

## A New Synthesis of 2,3-Disubstituted Indoles

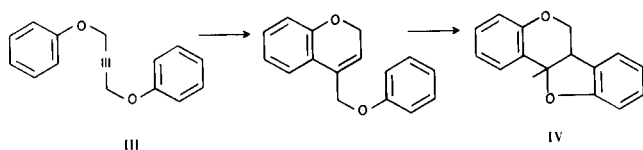
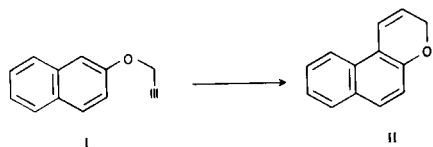
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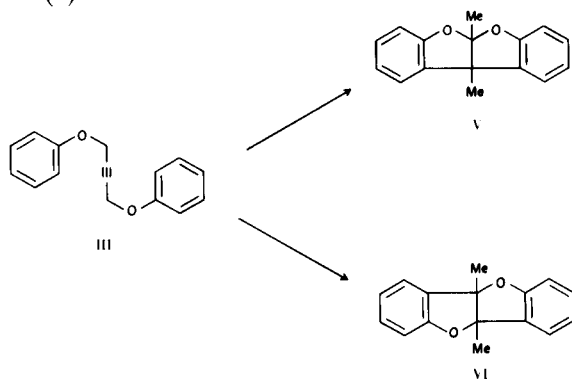
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A novel synthesis of 2,3-disubstituted indoles starting from *N*-alkyl-*N*-propynyl anilines is described. The reactions employed are analogous to the thermal rearrangement of aryl propynyl sulfoxides.

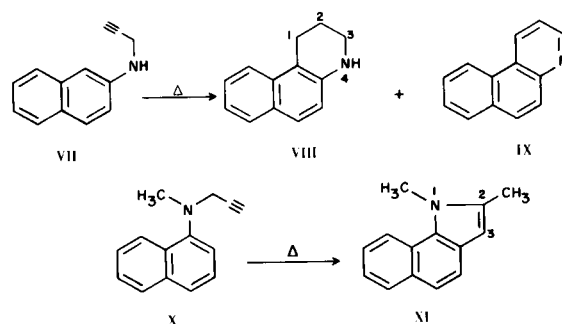
Although for three decades the *ortho* Claisen rearrangement of aryl propynyl ethers was considered a fruitless pursuit, two groups in 1963 independently demonstrated the great facility with which such a rearrangement occurs (1,2,3).



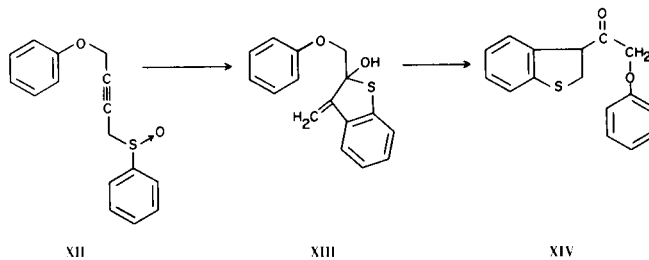
Subsequently versatility of the reaction was shown by Thyagarajan and coworkers in leading to the synthesis of benzofuro[2,3-*b*]benzofurans and benzofuro[3,2-*b*]benzofurans (4).



More recently, Zsindely and Schmid (5) showed that *N*-propargylnaphthylamines undergo *ortho* Claisen rearrangement to yield py-tetrahydrobenzoquinolines and benzoquinolines, whereas *N*-methyl propargylnaphthylamines under analogous conditions afford the indole derivative XI.



The interaction of the heteroatom and the triple bond in a Claisen rearrangement was modified in an intriguing manner by Thyagarajan and Majumdar (6,7) towards a novel synthesis of benzo[*b*]thiophenes (*vide infra*).



In a continuing effort to exploit this novel finding in obtaining other heterocycles, we describe in this paper a novel synthesis of 2,3-disubstituted indoles (8).

The condensation of *N*-methylaniline with 1-(2,4-dichlorophenoxy)-4-chloro-2-butyne readily afforded *N*-[4-(2,4-dichlorophenoxy)-2-butynyl]-*N*-methyl aniline XV.

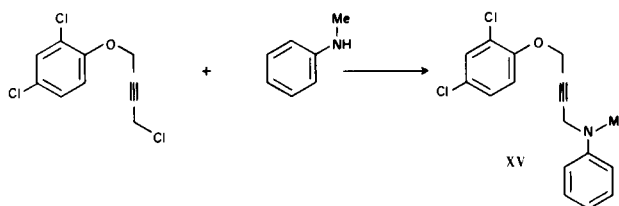
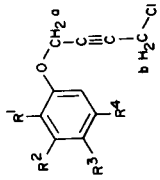


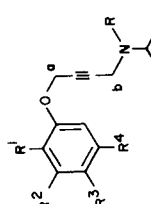
TABLE I  
1-Aryloxy-4-chloro-2-butyne



	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	M.p. or B.p., °C	% Yield	Molecular Formula	Analyses %		Found C	Found H	nmr (in δ)	
								Calcd. C	Calcd. H			a (t, 2H)	b (t, 2H)
<b>1</b> (c)	H	H	Cl	H								4.60	4.05
<b>2</b> (d)	Cl	H	Cl	H								4.50	3.97
<b>3</b>	H	H	Br	H	58-59	55	C <sub>10</sub> H <sub>8</sub> BrClO	46.26	3.08	46.28	2.90	4.60	4.05
<b>4</b>	H	CH <sub>3</sub>	H	CH <sub>3</sub>	116/0.03 mm	54	C <sub>12</sub> H <sub>13</sub> ClO	69.06	6.24	69.28	6.27	4.50	3.97
<b>5</b>	H	CH <sub>3</sub>	Cl	H	122/0.01 mm	52	C <sub>11</sub> H <sub>10</sub> Cl <sub>2</sub> O	57.64	4.37	57.52	4.35	4.53	4.03

(a) In carbon tetrachloride. (b) Coupling constants ~ 2 cps. (c) Reported by K. C. Majumdar and B. S. Thyagarajan, *Int. J. Sulfur Chem.*, A, 2, 93 (1972). (d) Reported by K. C. Majumdar and B. S. Thyagarajan, *ibid.*, A, 2, 153 (1972).

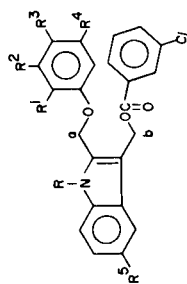
TABLE II  
N-[4-(Aryloxy)-2-butyne]-N-alkylanilines



	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	R <sup>5</sup>	M.p. or B.p., °C	% Yield	Molecular Formula	Analyses %		Found C	Found H	Found N	nmr (a) (in δ)	
									Calcd. C	Calcd. H				a (t, 2H)	b (t, 2H)
<b>1</b>	H	H	Cl	H	CH <sub>3</sub>	76-77	89.5	C <sub>17</sub> H <sub>16</sub> ClNO	71.46	5.60	71.67	5.72	4.83	4.55	4.00
<b>2</b>	H	H	Cl	H	C <sub>2</sub> H <sub>5</sub>	44-45	84.0	C <sub>18</sub> H <sub>18</sub> ClNO	72.12	6.01	72.38	6.15	4.66	4.54	3.96
<b>3</b>	Cl	H	Cl	H	CH <sub>3</sub>	96-97	91.0	C <sub>17</sub> H <sub>15</sub> Cl <sub>2</sub> NO	63.76	4.72	63.73	4.74	4.16	4.70	4.03
<b>4</b>	Cl	H	Cl	H	C <sub>2</sub> H <sub>5</sub>	41.5-42.5	88.0	C <sub>18</sub> H <sub>17</sub> Cl <sub>2</sub> NO	64.67	5.09	64.43	5.12	4.16	4.54	4.01
<b>5</b>	H	CH <sub>3</sub>	H	CH <sub>3</sub>	CH <sub>3</sub>	42-43	89.3	C <sub>19</sub> H <sub>21</sub> NO	81.70	7.53	81.75	7.76	4.85	4.56	4.01
<b>6</b>	H	CH <sub>3</sub>	H	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	156/0.005 mm	89.7	C <sub>20</sub> H <sub>23</sub> NO	81.91	7.85	81.70	7.84	4.74	4.58	4.00
<b>7</b>	H	H	Br	H	CH <sub>3</sub>	66-67	88.0	C <sub>17</sub> H <sub>16</sub> BrNO	61.84	4.85	61.91	4.79	4.12	4.55	4.00
<b>8</b>	H	H	Br	H	C <sub>2</sub> H <sub>5</sub>	57.5-58.5	89.5	C <sub>18</sub> H <sub>18</sub> BrNO	62.81	5.23	62.68	5.18	3.88	4.58	3.98
<b>9</b>	H	H	Br	H	CH <sub>3</sub>	81.5-82.5	90.4	C <sub>18</sub> H <sub>18</sub> BrNO	62.81	5.23	62.62	5.13	3.79	4.60	4.01
<b>10</b>	H	CH <sub>3</sub>	Cl	H	CH <sub>3</sub>	69-70	80.2	C <sub>18</sub> H <sub>18</sub> ClNO	72.12	6.01	72.12	5.96	4.74	4.54	4.00

(a) In deuteriochloroform. (b) Coupling constants ~ 2 cps.

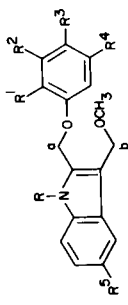
TABLE III  
2-(Aryloxy)methyl)-3-(*m*-chlorobenzoyloxymethyl)-1-alkylindoles



	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	R <sup>5</sup>	R	M.p., °C	% Yield	Molecular Formula	Analyses %			Found		nmr (a) (in δ)		
										Calcd.	C	H	N	C	H	N	a (s, 2H)
1	H	H	Cl	H	H	CH <sub>3</sub>	142-143	81.0	C <sub>24</sub> H <sub>19</sub> Cl <sub>2</sub> NO <sub>3</sub>	65.46	4.33	3.19	65.29	4.39	3.14	5.28	5.62
2	H	H	Cl	H	H	C <sub>2</sub> H <sub>5</sub>	144-145.5	82.6	C <sub>25</sub> H <sub>21</sub> Cl <sub>2</sub> NO <sub>3</sub>	66.08	4.63	3.08	65.93	4.67	3.04	5.28	5.62
3	Cl	H	Cl	H	H	CH <sub>3</sub>	114	86.5	C <sub>24</sub> H <sub>18</sub> Cl <sub>3</sub> NO <sub>3</sub>	60.71	3.82	2.95	60.89	3.81	2.85	5.35	5.58
4	Cl	H	Cl	H	H	C <sub>2</sub> H <sub>5</sub>	158.5-159.5	84.5	C <sub>25</sub> H <sub>20</sub> Cl <sub>3</sub> NO <sub>3</sub>	61.41	4.09	2.87	61.28	4.08	2.71	5.37	5.60
5	H	CH <sub>3</sub>	H	CH <sub>3</sub>	H	CH <sub>3</sub>	127-128	80.2	C <sub>26</sub> H <sub>24</sub> ClNO <sub>3</sub>	71.97	5.53	3.23	72.06	5.59	3.21	5.30	5.66
6	H	CH <sub>3</sub>	H	CH <sub>3</sub>	H	C <sub>2</sub> H <sub>5</sub>	116-117	67.5	C <sub>27</sub> H <sub>26</sub> ClNO <sub>3</sub>	72.40	5.81	3.13	72.33	5.85	3.02	5.28	5.64
7	H	H	Br	H	H	CH <sub>3</sub>	134.5-135.5	83.4	C <sub>24</sub> H <sub>19</sub> BrClNO <sub>3</sub>	59.45	3.92	2.89	59.59	3.89	2.94	5.28	5.61
8	H	H	Br	H	H	C <sub>2</sub> H <sub>5</sub>	145-146	84.0	C <sub>25</sub> H <sub>21</sub> BrClNO <sub>3</sub>	60.19	4.21	2.81	60.15	4.23	2.77	5.28	5.61
9	H	H	Br	H	CH <sub>3</sub>	CH <sub>3</sub>	130-131	86.3	C <sub>25</sub> H <sub>21</sub> BrClNO <sub>3</sub>	60.19	4.21	2.81	60.20	4.25	2.81	5.26	5.59
10	H	CH <sub>3</sub>	Cl	H	H	CH <sub>3</sub>	103-104	82.3	C <sub>25</sub> H <sub>21</sub> Cl <sub>2</sub> NO <sub>3</sub>	66.08	4.63	3.08	65.82	4.58	3.29	5.28	5.63

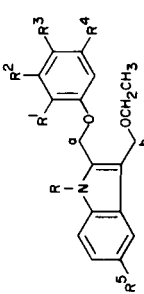
(a) In deuteriochloroform.

TABLE IV  
2-[Aryloxyethyl]-3-(methoxymethyl)-1-alkylindoles



1	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	R <sup>5</sup>	R	M.p., °C	% Yield	Molecular Formula	Calcd.		Analyses %			Found		nmr (a) (in δ)	
										C	H	N	C	H	N	a (s, 2H)	b (s, 2H)	
1	H	H	Cl	H	H	CH <sub>3</sub>	101.5-102.5	90.5	C <sub>18</sub> H <sub>18</sub> ClNO <sub>2</sub>	68.46	5.71	4.44	68.44	5.80	4.30	5.15	4.67	
2	H	H	Cl	H	H	C <sub>2</sub> H <sub>5</sub>	116-117	82.7	C <sub>19</sub> H <sub>20</sub> ClNO <sub>2</sub>	69.20	6.07	4.25	69.01	6.06	4.14	5.17	4.68	
3	Cl	H	Cl	H	H	CH <sub>3</sub>	131-132	92.0	C <sub>18</sub> H <sub>17</sub> Cl <sub>2</sub> NO <sub>2</sub>	61.72	4.89	4.00	61.69	4.72	3.83	5.25	4.67	
4	Cl	H	Cl	H	H	C <sub>2</sub> H <sub>5</sub>	129.5-130.5	87.1	C <sub>19</sub> H <sub>19</sub> Cl <sub>2</sub> NO <sub>2</sub>	62.64	5.22	3.85	62.52	5.26	3.74	5.27	4.67	
5	H	CH <sub>3</sub>	H	CH <sub>3</sub>	H	CH <sub>3</sub>	99.5-100.5	77.6	C <sub>20</sub> H <sub>23</sub> NO <sub>2</sub>	77.67	7.44	4.53	77.91	7.51	4.39	5.18	4.70	
6	H	CH <sub>3</sub>	H	CH <sub>3</sub>	H	C <sub>2</sub> H <sub>5</sub>	80-81	88.9	C <sub>21</sub> H <sub>25</sub> NO <sub>2</sub>	78.02	7.74	4.33	78.06	7.87	4.25	5.19	4.71	
7	H	H	Br	H	H	CH <sub>3</sub>	105.5-106.5	82.5	C <sub>18</sub> H <sub>18</sub> BrNO <sub>2</sub>	60.02	5.00	3.89	59.76	4.88	4.12	5.15	4.67	
8	H	H	Br	H	H	C <sub>2</sub> H <sub>5</sub>	131-133	86.1	C <sub>19</sub> H <sub>20</sub> BrNO <sub>2</sub>	60.98	5.35	3.74	60.76	5.29	3.69	5.15	4.67	
9	H	H	Br	H	CH <sub>3</sub>	CH <sub>3</sub>	102-102.5	86.6	C <sub>19</sub> H <sub>20</sub> BrNO <sub>2</sub>	60.98	5.35	3.74	60.77	5.29	3.68	5.17	4.66	
10	H	CH <sub>3</sub>	Cl	H	H	CH <sub>3</sub>	98-99	85.2	C <sub>19</sub> H <sub>20</sub> ClNO <sub>2</sub>	69.20	6.07	4.25	69.26	6.21	4.18	5.17	4.68	

TABLE V  
2-(Aryloxyethyl)-3-(ethoxymethyl)-1-alkylindoles

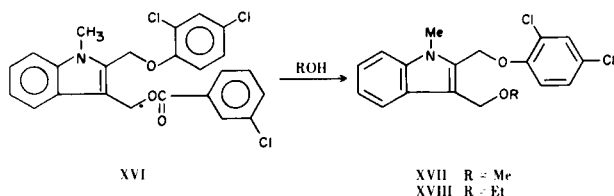


1	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	R <sup>5</sup>	R	M.p., °C	% Yield	Molecular Formula	Calcd.		Analyses %			Found		nmr (a) (in δ)	
										C	H	N	C	H	N	a (s, 2H)	b (s, 2H)	
1	H	H	Cl	H	H	CH <sub>3</sub>	90.5-91.5	84.5	C <sub>19</sub> H <sub>20</sub> ClNO <sub>2</sub>	69.30	6.08	4.26	69.53	6.22	4.15	5.17	4.74	
2	H	H	Cl	H	H	C <sub>2</sub> H <sub>5</sub>	110-111	85.1	C <sub>20</sub> H <sub>22</sub> ClNO <sub>2</sub>	69.87	6.40	4.08	69.80	6.44	3.97	5.21	4.75	
3	Cl	H	Cl	H	H	CH <sub>3</sub>	114-115	86.0	C <sub>19</sub> H <sub>19</sub> Cl <sub>2</sub> NO <sub>2</sub>	62.64	5.23	3.84	62.49	5.44	3.78	5.20	4.70	
4	Cl	H	Cl	H	H	C <sub>2</sub> H <sub>5</sub>	110-111	82.0	C <sub>20</sub> H <sub>21</sub> Cl <sub>2</sub> NO <sub>2</sub>	63.49	5.56	3.70	63.30	5.60	3.63	5.31	4.75	
5	H	CH <sub>3</sub>	H	CH <sub>3</sub>	H	CH <sub>3</sub>	74-75	80.8	C <sub>21</sub> H <sub>25</sub> NO <sub>2</sub>	78.02	7.74	4.33	77.80	7.57	4.07	5.18	4.75	
6	H	CH <sub>3</sub>	H	CH <sub>3</sub>	H	C <sub>2</sub> H <sub>5</sub>	84-85	76.4	C <sub>22</sub> H <sub>27</sub> NO <sub>2</sub>	78.34	8.01	4.15	78.35	8.11	4.08	5.19	4.75	
7	H	H	Br	H	H	CH <sub>3</sub>	99-100	78.5	C <sub>19</sub> H <sub>20</sub> BrNO <sub>2</sub>	60.98	5.35	3.74	60.73	5.18	3.62	5.18	4.72	
8	H	H	Br	H	H	C <sub>2</sub> H <sub>5</sub>	96.5-97.5	78.3	C <sub>20</sub> H <sub>22</sub> BrNO <sub>2</sub>	61.87	5.67	3.61	61.74	5.64	3.58	5.20	4.73	
9	H	H	Br	H	CH <sub>3</sub>	CH <sub>3</sub>	130-131	79.5	C <sub>20</sub> H <sub>22</sub> BrNO <sub>2</sub>	61.87	5.67	3.61	61.59	5.59	3.52	5.18	4.71	
10	H	CH <sub>3</sub>	Cl	H	H	CH <sub>3</sub>	87-88	80.3	C <sub>20</sub> H <sub>22</sub> ClNO <sub>2</sub>	69.87	6.40	4.08	70.20	6.52	3.81	5.20	4.75	

(a) In deuteriochloroform.

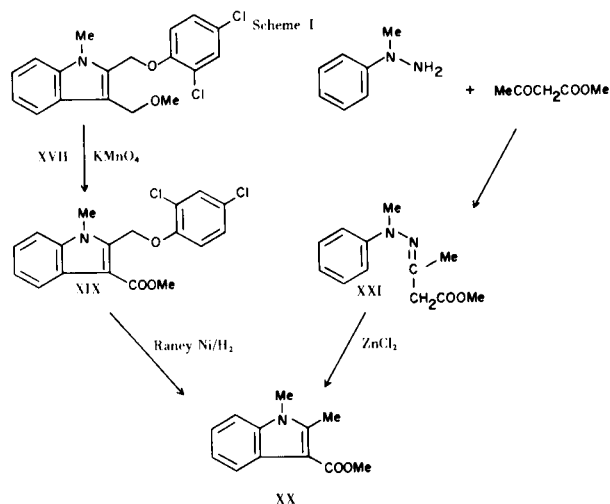
(a) In deuteriochloroform.

Treatment of XV with one equivalent of metachloroperbenzoic acid (MCPBA) in methylene chloride at room temperature over 12 hours gave a high yield of a product XVI melting at 114° and analyzing for C<sub>24</sub>H<sub>18</sub>Cl<sub>3</sub>NO<sub>3</sub>. The nmr spectrum of XVI showed a total of 11 aromatic protons, a gain of 4 over the starting compound. The mass spectrum indicated a molecular ion peak at 473 as well as the presence of three chlorine atoms. The infrared spectrum revealed the presence of a carbonyl group. Hydrolysis of XVI with aqueous alkali readily gave *m*-chlorobenzoic acid as a product. The nitrogen containing residue from this hydrolysis was a mixture of at least two components. These were difficult to separate. However, compound XVI upon treatment with methanol or ethanol rapidly eliminated the *m*-chlorobenzoate moiety with concomitant entry of the alkoxy group, to give XVII and XVIII. This facile displacement of the aryloxy function suggested a possible allylic displacement (9).



Additional synthetic confirmation for this structural assignment was obtained by the following sequence of reactions.

Oxidation of XVII with potassium permanganate in acetone solution afforded a good yield of a new compound XIX, melting at 191-192°. Infrared and nmr spectra of XIX confirmed the conversion of a methylene to a carbonyl group in this oxidation. Hydrogenolysis of XIX with Raney Nickel in refluxing *sec*-butyl alcohol gave a 44% yield of 1,2-dimethyl-3-carbomethoxy indole (XX). Independent synthesis of XX was readily achieved by the



Fischer cyclization of the hydrazone (XXI) from *N*-methyl-*N*-phenylhydrazine and methyl acetoacetate. The sequence of reactions involved is described in Scheme I.

The conversion of XIX to XX involves the elimination of the aryloxy moiety. Therefore, other analogues of XIX carrying different aryloxy groups should yield the same indole XX upon oxidation and hydrogenolysis. In the event, this proved to be so (*vide experimental*). Thus the formation of the indole from substituted *N*-methyl-*N*-propynyl anilines is clearly established.

The formation and involvement of the amine oxide in the conversion of XV into the indole XVI has decisively been demonstrated by us elsewhere (8). The generation of indoles from *N*-alkyl-*N*-propynyl anilines at ambient temperatures (20-25°) and in high yields (> 80%) is an entirely novel and intriguing approach hitherto unknown. The facility with which the aryloxy group in XVI can be displaced by nucleophiles opens up the possibility of synthesizing numerous aryl or alkyl aminomethyl derivatives, arylthiomethyl derivatives and aryloxymethyl derivatives of indoles by the present approach. The synthesis and biological activity of these derivatives will be reported in a subsequent publication.

## EXPERIMENTAL

The melting points were determined on a Mel-Temp apparatus with an ordinary thermometer and were not corrected. Nuclear magnetic resonance (nmr) spectra were obtained with a Varian A-60 spectrometer and Varian HA-100 spectrometer using carbon tetrachloride or deuteriochloroform as solvents and tetramethylsilane (TMS) as an internal standard. Mass spectral data were obtained on a Hitachi Perkin Elmer Model RMU-6E mass spectrometer. Microanalyses were performed by Mr. David Harsch.

### Synthesis of 1-Aryloxy-4-chloro-2-butyne.

These compounds were synthesized according to our earlier published procedure (7,10). Compounds thus obtained are listed in Table I.

### Synthesis of *N*-[4-Aryloxy-2-butyrynyl]-*N*-alkyl Anilines.

#### General Procedure.

1-Aryloxy-4-chloro-2-butyne (0.1 mole) and the secondary aniline (0.2 mole) were refluxed in 1-butanol (100 ml.) for 8-10 hours. The solvent was removed *in vacuo*. The residue was treated with chloroform (350 ml.), washed with water (three times) and dried (sodium sulfate). Removal of solvent gave a pale yellow viscous oil which was triturated with 50 ml. of ethanol-petroleum ether (30-60°) (1:5) and cooled to give a white solid. Recrystallization from petroleum-ether (30-60°) or benzene-petroleum ether gave pure products. The *N*-[4-Aryloxy-2-butyrynyl]-*N*-alkyl anilines prepared by this procedure are listed in Table II.

#### General Procedure for Oxidation and Rearrangement of the *N*-[4-Aryloxy-2-butyrynyl]-*N*-alkyl anilines.

*Meta*-chloroperbenzoic acid (11) [0.03 mole, 6.10 g. (85%)] in dichloromethane (200 ml.) was slowly added to a well-stirred solution of *N*-[4-aryloxy-2-butyrynyl]-*N*-alkyl aniline (0.03 mole)

dissolved in dichloromethane (150 ml.) at room temperature over a period of 30 minutes. The mixture was stirred for an additional 12 hours. The reaction mixture was washed with a 10% solution of potassium carbonate (three times, each with 300 ml. portions), then with saturated sodium chloride solution (two times) and dried (sodium sulfate). Concentration of the solution to 30-40 ml. and addition of petroleum ether (30-60°) gave a light brown solid. It was purified by recrystallization from benzene-petroleum ether (30-60°) or from methylene chloride-petroleum ether (30-60°). The 2-(aryloxymethyl)-3-(*m*-chlorobenzoyloxymethyl)-1-alkylindoles thus obtained are listed in Table III.

General Procedure for Alcoholysis of 2-(Aryloxymethyl)-3-(*m*-chlorobenzoyloxymethyl)-1-alkylindoles.

The alcoholysis was performed by dissolving the 2-(aryloxymethyl)-3-(*m*-chlorobenzoyloxymethyl)-1-alkylindole (2 g.) in absolute alcohol (methanol or ethanol, 40-70 ml.) by heating the mixture on a steam bath for about 5-15 minutes. The product was isolated by concentration of the solution and fractional recrystallization and purified by recrystallization from the same alcohol as was used in the reaction. The products 2-(aryloxymethyl)-3-methoxymethyl-1-alkylindoles and 2-(aryloxymethyl)-3-(ethoxymethyl)-1-alkylindoles thus obtained are listed in Tables IV and V respectively.

2-[(*p*-Chlorophenoxy)methyl]-3-(*m*-chlorobenzoyloxymethyl)-1-methylindole under similar treatment with allyl alcohol furnished a white solid, 2-[(*p*-chlorophenoxy)methyl]-3-(allyloxymethyl)-1-methylindole, m.p. 99-100°; yield 78.5%; nmr (deuteriochloroform): 3.72  $\delta$  (s, 3H), 3.90-4.20  $\delta$  (m, 2H), 4.75  $\delta$  (s, 2H), 5.0-5.45  $\delta$  (m, 3H), 5.17  $\delta$  (s, 2H), 6.80-7.85  $\delta$  (m, 8H); molecular ion peak at 341, 343.

*Anal.* Calcd. for C<sub>20</sub>H<sub>20</sub>ClNO<sub>2</sub>: C, 70.28; H, 5.86; N, 4.10. Found: C, 70.49; H, 5.94; N, 4.04.

Similar treatment of 2-[(2,4-dichlorophenoxy)methyl]-3-(*m*-chlorobenzoyloxymethyl)-1-methylindole with *t*-butyl alcohol gave a white solid, 2-[(2,4-dichlorophenoxy)methyl]-3-(*t*-butyloxymethyl)-1-methylindole, yield 83.6%, m.p. 141-142°, nmr (deuteriochloroform): 1.33  $\delta$  (s, 9H), 3.80  $\delta$  (s, 3H), 4.67  $\delta$  (s, 2H), 5.37  $\delta$  (s, 2H), 7.05-7.75  $\delta$  (m, 7H); molecular ion peak at 391, 393.

*Anal.* Calcd. for C<sub>21</sub>H<sub>23</sub>Cl<sub>2</sub>NO<sub>2</sub>: C, 64.29; H, 5.87; N, 3.57. Found: C, 64.15; H, 5.86; N, 3.42.

Potassium Permanganate Oxidation of 2-(Aryloxymethyl)-3-(methoxymethyl)-1-methylindoles.

2-[(2,4-Dichlorophenoxy)methyl]-3-(methoxymethyl)-1-methylindole (0.01 mole) was refluxed with potassium permanganate (40 g.) in acetone (300 ml.) for 10 hours with efficient stirring. The reaction mixture was cooled and filtered. Acetone was removed from the filtrate to give a solid (1.56 g.). The residue was extracted with ether (250 ml.). Removal of ether from the extract gave additional 0.6 g. solid. The combined solid was recrystallized from acetone to give a white solid, 2-[(2,4-dichlorophenoxy)methyl]-3-carbomethoxy-1-methylindole, yield 41.8%; m.p. 191-192°, ir (potassium bromide): 1712 cm<sup>-1</sup> (-C-OCH<sub>3</sub>);

nmr (deuteriochloroform): 3.87  $\delta$  (s, 3H), 3.95  $\delta$  (s, 3H), 5.82  $\delta$  (s, 2H); 7.10-7.40  $\delta$  (m, 6H), 8.0-8.25  $\delta$  (m, 1H), molecular ion peak at 364, 366.

*Anal.* Calcd. for C<sub>18</sub>H<sub>15</sub>Cl<sub>2</sub>NO<sub>3</sub>: C, 59.40; H, 4.17; N, 3.87. Found: C, 59.64; H, 4.13; N, 3.90.

Similar treatment of 2-[(*p*-chlorophenoxy)methyl]-3-(methoxymethyl)-1-methylindole with potassium permanganate gave a solid, 2-[(*p*-chlorophenoxy)methyl]-3-carbomethoxy-1-methylindole, 1.33 g. (40%), m.p. 157-158°; ir (potassium bromide): 1710 cm<sup>-1</sup>

(-C-OCH<sub>3</sub>); uv (methanol):  $\lambda$  max 295 m $\mu$ ; nmr (deuteriochloroform):

3.83  $\delta$  (s, 3H), 3.95  $\delta$  (s, 3H), 5.75  $\delta$  (s, 2H), 6.90-7.45  $\delta$  (m, 7H), 8.05-8.30  $\delta$  (m, 1H); molecular ion peak at 329, 331.

*Anal.* Calcd. for C<sub>18</sub>H<sub>16</sub>ClNO<sub>3</sub>: C, 65.55; H, 4.85; N, 4.24. Found: C, 65.51; H, 4.95; N, 4.16.

Hydrogenolysis of 2-(Aryloxymethyl)-1-methyl-3-carbomethoxyindole with Raney Nickel.

2-[(2,4-Dichlorophenoxy)methyl]-1-methyl-3-carbomethoxyindole (0.364 g., 0.001 mole) was refluxed with Raney Nickel (20 g.) in *sec*-butyl alcohol (100 ml.) for 40 hours with efficient stirring. Then the reaction mixture was cooled and filtered. Solvent was removed from the filtrate *in vacuo* to give a colorless oily solid. This was taken in ether (250 ml.) and washed with three-50 ml. portions of ice cold 3% aqueous potassium hydroxide solution, salt water, and water respectively. Then the ether solution was dried (sodium sulfate) and solvent was removed to give a white solid (0.11 g.). This was purified by chromatography over basic alumina, yielding 0.09 g. (44%); m.p. 141-142°; ir (potassium bromide): 1675 cm<sup>-1</sup> (-C-OCH<sub>3</sub>); uv (methanol):  $\lambda$

max 294 m $\mu$ ; nmr (deuteriochloroform): 2.66  $\delta$  (s, 3H), 3.52  $\delta$  (s, 3H), 3.92  $\delta$  (s, 3H), 7.10-7.40  $\delta$  (m, 3H), 8.0-8.25 (m, 1H); molecular ion peak 203.

*Anal.* Calcd. for C<sub>12</sub>H<sub>13</sub>NO<sub>2</sub>: C, 70.91; H, 6.45; N, 6.89. Found: C, 71.04; H, 6.59; N, 6.74.

Similar treatment of 2-[(*p*-chlorophenoxy)methyl]-1-methyl-3-carbomethoxyindole with Raney Nickel furnished the same indole derivative, 3-carbomethoxy-2-methyl-1-methylindole; yield 45%. There was no depression of m.p. with the same indole obtained from the above reaction.

Synthesis of 3-Carbomethoxy-2-methyl-1-methylindole. Preparation of *N*-Methyl-1-phenylhydrazine of Methyl Acetoacetate.

*N*-Methyl-1-phenylhydrazine (3.3 g.) was condensed with methyl acetoacetate (3.5 g.) in presence of sodium acetate (20 g.) in water-methanol solution under nitrogen, yield 3.2 g., m.p. 65-66°; molecular ion peak at 220.

*Anal.* Calcd. for C<sub>12</sub>H<sub>16</sub>N<sub>2</sub>O<sub>2</sub>: C, 65.45; H, 7.27; N, 12.73. Found: C, 65.28; H, 7.36; N, 12.69.

Fischer Cyclization of *N*-Methyl-*N*-phenylhydrazone of Methyl Acetoacetate.

The hydrazone (3.5 g.) was dissolved in dry cumene (100 ml.) under nitrogen. The anhydrous zinc chloride (17 g.) was added. The reaction mixture was refluxed for 3 hours. The mixture was filtered. From the yellow filtrate, solvent was removed under a vacuum to give a brown solid. This was purified by chromatography over basic alumina using benzene as eluent to give a white solid (0.8 g., 24.8%), m.p. 141-142°. This is identical in every respect with the product 3-carbomethoxy-2-methyl-1-methylindole obtained through rearrangement, methanolysis, permanganate oxidation and hydrogenolysis sequence.

*Anal.* Calcd. for C<sub>12</sub>H<sub>13</sub>NO<sub>2</sub>: C, 70.91; H, 6.45; N, 6.89. Found: C, 70.61; H, 6.42; N, 6.95.

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