senbrand, Deutsches Krebsforschungszentrum, Heidelberg, for providing us with samples of *N*-nitroso-*N*-benzylurea. This work was supported by Contract No. N01-CO-75380 with the National Cancer Institute, NIH, Bethesda, Md. 20014.

**Registry No.** 1, 775-11-1; 2, 72360-76-0; 3, 71171-58-9; 4, 4552-61-8; 5, 55043-75-9; $N^6$-benzyladenosine, 4294-16-0; 1-benzyladenosine, 4294-16-0; guanosine, 118-00-3; adenosine, 58-61-7.

## Structure of Deacetylviguiestenin (Tagitinin E). An Addendum[1]

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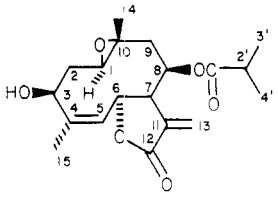
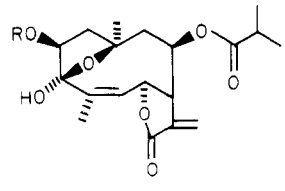
In a recent article[2] we presented complete stereochemical expressions for several sesquiterpene lactones from *Tithonia diversifolia* Hemsl., viz., tagitinin A, B (=deacetylwoodhousin), C, D (=tirotundin), and E,[3,4] as well as for some other related compounds. Since formulation of tagitinin E as the heliangolide **1** was based entirely on



**1**



**3a**, R = H
**b**, R = Ac

NMR analysis of a very small authentic sample, it was deemed desirable to adduce additional chemical proof. This has now been accomplished by relating tagitinin E to tagitinin C (**2**). The latter has been correlated previously[3] with deacetylwoodhousin (**3a**) whose structure is securely based on an X-ray analysis of **3b** (woodhousin).[5]

The correlation is shown in Scheme I. Zinc–acetic acid reduction of tagitinin C afforded **4**[6] which was epoxidized to **5**. The oxirane stereochemistry of **5** which is the same as that of several naturally occurring 1,10-epoxyheliangolides of confirmed structure[7] is dictated by the preferred "outside" approach of epoxidizing agent observed in at least two other thoroughly documented instances.[8] Protection of the $\alpha$-methylene-$\gamma$-lactone function by way of the morpholine adduct **6**[9] followed by $NaBH_4$ reduction furnished two alcohols, **7** and **8**.[10] The major product, **7**, was converted to a substance identical in all respects with tagitinin E. The minor product, **8**, afforded **9** whose stereochemistry at C-4 remains undefined. That at C-3 is probably the same as that of **1**.

In view of our formulation of tagitinin E as **1**, we concluded earlier[2] that deacetylviguiestenin, an apparently isomeric substance from *Viguiera stenoloba*,[11] might be the C-8 epimer of **1**. However, on reexamination of the evidence in the original report,[11] it seemed possible that the two substances might be identical, and, in fact, Romo de Vivar and co-workers have proposed formula **1** for deacetylviguiestenin in a second, more recent publication.[12] Since then, direct comparison has shown that deacetylviguiestenin and tagitinin E are indeed identical.[13] The name tagitinin E should therefore be stricken from the literature.

### Experimental Section

**Reduction of Tagitinin C.** A solution of 0.10 g of **2** in 2.5 mL of acetic acid and 1.5 mL of $H_2O$ was kept at 100 °C while 0.2 g of Zn dust was added over a 15-min period. After an additional hour at 100 °C (TLC monitoring) the mixture was neutralized with 10% aqueous $NaHCO_3$ and extracted with ether. The washed and dried extract was evaporated and the residue purified by preparative TLC (silica gel, solvent ethyl acetate–benzene, 9:1). The main fraction, **4**, was recrystallized from ethyl acetate–petroleum ether (bp 60–80 °C): mp 135–137 °C; yield 0.025 g; IR ($CHCl_3$) 1760, 1730, 1695, 1660, 1140, 860 $cm^{-1}$; NMR (60 MHz, $CDCl_3$) $\delta$ 6.35 and 5.78 (2 d, $J$ = 2 Hz, H-13), 5.1–5.5 (c, H-1, H-5, H-6, and H-8), 1.98 (H-14), 1.82 (H-15), 1.15 (d, $J$ = 7 Hz, H-3′ and H-4′); mass spectrum $m/e$ 332 ($M^+$), 262, 244, 71 (base peak).

Anal. Calcd for $C_{19}H_{24}O_5$: C, 68.66; H, 7.28. Found: C, 68.34; H, 7.18.

**Epoxidation of 4.** To 25 mg of **4** in 2 mL of $CHCl_3$ was added at 0 °C 0.5 mL of 8% perbenzoic acid in $CHCl_3$. After 12 h at 0 °C, the mixture was diluted with $CHCl_3$, washed with 10% aqueous $NaHCO_3$ and water, dried, and evaporated. Purification of the residue by preparative TLC (ethyl acetate–benzene, 4:1) gave 10 mg of **5** as a gum which exhibited the following: IR 1765, 1730, 1660, 1130, 1000 $cm^{-1}$; NMR 6.30 and 5.78 (2 d, $J$ = 2 Hz, H-13), 5.2–5.5 (c, H-5, H-6, and H-8), 3.50 (m, H-7), 1.98 (br, H-15), 1.25 (H-14), 1.08 (d, $J$ = 7 Hz, H-3′ and H-4′); mass spectrum $m/e$ 348 ($M^+$), 278, 260. A minor fraction appeared to be the epimeric epoxide but could not be purified satisfactorily.

Anal. Calcd for $C_{19}H_{24}O_6$: C, 65.50; H, 6.94. Found: C, 65.41; H, 7.12.

**Preparation of 1 and 9.** To 25 mg of **5** in 0.5 mL of EtOH at 0 °C was added 0.2 g of morpholine. After 12 h at 0 °C, the mixture was diluted with ice-cold water and extracted with $CHCl_3$. On evaporation of the washed and dried extract, 25 mg of adduct **6** was obtained as a gum which had the following: IR 5.2–5.6 (c, H-5, H-6, and H-8), 1.80 (br, H-15), 1.15 (H-14), 1.05 (d, $J$ = 7 Hz, H-3′ and H-4′); mass spectrum $m/e$ 435 ($M^+$), 417, 364, 348, 260, 100, 87.

Anal. Calcd for $C_{23}H_{33}O_7N$: mol wt 435.225 50. Found: mol wt 435.225 38.

To 25 mg of **6** in 0.6 mL of isopropyl alcohol was added 20 mg of $NaBH_4$. After the solution was stirred at −15 °C for 4 h, TLC

(1) Work at The Florida State University was supported in part by a U.S. Public Health Service grant (CA-13121) through the National Cancer Institute.

(2) Barua, N. C.; Sharma, R. P.; Madhusudanan, K. P.; Thyagarajan, G.; Herz, W.; Murari, R. *J. Org. Chem.* **1979**, *44*, 1831. Formula **2** of this paper was mislabeled tagitinin D instead of tagitinin B, and the NMR data in the last column of Table II are those of tagitinin E (**19a**), not **20a**.

(3) Pal, R.; Kulshreshta, D. K.; Rastogi, R. P. *Indian J. Chem.* **1976**, *14*, 77, 259; **1977**, *15*, 208.

(4) Examination of voucher specimens has proved correct our surmise that Pal et al. were dealing with *T. diversifolia* instead of *T. tagetiflora* Desf. which is an improper synonym for *T. rotundifolia* (Mill.) Blake.

(5) Herz, W.; Blount, J. F. *J. Org. Chem.* **1978**, *43*, 4887.

(6) The low yield (25%) of **4** can probably be attributed to the competing reduction of the $\alpha,\beta$-unsaturated lactone system.

(7) Several lactones of this type have been correlated with dihydroheliangin whose structure was established by X-ray crystallography (Nishikawa, M.; Kamiya, K.; Takabatake, A.; Oshio, H. *Tetrahedron* **1966**, *22*, 3601), without disturbing the epoxide function.

(8) (a) Herz, W.; Wahlberg, I. *J. Org. Chem.* **1973**, *38*, 2485. (b) Lee, K.-H.; Kimura, T.; Haruna, M.; McPhail, A. T.; Onan, K. D. *Phytochemistry* **1977**, *16*, 1068.

(9) Ananthasubramanian, L.; Govindan, S.; Deodhar, K. D.; Bhattacharyya, S. C. *Indian J. Chem.* **1978**, *16*, 191.

(10) For citations of other 1,4-reductions of $\alpha,\beta$-unsaturated ketones with $NaBH_4$, see: Jackson, W. R.; Zurqiyah, A. *J. Chem. Soc.* **1965**, 5280.

(11) Guerrero, C.; Ortega, A.; Diaz, E.; Romo de Vivar, A. *Rev. Latinoam. Quim.* **1973**, *4*, 118.

(12) Romo de Vivar, A.; Delgado, G.; Guerrero, C.; Reséndiz, J.; Ortega, A. *Rev. Latinoam. Quim.* **1978**, *9*, 171.

(13) Private communication from Dr. Romo de Vivar.

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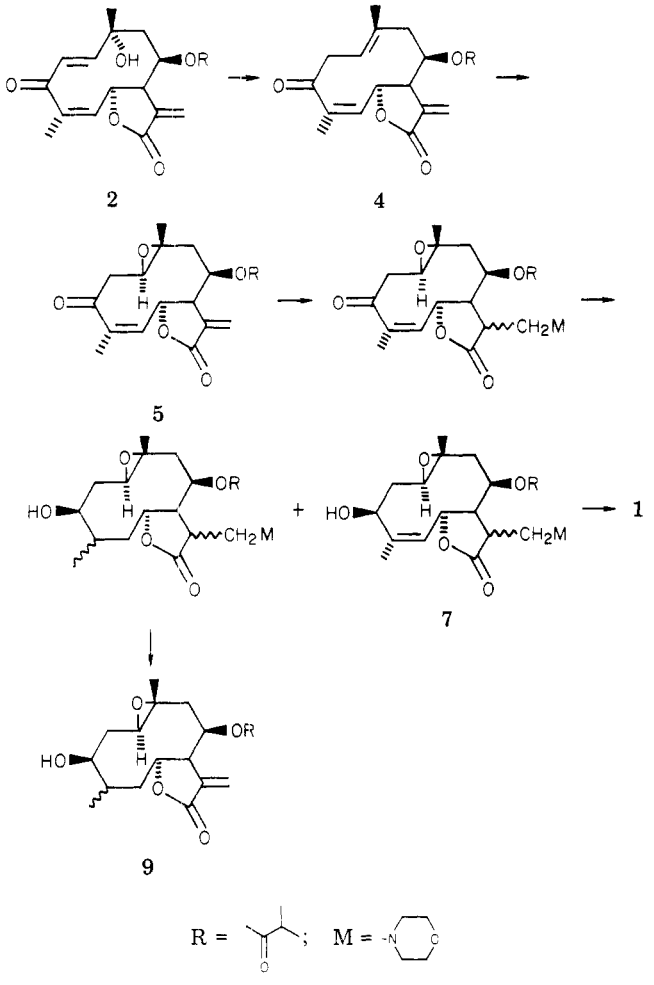
Scheme I



indicated that the starting material had been consumed, and the solution was diluted with water and extracted with $CHCl_3$. Evaporation of the washed and dried extract gave a residue which showed two spots on TLC. These were separated by preparative TLC (ethyl acetate–benzene, 3:1). The major product, **7**, was recrystallized from petroleum ether (bp 60–80 °C): yield 14 mg; mp 170 °C; IR 3500, 1725, 1110, 850 $cm^{-1}$; NMR 6.60 (dd, $J$ = 12, 2 Hz, H-6), 5.2–5.45 (c, H-5 and H-8), 4.40 (br, H-3), 1.80 (d, $J$ = 1.5 Hz, H-15), 1.25 (H-14), 1.15 (d, $J$ = 7 Hz, H-3′ and H-4′); mass spectrum $m/e$ 437 ($M^+$), 350, 349, 332, 262, 100, 87, 71 (base peak).

Anal. Calcd for $C_{23}H_{35}O_7N$: mol wt 437.241 14. Found: mol wt 437.241 06.

The minor product (**8**, yield 8 mg) was a gum: IR 3500, 1765, 1730, 1125 $cm^{-1}$; mass spectrum $m/e$ 439 ($M^+$), 352, 351, 264, 228. Because **8** had a tendency to decompose, it was immediately mixed with $CH_3I$,[9] kept overnight at room temperature, diluted with $CHCl_3$, washed with three 50-mL portions of 10% aqueous $NaHCO_3$ and water, dried, and evaporated. The residue (**9**, 6 mg) was a gum: IR 3500, 1765, 1730, 1100 $cm^{-1}$; NMR 6.25 and 5.70 (2 d, $J$ = 2.5 Hz, H-13), 5.2–5.5 (C, H-5 and H-8), 3.65 (br, H-3), 1.25 (H-14), 1.15 (d, $J$ = 7 Hz, H-3′ and H-4′), 1.05 (d, $J$ = 7 Hz, H-15); mass spectrum $m/e$ 352 ($M^+$), 337, 264, 246, 71.

Treatment of 12 mg of **7** with $CH_3I$ and workup in the manner described in the previous paragraph gave on evaporation of $CHCl_3$ 10 mg of **1**: mp 210 °C, after recrystallization from $CHCl_3$–hexane; mixture melting point with authentic tagitinin E (mp 210 °C) undepressed; identical on TLC (ethyl acetate–benzene, 1:9); IR, NMR, and mass spectra superimposable.

**Acknowledgment.** We thank Dr. R. P. Rastogi for a sample of authentic tagitinin E.

**Registry No.** **1**, 59979-58-7; **2**, 59979-56-5; **4**, 72301-72-5; **5**, 72301-73-6; **6**, 72301-74-7; **7**, 72301-75-8; **8**, 72301-76-9; **9**, 72301-77-0; morpholine, 110-91-8.

# Synthesis and Characterization of a Cyclic Acylammonium Chloride

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We were recently interested in the preparation of (2-chloroethyl)ureas for use as alkylating agents in the preparation of compounds for pharmacological evaluation. Specifically, we attempted first to synthesize (chloroethyl)urea **4**. *N*-Ethyl-*N*-(2-hydroxyethyl)-4-morpholinecarboxamide (**3**) was prepared in straightforward fashion from morpholinecarbonyl chloride (**1**) and 2-(ethylamino)ethanol (**2**) as shown in Scheme I. However, treatment of a chloroform solution of **3** with thionyl chloride or phosgene did not yield **4**, but rather a hygroscopic salt [$\nu$(C=O) 1800 $cm^{-1}$] which has been identified as **5**.

Treatment of **5** with sodium methoxide yielded a single product, which we assigned as carbamate **6** (Scheme II). An authentic sample of **6** was produced by treating methyl *N*-(2-chloroethyl)-*N*-ethylcarbamate (**10**) with morpholine. [(Chloroethyl)carbamate **10**, in turn, was prepared from the (hydroxyethyl)carbamate **8** and thionyl chloride. The main product of this reaction was 3-ethyl-2-oxazolidinone (**9**).] Interestingly, inner salt **5** could also be quantitatively prepared from **1** and *N*-ethylaziridine.

Treatment of **3** with 4-oxo-4*H*-1-benzopyran-2-carbonyl chloride (**11**) afforded the expected ester **12** (Scheme III) as a white solid (96% yield). However, when the piperidinyl analogues of **3** (**13a–d**) were treated with **11**, oils (**14a–d**) resulted which converted, upon standing for several days, to their corresponding acylammonium carboxylate salts (**15a–d**). These transformations were monitored by infrared and NMR spectroscopy. The liquid physical states of **14a–d** may be responsible for their conversions to **15a–d**, possibly via chloride catalysis. Another explanation for the stability of **12** and the instability of **14a–d** is that morpholine ($pK_a$ = 8.33)[1] is less basic than piperidine ($pK_a$ = 11.123)[1] or the methylpiperidines and is therefore less nucleophilic and less prone to initiate carboxylate displacement.

Acylammonium salts have been isolated or implicated as intermediates in other instances. For example, a series of (alkoxycarbonyl)trialkylammonium fluoroborates has been synthesized and used in peptide synthesis.[2] The use of 2,2,2-trichloroethyl chloroformate in the demethylation of tertiary amines[3] is a classic example of the intermediacy of acylammonium salts. In addition, perchlorate[4] and antimony pentachloride[5] salts of heterocycles having positive charge on nitrogen atoms which are adjacent to carbonyl groups have been reported.

## Experimental Section[6]

***N*-Ethyl-*N*-(2-hydroxyethyl)-4-morpholinecarboxamide (3).** A 29.9-g (0.200 mol) quantity of 4-morpholinecarbonyl

(1) "Handbook of Chemistry and Physics", 55th ed., R. C. Weast, Ed., CRC Press, Cleveland, OH, 1974, p D-127.
(2) J. V. Paukstelis and M. Kim, *J. Org. Chem.*, **39**, 1499 (1974).
(3) (a) T. A. Montzka, J. D. Matiskella, and R. A. Partyka, *Tetrahedron Lett.*, 1325 (1974); (b) M. Fieser and L. F. Fieser, "Reagents for Organic Synthesis", Vol. 5, Wiley, New York, 1975, pp 686–7.
(4) G. N. Dorofeenko, Y. I. Ryabukhin, and V. V. Mezheritskii, *Zh. Org. Khim.*, **10**, 2233 (1974).
(5) W. Flitsch and K. Gurke, *Angew. Chem.*, **87**, 38 (1975).

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