Experimental Section

General. Infrared spectra were recorded on a Perkin-Elmer 681 spectrophotometer. Optical rotations were measured with a Perkin-Elmer 137 polarimeter. Melting points (uncorrected) were determined on a Reichert Thermovar apparatus. Exact mass measurements and EIMS were obtained on a VG Micromass ZAB-2F instrument. The NMR experiments were performed on a Brucker WP-200 SY spectrometer. The ^1H couplings were verified by double-resonance experiments. The programs used for DEPT, HETCORR, NOEDIFF, and INAPT (J = 5 Hz, for maximum sensitivity) experiments were those furnished in the Bruker manual. Alumina, Merck, Art. 1077, 5581, and 1092, was used for CC, TLC, and PTLC, respectively. Visualization was effected with Dragendorff's reagent. All solvents, except ethanol, were distilled from glass prior to use. The known reisolated alkaloids were identified by comparison with authentic samples (melting point, IR, MS, and ^1H NMR data).

Isolation of Cardionine (1). Above-ground parts of plants of *Delphinium cardiopetalum* DC[2,3] (2.25 kg) were extracted in 80% EtOH by percolation for 4 days. After removing the solvent under vacuum, the ethanolic extract (238 g) was treated with 0.5 M HCl. The acid solution, washed with $CHCl_3$ and basified with NH_4OH to pH 8, with $CHCl_3$ extraction, gave 14 g of crude alkaloid material. The aqueous phase was then led to pH 12 with 25% NaOH, and extracted with $CHCl_3$ to yield 4 g of additional crude alkaloid material.

The pH 12 alkaloid fraction was chromatographed over alumina with EtOAc and mixtures of EtOAc–MeOH (99:1 to 90:10) to give two main fractions, F_1 (140 mg) and F_2 (2.51 g). Further CC and PTLC, when necessary, yielded cardionine (72 mg) and atisinium chloride[17] (1.95 g) from F_1 and F_2, respectively.

Cardionine (1) had mp 235 °C dec, crystallized from EtOAc: $[\alpha]_D$ 4.68° (c 0.13, EtOH); M^+, m/z 415.2362 for $C_{24}H_{33}NO_5$, Δ −0.4 mmu; IR (KBr) 3340 (br), 2900, 1720, 1260, 1195, 1160, 910, and 860 cm^{-1}; ^1H NMR ($CDCl_3$–CD_3OD, 1:1) δ 1.22 (6 H, d, J = 7 Hz, H-23 and H-24), 1.39 (3 H, s, H-18), 1.62 (1 H, s, H-5), 1.66 (1 H, d, J = 1.7 Hz, H-9), 2.36 (1 H, br d, J = 10.7 Hz, $W_{1/2}$ = 7.5 Hz, H-14), 2.51 (1 H, d, J = 11.8 Hz, H-19α), 2.63 (1 H, sept, J = 7 Hz, H-22), 2.73 (1 H, s, H-20), 3.18 (1 H, d, J = 11.8 Hz, H-19β), 3.86 (1 H, s, H-11α), 5.07 (1 H, d, J = 2 Hz, H-17e), 5.36 (1 H, d, J = 2 Hz, H-17z), and 5.73 (1 H, t, J = 2 Hz, H-15β); MS m/z (relative intensity) 415 (100) M^+, 344 (13), 329 (13), 328 (55), 327 (21), 298 (13), 162 (18), 160 (10), 137 (22), 91 (10), 60 (15), 45 (20), 43 (39), and 41 (18).

Isolation of 11-Acetylcardionine (2). Following the procedure already described, the ethanolic extract (145 g) from the aerial parts of plants of *Delphinium gracile* DC (1.45 kg) yielded pH 8 (6.4 g) and pH 12 (2.6 g) alkaloid fractions. The pH 8 alkaloid fraction was chromatographed over alumina with mixtures of hexane–EtOAc (80:20 to 10:90) and EtOAc to give three main fractions, F_1 (162 mg), F_2 (343 mg), and F_3 (184 mg). Further CC and PTLC yielded gracinine[4] (35 mg) and gadesine[18] (45 mg) from F_1, 11-acetylcardionine (42 mg), nudicaulidine[19] (80 mg), and dihydrogadesine[20] (38 mg) from F_2, and 13-acetylhetisinone[21] (110 mg) from F_3, respectively.

11-Acetylcardionine (2), isolated as a gum, had the following properties: $[\alpha]_D$ −5.71° (c 0.14, $CHCl_3$); M^+, m/z 457.2463 for $C_{26}H_{35}NO_6$, Δ −0.1 mmu; IR ($CHCl_3$) 3540, 3380 (br), 2895, 1710, 1230, 1140, 1050, and 895 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20 (6 H, d, J = 7 Hz, H-23 and H-24), 1.33 (3 H, s, H-18), 1.56 (1 H, s, H-5), 1.65 (1 H, d, J = 2 Hz, H-9), 2.04 (3 H, s, OAc), 2.32 (1 H, br d, J = 10.8 Hz, $W_{1/2}$ = 7.5 Hz, H-14), 2.37 (1 H, d, J = 12.2 Hz, H-19α), 2.59 (1 H, s, H-20), 2.63 (1 H, sept, J = 7 Hz, H-22), 3.08 (1 H, d, J = 12.2 Hz, H-19β), 4.99 (1 H, s, H-11α), 5.01 and 5.34 (1 H each, d, J = 2.5 Hz, H-17e and H-17z), and 5.68 (1 H, t, J = 2.2 Hz, H-15β); MS m/z (relative intensity) 457 (79) M^+, 414 (24), 397 (29), 370 (12), 369 (19), 326 (22), 310 (35), 309 (27), 308 (21), 298 (14), 188 (12), 163 (38), 162 (41), 161 (28), 160 (36), 137 (20), 105 (18), 91 (27), 79 (18), 77 (15), 71 (16), 55 (18), 43 (100), and 41 (46).

Derivatives 3 and 4. Cardionine (1) was treated with a mixture of dry pyridine and acetic anhydride (1 mL) for 12 h at 4 °C, toluene was added, and the solvent was removed under vacuum. The reaction mixture was chromatographed over alumina and eluted with EtOAc to give the neutral and basic diacetates 4 (12 mg) and 3 (13 mg), as resins. Analogous treatment of 11-acetylcardionine (15 mg) gave the same derivatives in similar yield.

The neutral diacetate (4): M^+, m/z 499.2554 for $C_{28}H_{37}NO_7$, Δ +1.6 mmu; IR ($CHCl_3$) 3280 (br), 2920, 1720, 1615, 1400, 1235, 1190, 1150, 1050, 1030, 980, and 920 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 (3 H, s, H-18), 1.14 (6 H, d, J = 7 Hz, H-23 and H-24), 1.67 (1 H, d, J = 3 Hz, H-9), 2.04 (3 H, s, OAc), 2.14 (3 H, s, NAc), 2.52 (1 H, sept, J = Hz, H-22), 2.99 and 3.31 (1 H each, d, J = 12.4 Hz, H-19α and H-19β), 3.97 (1 H, s, H-20), 5.16 (1 H, s, H-11α), 5.22 and 5.33 (1 H each, s, H-17e and H-17z), and 5.65 (1 H, s, H-15β); MS m/z (relative intensity) 499 (29) M^+, 458 (28), 457 (100), 456 (54), 414 (10), 369 (29), 368 (19), 326 (17), 310 (14), 309 (13), 308 (19), 291 (22), 162 (13), 161 (12), 160 (13), 711 (19), 69 (11), and 57 (21).

The basic diacetate (3): M^+, m/z 499.2550 for $C_{28}H_{37}NO_7$, Δ +2.0 mmu; IR (KBr), 3430 (br), 3170 (br), 2920, 1735, 1718, 1460, 1360, 1240, 1220, 1155, 1132, 1070, 1030, 970, and 900 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.03 (3 H, s, H-18), 1.17 (6 H, d, J = 7 Hz, H-23 and H-24), 2.01 and 2.04 (3 H each, s, 2 OAc), 2.32 (1 H, br d, J = 11 Hz, $W_{1/2}$ = 7.5 Hz, H-14), 2.34 (1 H, s, H-5), 2.43 (1 H, d, J = 12.6 Hz, H-7α), 2.43 (1 H, d, J = 12.5 Hz, H-19α), 2.54 (1 H, s, H-20), 2.57 (1 H, sept, J = 7 Hz, H-22), 2.96 (1 H, d, J = 12.5 Hz, H-19β), 4.95 (1 H, s, H-11α), 4.99 and 5.31 (1 H each, d, J = 2.5 Hz, H-17e and H-17z), 5.65 (1 H, t, J = 2 Hz, H-15β); MS m/z (relative intensity) 499 (29), 458 (28), 457 (100), 456 (54), 414 (10), 369 (29), 368 (19), 326 (17), 310 (14), 309 (13), 308 (19), 291 (22), 162 (13), 161 (12), 160 (13), 71 (19), 57 (21), and 55 (19).

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Registry No. 1, 123151-94-0; 2, 123151-95-1; 3, 123151-96-2; 4, 123151-97-3; atisinium chloride, 4758-99-0; gracinine, 107040-83-5; gadesine, 70420-60-9; nudicaulidine, 99815-81-3; dihydrogagesine, 70420-63-2; 13-acetylhetisinone, 82209-94-7.

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Synthesis and Structure of *as*-Triazinoquinazolines. 3[1,2]

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Recently, we reported the synthesis and structure of two isomeric *as*-triazinoquinazoline derivatives, viz., *as*-triazino[3,2-*b*]quinazolines and *as*-triazino[3,4-*b*]-quinazolines.[1,2] The present investigation reports our attempts to construct new *as*-triazino[4,3-*a*]quinazolines ring system. A convenient starting point in the synthetic pathway toward compound of type A depends on our recent findings that heterocyclic compounds containing an *N*-amino amide moiety ($CONNH_2$) can serve as a potential protecting group for obtaining certain isomeric condensed

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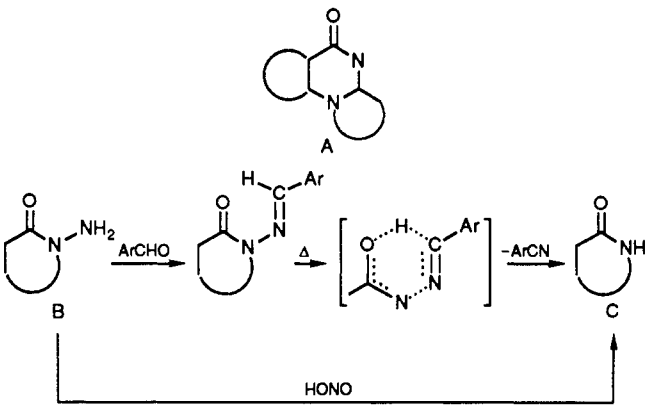
Table I

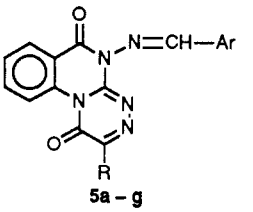
compd[a]	mp, °C	yield, %	recryst solvt	formula (MW)	anal. % calcd/found C	H	N
2a	205–7	93	NaOH/HCl	$C_{11}H_{11}N_5O_3$ (261.24)	50.57	4.24	26.81
					50.30	4.10	26.60
2b	212–3	95	NaOH/HCl	$C_{16}H_{13}N_5O_3$ (323.31)	59.44	4.05	21.66
					59.20	4.20	21.50
2c	205–6	94	NaOH/HCl	$C_{18}H_{15}N_5O_3$ (349.35)	61.89	4.33	20.05
					61.70	4.50	20.10
2d	195–7	94	NaOH/HCl	$C_{19}H_{17}N_5O_4$ (379.38)	60.15	4.52	18.46
					59.90	4.60	18.20
3a	278–9	70	acetic acid	$C_{11}H_9N_5O_2$ (243.23)	54.32	3.73	28.79
					54.40	3.50	28.80
3b	195–7	73	acetic acid	$C_{16}H_{11}N_5O_2$ (305.30)	62.95	3.63	22.94
					63.10	3.50	22.80
3c	234–6	72	DMF	$C_{18}H_{13}N_5O_2$ (331.34)	65.25	3.95	21.14
					65.50	3.70	21.20
3d	248–9	88	acetic acid	$C_{19}H_{15}N_5O_3$ (361.36)	63.15	4.18	19.38
					63.00	3.90	19.10

[a] **3a**, UV λ_{max} (log ϵ) = 265 (3.98), 270 (3.35) nm; **3b**, 212 (5.1), 272 (4.6) nm; **3c**, 296 (4.6) nm; **3d**, 390 (4.3) nm. **3a**, IR 3350, 3300 (NH), 1735, 1655 (C=O) cm^{-1}; **3d**, 3325, 3225 (NH), 1710, 1680 (C=O) cm^{-1}.

Scheme I



systems.[3] The *N*-amino amide groups undergo facile removal by the action of nitrous acid[3,4] or by condensation with aldehydes followed by thermolysis[5] as shown in Scheme I. The latter reaction was suggested to be a thermally allowed concerted reaction (similar to the reteroene reactions[6]). We, therefore, used this strategy to selectively and unequivocally synthesize the target compounds 6 (Scheme II). Thus condensation of 3-amino-2-hydrazinoquinazolin-4(1*H*)-one (1) with α-keto acids, namely, pyruvic acid, phenylglyoxylic acid, benzylidenepyruvic acid, and *p*-methoxybenzylidenepyruvic acid led to the formation of the corresponding α-keto acid hydrazones **2a–d**, respectively. Cyclization of the latter was readily effected by heating under reflux in acetic acid for 3–5 h to afford the corresponding 5-amino-1,6-dioxo-5,1-dihydro-1*H*-*as*-triazino[4,3-*a*]quinazolines **3a–d**, respectively. Tetrazepinoquinazolines **4** are also expected as a reaction products from cyclization of compounds **2a–d**; however, this was excluded based on the ready condensation of these products with the appropriate aromatic aldehydes to give the corresponding 5-arylideneamino derivatives **5a–g**. Moreover, the reaction of compounds



5a – g

	R	Ar
a	Ph	Ph
b	Ph	*p*-$MeOC_6H_4$
c	Ph	*p*-ClC_6H_4
d	PhCH=CH	*p*-$MeOC_6H_4$
e	PhCH=CH	*p*-ClC_6H_4
f	*p*-$MeOC_6H_4CH$=CH	Ph
g	*p*-$MeOC_6H_4CH$=CH	*p*-ClC_6H_4

3a–d with nitrous acid led to the unprecedented selective synthesis of the corresponding 1,6-dioxo-5,6-dihydro-1*H*-*as*-triazino[4,3-*a*]quinazolines **6a–d**, respectively. Compounds **6** were also obtained along with benzonitrile either by pyrolysis of the appropriate arylideneamino derivatives **5** or by direct reaction of compounds **3** with aromatic aldehydes at 180–200 °C for 1 h. The reaction of compound **6b** with diazomethane was shown to give mainly **7**. The latter was shown to be different from the other possible expected isomeric product **8a** obtained from 2-hydrazino-3-methylquinazolin-4(3*H*)-one (**9**). Moreover, an O-methylated product is not favored on the basis of the appearance of two carbonyl bands and also the presence of a N-CH_3 signal at δ 3.78 in the expected region for such N-methylated triazinoquinazolines (the isomeric 1-methyltriazino[3,4-*b*]quinazoline-4,6-dione showed an N-CH_3 signal at δ 3.92[1]). Thus condensation of **9** with phenylglyoxylic acid gave the corresponding hydrazone **10a**, which was readily cyclized into **8a** by the action of acetic anhydride. On the other hand, attempts to cyclize compound **10a** by heating in dimethylformamide led to decarboxylation, and the benzaldehyde hydrazone **11** was obtained. The latter was alternatively synthesized by the reaction of benzaldehyde with compound **9**.

Experimental Section

All melting points are uncorrected. The UV spectra were measured in methanol, with a Unicam Model SP 1750 spec-

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Scheme II

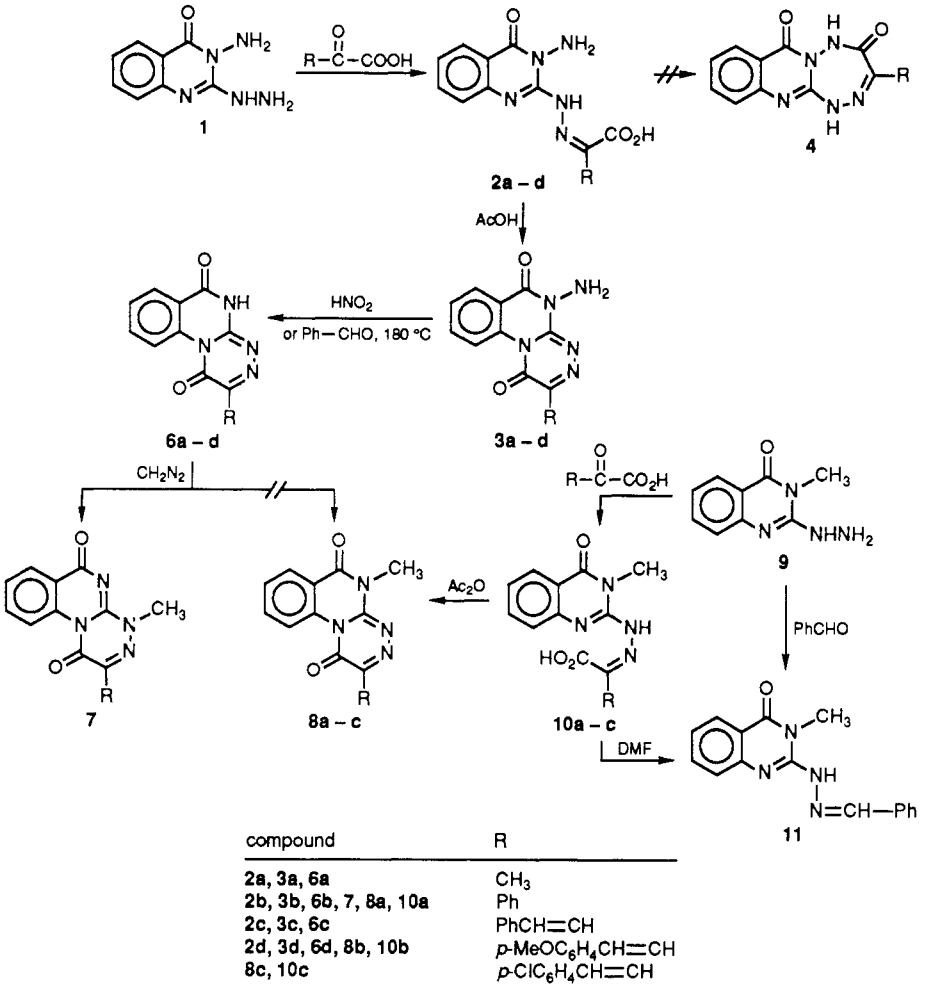

Table II

compd[a]	mp, °C	yield, %	recryst solvt	formula (MW)	anal.[b] % calcd/found C	H	N
5a	248–9	95	acetic acid	$C_{23}H_{15}N_5O_2$ (393.41)	70.22	3.84	17.80
					70.10	3.60	17.60
5b	230–2	93	DMF/alc	$C_{24}H_{17}N_5O_3$ (423.43)	68.08	4.05	16.45
					68.10	4.20	16.40
5c	257–8	96	butanol	$C_{23}H_{14}N_5O_2Cl$ (427.85)	64.57	3.30	16.37
					64.70	3.10	16.20
5d	222–3	95	butanol	$C_{26}H_{19}N_5O_3$ (449.47)	69.48	4.26	15.58
					69.40	4.30	15.60
5e	238–9	95	butanol	$C_{25}H_{16}N_5O_2Cl$ (453.89)	66.16	3.55	15.43
					66.20	3.40	15.60
5f	284–6	94	DMF	$C_{26}H_{19}N_5O_3$ (449.47)	69.48	4.26	15.58
					69.60	4.10	15.50
5g	232–4	93	butanol	$C_{26}H_{18}N_5O_3Cl$ (483.92)	64.53	3.75	14.47
					64.20	3.90	14.50
6a	>300	80	DMF	$C_{11}H_8N_4O_2$ (228.21)	57.89	3.53	24.55
					57.10	3.40	24.60
6b	>300	78	DMF	$C_{16}H_{10}N_4O_2$ (290.28)	66.20	3.47	19.30
					66.10	3.20	19.20
6c	>300	81	DMF	$C_{18}H_{12}N_4O_2$ (316.32)	68.35	3.82	17.71
					68.10	3.60	17.80
6d	>300	79	DMF	$C_{19}H_{14}N_4O_3$ (346.35)	65.89	4.07	16.18
					66.00	4.10	16.30

[a] **6a**, UV λ_{max} (log ϵ) = 230 (5.34), 252 (4.72) nm; **6b**, 272 (4.44) nm; **6c**, 288 (4.23), 332 (3.90) nm; **6d**, 370 (4.60) nm. **6a**, IR 3200 (NH), 1740, 1660 (C=O) cm^{-1}; **6c**, 3200 (NH), 1750, 1680 (C=O) cm^{-1}. [b] **5c**: Cl, calcd 8.28, found 8.00. **5e**: Cl, calcd 7.81, found 8.10. **5g**: Cl, calcd 7.32, found 7.50.

trometer. The ^1H NMR spectra were determined on a Varian EM 390 90-MHz spectrometer in $CDCl_3$ using TMS as an internal standard. The IR spectra (KBr) were recorded with a Unicam SP 1200 infrared spectrophotometer. Compounds prepared by different procedures were confirmed by mixed melting points and by identity of IR spectra.

Preparation of α-Keto Acid Hydrazones 2a–d. Compound 1[7] (0.01 mol) was heated under reflux with the appropriate α-keto

Table III

compd[a]	mp, °C	yield, %	recryst solvt	formula (MW)	anal.[b] % calcd/found C	H	N
8a	195-7	88	ethanol	$C_{17}H_{12}N_4O_2$ (304.31)	67.10	3.97	18.41
					67.30	4.10	18.20
8b	248-9	85	acetic acid	$C_{20}H_{16}N_4O_3$ (360.38)	66.66	4.48	15.55
					66.90	4.30	15.30
8c	227-9	85	acetic acid	$C_{19}H_{13}N_4O_2Cl$ (364.79)	62.56	3.59	15.36
					62.30	3.60	15.20
10a	183-5	93	acetic acid	$C_{17}H_{14}N_4O_3$ (322.33)	63.35	4.38	17.38
					63.50	4.30	17.50
10b	220-2	95	acetic acid	$C_{20}H_{18}N_4O_4$ (378.39)	63.49	4.79	18.81
					63.30	4.90	14.60
10c	215-7	93	acetic acid	$C_{19}H_{15}N_4O_3Cl$ (382.81)	59.62	3.95	14.64
					59.40	4.20	14.40

[a] **8a**, UV λ_{max} (log ϵ) = 216 (4.99), 315 (4.30) nm; IR 1690, 1650 (C=O) cm^{-1}; ^1H NMR δ 3.78 (s, 3 H, NMe), 7.40-8.40 (m, 9 H, ArH). [b] **8c**: Cl, calcd 9.72, found 10.00. **10c**: Cl, calcd 9.26, found 9.50.

acid (0.01 mol) in water (20 mL) for 15 min, during which time a crystalline precipitate began to separate. After cooling, the product was collected, dried and purified by dissolving in aqueous 5% NaOH solution, filtered, and reprecipitated with concentrated hydrochloric acid as yellow precipitates of **2a-d** in almost quantitative yield (Table I).

5-Amino-1,6-dioxo-5,6-dihydro-1*H*-*as*-triazino[4,3-*a*]-quinazolines 3a-d. Each of compounds **2a-d** (0.01 mol) was heated under reflux in glacial acetic acid (20 mL) for 3-5 h. The product obtained upon cooling was collected and crystallized from acetic acid as yellow crystals of **3a-d** (Table I).

5-(Arylideneamino)triazinoquinazolines 5a-g. General Procedure. The following exemplifies the procedure. Compound **3b** (0.01 mol) was heated under reflux in glacial acetic acid (15 mL) with benzaldehyde (0.01 mol) and fused sodium acetate (2 g) for 1-2 h, during which time a crystalline precipitate began to separate. After cooling, the product was collected, dried, and crystallized from acetic acid as yellow crystals of **5a** (Table II).

Action of Nitrous Acid on 3a-d. To a suspension of each of **3a-d** (0.5 g) in 6 N HCl (10 mL) was added dropwise while cooling and stirring sodium nitrite solution (0.5 g in 15 mL of water). The reaction mixture was left at room temperature for 15 min. The solid obtained was collected, washed with water, and crystallized from DMF as yellow crystals of **6a-d** (Table II).

Thermal Deamination of Compounds 3b,d. A mixture of each of **3b** and **3d** (0.01 mol) was heated at 180-200 °C in an oil bath with benzaldehyde (0.011 mol) for 2 h, during which time benzonitrile was noticeably evolved (and identified by IR and GC after extraction with chloroform from the reaction vessels). After cooling, the residue was triturated with ethanol. The obtained products were then crystallized from DMF as yellow crystals and were proved to be **6b** and **6d**, respectively.

Pyrolysis of Compound 5a. Compound **5a** (0.5 g) was heated at 250 °C (metal bath) for 30 min during which time benzonitrile was noticeably evolved. The solid remained was crystallized from DMF into compound **6b**.

Action of Diazomethane on 6b. An ethereal solution of diazomethane (prepared from 3 g of *N*-methyl-*N*-nitrosourea and 50 mL of ether) was added to 1 g of compound **6b**. After standing overnight in the refrigerator, the solution was evaporated at room temperature. The remaining solid was crystallized from ethanol into yellow crystals of **7**, mp 199 °C, yield 88%. Anal. Calcd. for $C_{17}H_{12}N_4O_2$ (304.31): C, 67.10; H, 3.97; N, 19.41. Found: C, 66.90; H, 3.80; N, 18.20. UV λ_{max} = 218, 270 nm; IR (KBr) 1720, 1695 (C=O) cm^{-1}; ^1H NMR δ 3.68 (s, 3 H, NMe), 7.35-8.35 (m, 9 H, Ar H).

Preparation of α-Keto Acid Hydrazones 10a-c. Compound **9**[8] (0.01 mol) was heated under reflux with the appropriate α-keto acid (0.01 mol) in ethanol (20 mL) for 15 min, during which time a crystalline precipitate began to separate. After cooling, the product was collected, dried, and crystallized from acetic acid as yellow crystals of **10a-c** (Table III).

Preparation of Compound 11. (a) A solution of compound **10b** (0.5 g) in DMF (10 mL) was heated under reflux for 2 h, cooled, and then diluted with water. The precipitate was collected and recrystallized from ethanol into yellow crystals of **11**, mp 158 °C, yield 72%. Anal. Calcd for $C_{16}H_{14}N_4O$ (278.32): C, 69.05; H, 5.07; N, 20.13. Found: C, 69.10; H, 4.80; N, 20.20.

(b) A solution of compound **9** (0.01 mol) and benzaldehyde (0.01 mol) in ethanol (15 mL) was heated under reflux for 10 min. The solid obtained upon cooling was crystallized from ethanol and proved to be **11** (mixed mp), yield 92%; ^1H NMR δ 3.56 (s, 3 H, NMe), 7.06-8.26 (m, 9 H, Ar H), 8.56 (s, 1 H, benzal CH), 9.36 (s, 1 H, NH).

Registry No. **1**, 19062-39-6; **2a**, 123565-87-7; **2b**, 123565-88-8; **2c**, 123593-02-2; **2d**, 123565-89-9; **3a**, 123565-90-2; **3b**, 123565-91-3; **3c**, 123565-92-4; **3d**, 123565-93-5; **5a**, 123565-94-6; **5b**, 123565-95-7; **5c**, 123565-96-8; **5d**, 123565-97-9; **5e**, 123565-98-0; **5f**, 123565-99-1; **5g**, 123566-00-7; **6a**, 123566-01-8; **6b**, 123566-02-9; **6c**, 123566-03-0; **6d**, 123566-04-1; **7**, 123566-05-2; **8a**, 123566-06-3; **8b**, 123566-07-4; **8c**, 123566-08-5; **9**, 61507-80-0; **10a**, 123593-03-3; **10b**, 123566-09-6; **10c**, 123566-10-9; **11**, 123566-11-0; *p*-ClC_6H_4CH=$CHCOCO_2H$, 33185-97-6; PhCHO, 100-52-7; *p*-$MeOC_6H_4CHO$, 123-11-5; P-ClC_6H_4CHO, 104-88-1; pyruvic acid, 127-17-3; phenylglyoxylic acid, 611-73-4; benzylidinepyruvic acid, 17451-19-3; *p*-methoxybenzylidenepyruvic acid, 17451-21-7; benzonitrile, 100-47-0.

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Microbiological Transformations. 13. A Direct Synthesis of Both *S* and *R* Enantiomers of 5-Hexadecanolide via an Enantioselective Microbiological Baeyer-Villiger Reaction

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The conversion of ketones to esters or lactones, i.e., the Baeyer-Villiger reaction,[1] is obviously one of the very important reactions in organic synthesis. However, the corresponding asymmetric Baeyer-Villiger reaction seems, up to now, to be unknown in the chemical literature. On the other hand, various studies have shown that "biological Baeyer-Villiger" reactions are involved in the oxidative degradation of a wide variety of organic compounds,[2] e.g.,

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