stirred for 90 min and then 0.71 g (5 mmol) of methyl iodide was added slowly. After another 5 min of stirring, 50 ml of water was added and the product was isolated in usual fashion. Recrystallization from aqueous methanol yielded 0.515 g (50%) of white crystals: mp 103–104°; NMR ($CDCl_3$) δ 2.49 (s, 3 H, CH_3), 2.79 (d, 3 H, J = 5.0 Hz, NCH_3), 5.9–6.2 (m, 1 H, NH), 6.5–8.1 (m, 8 H, aromatic).

On the basis of this and other evidence the compound is tentatively identified as 2-(*N*-methylamino)-2′-methyldiphenyl sulfone (**2j**).

A similar solution of dianion was prepared from 1.7 g (6.9 mmol) of **1a** in 15 ml of dry THF and treated dropwise with 1.05 g (10 mmol) of benzaldehyde. After stirring for another 15 min the mixture was quenched with water and the product was isolated. The resulting viscous oil was purified by chromatography on silica gel, eluting with carbon tetrachloride–chloroform. This yielded 2.07 g (85%) of clear oil which crystallized on standing: mp 115–116°; NMR ($CDCl_3$) δ 2.63 (d, 3 H, J = 5.0 Hz, NCH_3), 3.57 (broadened d, 1 H, J = 4.0 Hz, OH), 6.05 (broadened d, 1 H, J = 4.0 Hz, C-H), 6.4–7.9 (m, 14 H, aromatic and NH).

On the basis of this and subsequent evidence, the material is tentatively assigned structure **7**.

Preparation of 10-Methyl-11-phenyldibenzo[*b,f*][1,4]thiazepin 5,5-Dioxide (8). To 2.07 g (5.86 mmol) of alcohol **7** was added 150 mg of anhydrous zinc chloride. The neat mixture was then heated at 115–120° under a nitrogen atmosphere for 40 min. At this point the mixture had solidified. After cooling, 50 ml of water was added and the mixture was extracted with chloroform. After drying with magnesium sulfate, removal of solvent, and recrystallization from aqueous ethanol, 1.45 g (73%) of a white solid was obtained: mp 211–212°; NMR ($CDCl_3$) δ 2.95 (s, 3 H, NCH_3), 6.02 (broadened s, 1 H, CH), 6.67–7.55 (m, 13 H, aromatic); mass spectrum *m/e* 335 (parent), 306, 270.

Anal. Calcd for $C_{20}H_{16}NO_2S$: C, 71.62; H, 5.11. Found: C, 71.31; H, 5.12.

Registry No.—**1a**, 90-10-8; **1e**, 35088-88-1; **1g**, 53973-86-7; **5**, 53973-87-8; **7**, 53973-88-9; **8**, 53973-89-0; 2,6-dimethylaniline, 87-62-7; benzenesulfonyl chloride, 98-09-9.

References and Notes

(1) (a) Supported in part by the U.S. Public Health Service (Research Grant No. R01-AM11419 from the National Institute of Arthritis and Metabolic Diseases), and by the Alfred P. Sloan Foundation. (b) Presented in part at the 165th National Meeting of the American Chemical Society, Dallas, Texas, April 1973, Abstract ORGN 093. (c) Some similar results have been since reported by D. Hellwinkel and M. Supp, *Angew. Chem.*, **86**, 273 (1974).
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A Novel and Efficient Route to 5-Arylated γ-Lactones

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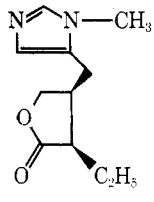
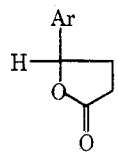
Title compounds (IV) were prepared by oxidation of lactols I with Ag_2CO_3 on Celite in refluxing xylene. Lactols I were obtained from reaction of ketones II with organomagnesium compound III and subsequent hydrolysis of the products V in 10% sulfuric acid. Prepared were the following compounds IV (R_1, R_2 given): H, 3-pyridyl; H, 4-pyridyl; H, 1-benzylimidazol-2-yl; H, 1-methylimidazol-2-yl; H, 1-benzyl-2-methylimidazol-5-yl; H, 1-benzyl-2-isopropylimidazol-5-yl; H, 1,2-dimethylimidazol-5-yl; phenyl, phenyl.

In our current research program we were interested in lactones of type I, bearing an imidazole or pyridine moiety at the 5 position, in order to examine their anticholinergic activities compared to pilocarpine (1). A survey of the literature revealed that there are no convenient methods to synthesize lactones of this particular type, because of the difficult availability of the required starting materials or inconvenient experimental conditions of the documented methods.



1



I

However, in a recent report,[2] benzimidazoles could be synthesized by reaction of readily available carboxaldehydes with the Grignard derivative of 2-(2-bromoethyl)-dioxolane-1,3 (**3**)[3] and subsequent cyclization in alcoholic medium. It was established that these reactions proceed *via* lactols as intermediates, which in fact could be isolated. With this consideration in mind, it was obvious that oxidation of the lactols might afford the required lactones.

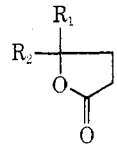
Reaction of the aldehyde **2d** with Grignard derivative **3** in tetrahydrofuran gave **4d**, which upon refluxing in 10% sulfuric acid afforded lactol **5d**. Oxidation of this lactol with convenient reagents such as permanganate, chromous trioxide, manganese dioxide, and silver oxide did not provide the desired lactone **6d**.

At that stage our attention was focussed to the work of Fetizon, *et al.*,[4] who reported that lactones should be generated from 1,5-diols in one simple oxidative conversion by silver carbonate on Celite.

There is much evidence that this reaction proceeds *via* the lactol stage.[5] Indeed, on refluxing lactol **5d** with silver carbonate on Celite, in xylene as solvent, lactone **6d** could be obtained in a 51% yield. Treatment of lactols **5a–c** and **5e,f** under similar conditions gave in moderate to good yields lactones **6a–c** and **6e,f**.

Further elucidation of this reaction showed that this method is not restricted to heterocyclic compounds. So, on

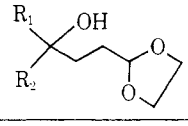
Table I[b]
Lactones



Compd	Yield, %	Mp, °C	Deriv	Mp, °C	Empirical formula
6a	55		Picrate	131–132	$C_9H_9NO_2$
6b	48	56–57	Picrate	152–153	$C_9H_9NO_2$
6c	51	132–132.5			$C_{17}H_{26}N_2O_2$
6d	61	117.5–118.5			$C_{15}H_{16}N_2O_2$
6e	49	88–89			$C_9H_{12}N_2O_2$
6f	25	76–76.5			$C_{14}H_{14}N_2O_2$
6g	22		Picrate	147–149	$C_8H_{10}N_2O_2$
6h[a]	71	86–88			$C_{16}H_{14}O_2$

[a] H. A. Staab, K. Wendel, and A. P. Datta, *Justus Liebigs Ann. Chem.*, **694**, 78 (1966): mp 91–92°. [b] Satisfactory analytical data (±0.3% for C, H, N) were reported for compounds **6a–g**.

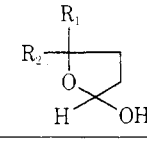
Table II[c]
Open-Chain Precursors



Compd	Yield, %	Mp, °C	Empirical formula
4a	91[a]		$C_{11}H_{15}NO_3$
4b	95	68.5–69.5	$C_{11}H_{15}NO_3$
4c[b]	96	90–91	$C_{19}H_{26}N_2O_3$
4d[b]	84	108–110	$C_{17}H_{22}N_2O_3$
4e	70	106–107	$C_{11}H_{18}N_2O_3$
4f	88	85–86	$C_{16}H_{20}N_2O_3$
4g	80[a]		$C_{10}H_{16}N_2O_3$
4h	90	76.5–77	$C_{18}H_{20}O_3$

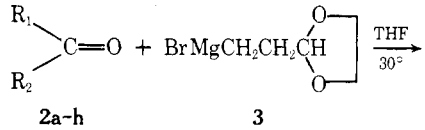
[a] Product was obtained as an oil; the nmr data were consistent with the assigned structure. [b] H. J. J. Loozen and E. F. Godefroi, *J. Org. Chem.*, **38**, 3495 (1973). [c] Satisfactory analytical data (±0.3% for C, H, N) were reported for compounds **4b,e,f** (C and H for **4h**).

Table III[c]
Lactols

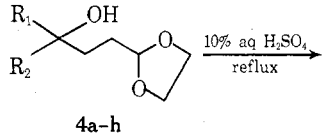


Compd	Yield, %	Mp, °C	Empirical formula
5a	95[a]		$C_9H_{11}NO_2$
5b	84	117–118	$C_9H_{11}NO_2$
5c[b]	92	138–139	$C_{17}H_{22}N_2O_2$
5d[b]	84	99–100	$C_{15}H_{18}N_2O_2$
5e	94[a]		$C_9H_{14}N_2O_2$
5f	82	117–119	$C_{14}H_{16}N_2O_2$
5g	76	146–148	$C_8H_{12}N_2O_2$
5h	74	122–124	$C_{16}H_{16}O_2$

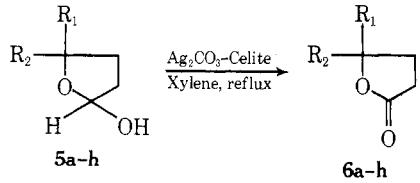
[a] Yield based on crude oil; nmr was consistent with the assigned structure. [b] H. J. J. Loozen and E. F. Godefroi, *J. Org. Chem.*, **38**, 3495 (1973). [c] Satisfactory analytical data (±0.3% for C, H, N) were reported for compounds **5b, 5f,** and **5g** (C and H for **5h**).



2a–h **3**



4a–h



5a–h **6a–h**

a, R_1 = 3-pyridyl; R_2 = H
b, R_1 = 4-pyridyl; R_2 = H
c, R_1 = 1-benzyl-2-isopropylimidazol-5-yl; R_2 = H
d, R_1 = 1-benzyl-2-methylimidazol-5-yl; R_2 = H
e, R_1 = 1,2-dimethylimidazol-5-yl; R_2 = H
f, R_1 = R_1 = 1-benzylimidazol-2-yl; R_2 = H
g, R_1 = 1-methylimidazol-2-yl; R_2 = H
h, R_1 = R_2 = phenyl

starting from benzophenone (**2h**) in a three-step sequence 5,5-diphenylbutyrolactone was obtained in 50% overall yield. The results are summarized in Table I–III.

Experimental Section

General. Melting points were determined on a Mettler apparatus and are uncorrected. Nmr data (Varian A-60, TMS as an internal standard) were consistent with the assigned structures. The intermediate oils **5a, 5e, 4a,** and **4f** were characterized by means of nmr and were converted as is into the products offered in Table I and II. Microanalyses were performed in our laboratories by Messrs. H. Eding and P. van den Bosch.

Starting Materials. Benzophenone and the pyridine carboxaldehydes were commercially available. The aldehydes **2c–e** were prepared as reported.[6] Aldehyde **2g** was obtained analogously: (a) from 1-methylimidazole to the 2-hydroxymethyl derivative (aqueous formaldehyde; 72 hr reflux; 51% yield), mp 91–92.5° (ethanol–$(i\text{-Pr})_2O$); (b) from oxidation (MnO_2–benzene)[7] of the corresponding carbinol to **2g** (71%), bp 90–95° (6 mm). Aldehyde **2f** was prepared by oxidation of the corresponding carbinol[8] with MnO_2 in 75% yield, bp 117–125° (0.01 mm).

All lactones, lactols, and their open-chained precursors have been compiled in the corresponding tables. The general preparation of the lactones is illustrated by the synthesis of **6b.**

1-(1,3-Dioxolan-2-yl)-3-hydroxy-3(4-pyridyl)propane (4b). To a solution of **3** in THF, prepared from 5 g (0.026 mol) of the bromide[3] and 0.65 g (0.26 g-atom) of Mg, was added dropwise with stirring a solution of 2.14 g (0.02 mol) of pyridine-4-carboxal-

dehyde in 10 ml of dry ether. After 2 hr the mixture was poured into 100 ml of 10% NH_4Cl solution. Extraction of the reaction product with chloroform and washing, drying, and evaporating of the solvent left 3.9 g (95%) of a solid: mp (benzene–petroleum ether) 68.5–69.5°; nmr ($CDCl_3$) δ 1.64–1.92 (m, 4, $-CH_2CH_2-$), 3.72–4.03 (m, 4, dioxolane protons); ir (KBr) 3300 cm^{-1} broad OH absorption.

4-Hydroxy-4-pyridylbutanal (as Hemiacetal 5b). A solution of 3.6 g (0.017 mol) of **4b** in 50 ml of 10% aqueous sulfuric acid was refluxed for 30 min. The mixture was cooled, made alkaline with 5 *N* NaOH, and extracted with chloroform. After drying and evaporation of the solvent the residual oil was chromatographed over SiO_2 ($CHCl_3$–2% CH_3OH as eluent) and afforded 2.3 g (8) of **5b**: mp ($CHCl_3$–(*i*-Pr)$_2O$) 117–118°; nmr ($CDCl_3$) δ 1.38–2.70 (m, 4, $-CH_2CH_2-$), 8.04 (ab, 4, pyridine protons); the ir spectrum (KBr) showed no C=O absorption, only broad OH band at 3300 cm^{-1}.

Dihydro-5-(4-pyridyl)-2(3*H*)-furanone (6b). To a solution of 0.33 g (0.002 mol) of **5b** in 20 ml of xylene was added 5.9 g of Ag_2CO_3–Celite (prepared according to the method of Fetizon; five times molar excess). The mixture was refluxed with stirring for 0.5 hr (on monitoring the reaction by tlc). After filtering the reaction mixture and stripping off the solvent, 0.16 g (48%) of **6** was obtained, as a solid: mp 56–57°; ir (KBr) strong C=O lactone absorption at 1760 cm^{-1}; nmr ($CDCl_3$) δ 1.93–3.18 (m, 4, $-CH_2CH_2-$), 5.57 (t, 1, CH), 8.00 (ab, 4, pyridine protons).

Registry No.—**2a**, 500-22-1; **2b**, 872-85-5; **2c**, 39269-79-9; **2d**, 39269-74-4; **2e**, 24134-12-1; **2f**, 10045-65-5; **2f** corresponding carbinol, 5376-10-3; **2g**, 13750-81-7; **2g** corresponding carbinol, 17334-08-6; **2h**, 119-61-9; **4a**, 53798-67-7; **4b**, 53798-68-8; **4c**, 41030-03-9; **4d**, 41030-01-7; **4e**, 53798-69-9; **4f**, 53798-70-2; **4g**, 53798-71-3; **4h**, 53798-72-4; **5a**, 53798-73-5; **5b**, 53798-74-6; **5c**, 41030-06-2; **5d**, 53798-75-7; **5e**, 53821-45-7; **5f**, 53798-76-8; **5g**, 53798-77-9; **5h**, 53798-78-0; **6a**, 20971-79-3; **6a** picrate, 53798-79-1; **6b**, 53798-80-4; **6b** picrate, 53798-81-5; **6c**, 53798-82-6; **6d**, 53798-83-7; **6e**, 53798-84-8; **6f**, 53798-85-9; **6g**, 53798-86-0; **6g** picrate, 53798-87-1; **6h**, 7746-94-3; 2-(1,3-dioxolan-2-yl)ethyl bromide, 18742-02-4; 1-methylimidazole, 616-47-7.

References and Notes

(1) Address correspondence to this author.
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Quinazolines and 1,4-Benzodiazepines. LXX.[1] *v*-Triazolo[1,5-*a*][1,4]benzodiazepines

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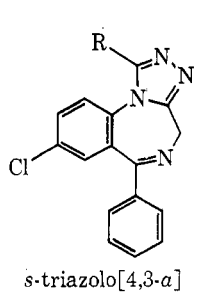
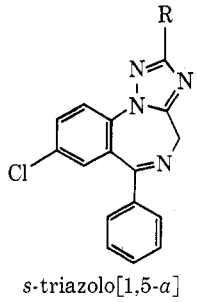
The cycloaddition reaction of 2-azido-5-chlorobenzophenone with dimethyl acetylenedicarboxylate provides 1-(2-benzoyl-4-chlorophenyl)-1*H*-1,2,3-triazole-4,5-dicarboxylic acid dimethyl ester. The oxime of this ketone undergoes reductive cyclization with zinc in acid which, together with subsequent transformations, give the first examples of the new tricyclic ring system named in the title.

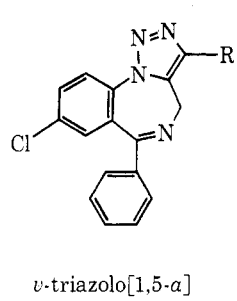
1,4-Benzodiazepines embellished with a triazole ring have been the subject of several recent reports in both the journal[2,3] and patent[4–7] literature. Compounds of types **1**[2–6] and **2**[7] are known compounds and represent the two possible ring systems in which an *s*-triazole ring is fused to the 1,2 positions of a 1,4-benzodiazepine. The third possible ring system of this type in which a *v*-triazole is so incorporated is exemplified in compounds **3** and **4**. A synthesis of such previously unknown compounds is the subject of this paper.



s-triazolo[4,3-*a*]
1

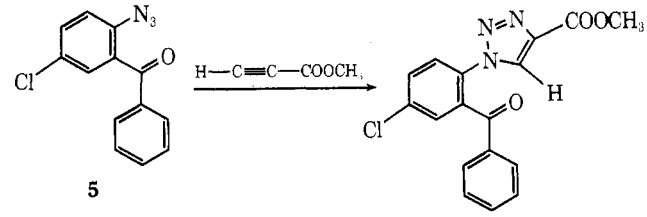


s-triazolo[1,5-*a*]
2



v-triazolo[1,5-*a*]
3, R = H
4, R = CH_3

Of the several methods for the synthesis of *v*-triazoles,[8] the cycloaddition of acetylene derivatives to azides[9] appeared to be most applicable in the present instance, particularly since the appropriate azide **5** is readily accessible[10] from (commercially available) 2-amino-5-chlorobenzophenone. We initially anticipated a direct, essentially one-step synthesis of **3** by cycloaddition–condensation of propargyl amine with the azido ketone **5**. After numerous trials it became clear that a more reactive acetylene was necessary. Methyl propiolate reacts with **5** at room temperature to produce a single, crystalline adduct. However, while it was not clear from spectral data which of the two regiochemical modes of cycloaddition prevailed, our sustained inability to produce a tricyclic derivative from the adduct forced us to conclude that it has structure **6**. This result could have been predicted by analogy with the cycloaddition of phenyl azide and methyl propiolate in which the 1,4-disubstituted triazole is the major product (the 1,4 to 1,5 isomer ratio is approximately 7:1).[11]



5 **6**

This question of regiochemistry in the cycloadduct was simply avoided by using dimethyl acetylenedicarboxylate as the 1,3-dipolarophile. The resulting adduct **7** was converted to its oxime **9** and reductively cyclized to the lactam **10** as shown in Scheme I. Better yields of the cycloaddition