 7.56(d, 1H, $J$ = 12.7), 7.64 (t, 1H, $J$ = 7.4), 7.92 (d, 1H, $J$ = 8.4), 8.03 (d, 1H, $J$ = 8.4). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 14.5, 21.4 (2 × C), 45.0, 48.8, 50.5, 85.9, 122.6, 123.7, 123.8, 126.4, 127.2, 129.5, 130.2, 133.4, 144.5, 147.0, 147.1,155.1, 169.9. ESI MS: 325 ($M^{+1}$) Anal. Calcd for $C_{20}H_{24}N_2O_2$: C 74.07; H 7.41; N 8.64. Found: C 74.31; H 7.59; N 8.82.

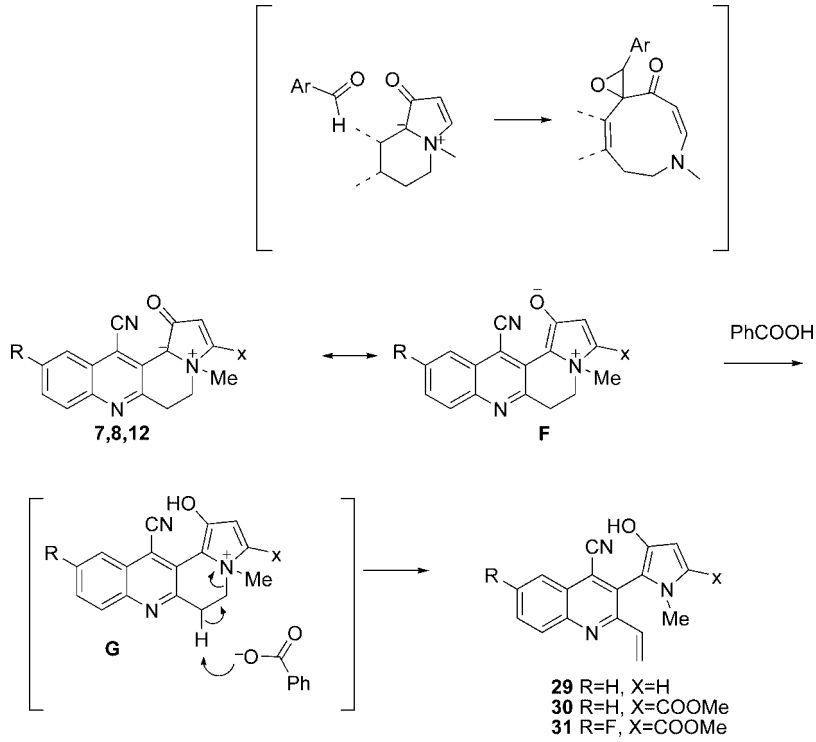
**General Procedure for Acetylation of Compounds (7−14).** To the solution of a compound (**7**−**14**) (0.6 mmol) in 20 mL of dichloromethane was added 0.07 g (0.66 mmol) of freshly distilled acetic anhydride in one portion, and the reaction mixture was stirred for 24 h at room temperature. The reaction mixture was subsequently treated with 20 mL of 10% $Na_2CO_3$ and 20 mL of water. The organic layer was dried over $MgSO_4$, the solvent was removed, and the resulted yellowish oil was crystallized from diethyl ether to give compounds **17**−**24.**

**10-Bromo-12-cyano-1,5,6,12b-tetrahydrobenzo[*b*]pyrrolo[2,1-*f*]-1,6-naphthyridine-1-yl Acetate (20).** Yellow solid 0.18 g (yield 78%), mp 186−188 °C. $^1$H NMR (400 MHz, $CDCl_3$): 2.44(s, 3H), 3.40(t, 2H, $J$ = 5.9), 4.23(t, 2H, $J$ = 5.9), 6.38(d, 1H, $J$ = 2.6), 6.86(d, 1H, $J$ = 2.6), 7.80(d, 1H, $J$ = 8.5), 7.90(d, 1H, $J$ = 8.5), 8.37(s, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 21.6, 34.7, 44.0, 45.8, 104.1, 107.9, 113.8, 115.5, 122.6, 123.0, 125.7, 127.0, 130.7,133.2, 138.7, 143.1, 155.5, 168.4. EI MS *m*/*z*, (I %) 382($M^+$,1); 339(41); 286(7); 260(18); 204(8); 177(10), 151(7), 100(6), 75(7), 53(8), 43(100). Anal. Calcd for $C_{18}H_{12}BrN_3O_2$: C 56.54; H 3.14; N 10.99. Found: C 56.37; H 3.37; N 10.83.

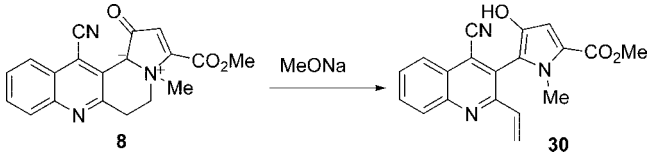
**General Procedure for Reactions of Ylides 7 and 8 with Cyclopropanecarbonyl Chloride or MsCl.** To the solution of the corresponding ylide (0.6 mmol) and 0.07 g (0.66 mmol) of $NEt_3$ in 30 mL of dichloromethane was added 0.07 g (0.66 mmol) of cyclopropanecarbonyl chloride or 0.08 g (0.66 mmol) of mesyl chloride in one portion, and the reaction mixture was stirred at room temperature for 12−18 h (TLC monitoring, ethyl acetate). The reaction mixture was subsequently treated with 20 mL of 10% citric acid, 20 mL of 10% $Na_2CO_3$, and 20 mL of water. The organic layer was dried over $Na_2SO_4$ and evaporated to dryness. The resulting viscous oil was triturated with diethyl ether to give crystalline product, which was recrystallized from ethyl acetate/hexane mixture.

**Methyl 12-Cyano-1-[(cyclopropylcarbonyl)oxy]-5,6-dihydrobenzo[*b*]pyrrolo[2,1-*f*][1,6]naphthyridine-3-carboxylate (26).** Yellow solid (yield 93%), mp 180−182 °C. $^1$H NMR (400 MHz, $CDCl_3$): 1.05(m,2H), 1.18(m,2H), 2.03(m,1H), 3.41(t, 2H, $J$ = 6.2), 3.87 (s, 3H), 4.85(t, 2H, $J$ = 6.2), 7.08 (s, 1H), 7.72(t, 1H, $J$ =

**SCHEME 9. Hoffman-like Cleavage of the Tetrahydropyridine Ring in Compounds 7, 8, and 12 under the Action of Benzoic Acid**




**SCHEME 10. Hoffman-like Cleavage of 8**




7.3), 7.81(t, 1H, $J$ = 7.3), 8.10(d, 1H, $J$ = 8.1), 8.28(d, 1H, $J$ = 8.1). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 9.8, 13.3, 33.8, 41.2, 51.7, 110.7, 112.5, 115.0, 119.9, 121.7, 123.9, 125.1, 126.3, 128.8, 129.1, 130.9, 137.3, 144.7, 155.6, 160.9, 172.2. ESI MS: 388($M^+$ + 1). Anal. Calcd for $C_{22}H_{17}N_3O_4$: C 68.21; H 4.39; N 10.85. Found: C 68.00; H 4.49; N 10.92.

**Methyl 12-Cyano-1-[(methylsulfonyl)oxy]-5,6-dihydrobenzo-[*b*]pyrrolo[2,1-*f*][1,6]naphthyridine-3-carboxylate (28).** Pale-red solid (yield 73%), mp 222−224 °C. $^1$H NMR (400 MHz, $CDCl_3$): 3.33(s,3H), 3.45(t, 2H, $J$ = 6.2), 3.89(s, 1H), 4.85(t, 2H, $J$ = 6.2), 7.12(s, 1H), 7.73(t, 1H, $J$ = 7.6), 7.82(t, 1H, $J$ = 7.6), 8.11(d, 1H, $J$ = 8.3), 8.27(d, 1H, $J$ = 8.3). $^{13}$C NMR (100 MHz, DMSO): $\delta$ 33.8, 37.8, 41.6, 51.9, 110.6, 112.8, 115.1, 121.4, 121.9, 123.0, 125.3, 126.12, 129.0, 129.2, 131.3, 133.4, 145.2, 155.3, 160.6. EI-MS: *m*/*z* (%): 397 ($M^+$, 10); 318(100); 230(12); 206(16); 191(9); 178(6); 152(7), 102(5), 79(38), 59(10), 53(22). Anal. Calcd for $C_{19}H_{15}N_3O_5S$: C 57.42; H 3.78; N 10.58. Found: C 57.25; H 3.60; N 10.76.

**General Procedure for Reaction of Ylides 7, 8, and 12 with Benzoic Acid.** To the solution of the ylide (**7**, **8**, **12**) (0.6 mmol) in 20 mL of dichloromethanewas added 0.08 g (0.66 mmol) of benzoic acid in one portion, and the reaction mixture was stirred for 24 h at room temperature. The reaction mixture was subsequently treated with 20 mL of 10% $Na_2CO_3$ and 20 mL of water. The organic layer was dried over $MgSO_4$, and the solvent was removed to give crystalline compounds **29**−**31**.

**Methyl 5-(4-Cyano-2-vinylquinolin-3-yl)-4-hydroxy-1-methyl-1*H*-pyrrole-2-carboxylate (30).** Yellow solid (yield 35%), mp 200−202 °C. $^1$H NMR (400 MHz, $CDCl_3$): 3.58(s, 3H), 3.84(s, 3H), 5.61(d, 1H, $J$ = 10.8), 6.57(d, 1H, $J$ = 16.1), 6.65−6.71(m,1H), 6.69(s, 1H), 7.09(bs,1H(-OH)), 7.65(t, 1H, $J$ = 7.3), 7.84(t, 1H, $J$ = 7.3), 8.06(d, 1H, $J$ = 8.1), 8.16(d, 1H, $J$ = 8.1). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 33.9, 51.6, 106.2, 114.4, 118.3, 121.5, 122.2, 124.5, 124.7, 125.2, 126.3, 129.2(2 × C), 132.2, 132.6, 142.1, 147.0, 155.5, 161.5. ESI MS: 334($M^+$+1). Anal. Calcd for $C_{19}H_{15}N_3O_3$: C 68.46; H 4.50; N 12.61. Found: C 68.25; H 4.67; N 12.39.

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**Supporting Information Available:** $^1$H and $^{13}$C NMR, EI or ESI mass spectra, and elemental analysis data for compounds **1**−**31**; CIF files for all X-ray analyses mentioned. This material is available free of charge via the Internet at http://pubs.acs.org.

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