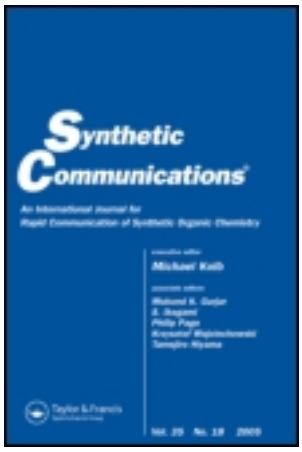
This article was downloaded by: [Moskow State Univ Bibliote]
On: 28 November 2013, At: 05:04
Publisher: Taylor & Francis
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

SYNTHESIS OF NEW 3-SUBSTITUTED AND SPIRO 1,5-BENZODIAZEPIN-2-ONES UNDER PHASE-TRANSFER CATALYSIS CONDITIONS

H. Abdel-Ghany , A. M. El-Sayed , A. Khodairy & H. Salah

Published online: 09 Nov 2006.

To cite this article: H. Abdel-Ghany , A. M. El-Sayed , A. Khodairy & H. Salah (2001) SYNTHESIS OF NEW 3-SUBSTITUTED AND SPIRO 1,5-BENZODIAZEPIN-2-ONES UNDER PHASE-TRANSFER CATALYSIS CONDITIONS, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 31:16, 2523-2535, DOI: 10.1081/SCC-100105132

To link to this article: http://dx.doi.org/10.1081/SCC-100105132

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at http://www.tandfonline.com/page/terms-and-conditions

SYNTHETIC COMMUNICATIONS, 31(16), 2523–2535 (2001)

Downloaded by [Moskow State Univ Bibliote] at 05:04 28 November 2013

SYNTHESIS OF NEW 3-SUBSTITUTED AND SPIRO 1,5-BENZODIAZEPIN-2-ONES UNDER PHASE-TRANSFER CATALYSIS CONDITIONS

H. Abdel-Ghany,* A. M. El-Sayed, A. Khodairy, and H. Salah

Department of Chemistry, Faculty of Science, Sohag, Egypt

ABSTRACT

1,3-Dihydro-4-phenyl-1,5-benzodiazepin-2-one **1** was treated with bromine in 1:1 molar ratio to get the corresponding 3-bromo derivative **2** which in turn reacted with different nucleophiles to get the corresponding 3-substituted derivatives **3–11**. The cyclized compounds $\mathbf{4_a}$, $\mathbf{5_a}$, $\mathbf{7_{a,b}}$, and $\mathbf{9_{a–c}}$ were achieved on refluxing compounds **4, 5,** $\mathbf{6_{a,b}}$, or $\mathbf{8_{a–c}}$ respectively in diphenyl ether. Compound **1** was benzoylated with benzoyl chloride to give the corresponding 1-benzoyl derivative **12** which reacted with bromine in 1:2 molar ratio to yield the corresponding 3,3-dibromo derivative **13**. Spiro benzodiazepines $\mathbf{14_{a–d}}$**–16** were obtained by reacting compound **13** with the proper bidentates. Compound **1** was treated with formaldehyde and secondary amines or thiols to give Mannich bases or sulphides **17–21**, respectively.

*Corresponding author.

Copyright © 2001 by Marcel Dekker, Inc. www.dekker.com

ORDER REPRINTS

The pharmacological activities[1-7] of 1,5-benzodiazepin-2-ones prompted us to continuate our previous work on the synthesis of fused and 3-substituted-1,5 benzodiazepines[8,9].

RESULTS AND DISCUSSION

3-Bromo-1,3-dihydro-1,5-benzodiazepin-2-one **2** was prepared from the reaction of 1,3-dihydro-4-phenyl-1,5 benzodiazepin-2-one **1** with an equimolar amount of bromine in chloroform as a solvent. This compound is proven to be a good starting material for the synthesis of 4-phenyl-3-substituted-1(H)-1,5-benzodiazepin-2-ones, where it was reacted with phthalimidoethanol, cystamine hydrochloride, guanidine hydrochloride, ethyl mercaptoacetate, ethyl glycinate hydrochloride, *o*-phenylenediamine, *o*-aminothiophenol, catechol, *p*-phenylenediamine, *p*-aminobenzoic acid, hydroquinone or resorcinol to give the corresponding 3-substituted derivatives **3, 4, 5, $6_{a,b}$, 8_{a-c}, 10_{a-c}** or **11**, respectively (cf. Scheme 1, Table 1).

The reaction was performed under phase-transfer catalysis conditions using solid-liquid phase system, where the reactants in dioxane formed the organic phase in which potassium carbonate was suspended. The reaction was catalyzed with tetrabutylammonium bromide (TBAB). The reaction pathway was assumed to proceed via two catalytic cycles. The first one, namely proton abstraction, takes place on the surface of solid carbonate. The formed anion then migrates as an ion pair with the catalyst cation into the organic phase where the second cycle concerned with the substitution reaction takes place in order of reactivity $S^- > N^- > O^-$.

On refluxing compounds **4, 5, $6_{a,b}$** or **8_{a-c}** in diphenyl ether gave the corresponding cyclized products **4_a, 5_a, $7_{a,b}$** or **9_{a-c}**, respectively.

Treatment of compound **1** with benzoyl chloride in pyridine as a solvent and catalyst afforded 1-benzoyl-4-phenyl-3(H)-1,5-benzodiazepin-2-one **12**, which in turn reacted with bromine in 1:2 molar ratio at room temperature in chloroform to give 1-benzoyl-3,3-dibromo-4-phenyl-1,5-benzodiazepin-2-one **13**. This compound is a building block for the synthesis of spiro heterocyclic systems attached to benzodiazepine moeity, where it was treated with ethylenediamine, ethanolamine, cystamine hydrochloride, 2-mercaptoethanol, *o*-phenylenediamine, *o*-aminophenol, *o*-aminothiophenol, catechol or thiosemicarbazide using phase-transfer catalysis technique [dioxane/potassium carbonate/tetrabutylammonium bromide (TBAB)] to give the corresponding spiro (1, 5) benzodiazepin-2-one derivatives **14_{a-d}–16**, respectively (cf. Scheme 2, Table 1).

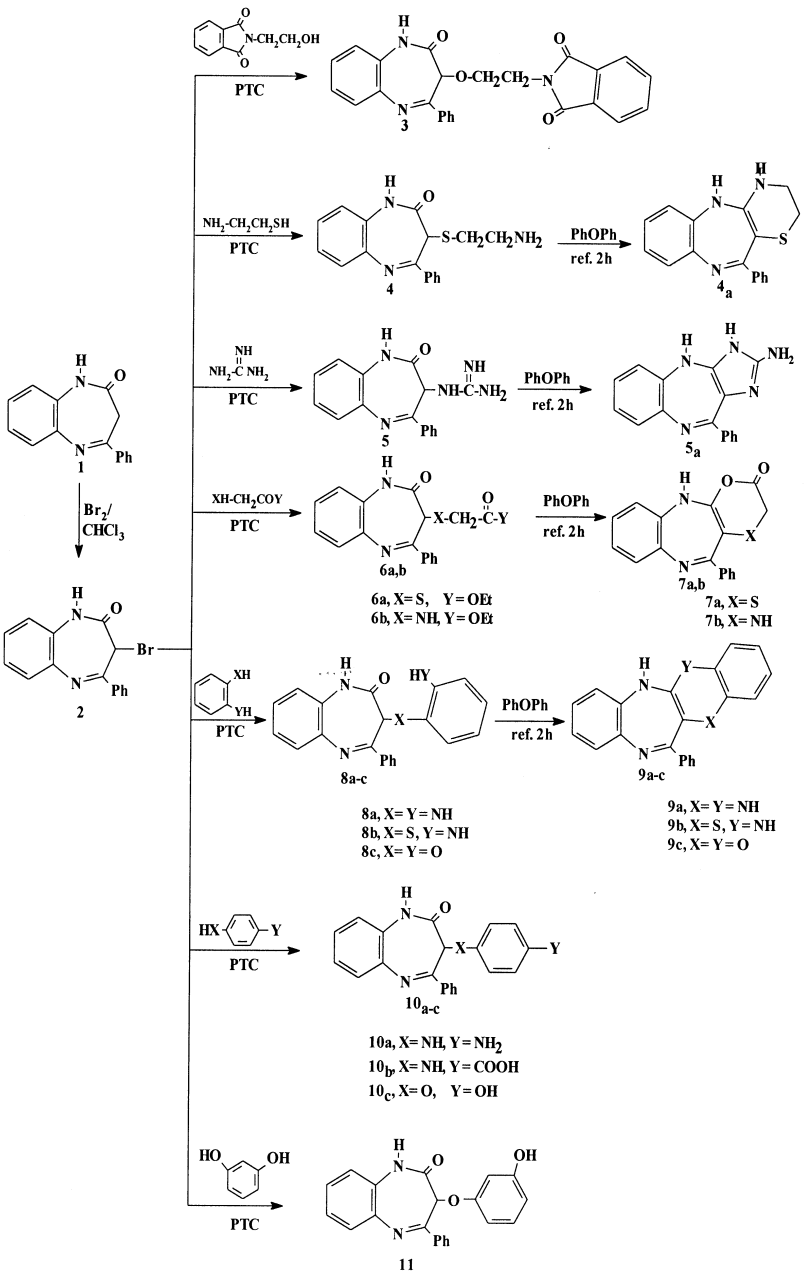
The reaction mechanism should be followed as explained before and can be illustrated as in Figure A.

Downloaded by [Moskow State Univ Bibliote] at 05:04 28 November 2013

Copyright © Marcel Dekker, Inc. All rights reserved.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

ORDER REPRINTS



Scheme 1.

Downloaded by [Moskow State Univ Bibliote] at 05:04 28 November 2013

Copyright © Marcel Dekker, Inc. All rights reserved.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

ORDER REPRINTS

Table 1. Analytical and Spectral Data of the Prepared Compounds

Comp. No.	M.P.(°C)[a] Crystaliz. Solvent	Yield (%)	Mol. From. (Mol.wt.)	Analytical Data (cal./found)[b] C	H	N	S
3	90 ethanol	62	$C_{25}H_{19}N_3O_4$ (425.45)	70.58 70.30	4.50 4.22	9.88 9.66	
4	108 ethanol	80	$C_{17}H_{17}N_3O$ S (311.41)	65.57 65.80	5.5 5.71	13.49 13.65	10.30 10.51
4_a	165 ethanol	68	$C_{17}H_{15}N_3S$ (293.39)	69.60 69.83	5.15 5.31	14.32 14.60	10.93 10.71
5	145 methanol	82	$C_{16}H_{15}N_5O$ (293.34)	65.51 65.30	5.15 5.35	23.88 23.60	
5_a	171 ethanol	70	$C_{16}H_{13}N_5$ (275.32)	69.80 69.63	4.76 4.95	25.44 24.13	
6_a	185 methanol	67	$C_{19}H_{18}N_2O_3S$ (354.43)	64.39 64.61	5.12 5.35	7.90 7.60	9.05 9.30
6_b	101 ethanol	42	$C_{19}H_{19}N_3O_3$ (337.38)	67.64 67.81	5.68 5.63	12.46 12.30	
7_a	187 methanol	60	$C_{17}H_{12}N_2O_2S$ (308.36)	66.22 66.50	3.92 3.63	9.08 9.31	10.40 10.23
7_b	182 ethanol	30	$C_{17}H_{13}N_3O_2$ (291.31)	70.09 70.33	4.50 4.73	14.42 14.75	
8_a	130 dioxane	76	$C_{21}H_{18}N_4O$ (342.4)	73.66 73.81	5.3 5.52	16.36 16.60	
8_b	117 ethanol	89	$C_{21}H_{17}N_3O$ S (359.45)	70.17 70.40	4.77 4.44	11.69 11.83	8.92 8.70
8_c	177 ethanol	45	$C_{21}H_{16}N_2O_3$ (344.37)	73.24 73.60	4.68 4.81	8.14 8.35	
9_a	240 ethanol	68	$C_{21}H_{16}N_4$ (324.39)	77.76 77.43	4.97 4.67	17.27 17.00	
9_b	192 methanol	76	$C_{21}H_{15}N_3S$ (341.44)	73.87 73.63	4.43 4.73	12.31 12.53	9.39 9.14
9_c	280 methanol	34	$C_{21}H_{14}N_2O_2$ (326.36)	77.29 77.00	4.32 4.63	8.58 8.71	
10_a	160 methanol	60	$C_{21}H_{18}N_4O$ (342.41)	73.66 73.83	5.20 5.60	16.36 16.02	
10_b	154 dioxane	30	$C_{22}H_{17}N_3O_3$ (371.40)	71.15 71.35	4.61 4.83	11.31 11.61	
10_c	151 methanol	32	$C_{21}H_{16}N_2O_3$ (344.37)	73.24 73.54	4.68 4.93	8.14 8.39	

(*continued*)

Downloaded by [Moskow State Univ Bibliote] at 05:04 28 November 2013

Copyright © Marcel Dekker, Inc. All rights reserved.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

ORDER REPRINTS

Table 1. Continued

Comp. No.	M.P.(°C)[a] Crystaliz. Solvent	Yield (%)	Mol. From. (Mol.wt.)	Analytical Data (cal./found)[b] C	H	N	S
11	260 ethanol	45	$C_{21}H_{16}N_2O_3$ (344.37)	73.24 73.00	4.68 4.90	8.14 8.35	
12	170 ethanol	90	$C_{22}H_{16}N_2O_2$ (340.38)	77.63 77.44	4.74 4.94	8.32 8.45	
13	298 benzene	72	$C_{22}H_{14}N_2O_2Br_2$ (498.19)	53.04 53.30	2.83 2.66	5.62 5.45	
14_a	95 ethanol	52	$C_{24}H_{20}N_4O_2$ (396.46)	72.71 72.52	5.08 5.30	14.13 14.40	
14_b	275 ethanol	79	$C_{24}H_{19}N_3O_3$ (397.44)	72.53 72.69	4.82 4.62	10.57 10.79	
14_c	123 methanol	81	$C_{24}H_{19}N_3O_2S$ (413.50)	69.71 69.92	4.63 4.78	10.16 10.35	7.75 7.90
14_d	284 ethanol	63	$C_{24}H_{18}N_2O_3S$ (414.49)	69.55 69.31	4.38 4.75	6.76 6.81	7.74 7.95
15_a	270 ethanol	65	$C_{28}H_{20}N_4O_2$ (444.50)	75.66 75.45	4.53 4.75	12.60 12.85	
15_b	258 methanol	60	$C_{28}H_{19}N_3O_3$ (445.48)	75.49 75.31	4.30 4.51	9.43 9.69	
15_c	120 ethanol	84	$C_{28}H_{19}N_3O_2S$ (461.55)	72.86 72.95	4.15 4.35	9.10 9.35	6.95 6.61
15_d	113 ethanol	71	$C_{28}H_{18}N_2O_4$ (446.47)	75.33 75.00	4.06 4.31	6.28 6.00	
16	84 ethanol	40	$C_{23}H_{17}N_5O_2S$ (427.49)	64.62 64.31	4.01 4.40	16.38 16.20	7.50 7.69
17	104 benzene	63	$C_{21}H_{23}N_3O$ (333.43)	75.65 75.41	6.95 6.75	12.60 12.82	
18	138 benzene	60	$C_{20}H_{21}N_3O_2$ (335.41)	71.62 71.82	6.31 6.08	12.53 12.75	
19	132 ethanol	52	$C_{36}H_{34}N_6O_2$ (582.70)	74.21 71.52	5.88 5.97	14.42 14.62	
20	152 dioxane	92	$C_{23}H_{17}N_3O_2S$ (399.47)	69.15 69.35	4.29 4.00	10.52 10.69	8.03 8.30
21	196 ethanol	88	$C_{22}H_{24}N_2O$ S (364.51)	72.49 72.33	6.64 6.80	4.68 7.88	8.80 8.63

[a]Uncorrected; [b] Satisfactory microanalysis obtained C; ±0.35, H; ±0.40, N; ±0.30.

(continued)

Downloaded by [Moskow State Univ Bibliote] at 05:04 28 November 2013

Copyright © Marcel Dekker, Inc. All rights reserved.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

ORDER REPRINTS

Table 1. Continued

Com. No.	IR (cm^{-1})[c]	^{1}H-NMR (δ, ppm)[d]
3	3230(NH); 1692, 1672(2CO).	9.60 (s, 1H, NH); 7.90-6.70 (m, 13H, arom.); 4.80 (s, 1H, CH); 3.90-3.40 (m, 4H, $2CH_2$).
4	3374, 3310, 33205(NH, NH_2); 1678(CO).	9.30 (s, 1H, NH); 7.60-6.50 (m, 9H, arom.); 4.80 (s, 1H, CH); 3.60-3.30 (m, 4H, $2CH_2$); 3.20-2.80 (br, 2H, NH_2).
4_a	3413, 3280(2NH).	10.30 (s, 1H, NH); 9.70 (s, 1H, NH); 7.80-6.10 (m, 9H, arom); 3.10-2.80 (m, 4H, $2CH_2$).
5	3383, 3360, 3150, 3300, 3254(3NH, NH_2); 1665(CO).	10.55 (s, 1H, NH); 9.85 (s, 1H, NH); 7.70-6.60 (m, 10H, arom. + NH); 6.25 (s, 2H, NH_2); 4.15 (s, 1H, CH).
5_a	3415, 3300, 3190, 3120(2NH, NH_2).	9.90 (s, 1H, NH); 9.30 (s, 1H, NH); 7.80-6.70 (m, 9H, arom.); 5.80 (s, 2H, NH_2).
6_a	3420(NH); 1724, 1668(2CO).	10.55 (s, 1H, NH); 8.30-7.10 (m, 9H, arom.); 4.70-4.10 (m, 3H, $CH + CH_2$); 3.70 (s, 2H, CH_2); 1.30-0.80 (t, 3H, CH_3).
6_b	3340, 3260(2NH); 1720, 1674(2CO).	10.30 (s, 1H, NH); 9.80 (s, 1H, NH); 8.30-6.90 (m, 9H, arom.); 4.50-4.10 (q, 2H, CH_2); 3.80 (s, 1H, CH), 3.40 (s, 2H, CH_2); 1.40-1.00 (t, 3H, CH_3).
7_a	3342(NH); 1701(CO).	10.10 (s, 1H, NH); 7.80-6.30 (m, 9H, arom.); 4.40 (s, 2H, CH_2).
7_b	3321, 3211(2NH), 1711(CO).	10.25 (s, 1H, NH); 9.35 (s, 1H, NH); 8.10-7.10 (m, 9H, arom.); 4.30 (s, 2H, CH_2).

(*continued*)

Downloaded by [Moskow State Univ Bibliote] at 05:04 28 November 2013

Copyright © Marcel Dekker, Inc. All rights reserved.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

ORDER REPRINTS

Table 1. Continued

Com. No.	IR (cm^{-1})[c]	^{1}H-NMR (δ, ppm)[d]
8_a	3416, 3360, 3259, 3157(NH_2); 1686(CO).	10.30 (s, 1H, NH); 9.55 (S, 1H, NH); 8.30-6.90 (m, 13H, arom.); 5.85 (s, 2H, NH_2); 3.65 (s, 1H, CH).
8_b	3345(NH); 3310, 3200, (NH_2); 1686(Co).	10.35 (s, 1H, NH); 9.90-6.30 (m, 13H, arom.); 4.50 (s, 2H, NH_2); 3.10 (s, 1H, CH).
8_c	3441(OH); 3320(NH); 1674 (CO).	10.85 (s, 1H, NH); 8.40-7.10 (m, 13H, arom.); 3.60 (s, 1H, OH); 3.40 (s, 1H, CH).
9_a	3417, 3286, 3274(3NH).	10.35 (s, 1H, NH); 9.70-9.40 (br, 2H, 2NH); 7.80-6.30 (m, 13H, arom.).
9_b	3414, 3240(NH_2).	9.90 (s, 1H, NH); 9.15 (s, 1H, NH); 7.80-6.20 (m, 13H, arom.).
9_c	3396(NH).	10.25 (s, 1H, NH); 8.20-7.10 (m, 13H, arom.).
10_a	3424, 3350, 3232, 3120(2NH, NH_2); 1691(CO).	10.50 (s, 1H, NH); 9.70 (s, 01H, NH); 8.00-6.80 (m, 13H, arom.); 4.80 (s, 2H, NH_2); 3.60 (s, 1H, CH).
10_b	3421(OH); 3188, 3140(2NH); 1715, 1685(2CO).	11.45 (s, 1H, OH); 10.30 (s, 1H, NH); 9.20 (s, 1H, NH); 8.20-6.80 (m, 13H, arom.); 3.60 (s, 1H, CH).
10_c	3410(OH); 3200(NH); 1682(CO).	10.85 (s, 1H, OH); 10.40 (s, 1H, NH); 7.90-6.20 (m, 13H, arom.); 3.40 (s, 1H, CH).
11	3412(OH); 3220(NH); 1684(CO).	10.75 (s, 1H, OH); 9.75 (s, 1H, NH); 8.10-6.20 (m, 13H, arom.); 3.40 (s, 1H, CH).
12	1741, 1674(2CO).	8.60-7.10 (m, 14H, arom.), 6.00 (s, 1H, H_a), 5.60 (s, 1H, H_b).
13	1751, 1695(2CO), 603(C-Br).	8.60-7.30 (m, 14H, arom.).

(*continued*)

Downloaded by [Moskow State Univ Bibliote] at 05:04 28 November 2013

Copyright © Marcel Dekker, Inc. All rights reserved.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

ORDER REPRINTS

Table 1. Continued

Com. No.	IR (cm^{-1})[c]	^{1}H-NMR (δ, ppm)[d]
14_a	3310, 3308(2NH); 1720, 1688(2CO).	9.60-9.30 (br, 2H, 2NH); 8.30-7.10 (m, 14H, arom.); 3.20-2.70 (br, 4H, $2CH_2$).
14_d	1723, 1686(2CO).	8.10-6.40 (m, 14H, arom.); 3.90-3.60 (t, 2H, OCH_2). 3.20-2.80 (t, 2H, sCH_2).
15_a	3164, 3161(2NH); 1725, 1690(2CO).	9.50-9.10 (br, 2H, 2NH); 8.10-7.60 (m, 18H, arom.).
15_b	3163(NH); 1726, 1697(2CO).	9.70 (s, 1H, NH); 8.30-6.70 (m, 18H, arom.).
15_c	3165(NH); 1727, 1692(2CO).	9.60 (s, 1H, NH); 8.20-6.50 (m, 18H, arom.).
15_d	1719, 1684(2CO).	8.20-6.60 (m, 18H, arom.).
16	3420, 3314, 3210(NH, NH_2); 1718, 1684(2CO).	9.30 (S, 1H, NH); 8.20-7.10 (m, 14H, arom.); 6.20 (s, 2H, NH_2).
17	1670(CO).	8.60-7.10 (m, 9H, arom); 4.30 (s, 2H, N-CH_2-N); 3.70-3.30 (br, 2H, CH); 2.00-1.40 [br, 4H, $N(CH_2)_2$]; 1.20-0.60 (m, 6H, $3CH_2$).
18	1662(CO).	8.50-7.10 (m, 9H, arom.); 4.70 (s, 2H, N-CH_2-N); 4.25 (s, 2H, CH_2); 4.15-3.80 [t, 4H, $O(CH_2)_2$]; 3.40-3.10 [t, 4H, $N(CH_2)_2$].
19	1670(CO).	8.70-7.00 (m, 18H, arom.); 4.60 (s, 4H, 2N-CH_2-N) 3.45 (s, 4H, $2CH_2$); 2.05-1.60 [br, 8H, $N(CH_2)_4$ N)].
20	1666(CO).	8.10-7.10 (m, 13H, arom.); 4.70 (s, 2H, N-CH_2-S); 3.50 (s, 2H, CH_2).
21	1668(CO).	8.00-7.50 (m, 4H, arom.); 4.50 (s, 2H, N-CH_2-S); 3.50-2.90 (t, 1H, CH), 2.50-1.60 (m, 10H, $5CH_2$).

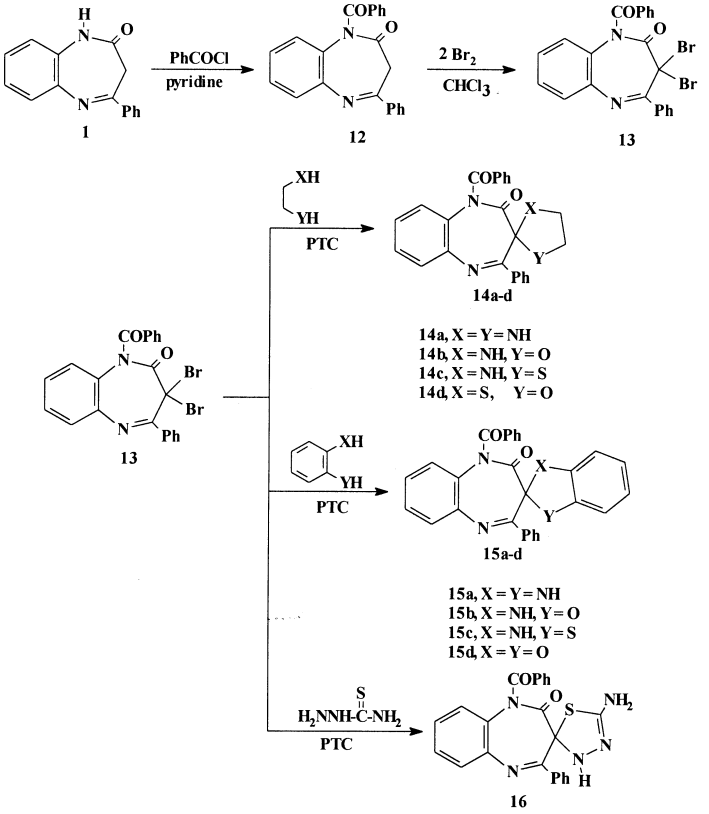
[c]Measured by Nicolet FT-IR 710 spectrophotometer.
[d]Measured by a varian EM 360 L spectrometer at 60 MHz using TMS as internal standard and DMSO as a solvent.

Downloaded by [Moskow State Univ Bibliote] at 05:04 28 November 2013

Copyright © Marcel Dekker, Inc. All rights reserved.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

ORDER REPRINTS



Scheme 2.

Also, compound **1** was subjected to react with formaldehyde and piperidine, morpholine, piperazine, 2-mercaptobenzoxazole or cyclohexylmercaptane, the corresponding Mannich bases **17–21** were obtained (cf. Scheme 3, Table 1).

EXPERIMENTAL

Synthesis of 3-bromo-1,3-dihydro-4-phenyl-1,5-benzodiazepin-2-one 2

To a stirred solution of compound **1** (4.72 g, 0.02 mol) in chloroform (50 mL), solution of bromine (1.91 mL, 0.02 mol) in chloroform (15 mL) was added dropwise. Stirring was continued until the evolution of HBr gas

Downloaded by [Moskow State Univ Bibliote] at 05:04 28 November 2013

Copyright © Marcel Dekker, Inc. All rights reserved.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

ORDER REPRINTS

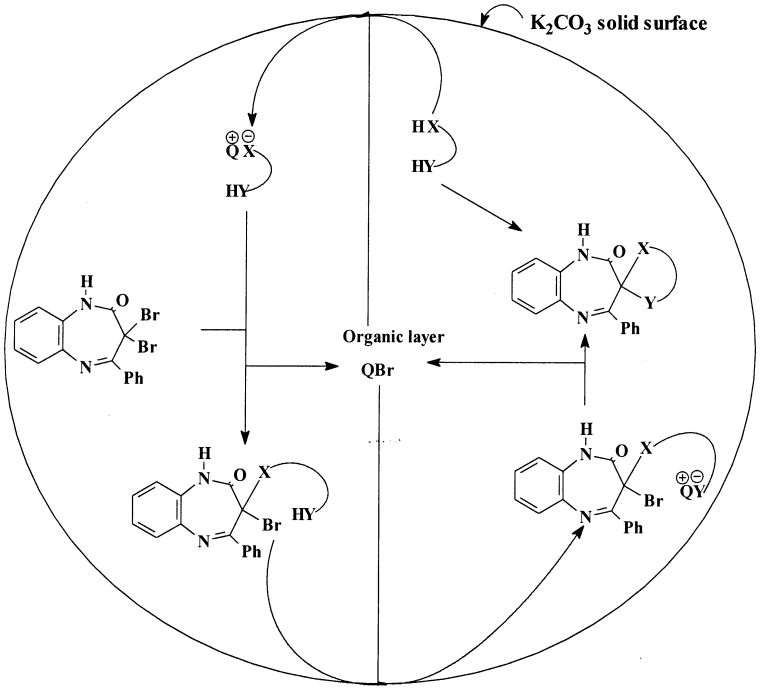


Figure A.

ceased. The precipitated solid was filtered off and crystallized from chloroform (cf. Table 1, Scheme 1).

Synthesis of 4-phenyl-3-substituted-1(H)-1,5 benzodiazepin-2-one 3, 4, 5, $6_{a,b}$, 8_{a-c}, 10_{a-c} and 11: (General procedure)

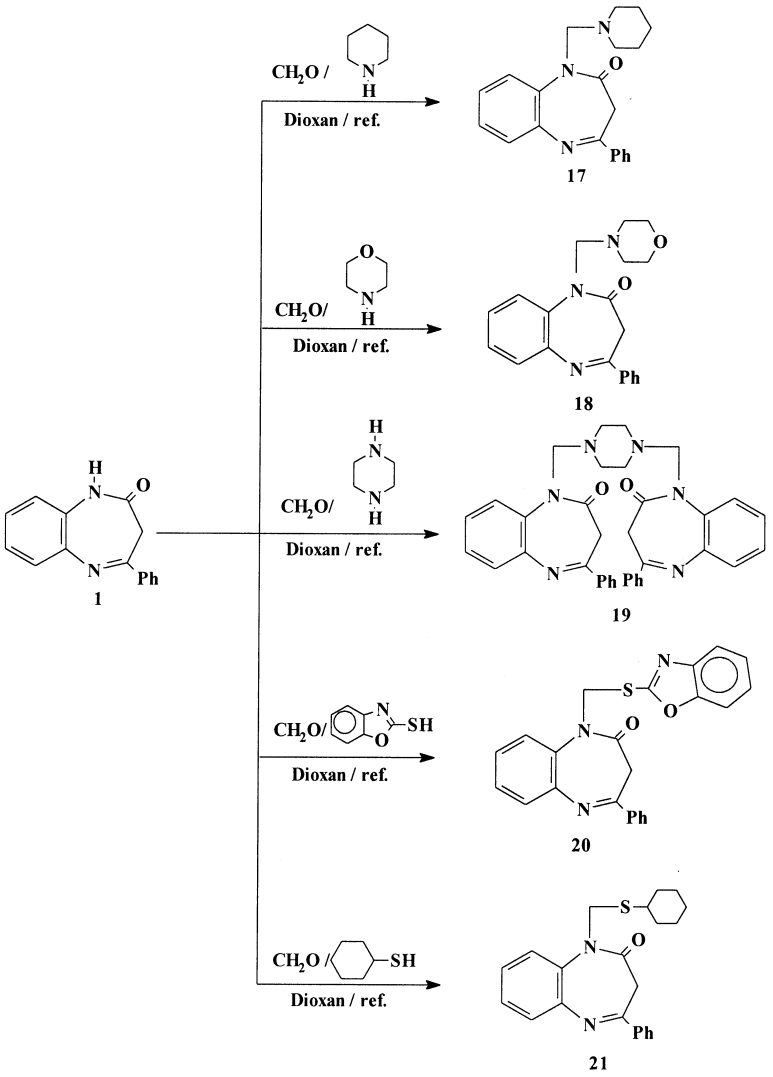
A mixture of anhydrous potassium carbonate (3 g), dry dioxane (30 mL), compound **2** (0.003 mol), the appropriate reactant (0.003 mol), namely phthalimidoethanol (0.57 g), cystamine hydrochloride (0.94 g), guanidine hydrochloride (0.28 g), ethyl mercaptoacetate (0.33 g), ethyl glycinate hydrochloride (0.41 g), *o*-phenylenediamine (0.32 g), *o*-aminothiophenol (0.32 g), catechol (0.33 g), *p*-phenylenediamine (0.33 g), *p*-aminobenzoic acid (0.41 g), hydroquinone (0.33 g) or resorcinol (0.33 g) and a catalytic amount of tetrabutylammonium bromide [TBAB] (0.003 g) was stirred over different periods of time at the appropriate temperature (cf. Table 1), till completion of the reaction (*TLC*). The reaction mixture was filtered off

Downloaded by [Moskow State Univ Bibliote] at 05:04 28 November 2013

Copyright © Marcel Dekker, Inc. All rights reserved.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

ORDER REPRINTS



Scheme 3.

and the filtrate evaporated *in vacuo*. The residue was triturated with pet. ether (40–60°C) to give a solid crystallized from the appropriate solvent (cf. Table 1, Scheme 1)

Note: Compound **11** was obtained by dissolving the carbonate in water (30 mL) followed by acidification and collected by filtration.

Downloaded by [Moskow State Univ Bibliote] at 05:04 28 November 2013

Copyright © Marcel Dekker, Inc. All rights reserved.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

ORDER REPRINTS

Synthesis of Compounds 4_a, 5_a, $7_{a,b}$, and $9_{a\text{-}c}$: (General Procedure)

0.005 Mol of compound **4** (1.55 g), **5** (1.64 g), $\mathbf{6_a}$ (1.77 g), $\mathbf{6_b}$ (1.68 g), $\mathbf{8_a}$ (1.71 g), $\mathbf{8_b}$ (1.77 g) or $\mathbf{8_c}$ (1.72 g) were dissolved in diphenyl ether (15 mL) and refluxed for 90 min. After cooling, the reaction mixture was poured into pet. ether 40–60°C. The separated solid was collected by filtration and crystallized from the suitable solvent (cf. Table 1, Scheme 3).

Synthesis 1-benzoyl-4-phenyl-3(H)-1,5-benzodiazepin-2-one 12

To a stirred solution of compound **1** (4.72 g, 0.02 mol) in dry pyridine (20 mL), benzoyl chloride (2.32 mL, 0.02 mol) was added dropwise at room temperature. The stirring was continued for 30 min. and the reaction mixture was refluxed for 7 hr, poured into ice cold water. The separated solid was collected by filtration and crystallized from absolute ethanol (cf. Table 1, Scheme 1).

Synthesis 1-benzoyl-3,3-dibromo-4-phenyl-1,5-benzodiazepin-2-one 13

To a solution of compound **12** (7.47 g, 0.015 mol) in chloroform (50 mL), a solution of bromine (2.68 mL, 0.03 mol) in chloroform (25 mL) was added dropwise during the stirring. The stirring was continued till the evolution of HBr gas ceased. The precipitated solid was filtered off and crystallized from chloroform (cf. Table 1, Scheme 2).

Synthesis of Compounds $14_{a\text{-}d}$, $15_{a\text{-}d}$ and 16: (General Procedure)

A mixture of compound **13** (0.99 g, 0.002 mol), dry dioxane (30 mL), anhydrous potassium carbonate (3 g), catalytic amount of tetrabutylammonium bromide [TBAB] (0.003 g) was treated with the suitable reactant (0.002 mol) namely, ethylenediamine (0.13 mL), ethanolamine (0.12 mL), cystamine hydrochloride (0.22 g), 2-mercaptoethanol (0.41 mL), *o*-phenylenediamine (0.21 g), *o*-aminophenol (0.21 g), *o*-aminothiophenol (0.21 mL), catechol (0.22 g) or thiosemicarbazide (0.18 g). The reaction mixture was stirred over different periods of time at the appropriate temperature (cf. Table 1, Scheme 3), till the completion of the reaction (TLC).The reaction mixture was filtered off and the filtrate evaporated *in vacuo*. The solid

Downloaded by [Moskow State Univ Bibliote] at 05:04 28 November 2013

Copyright © Marcel Dekker, Inc. All rights reserved.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

ORDER REPRINTS

residue was washed with water and crystallized from the appropriate solvent (cf. Table 1, Scheme 1).

Synthesis of Compounds 17–21: (General Procedure)

To a stirred solution of compound **1** (0.003 mol) in dioxane (20 mL), formaline solution (1 mL) and the suitable reagent (0.003 mol) including, piperidine (0.3 mL), morpholine (0.26 mL), piprazine (0.12 g, 0.0015 mol), cyclohexylmercaptane (0.36 mL) or 2-mercaptobenzoxazole (0.45 g) were added. The reaction mixture was refluxed for 3 hr. The precipitated solid was filtered off, washed with water and crystallized from the appropriate solvent (cf. Table 1, Scheme 3).

REFERENCES

1. Guidan, C.; Greiveldinger, F.; Balette, B.; Loppinet, V. Soc. Pharm. Biol. Lorraine, **1975**, *1*, 29.
2. Bauer, A.; Weber, K.H.; Dannlberg, F. Ger. Offen. **1974**, *2*, 306. C.A. **1975**, *32*, 43312.
3. Nawrocka, W.; Liszkiewicz, H.; Nawojsk, A.; Wilimowski, M.; Kdzierska-Godzik, L.; Barezyska, J.; Wojew dzki, W.; Du, E.; Szel, G.A.; Ruthowska, M. Pol. Pharmacol. Pharm. **1991**, *43*(6), 495.
4. Khan, H.; Bano, Q.; Nizamuddin, J. Agric. Food Chem. **1995**, *43*(10), 2719.
5. Fray, M.J.; Cooper, K.; Parry, M.J.; Richardsan, K.; Steele, J. J. Med. Chem. **1995**, *38*(18), 3514.
6. Nawrocka, W.; Rutkowska, M.; Szelag, A.; Barczynska, J.; Kedzierska-Gozdzik, L. Acta. Pol. Pharm. **1996**, *53*(6), 425.
7. Nawocka, W.; Sztuba, B.; Rutkowska, M.; Barczynska, J.; Opolski, A.; Wietrzyk, J. Acta. Pol. Pharm. **1998**, *55*(5), 397.
8. Abdel-Ghany, H.; El-Sayed, A.M.; Sultan, A.A.; El-Shafei, A.K. Synth. Comm. **1990**, *20*(6), 893.
9. El-Sayed, A.M.; Abdel-Ghany, H.; and El-Saghier, A.M.M. Synth. Comm. **1999**, *29*(20), 3561.

Received in the USA November 10, 2000

Downloaded by [Moskow State Univ Bibliote] at 05:04 28 November 2013

Copyright © Marcel Dekker, Inc. All rights reserved.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

Downloaded by [Moskow State Univ Bibliote] at 05:04 28 November 2013

Request Permission or Order Reprints Instantly!

Interested in copying and sharing this article? In most cases, U.S. Copyright Law requires that you get permission from the article's rightsholder before using copyrighted content.

All information and materials found in this article, including but not limited to text, trademarks, patents, logos, graphics and images (the "Materials"), are the copyrighted works and other forms of intellectual property of Marcel Dekker, Inc., or its licensors. All rights not expressly granted are reserved.

Get permission to lawfully reproduce and distribute the Materials or order reprints quickly and painlessly. Simply click on the "Request Permission/Reprints Here" link below and follow the instructions. Visit the U.S. Copyright Office for information on Fair Use limitations of U.S. copyright law. Please refer to The Association of American Publishers' (AAP) website for guidelines on Fair Use in the Classroom.

The Materials are for your personal use only and cannot be reformatted, reposted, resold or distributed by electronic means or otherwise without permission from Marcel Dekker, Inc. Marcel Dekker, Inc. grants you the limited right to display the Materials only on your personal computer or personal wireless device, and to copy and download single copies of such Materials provided that any copyright, trademark or other notice appearing on such Materials is also retained by, displayed, copied or downloaded as part of the Materials and is not removed or obscured, and provided you do not edit, modify, alter or enhance the Materials. Please refer to our Website User Agreement for more details.

Order now!

Reprints of this article can also be ordered at

http://www.dekker.com/servlet/product/DOI/101081SCC100105132