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Short Communication

Reissert Epoxides: Novel Oxidation Products of Quinoline Reissert Compounds

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Summary. Treatment of quinoline Reissert compounds with *m*-chloroperoxybenzoic acid gave epoxides which are remarkably stable in crystalline state, but reactive in solution versus nucleophiles. They represent useful intermediates to regioselectively functionalized quinolines.

Keywords. Quinolines; Reissert compounds; Reissert epoxides.

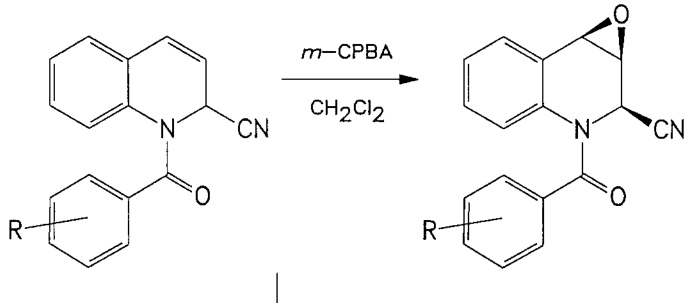
Reissert-Epoxide: Neue Oxidationsprodukte von Chinolin-Reissert-Verbindungen (Kurze Mitt.)

Zusammenfassung. Chinolin-Reissert-Verbindungen lassen sich mit *m*-Chlorperbenzoesäure zu Epoxiden oxidieren, die als kristalline Substanzen bemerkenswert stabil sind, in Lösung aber mit Nucleophilen bereitwillig reagieren. Sie stellen nützliche Zwischenprodukte zu regioselektiv funktionalisierten Chinolin-Derivaten dar.

To the best of our knowledge, defined oxidation products of Reissert compounds are only known from isoquinoline Reissert compounds. The oxidation takes place on the 3,4-double bond, as described for the addition of HOCl or $Tl(NO_3)_3/MeOH$ [1]. In contrary, the quinoline analogues show a different reaction behaviour depending on the substituents of the benzene ring. These afford ring contracted indoline derivatives, or undergo oxidative debenzoylation [1].

We now report the first synthesis of Reissert epoxides (**2**) by oxidation of common quinoline Reissert compounds (**1**) with *m*-chloroperoxybenzoic acid. It is a remarkable observation that the 3,4-double bond can be functionalized to the oxirane moiety preserving the ring system and the residual substitution pattern too. The resulting oxidation products possess considerable stability in solid state and are stable to the conditions employed in conventional purification techniques. With nucleophiles, they act as useful key intermediates whose reactions are examined in ongoing studies [2].

The spectroscopic data of five selected Reissert epoxides are described in the experimental part. The proposed structure was additionally supported by spectroscopic results. The epoxide moiety was affirmed by its typical high $^1J(C,H)$



1 **2**

a	H
b	4–CH_3
c	4–OCH_3
d	3,4,5–$(OCH_3)_3$
e	4–NO_2

Only relative stereochemistry shown

couplings, obtained by a gate-decoupled ^{13}C spectrum of **2a**: 187.5 Hz (4-C), 185.6 Hz (3-C), 2-C gave a value of 151.0 Hz [3]. Adequate to Reissert compounds, the IR spectra of **2** showed no band attributable to the CN group [4]. It is noteworthy that the epoxidation afforded only the *syn*-diastereomers as shown by the (400 MHz)-^1H and ^{13}C spectra. The relative configuration was deduced from the ^3J(2-H, 3-H) coupling constants and additional NOE experiments, and was assumed as (2*RS*,3*SR*,4*RS*).

Similar epoxides were also obtained from Reissert analogues with different substituted benzoyl groups. In all cases, the epoxides were produced in good to excellent yields.

Experimental Part

Preparation of Reissert Epoxides (General Procedure)

The quinoline Reissert compound (1 mmol) and *m*-chloroperoxybenzoic acid (1.5 mmol) were stirred in methylene chloride (10 ml) at room temperature until complete conversion was indicated by TLC (2–3 h). Then the reaction mixture was treated with 2*N* sodium carbonate solution (10 min). Separation of the organic phase, followed by extraction of the aqueous layer with methylene chloride, afforded, after drying and evaporating, the crystalline Reissert expoxide.

1-Benzoyl-2-cyano-3,4-epoxy-1,2,3,4-tetrahydroquinoline (**2a**)

Yield: 92%. Colorless crystals from ethyl acetate, m.p. 166–167 °C. ^1H NMR (400 MHz/*DMSO-d*$_6$): $\delta = 8.00$–7.05 (m, 9H, arom. H), 6.45 (d, 1H, $J = 2.5$ Hz, 2-H), 4.55 (dd, 1H, $J = 2.5$ Hz, $J = 4.5$ Hz, 3-H), 4.45 (d, 1H, $J = 4.5$ Hz, 4-H). ^{13}C NMR (20.12 MHz/$CDCl_3$ + *DMSO-d*$_6$ (1 + 1): $\delta = 168.1$ (Ar–CO–N), 133.5, 132.4 (1′-C and 8a-C), 129.6, 128.6, 127.5, 127.2, 126.6, 124.8, 124.7 (5-C, 6-C, 7-C, 8-C, 2′-C and 6′-C, 3′-C and 5′-C, 4′-C), 122.9 (4a-C), 108.5 (CN), 57.8 (4-C), 48.9 (3-C), 40.2 (2-C). IR (KRr) 1670 (ν_{amide}). MS (*m*/*z*) 249 (M^+ – HCN). Anal. calcd. for $C_{17}H_{12}N_2O_2$: C 73.90, H 4.38, N 10.14; found C 73.78, H 4.32, N 10.13.

2-Cyano-3,4-epoxy-1-toluoyl-1,2,3,4-tetrahydroquinoline (**2b**)

Yield: 82%. Colorless crystals from diethylether, m.p. 170–172 °C. ^{1}H NMR (80 MHz/$CDCl_3$): $\delta = 7.60$–6.95 (m, 7H, arom. H), 6.57 (m, 1H, arom. H), 6.22 (d, 1H, $J = 2.5$ Hz, 2-H), 4.28 (dd, 1H, $J = 2.5$ Hz, $J = 4.5$ Hz, 3-H), 4.15 (d, 1H, $J = 4.5$ Hz, 4-H), 2.26 (s, 3H, CH_3). ^{13}C NMR (20.12 MHz/$CDCl_3$): $\delta = 169.7$ (Ar–CO–N), 141.6 (4′-C), 135.1 (8a-C), 130.4 (1′-C), 129.8, 129.0, 128.9, 128.6, 126.3, 125.9 (5-C, 6-C, 7-C, 8-C, 2′-C and 6′-C, 3′-C and 5′-C), 123.6 (4a-C), 114.6 (CN), 59.1 (4-C), 50.7 (3-C), 41.3 (2-C), 21.2 (4′-CH_3). IR (KBr) 1670 (ν_{amide}). MS (m/z) 263 ($M^+ - HCN$). Anal. calcd. for $C_{18}H_{14}N_2O_2$: C 74.47, H 4.86, N 9.65; found C 74.40, H 4.70, N 9.60.

2-Cyano-3,4-epoxy-1-(4-methoxybenzoyl)-1,2,3,4-tetrahydroquinoline (**2c**)

Yield: 75%. Colorless crystals from diethylether, m.p. 145–147 °C. ^{1}H NMR (80 MHz/$CDCl_3$): $\delta = 7.60$–6.50 (m, 8H, arom. H), 6.20 (d, 1H, $J = 2.5$ Hz, 2-H), 4.28 (dd, 1H, $J = 2.5$ Hz, $J = 4.5$ Hz, 3-H), 4.13 (d, 1H, $J = 4.5$ Hz, 4-H), 3.80 (s, 3H, OCH_3). ^{13}C NMR (20.12 MHz/$CDCl_3$): $\delta = 169.5$ (Ar–CO–N), 161.9 (4′-C), 135.5 (8a-C), 131.2 (2′-C and 6′-C), 129.9, 129.3, 128.4, 125.9 (5-C, 6-C, 7-C, 8-C), 125.4 (1′-C), 123.6 (4a-C), 113.4 (3′-C and 5′-C), 114.8 (CN), 59.4 (4-C), 55.2 (OCH_3), 50.9 (3-C), 41.6 (2-C). IR (KBr) 1670 (ν_{amide}). MS (m/z) 279 ($M^+ - HCN$). Anal. calcd. for $C_{18}H_{14}N_2O_3$: C 70.58, H 4.61, N 9.15; found C 70.43, H 4.55, N 9.12.

2-Cyano-3,4-epoxy-1-(3,4,5-trimethoxybenzoyl)-1,2,3,4-tetrahydroquinoline (**2d**)

Yield: 74%. Purification by SC (Silica gel (60 mesh); diethylether/petroleum ether = 2 + 1) afforded a white solid, m.p. 147–152 °C. ^{1}H NMR (80 MHz/$CDCl_3$): $\delta = 7.60$–6.50 (m, 6H, arom. H), 6.21 (d, 1H, $J = 2.5$ Hz, 2-H), 4.27 (dd, 1H, $J = 2.5$ Hz, $J = 4.5$ Hz, 3-H), 4.12 (d, 1H, $J = 4.5$ Hz, 4-H), 3.84, 3.81, two rotamers (s, 3H, 4-OCH_3), 3.65, 3.63, two rotamers (s, 6H, 3-OCH_3 and 5-OCH_3). ^{13}C NMR (20.12 MHz/$CDCl_3$): $\delta = 169.3$ (Ar–CO–N), 152.5 (3′-C and 5′-C), 140.5 (4′-C), 135.2 (8a-C), 127.9 (1′-C), 129.7, 129.3, 126.3, 126.0 (5-C, 6-C, 7-C, 8-C), 123.5 (4a-C), 114.6 (CN), 106.6 (2′-C and 6′-C), 60.6 (4′-OCH_3), 59.2 (4-C), 55.8 (3′-OCH_3 and 5′-OCH_3), 50.7 (3-C), 41.5 (2-C). IR (KRr) 1665 (ν_{amide}). MS (m/z) 339 ($M^+ - HCN$). Anal. calcd. for $C_{20}H_{18}N_2O_5$: C 65.57, H 4.95, N 7.65; found C 65.81, H 4.69, N 7.59.

2-Cyano-3,4-epoxy-1-(4-nitrobenzoyl)-1,2,3,4-tetrahydroquinoline (**2e**)

Yield: 76%. Yellow crystals from methylene chloride/diethylether, m.p. 176–181 °C. ^{1}H NMR (80 MHz/$CDCl_3$): $\delta = 8.12$ (d, 2H, $J = 8.5$ Hz, 3′-H, 5′-H), 7.65–6.95 (m, 5H, arom. H), 6.48 (dd, 1H, $J = 7.5$ Hz, $J = 1.5$ Hz, arom. H), 6.31 (d, 1H, $J = 2.5$ Hz, 2-H), 4.32 (dd, 1H, $J = 2.5$ Hz, $J = 4.5$ Hz, 3-H), 4.20 (d, 1H, $J = 4.5$ Hz, 4-H). ^{13}C NMR (20.12 MHz/*DMSO*-d_6): $\delta = 167.8$ (Ar–CO–N), 148.4 (4′-C), 140.1 (1′-C), 134.1 (8a-C), 130.4, 129.8, 129.4, 126.9, 126.5, 123.5 (5-C, 6-C, 7-C, 8-C 2′-C and 6′-C, 3′-C and 5′-C), 124.8 (4a-C), 115.4 (CN), 59.0 (4-C), 49.9 (3-C), 41.7 (2-C). IR (KBr) 1680 (ν_{amide}). MS (m/z) 294 ($M^+ - HCN$). Anal. calcd. for $C_{17}H_{11}N_3O_4$: C 63.55, H 3.45, N 13.07; found C 63.28, H 3.25, N 13.04.

References

[1] Scriven E. F. V. (1984) Pyridines and Their Benzo Derivatives: (ii) Reactivity at Ring Atoms. In: Boulton A. J., McKillop A. J. (eds.) Comprehensive Heterocyclic Chemistry, Vol. 2. Pergamon Press, Oxford, p. 251, and references cited therein

[2] Kratzel M., Hiessböck R. (in preparation)

[3] Kalinowski H.-O., Berger S., Braun S. (1984) ^{13}C-NMR-Spektroskopie. Thieme, Stuttgart, p. 448

[4] Popp F. D., Blount W., Melvin P. (1961) J. Org. Chem. **26**: 4930

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