Table II
Spectral Data

Vinylcyclopropane	Ir, cm^{-1} [a]	Nmr, τ [b]	Mass, m/e
1-i	>3000, 1726, 1638, 994, 912	3.87–4.96 (m, 3 H) 5.80 (two q, 4 H) 7.57–7.60 (m, 3 H) 8.73 (two t, 6 H)	212 (M^+)
1-ii	>3000, 1722, 1648, 967, 748, 692	2.78 (s, 5 H) 3.36 (d, J = 17 Hz, 1 H) 3.62–4.10 (m, 1 H) 5.86 (two q, 4 H) 7.26–7.65 (m, 3 H) 8.78 (two t, 6 H)	
1-iii	>3000, 1728, 1650, 960, 748, 693	2.72 (s, 5 H) 3.45 (d, J = 16 Hz, 1 H) 3.90–4.48 (m, 1 H) 6.32 (two s, 3 H) 7.60–9.12 (m, 4 H)	202 (M^+) 171 143
1-v	>3000, 1726, 1670, 968	3.86–4.87 (m, 2 H) 5.86 (two q, 4 H) 7.50–7.73 (m, 3 H) 8.34 (d, 3 H) 8.73 (two t, 6 H)	
1-viii	>3000, 1734, 1640, 995, 910	4.50–5.12 (m, 3 H) 6.30 (two s, 3 H) 7.67–9.18 (m, 4 H)	126 (M^+) 95 67

[a] Neat. [b] $CDCl_3$ solution (TMS reference).

undergoes the coupling reaction, and that **2** reacts with α,β-unsaturated carbo esters faster than with organic halides.

Experimental Section

All halides employed were prepared by the reaction of the corresponding aldehyde and PCl_5. 1,3-Dichloropropene and olefins were commercial reagents, purified by distillation after drying over molecular sieves.

Reaction of Allylidene Dichloride with Diethyl Fumarate in the Copper–Isonitrile System. Allylidene dichloride, 0.56 g (5 mmol), was added dropwise with stirring during 45 min to a mixture of metallic copper powder, 1.27 g (20 mg-atoms) (prepared by the reduction of $CuSO_4$ with zinc powder), *tert*-butyl isocyanide, 3.32 g (40 mmol), and diethyl fumarate, 1.72 g (10 mmol) in benzene (5 ml) at 80°, and the reaction mixture was heated for 12 hr. The mixture was triturated with ether, and the precipitated CuCl–isonitrile complex was removed by filtration. The filtrate was concentrated and distilled *in vacuo* to isolate 1-vinyl-*trans*-2,3-bis(ethoxycarbonyl)cyclopropane (67%), uncontaminated with its isomer as judged by tlc. The structure of the product was confirmed by spectral (Table II) and elemental analysis.

Reaction of *trans*-Cinnamylidene Dichloride with Methyl Acrylate in the Copper–Isonitrile System. *trans*-Cinnamylidene dichloride, 0.93 g (5 mmol), in benzene (3 ml) was added with stirring during 45 min to a mixture of metallic copper, 1.27 g (20 mg-atoms), *tert*-butyl isocyanide, 3.32 g (40 mmol), methyl acrylate, 0.86 g (10 mmol), and benzene (5 ml) at 80°. The reaction mixture was stirred at 80° for 12 hr. Work-up of the mixture according to the above procedure afforded a mixture of *cis*- and *trans*-1-(*trans*-styryl)-2-methoxycarbonylcyclopropane in 66% yield. Reactions of 1,3-dichloropropene with diethyl fumarate and methyl acrylate by copper–isonitrile system were carried out in similar ways.

Registry No.—*tert*-Butyl isocyanide, 7188-38-7; cyclohexyl isocyanide, 931-53-3; copper, 7440-50-8.

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Friedländer Synthesis and Rearrangement of 10-(*o*-Fluorophenyl)-1,4-ethanobenzo[*b*]-1,5-naphthyridines to Benzo[*b*]indolo[3,2,1-*d,e*]-1,5-naphthyridines

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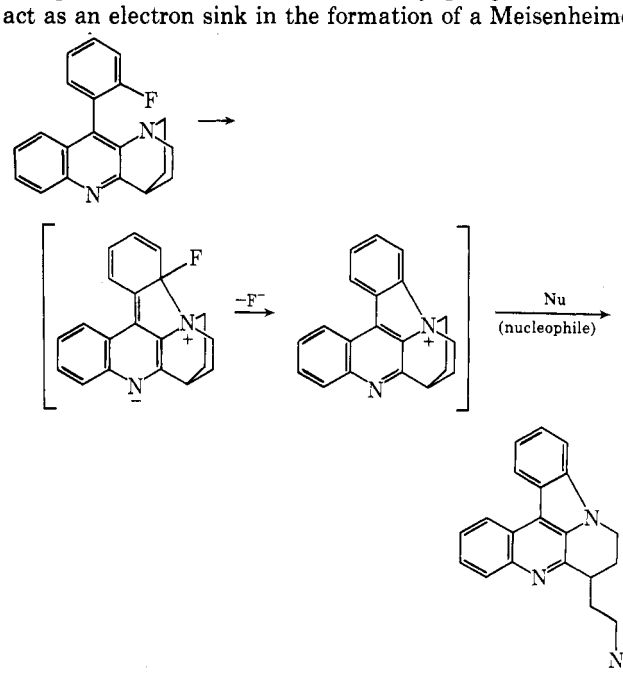
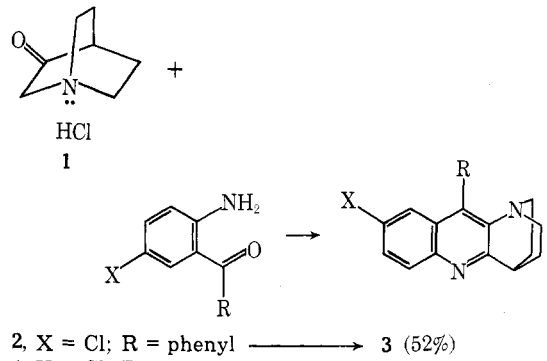
The rearrangement of suitably functionalized 2-arylmethylene quinuclidines to tetrahydropyrido[1,2-*a*]indoles[1] provides ready access to this ring system and proved to be of great value in a recently completed total synthesis of dihydroeburnamenine.[2] An extension of this arrangement to a different category of quinuclidine derivatives is described in this note. The reactions involve nucleophilic attack on an aromatic ring by the quinuclidine nitrogen and are therefore favored by groups which can act as an electron sink in the formation of a Meisenheimer



complex. A quinoline ring could presumably serve in this capacity and the rearrangement outlined below was conceived on this basis.

The expectation that ring opening of the quinuclidinium ion will proceed by substitution rather than elimination can be based on stereoelectronic constraints on the latter process.[3]

The starting materials for the planned rearrangement reaction would be readily available if Friedländer quinoline syntheses could be effected using 3-quinuclidinone and *o*-aminobenzophenones. Although attempts to carry out the condensation with base catalysis (NaOEt in EtOH) were fruitless, acid catalysis[4] (HCl in EtOH) gave satisfactory results and the three examples listed below were carried out with the indicated yields.

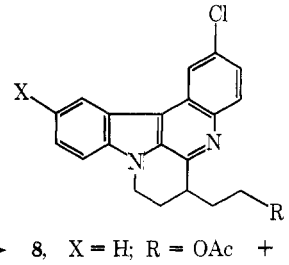


HCl

1

2, X = Cl; R = phenyl ⟶ 3 (52%)
4, X = Cl; R = 2-fluorophenyl ⟶ 5 (50%)
6, X = H; R = 2-pyridyl ⟶ 7 (55%)
10, X = Cl; R = 2-fluoro-5-nitrophenyl

The rearrangement of compound **5** proceeded with great reluctance, refluxing in triglyme for 20 hr being necessary for complete disappearance of starting material. These vigorous conditions induced secondary reactions leading to formation of a significant amount of a reduced product **9** as well as minor amounts of other by-products.



5 $\xrightarrow{KOAc/\Delta}$ 8, X = H; R = OAc + 9, X = R = H

$\downarrow KNO_3/H_2SO_4$

10 $\xrightarrow{KOAc/\Delta}$ 11, X = NO_2; R = OH

Compounds **8** and **9** have close R_f values, resulting in substantial product losses during their chromatographic separation. The verification of product structures by spectroscopic methods is straightforward; in particular the appearance of a triplet or multiplet near 4.2 ppm in their nmr spectra is characteristic of the indolic NCH_2CH_2 unit.

It appeared that one could expedite the rearrangement by further activation of the fluorine atom toward nucleophilic displacement. To this end compound **5** was nitrated. The nitrated product **10** now underwent smooth rearrangement in refluxing diglyme, the reaction was complete in 3 hr, and the product (**11**) was easily isolated by direct crystallization provided an acid hydrolysis of the acetoxy group was included in the work-up procedure.

Experimental Section[5]

8-Chloro-10-phenyl-3,4-dihydro-2*H*-1,4-ethanobenzo[*b*]-1,5-naphthyridine (3). A solution of 2-amino-5-chlorobenzophenone (**2**, 46.4 g, 0.2 mol) and 3-quinuclidinone hydrochloride (**1**, 32.4 g, 0.2 mol) in ethanol (500 ml) was saturated with dry hydrogen chloride and then heated under reflux for 4 days. The solution was then diluted with water, made basic by addition of sodium carbonate, and extracted with methylene chloride. The extract was dried over sodium sulfate, treated with charcoal, filtered through Celite, and evaporated. Recrystallization from methylene chloride–ethanol gave 33.1 g (52%) of yellow crystals. Either by two additional recrystallizations or by vacuum sublimation, colorless crystals, mp 235–237°, were obtained: ir (Nujol) 1600 and 1560 cm^{-1}; nmr ($CDCl_3$) 2.0 (m, 4 H), 2.4–3.3 (m, 4 H), 3.5 (m, 1 H, bridgehead), 7.2–7.7 (m, 7 H), and 8.03 ppm (d, J = 9 Hz, 1 H); mass spectrum m/e 320 (M^+).

Anal. Calcd for $C_{20}H_{17}ClN_2$: C, 74.88; H, 5.34; N, 8.73; Cl, 11.05. Found: C, 74.87; H, 5.35; N, 8.51; Cl, 11.09.

8-Chloro-10-(2-fluorophenyl)-3,4-dihydro-2*H*-1,4-ethanobenzo[*b*]-1,5-naphthyridine (5). Condensation of 2-amino-5-chloro-2′-fluorobenzophenone (**4**)[6] with 3-quinuclidinone hydrochloride (1 mol of each, 6 days reflux) as described above afforded 170 g (50%) of crude **5** in two crops. A recrystallized sample provided colorless crystals: mp 230–230.5°; ir (Nujol) 1625 and 1580 cm^{-1}; nmr ($CDCl_3$) 2.0 (m, 4 H), 2.5–3.4 (m, 4 H), 3.5 (m, 1 H, bridgehead), 7.0–7.8 (m, 6 H), and 8.1 ppm (d, J = 8 Hz, 1 H); mass spectrum m/e 338 (M^+).

Anal. Calcd for $C_{20}H_{16}ClFN_2$: C, 70.90; H, 4.76; N, 8.27. Found: C, 70.79; H, 4.67; N, 8.26.

10-(2-Pyridyl)-3,4-dihydro-2*H*-1,4-ethanobenzo[*b*]-1,5-naphthyridine (7). Condensation of 2-(*o*-aminobenzoyl)pyridine (**6**)[7] with 3-quinuclidinone hydrochloride (0.125 mol of each, 20 hr reflux) as described above afforded 28 g of crude product. Recrystallization from methylene chloride–ether gave 20 g (55%) of pure, colorless compound **7**, mp 209–210°. The mother liquor afforded 3 g of an impurity derived from self-condensation of compound **6**. Compound **7** had ir (Nujol) bands at 1590 and 1565 cm^{-1}; nmr ($CDCl_3$) 2.0 (m, 4 H), 2.4–3.4 (m, 4 H), 3.5 (m, 1 H, bridgehead), 7.2–8.3 (m, 7 H), and 8.8 ppm (d, J = 4 Hz, 1 H); mass spectrum m/e 287 (M^+).

Anal. Calcd for $C_{19}H_{17}N_3$: C, 79.42; H, 5.96; N, 14.62. Found: C, 79.54; H, 5.89; N, 14.67.

Rearrangement of 5 to 8-(2-Acetoxyethyl)-12-chloro-7,8-dihydro-6*H*-benzo[*b*]indolo[3,2,1-*d*,*e*]-1,5-napthyridine (8) and 8-Ethyl-12-chloro-7,8-dihydro-6*H*-benzo[*b*]indolo[3,2,1-*d*,*e*]-1,5-napthyridine (9). A mixture of compound **5** (22 g) and potassium acetate (22 g) in triglyme (200 ml) was stirred and heated to reflux under argon for 20 hr. The mixture was cooled, diluted with water, and extracted with benzene. The benzene layer was washed three times with dilute aqueous Na_2CO_3 to remove triglyme, dried, and evaporated. The residue was chromatographed on a silica gel column using a 5:1:1 mixture of hexane, ethyl acetate, and ethanol as the eluent. The fractions observed by tlc to contain compound **8** (more polar product) were combined and evaporated, and the residue was recrystallized from ethyl acetate–ethanol to give 2.3 g (9%) of pale yellow crystals: mp 133°; ir (Nujol) 1730, 1610, 1590, and 1510 cm^{-1}; nmr ($CDCl_3$) 1.7–3.0 (m, 4 H), 2.10 (s, 3 H), 3.35 (m, 1 H), 4.24 (m, 2 H), 4.46 (t, J = 7 Hz, 2 H), 7.2–7.7 (m, 4 H), 8.10 (d, J = 9 Hz, 1 H), and 8.28 (m, 2 H); mass spectrum m/e (rel intensity) 291 (50), 292 (100), and 378 (M^+).

Anal. Calcd for $C_{22}H_{19}ClN_2O_2$: C, 69.75; H, 5.06; N, 7.39. Found: C, 69.90; H, 5.09; N, 7.20.

Evaporation of the earlier fractions gave 1.1 g (5%) of compound **9**, which crystallized from ether–hexane (can also be vacuum sublimed) as pale yellow crystals: mp 150–151°; ir (Nujol) 1620, 1605, 1580, and 1510 cm^{-1}; nmr ($CDCl_3$) 1.20 (t, J = 7 Hz, 3 H), 1.4–2.7 (m, 4 H), 3.2 (m, 1 H), 4.26 (t, J = 6 Hz, 2 H), 7.2–7.7 (m, 4 H), 8.15 (d, J = 9 Hz, 1 H), and 8.35 (m, 2 H); mass spectrum m/e (rel intensity) 291 (58), 292 (100), and 320 (M^+).

Anal. Calcd for $C_{20}H_{17}ClN_2$: C, 74.88; H, 5.34; N, 8.73; Cl, 11.05. Found: C, 74.79; H, 5.30; N, 8.68; Cl, 11.31.

8-Chloro-10-(2-fluoro-5-nitrophenyl)-3,4-dihydro-2*H*-1,4-ethanobenzo[*b*]-1,5-naphthyridine (10). Compound **5** (150 g) was added in portions to concentrated sulfuric acid (300 ml). The resulting solution was stirred and cooled in an ice–water bath while potassium nitrate (200 g) was added at such a rate as to maintain the temperature in the range 40–45°. After stirring for an additional 20 min, the solution was poured over crushed ice and made basic with aqueous Na_2CO_3. The product was collected, washed with water, and dried. Recrystallization from methylene chloride–

ethanol gave 165 g (97%) of **10** in two crops. An analytical sample was obtained by a second recrystallization, giving colorless crystals: mp 248°; ir (Nujol) 1640, 1620, 1590, 1530, and 1350 cm^{-1}; nmr ($CDCl_3$) 2.0 (m, 4 H), 2.6–3.4 (m, 4 H), 3.55 (m, 1 H, bridgehead), 7.3–7.8 (m, 3 H), and 8.0–8.6 (m, 3 H); mass spectrum *m/e* 383 (M^+).

Anal. Calcd for $C_{20}H_{15}ClFN_3O_2$: C, 62.59; H, 3.94; N, 10.95; Cl, 9.24; F, 4.95. Found: C, 62.40; H, 3.57; N, 10.90; Cl, 9.24; F, 5.10.

12-Chloro-7,8-dihydro-8-(2-hydroxyethyl)-2-nitro-6*H*-benzo[*b*]indole[3,2,1-*d*,*e*]-1,5-naphthyridine (11). A mixture of compound **10** (140 g) and potassium acetate (170 g) in diglyme (1 l.) was stirred and heated to reflux under argon for 3 hr. After cooling, water (600 ml) and concentrated HCl (300 ml) were added and the resulting mixture was heated on the steam bath for 4 hr. An additional 100 ml of concentrated HCl was then added and heating was continued for 1 hr. The mixture was then poured into excess aqueous Na_2CO_3 and extracted several times with methylene chloride. The combined extract was treated with charcoal, dried over sodium sulfate, and evaporated to leave a yellow solid. This was triturated with ethanol, chilled, filtered, washed with ethanol, and dried to give 58.2 g (42%) of compound **11**. Recrystallization from methylene chloride–ethanol gave light yellow needles: mp 219–220° dec; ir (Nujol) 3200, 1640, 1600, 1525, and 1330 cm^{-1}; nmr (TFA, external TMS) 2.1 (m, 4 H), 3.4–4.0 (m, 3 H), 3.50 (s, OH or NH^+), 4.22 (m, 2 H), 7.3–8.5 (m, 6 H), and 9.25 ppm (s, NH^+ or OH); mass spectrum *m/e* (rel intensity) 336 (40), 337 (100), and 381 (M^+).

Anal. Calcd for $C_{20}H_{16}ClN_3O_3$: C, 62.92; H, 4.22; N, 11.01. Found: C, 62.55; H, 4.23; N, 10.77.

If the reaction mixture was diluted with water, the acetate of **11** precipitated. This compound was difficult to crystallize but was characterized by ir (Nujol) 1735, 1640, 1590, 1520, and 1330 cm^{-1} and mass spectrum *m/e* (rel intensity) 336 (30), 337 (100), and 423 (M^+).

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Registry No.—**1**, 1193-65-3; **2**, 719-59-5; **3**, 21820-07-5; **4**, 784-38-3; **5**, 51230-56-9; **6**, 42471-56-7; **7**, 51230-57-0; **8**, 51230-58-1; **9**, 51230-59-2; **10**, 51230-60-5; **11**, 51230-61-6; **11** acetate, 51230-62-7.

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Ejection of the 19-Methyl Group in Tetracyclic Triterpenes

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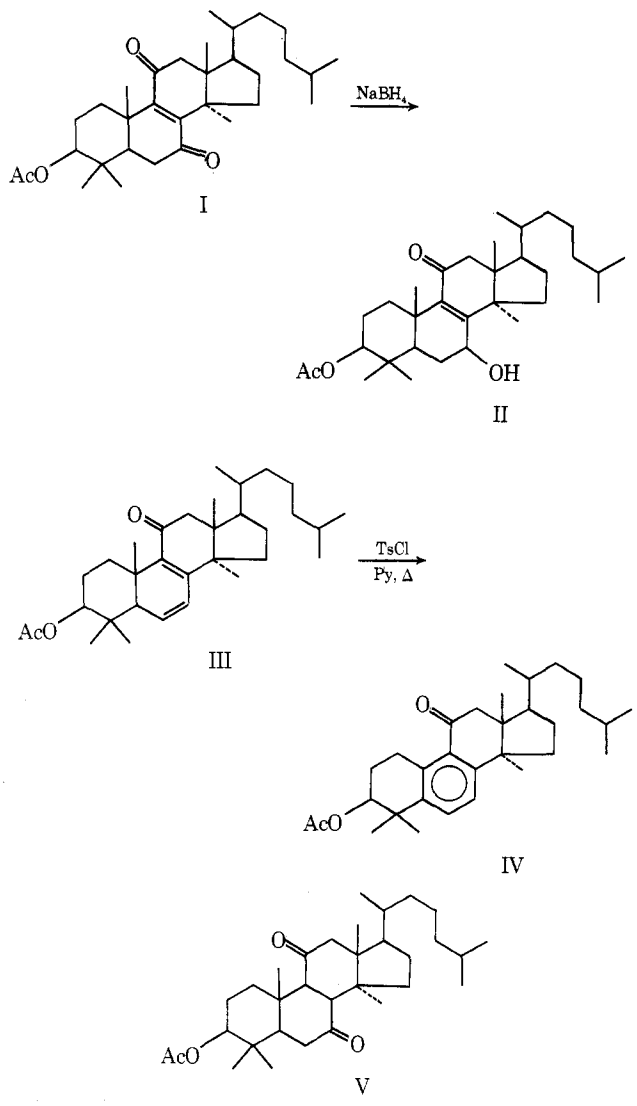
While ways to transform the lanostane skeleton to the cucurbitacin skeleton (a terpene family having potential antileukemic properties)[1] were being explored, a novel ejection of the 19-methyl group concurrently with B-ring aromatization (IV) was observed.[2] Only a few examples of B-ring aromatization of tetracyclic triterpenes have been cited.[3] This reaction (II or III to IV) seems to be unique from these other examples[3] in that it occurs under nonreducing conditions. Pyrolytic conditions led to a similar B-ring aromatization in a steroid system, but ionic conditions produced anthrasteroids instead.[4]

Scheme I



Results

The enedione I was reduced (Scheme I) with sodium borohydride in the presence of ethyl acetate to give the 7β-hydroxy II and 7α-hydroxy products in a 3:1 ratio. Reaction of II with excess gaseous BF_3 in carbon tetrachloride for 1 day or refluxing with a tenfold excess of *p*-toluenesulfonyl chloride (TsCl) in benzene for 3 hr yielded approximately a 1:3 mixture of III and V, respectively. Treatment of II with a tenfold excess of TsCl in pyridine (or collidine) first at 25° for 2 days and then subsequently at refluxing temperature for 2 days gave a 20–30% yield of IV and approximately a 30% yield of V; using benzene instead of pyridine as a solvent gave, under otherwise identical conditions, 16% of I, 11% of III, 11% of IV, and 56% of V. Reaction of II with 1.5 equiv of TsCl in pyridine under the above prescribed conditions produced 19% of I and 51% of V but *no* IV.

Treatment of the 7α-hydroxy isomer of II with a tenfold excess of TsCl in pyridine under identical conditions as above produced some V with unidentified products and no III or IV. When II or III was heated at reflux in pure pyridine or glacial acetic acid for 2 days, no reaction occurred. However, dienone III was converted quantitatively into IV by refluxing for 2 days in pyridine containing TsCl (Scheme I), thus confirming III as an essential intermedi-