1-Alkoxycarbonyl- and 1-Acyl-*v*-triazolo[4,5-*b*]-pyridine/Hydrogen Peroxide Oxygenating Systems

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Epoxidation of alkenes and oxidation of thioanisole to the corresponding sulfoxide was achieved using the 1-alkoxycarbonyl- or 1-acyl-*v*-triazolo[4,5-*b*]pyridine/hydrogen peroxide systems. High yields of epoxide or sulfoxide were observed when some amide-type triazolides were employed for the oxidizing method.

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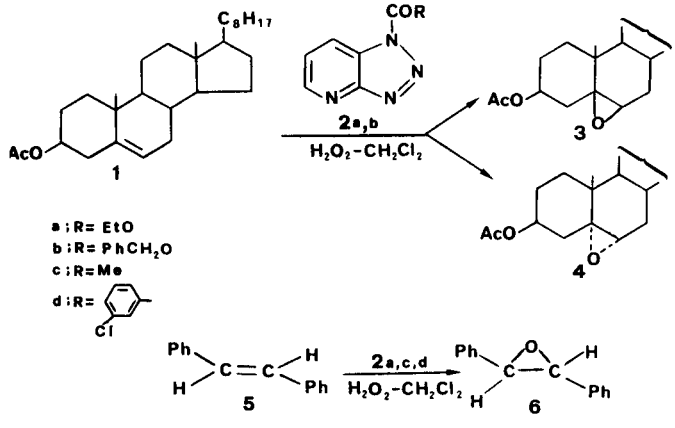
In a previous paper [1] we have reported the utility of some 1-alkoxycarbonyl- or 1-acyl-*v*-triazolo[4,5-*b*]pyridines for selective *N*-acylations of hydroxyamino esters and for transacylations of alcohols. As further applications of the title compounds we wish now to describe the epoxidation of alkenes and the oxidation of thioanisole using the following triazolide/hydrogen peroxide method. All the reactions were performed in a biphasic system by adding 30% aqueous hydrogen peroxide to a dichloromethane solution of a mixture of triazolide and alkene (or sulfide), and stirring at room temperature.

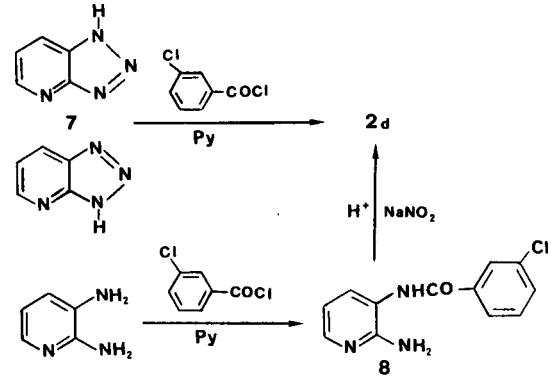
Epoxidation of cholesteryl acetate (**1**) was carried out using either 1-ethoxycarbonyl-*v*-triazolo[4,5-*b*]pyridine (**2a**) [2] or the corresponding benzyloxycarbonyl derivative **2b** [1]. While a greater α/β epoxide (**4/3**) ratio was observed with **2b**, the overall yields were in both cases high. A lower (58%) amount of (±)-*trans*-2,3-diphenyloxirane (**6**) was instead obtained when the oxidation with **2a**/hydrogen peroxide was performed on *trans*-stilbene (**5**).

Scheme 1



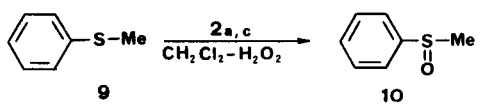
The extension of the use of the amide-type triazolides for the epoxidation of alkenes seemed to be promising. In fact the treatment of **5** with 1-acetyl-1*H*-*v*-triazolo[4,5-*b*]-pyridine (**2c**) [1] /hydrogen peroxide, under conventional conditions, afforded the epoxide **6** in a yield similar to that obtained using the urethane-type triazolide **2a**. Furthermore the above inert alkene **5** was converted to **6** in a 94% yield when 1-(*m*-chlorobenzoyl)-1*H*-*v*-triazolo[4,5-*b*]pyridine (**2d**) was employed for the oxidizing system. The 1-*m*-chlorobenzoyl derivative **2d** was obtained both by the usual direct acylation [1,2] of unsubstituted *v*-triazolo-[4,5-*b*]pyridine (**7**) [1] and by cyclization of 2-amino-3-(*m*-chlorobenzoylamino)pyridine (**8**) with sodium nitrite in aqueous acetic acid. The intermediate monoamide **8** was prepared by treatment of a THF solution of 2,3-diaminopyridine with *m*-chlorobenzoyl chloride.

Scheme 2



Although an analogous biphasic method for the epoxidation of alkenes has been recently reported [3], its application to oxidation of sulfides was, to our knowledge, not extended. Thus, as the first example of a new procedure for the oxidation of sulfides, the conversion of thioanisole (**9**) to sulfoxide **10** was achieved in a 66% yield by treatment with the triazolide **2a**/hydrogen peroxide system.

Scheme 3



Finally a nearly quantitative yield of sulfoxide **10** was observed with the amide-type triazolide **2c**. No attempt was made to isolate the peroxycarbonic acids or peroxy-

acids probably involved [3] in the above applications of our oxygenating method.

An overall analysis of our results shows that both the urethane- and the amide-type derivatives may be conveniently employed for oxidations of alkenes and sulfides performed in mild conditions.

Table

Epoxidation of *trans*-Stilbene (**5**)

Triazolide	Epoxide % [a]	Alkene Recovered %
2a	58	27
2c	55	39
2d	94	traces

[a] Isolated yield.

EXPERIMENTAL

Melting points were determined with a Büchi oil bath apparatus and are uncorrected. Optical rotations were taken at 20° with a Schmidt-Haensch Polartronic D polarimeter in a 1 dm cell. Infrared spectra (potassium bromide, unless otherwise specified) were recorded with a Perkin-Elmer 983 spectrophotometer. The ^{1}H nmr spectra were measured with a Varian EM-390 spectrometer using, unless otherwise specified, deuteriochloroform as the solvent (TMS as the internal standard). The coupling constants of resolved pyridinic signals for all described compounds are those reported at footnote of table I of our previous paper [1]. Merck silica gel 60 (230-400 mesh) was used for column chromatography; preparative layer chromatography (plc) was carried out with Merck F_{254} silica gel. The drying agent was sodium sulfate. Dry pyridine (Py) and tetrahydrofuran (THF) were used. Aqueous hydrogen peroxide (30% w/w; Carlo Erba) was used. All the oxidations were carried out in carefully sealed flasks at room temperature.

Epoxidation of Cholesteryl Acetate (**1**).

To a solution of cholesteryl acetate (**1**) (0.225 mmole) and 1-ethoxycarbonyl-1*H*-*v*-triazolo[4,5-*b*]pyridine (**2a**) [2] (0.45 mmole) in dichloromethane (0.5 ml) aqueous hydrogen peroxide (0.46 ml) was added. After stirring for 6 hours, dichloromethane was added in excess. The organic layers, washed with saturated aqueous sodium carbonate and water, were dried and evaporated under *vacuum*. The residue was chromatographed by plc (dichloromethane as eluent) to give the less polar β-epoxide **3** (0.028 g) and the molar α-epoxide **4** (0.064 g) (92% overall yield). Optical rotations and mps of both epoxides were in accord with literature data [4].

Compound **3** had ir: 2951, 1735, 1251, 1040 cm^{-1}; nmr: δ 0.63 (3H, s, 13-CH_3), 1.00 (3H, s, 10-CH_3), 2.00 (3H, s, CH_3-CO), 3.07 (1H, d, J = 3 Hz, 6 α-H), 4.81 (1H, m, 3α-H).

Compound **4** had ir: 2950, 1729, 1239, 1030 cm^{-1}; nmr: δ 0.61 (3H, s, 13-CH_3), 1.06 (3H, s, 10-CH_3), 1.98 (3H, s, CH_3-CO), 2.87 (1H, d, J = 4 Hz, 6β-H), 4.97 (1H, m, 3α-H).

Epoxidation of **1** with 1-benzyloxycarbonyl-1*H*-*v*-triazolo[4,5-*b*]pyridine (**2b**) [1] was carried out as above using a double amount of hydrogen peroxide and stirring for 24 hours. The epoxides **3** and **4** were obtained in 97% overall yield, and the α/β molar ratio was 3.3 (by nmr analysis on the basis of the intensities of 6-H signals).

2-Amino-3-(*m*-chlorobenzoylamino)pyridine (**8**).

To a stirred suspension of 2,3-diaminopyridine (2 mmoles) in THF (8 ml) and Py (0.21 ml), cooled at 0°, *m*-chlorobenzoyl chloride (2.2 mmoles) was added dropwise. After stirring at 0° for 15 minutes and at room temperature for 3 hours, ethyl acetate was added in excess. The organic layers, washed with saturated aqueous sodium carbonate and water, were dried and evaporated under *vacuum*. The residue (0.48 g) was chromatographed on a column of silica (1:40). Elution with dichloromethane-methanol (95:5) afforded pure amide **8** (0.354 g, 72%), mp 138-140° (ethyl acetate); ir: 3377, 3317, 1637, 1514 cm^{-1}; nmr (methanol-d_4): δ 6.74 (1H, dd, 5-H), 7.49-7.73 and 7.87-8.14 (6H, two m, 4-H and 5-H superimposed on aromatics).

Anal. Calcd. for $C_{12}H_{10}ClN_3O$: C, 58.19; H, 4.07; Cl, 14.32; N, 16.97. Found: C, 57.78; H, 4.05; Cl, 14.71; N, 16.55.

1-(*m*-Chlorobenzoyl)-1*H*-*v*-triazolo[4,5-*b*]pyridine (**2d**).

To a stirred suspension of unsubstituted-*v*-triazolo[4,5-*b*]pyridine (**7**) [1] (5.29 mmoles) in THF (21 ml) and Py (2.1 ml), cooled at 0°, 5.29 mmoles of *m*-chlorobenzoyl chloride were added. After stirring at 0° for 30 minutes and at room temperature for 2 hours, ethyl acetate was added in excess. The organic phase was washed with 2*N* hydrochloric acid and water, dried and evaporated under *vacuum*. The ^{1}H nmr analysis [2] of the residue (1.33 g) showed, besides the title compound **2d**, a small amount of isomeric 3-substituted triazolide. Complete conversion to **2d** was performed by stirring a solution of the mixture (0.13 g) in THF (2 ml), containing Py (0.2 ml), triazolopyridine **7** (0.013 g) and *m*-chlorobenzoyl chloride (0.009 g), at room temperature for 24 hours. Work up as above gave pure **2d** (0.14 g), mp 130-131° (ethyl acetate-ether); ir: 1722, 1594, 1569 cm^{-1}; nmr: δ 7.49-7.83 (3H, m, 6-H superimposed on aromatics), 8.21-8.39 (2H, m, aromatics), 8.80 (1H, dd, 7-H), 8.96 (1H, dd, 5-H).

Anal. Calcd. for $C_{12}H_7ClN_4O$: C, 55.71; H, 2.73; Cl, 13.71; N, 21.66. Found: C, 55.58; H, 2.77; Cl, 13.99; N, 21.39.

The title compound **2d** was also obtained by treatment of a solution of the monoamide **8** (1.42 mmoles) in water (4 ml) and acetic acid (1 ml), cooled at 0°, with sodium nitrite (0.14 g). After stirring at room temperature for 30 minutes, ethyl acetate was added in excess. The organic layers, washed with 2*N* hydrochloric acid and water, were dried and evaporated under *vacuum* to give pure **2d** (0.312 g, 86%).

Epoxidation of *trans*-Stilbene (**5**).

To a solution of 1 mmole of the title alkene **5** and 3 mmoles of the triazolide **2a** or **2c** (2 mmoles in the case of **2d**) in dichloromethane (3 ml), aqueous hydrogen peroxide (3.06 ml) was added. The biphasic system was stirred for 24 hours. Usual work up as in the previous oxidations gave a residue which was chromatographed on a silica column (1:50). Elution with *n*-pentane afforded (see Table) starting material and (±)-*trans*-2,3-diphenyloxirane (**6**), mp 68-69° (*n*-hexane) (with a Kofler hot-stage apparatus), lit 68-69° [5]; ir: 748, 697, 611 cm^{-1}; nmr: δ 3.89 (2H, s, oxirane protons), 7.41 (10H, s, aromatics).

Oxidations of Thioanisole (**9**).

To a solution of the title sulfide **9** (0.433 mmole) and **2a** (0.433 mmole) in dichloromethane (0.9 ml), aqueous hydrogen peroxide (0.44 ml) was added. The mixture was stirred for 21 hours and dichloromethane was added in excess. The organic layers were washed with water, dried and evaporated to give a residue which was chromatographed on a silica column (1:30). Elution with dichloromethane and dichloromethane-ether (95:5) afforded pure oily methyl phenyl sulfoxide (**10**) (0.04 g, 66%); ir (chloroform): 1090, 1071, 1037 cm^{-1}; nmr: δ 2.70 (3H, s, CH_3), 7.50-7.84 (5H, m, aromatics). Our spectral data were identical to those of an authentic sample [6].

Oxidation of **9** (1 mmole) in dichloromethane (1 ml) with triazolide **2c** (1 mmole) was carried out using 0.51 ml of aqueous hydrogen peroxide. After stirring for 5 hours and work up as above, final chromatography afforded pure sulfoxide **10** (0.136 g, 97%).

REFERENCES AND NOTES

[1] I. Torrini, G. Pagani Zecchini, F. Agrosì, and M. Paglialunga Paradisi, *J. Heterocyclic Chem.*, **23**, 1459 (1986).

[2] G. Pagani Zecchini, I. Torrini, and M. Paglialunga Paradisi, *ibid.*, **22**, 313 (1985).

[3] Y. Tsunokawa, S. Iwasaki, and S. Okuda, *Chem. Pharm. Bull.*, **31**, 4578 (1983).

[4] P. A. Plattner, T. Petrzilka, and W. Lang, *Helv. Chim. Acta*, **27**, 513 (1944).

[5] D. J. Reif and H. O. House, *Org. Synth.*, Coll. Vol. IV, 860 (1963).

[6] C. C. Price and J. J. Hydock, *J. Am. Chem. Soc.*, **74**, 1943 (1952).