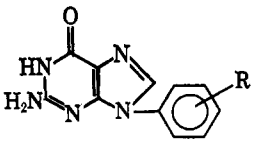
TABLE IV
PHYSICAL PROPERTIES OF



No.	R	Method[a]	Yield, %	Mp (dec), °C[b]	Formula[c]
4	*m*-NHCOC$_6$H$_3$-2-Me-5-SO$_2$F	A	34	310	$C_{19}H_{15}FN_6O_4S$
5	*m*-NHCOC$_6$H$_3$-2-MeO-5-SO$_2$F	A	22	290	$C_{19}H_{15}FN_6O_5S$
6	*m*-NHCOC$_6$H$_3$-4-Cl-3-SO$_2$F	A	29	315	$C_{18}H_{12}ClFN_6O_4S \cdot H_2O$
7	*m*-NHCOC$_6$H$_2$-2,4-Me$_2$-5-SO$_2$F	A	18	296	$C_{20}H_{17}FN_6O_4S \cdot H_2O$
8	*m*-NHCOC$_6$H$_2$-2,4-Cl$_2$-5-SO$_2$F	A	20	300	$C_{18}H_{11}Cl_2FN_6O_4S$
10	*m*-NHCOC$_6$H$_3$-3-Cl-4-SO$_2$F	A	26	320	$C_{18}H_{12}ClFN_6O_4S$
11	*m*-NHCOC$_6$H$_3$-3-Me-4-SO$_2$F	A	23	320	$C_{19}H_{15}FN_6O_4S$
12	*m*-NHCOC$_6$H$_4$-Cl-*o*	A	32	320	$C_{18}H_{13}ClN_6O_2$
13	*m*-NHCOC$_6$H$_4$-Cl-*m*	A	21	320	$C_{18}H_{13}ClN_6O_2 \cdot H_2O$
14	*m*-NHCOC$_6$H$_3$-2,4-Cl$_2$	A	28	310	$C_{18}H_{12}Cl_2N_6O_2 \cdot H_2O$
16	*m*-NHCONHC$_6$H$_3$-3-Me-4-SO$_2$F	B	57	258	$C_{19}H_{16}FN_7O_4S$
18	*m*-NHCONHC$_6$H$_3$-2-Me-5-SO$_2$F	B	68	220	$C_{19}H_{16}FN_7O_4S$
19	*m*-NHCONHC$_6$H$_3$-4-Cl-3-SO$_2$F	B	67	320	$C_{18}H_{13}ClFN_7O_4S$
20	*m*-NHCONHC$_6$H$_2$-2,4-Me$_2$-5-SO$_2$F	B	50	300	$C_{20}H_{18}FN_7O_4S \cdot 0.5H_2O$
21	*p*-O(CH$_2$)$_2$-NHCOC$_6$H$_3$-2-Me-5-SO$_2$F	A	27	258–261	$C_{21}H_{19}FN_6O_5S$
22	*p*-O(CH$_2$)$_2$-NHCOC$_6$H$_3$-2-MeO-5-SO$_2$F	A	32	237	$C_{21}H_{19}FN_6O_6S$
23	*p*-O(CH$_2$)$_2$-NHCOC$_6$H$_3$-4-Cl-3-SO$_2$F	A	53	265	$C_{20}H_{16}ClFN_6O_5S$
24	*p*-O(CH$_2$)$_2$-NHCOC$_6$H$_2$-2,4-Me$_2$-5-SO$_2$F	A	40	273–275	$C_{22}H_{21}FN_6O_5S$
26	*p*-O(CH$_2$)$_2$-NHCONHC$_6$H$_3$-2-Me-5-SO$_2$F	B	36	207	$C_{21}H_{20}FN_7O_5S \cdot H_2O$
27	*p*-O(CH$_2$)$_2$-NHCONHC$_6$H$_3$-4-Cl-3-SO$_2$F	B	42	238–242	$C_{20}H_{17}ClFN_7O_5S$
28	*p*-O(CH$_2$)$_2$-NHCONHC$_6$H$_2$-2,4-Me$_2$-5-SO$_2$F	B	34	225	$C_{22}H_{22}FN_7O_5S \cdot H_2O$
30	*p*-O(CH$_2$)$_2$NHCONHC$_6$H$_3$-3-Me-4-SO$_2$F	B	47	241	$C_{21}H_{20}FN_7O_5S \cdot 0.5H_2O$
31	*p*-O(CH$_2$)$_2$NHCONHC$_6$H$_3$-3-Cl-4-SO$_2$F	B	57	229	$C_{20}H_{17}ClFN_7O_5S \cdot 0.5CH_3OCH_2CH_2OH$
32[d]	*p*-O(CH$_2$)$_2$NHCONHCH$_2$C$_6$H$_4$-SO$_2$F-*p*	B	48	286	$C_{21}H_{20}FN_7O_5S$

[a] For method A see B. R. Baker and W. F. Wood, *J. Med. Chem.*, **11**, 650 (1968); for method B see ref 6; yields of anal. pure material. [b] All compds were recrystd from $CH_3OCH_2CH_2OH$–H_2O. [c] All compds were analyzed for C, H, and N. [d] See B. R. Baker and M. Cory, *J. Med. Chem.*, **14**, 805 (1971), for intermediate carbamate.

Irreversible Enzyme Inhibitors. 186.[1,2] Irreversible Inhibitors of the C'1a Component of Complement Derived from *m*-(Phenoxypropoxy)benzamidine by Bridging to a Terminal Sulfonyl Fluoride[3]

B. R. BAKER* AND MICHAEL CORY

Department of Chemistry, University of California at Santa Barbara, Santa Barbara, California 93106

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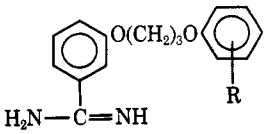
A series of 21 derivatives of *m*-(phenoxypropoxy)-, *m*-(phenoxybutoxy)-, *m*-(phenoxyethoxy)-, and *m*-(phenylbutyl)benzamidine bridged from the ortho position of the Ph moiety to a terminal SO_2F were synthesized, then investigated as irreversible inhibitors of the C'1a component of complement. The 2 most effective compds were *m*-[*o*-(2-chloro-5-fluorosulfonylphenylureido)phenoxybutoxy]benzamidine (**25**) and the corresponding propoxy compd (**17**) which showed 50% irreversible inhibition of C'1a at about 5 and 8 μM, respectively; these 2 compounds were also potent inhibitors of whole complement when assayed by inhibition of lysis of sheep red blood cells by hemolysin and complement.

The possible medicinal utility of inhibitors of serum complement for organ transplantation[4] and in treatment of some arthritic states[4] has been discussed previously.[3,5] The serum complement system involves 11 distinct proteins for killing invading organisms or for lysis of foreign mammalian cells.[4] The most powerful inhibitor of serum complement known to date[3] is the benzamidine meta bridged to SO_2F (**1**); however, **1** is not an irreversible inhibitor of the C'1a component of complement.[3] In contrast, the ortho-bridged SO_2F



1, R = *m*-NHCONHC$_6$H$_4$SO$_2$F-*p*
2, R = *o*-NHCOC$_6$H$_4$SO$_2$F-*m*

(1) This work was generously supported by Grant CA-08695 from the National Cancer Institute, U. S. Public Health Service.

(2) For the previous paper in this series see B. R. Baker and H.-U. Siebeneick, *J. Med. Chem.*, **14**, 802 (1971).

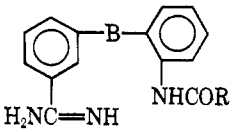
(3) For the previous paper on complement see B. R. Baker and M. Cory, *ibid.*, **14**, 119 (1971).

(4) H. J. Müller-Eberhard, *Advan. Immunol.*, **8**, 1 (1968).

(5) B. R. Baker and E. H. Erickson, *J. Med. Chem.*, **12**, 408 (1969).

TABLE I

INHIBITION OF WHOLE COMPLEMENT AND IRREVERSIBLE INHIBITION[a] OF ITS C'1A COMPONENT BY



No.	B	R	Inhib, m*M*	C'1a,[b] % inactvn	Whole complement % inhibn[c]	Whole complement % lysis[d]
2[e]	$O(CH_2)_3O$	$C_6H_4SO_2F$-*m*	0.25	89	80	9
			0.125	84	64	
			0.062	70		
			0.031	29		
3[e]	$O(CH_2)_3O$	$C_6H_4SO_2F$-*p*	0.125	16	38	6
			0.062		23	
4[e]	$O(CH_2)_3O$	C_6H_5	0.5	−13	90	10
			0.25	−8	83	
			0.125		32	
5	$O(CH_2)_3O$	C_6H_3-2-Cl-5-SO_2F	0.125[f]	98	51	0
			0.062	81	8	
			0.031	41		
6	$O(CH_2)_3O$	C_6H_3-2-Me-5-SO_2F	0.50	95		80
			0.25	81	82	3
			0.125	56	91	
			0.062	27	60	
			0.031		36	
7	$O(CH_2)_3O$	C_6H_3-2-MeO-5-SO_2F	0.062[f]	9	15	2
8	$O(CH_2)_3O$	C_6H_2-2,4-Cl_2-5-SO_2F	0.062[f]	92	63	0
			0.031	89	23	
			0.015	76		
			0.0077	42		
9	$O(CH_2)_3O$	C_6H_2-2,4-Me_2-5-SO_2F	0.125	90		85
			0.062	79	59	
			0.031	59	24	
			0.015	18		
10	$O(CH_2)_3O$	$CH_2C_6H_4SO_2F$-*p*	0.25[f]	97	72	11
			0.125	93	69	3
			0.062	75	45	
			0.031	47		
11	$O(CH_2)_3O$	$CH_2OC_6H_4SO_2F$-*p*	0.125[f]	81	66	0
			0.062	51	44	
12	$O(CH_2)_3O$	$(CH_2)_2C_6H_4SO_2F$-*p*	0.125[f]	80	70	0
			0.062	51	46	
13	$O(CH_2)_3O$	$(CH_2)_4C_6H_4SO_2F$-*p*	0.125[f]	73	29	33
			0.062	59	51	2
			0.031		25	
14	$O(CH_2)_3O$	NHC_6H_5	0.125[f]		52	0
			0.062		34	
15[e]	$O(CH_2)_3O$	$NHC_6H_4SO_2F$-*p*	0.25	40	61	21
			0.125	15	57	9
			0.062		51	
			0.031		26	
16	$O(CH_2)_3O$	$NHC_6H_4SO_2F$-*m*	0.125[f]	100	65	12
			0.062	99	70	0
			0.031	87	34	0
			0.015	49		
17	$O(CH_2)_3O$	NHC_6H_3-2-Cl-5-SO_2F	0.125[f]	95	74	11
			0.062	96	80	0
			0.031	95	60	
			0.015	78	32	
			0.0077	41		
18	$O(CH_2)_3O$	NHC_6H_3-4-Cl-3-SO_2F	0.062[f]	30	53	9
			0.031		36	
19	$O(CH_2)_3O$	NHC_6H_3-4-Me-3-SO_2F	0.062[f]	0	43	2
			0.031		31	
20	$O(CH_2)_3O$	NHC_6H_2-2,4-Me_2-5-SO_2F	0.062[f]	28	38	0
21	$O(CH_2)_3O$	$NHCH_2C_6H_4SO_2F$-*p*	0.25[f]	92	74	5
			0.125	70	54	
			0.062	43		
22	$O(CH_2)_3O$	$NH(CH_2)_2C_6H_4SO_2F$-*p*	0.125[f]	71	69	0
			0.062	43	51	

TABLE I (*Continued*)

No.	B	R	Inhib, m*M*	C'1a,[b] % inactvn	Whole complement— % inhibn[c]	Whole complement— % lysis[d]
23	$O(CH_2)_2O$	NHC_6H_3-2-Cl-5-SO_2F	0.125[f]	59	61	0
			0.062	39	28	
24	$O(CH_2)_4O$	C_6H_4-4-Me-3-SO_2F	0.125[f]		48	14
			0.062	24[f]	56	3
			0.031		25	
25	$O(CH_2)_4O$	NHC_6H_3-2-Cl-5-SO_2F	0.062[f]	100	86	4
			0.031	100	77	
			0.015	92	50	
			0.0077	61		
			0.0039	39		
26	$(CH_2)_4$	$NHC_6H_4SO_2F$-*m*	0.125[f]	71	55	12
			0.062	46	58	0
			0.031		30	
27	$(CH_2)_4$	$NHC_6H_4SO_2F$-*p*	0.125[f]		42	26
			0.062	10[f]	61	
			0.031	0	33	

[a] The technical assistance of Pauline Minton is acknowledged. [b] Inhibitor incubated 10 min at 37° with C'1a, then remainder of complement added as previously described.[3] [c] Lysis of sheep red blood cells by guinea pig complement as previously described.[5] [d] Lysis by the compd in the absence of complement expressed as per cent of total lysis possible.[5] [e] Data from ref 3. [f] Maximum solubility.

2 is a powerful irreversible inhibitor of the C'1a component of complement, but is only 0.125 as effective as **1** on the whole complement system.[3] Therefore a study was undertaken to see if the potency of the ortho-bridged sulfonyl fluoride **2** against whole complement or C'1a or both could be increased by molecular manipulation of **2**; the results are the subject of this paper.

Biological Results.—The compds in Table I were compared by the concn necessary to give 50% inactivation when incubated with C'1a at 37° for 10 min. The reasons why inactivation can be incomplete have been discussed previously.[3]

The first series of compds were derived from *o*-benzanilide by bridging to benzamidine with $O(CH_2)_3O$. Of the 2 parent compds, the *m*-SO_2F derivative **2** was considerably more effective as an irreversible inhibitor of C'1a than the corresponding *p*-SO_2F derivative **3**.[3] Introduction of a 2-Me (**6**) substituent on the benzamido moiety of **2** decreased the effectiveness about 2-fold; the 2-MeO (**7**) reduced activity even more. Activity was enhanced less than 2-fold by introduction of a 2-Cl substituent (**5**). However introduction of 2,4-Cl_2 substituents (**8**) increased activity 4-fold, **8** being the most active of the benzamide series; in contrast, introduction of 2,4-Me_2 substituents (**9**) did not change the activity.

Insertion of a CH_2 group (**10**) next to the *p*-benzenesulfonyl fluoride moiety of **3** increased activity at least 8-fold; this activity was maintained when CH_2O (**11**), $(CH_2)_2$ (**12**), or $(CH_2)_4$ (**13**) groups were inserted, but activity was not increased.

The second series of compds were derived from an *o*-phenylureido substituent (**14**). The parent *m*-SO_2F derivative **16** was again more effective in inactivating C'1a than the *p*-SO_2F derivative (**15**) by a factor of 16-fold. Introduction of a 2-Cl atom (**17**) on **16** enhanced activity about 2-fold. Introduction of 4-Cl (**18**), 4-Me (**19**), or 2,4-Me_2 (**20**) on **16** considerably reduced the activity. Insertion of a CH_2 (**21**) or $(CH_2)_2$ (**22**) group next to the *p*-$C_6H_4SO_2F$ moiety of **15** enhanced activity 4-fold.

The most active compd of this phenylureido series was the 2-Cl derivative **17** which showed 50% inhibition at about 8 μM. Therefore this 2-chloro-5-fluorosulfonylphenylureido moiety of **17** was held constant while the length of the $O(CH_2)_3O$ bridge was varied. The $O(CH_2)_2O$ bridge (**23**) gave an 8-fold less effective compd while the $O(CH_2)_4O$ bridge (**25**) increased the effectiveness by a factor of 2. Replacement of the $O(CH_2)_3O$ bridge of **16** by $(CH_2)_4$ (**26**) decreased effectiveness 4-fold; this result can be attributed to the more restricted ground state conformation of the bridge (B) in **26** than in **16** which apparently restricts **26** from assuming easily the required conformation for maximum binding to the C'1a component. The greater efficiency of **16** than of **26** on whole complement can also be rationalized in the same way.

The 2 most active compds in Table I for irreversible inhibition of C'1a are the 2-chloro-5-fluorosulfonylphenylureido derivatives, **25** and **17**, which gave 50% inactivation at about 5 and 8 μM, resp. These 2 compds are also the most effective in Table I on whole complement; however, **25** is still only 0.5 as effective as **1**[3] on the whole complement system. Since Cl is present in large excess in whole complement it is possible that **25** is not active enough to make C'1a rate limiting in the whole system assay.

Chemistry.—The intermediate substituted *m*-(phenoxyalkoxy)benzonitriles **28** and **29** were prepared by the previously described alkylation of *m*-cyanophenol (method A);[6] these were converted to the amidines **30** and **31** through the imino ether hydrochlorides (method B).[7] Catalytic reduction of the NO_2 group with 5% Pd/C (method C)[7] gave crystalline aminoamidine salts **32** and **33** which could be acylated to the desired amides or ureas (methods D and E).[3]

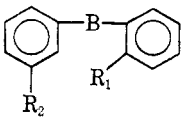
The butadiene **34** was prepared by a Wittig reaction of *m*-cyanobenzyltriphenylphosphonium bromide[5] and *o*-nitrocinnamaldehyde. Catalytic reduction of **34** with Pd/C catalyst (method C) and conversion of the crude oil to the amidine (method B) gave **35**.

The SO_2F-substituted acyl chlorides and *O*-(*p*-nitrophenyl) carbamates[8] used in methods D and E were prepared in these laboratories by published proce-

(6) B. R. Baker and E. H. Erickson, *J. Med. Chem.*, **10**, 1123 (1967).
(7) B. R. Baker and E. H. Erickson, *ibid.*, **11**, 245 (1968).
(8) B. R. Baker and N. M. J. Vermeulen, *ibid.*, **12**, 74 (1969).

TABLE II

PHYSICAL CONSTANTS OF



No.	R_1	R_2	B	Method[a]	Yield, %	Mp, °C	Formula[b]
5	$NHCOC_6H_3$-2-Cl-5-SO_2F	$C(NH_2)$=NH·TsOH	$O(CH_2)_3O$	D[c]	20[d]	163–165	$C_{30}H_{29}N_3ClFO_8S_2 \cdot 0.25H_2O$
6	$NHCOC_6H_3$-2-Me-5-SO_2F	$C(NH_2)$=NH·TsOH	$O(CH_2)_3O$	D[c]	28[d]	148–151	$C_{31}H_{32}FN_3O_8S_2$
7	$NHCOC_6H_3$-2-MeO-5-SO_2F	$C(NH_2)$=NH·TsOH	$O(CH_2)_3O$	D[e]	18[f]	222–224	$C_{31}H_{32}FN_3O_9S_2 \cdot H_2O$
8	$NHCOC_6H_2$-2,4-Cl_2-5-SO_2F	$C(NH_2)$=NH·TsOH	$O(CH_2)_3O$	D[g]	17[d]	196–198	$C_{30}H_{28}Cl_2FN_3O_8S_2$
9	$NHCOC_6H_2$-2,4-Me_2-5-SO_2F	$C(NH_2)$=NH·picrate	$O(CH_2)_3O$	D[g]	22[f]	214–215	$C_{31}H_{29}FN_6O_{12}S$
10	$NHCOCH_2C_6H_4SO_2F$-*p*	$C(NH_2)$=NH·picrate	$O(CH_2)_3O$	D[h]	63[f]	202–204	$C_{30}H_{27}FN_6O_{12}S \cdot 0.25H_2O$
11	$NHCOCH_2OC_6H_4SO_2F$-*p*	$C(NH_2)$=NH·TsOH	$O(CH_2)_3O$	D[i]	63[f]	189–191	$C_{31}H_{32}FN_3O_4S_2$
12	$NHCO(CH_2)_2C_6H_4SO_2F$-*p*	$C(NH_2)$=NH·TsOH	$O(CH_2)_3O$	D[j]	40[f]	205–207	$C_{32}H_{34}FN_3O_8S_2$
13	$NHCO(CH_2)_4C_6H_4SO_2F$-*p*	$C(NH_2)$=NH·TsOH	$O(CH_2)_3O$	D[j]	52[k]	163–165	$C_{34}H_{38}FN_3O_8S_2$
14	$NHCONHC_6H_5$	$C(NH_2)$=NH·picrate	$O(CH_2)_3O$	E[l]	48[m]	183–185	$C_{29}H_{27}H_7O_{10}$
16	$NHCONHC_6H_4SO_2F$-*m*	$C(NH_2)$=NH·TsOH	$O(CH_2)_3O$	E[n]	35[f]	195–197	$C_{30}H_{31}FN_4O_8S_2$
17	$NHCONHC_6H_3$-2-Cl-5-SO_2F	$C(NH_2)$=NH·TsOH	$O(CH_2)_3O$	E[n]	49[f]	183–185	$C_{30}H_{30}ClFN_4O_8S_2 \cdot 1.5H_2O$
18	$NHCONHC_6H_3$-4-Cl-3-SO_2F	$C(NH_2)$=NH·TsOH	$O(CH_2)_3O$	E[g]	47[f]	148–150	$C_{30}H_{30}ClFN_4O_8S_2$
19	$NHCONHC_6H_3$-4-Me-3-SO_2F	$C(NH_2)$=NH·TsOH	$O(CH_2)_3O$	E[o]	58[o]	157–159	$C_{31}H_{23}FN_4O_8S_2 \cdot H_2O$
20	$NHCONHC_6H_2$-2,4-Me_2-5-SO_2F	$C(NH_2)$=NH·TsOH	$O(CH_2)_3O$	E[g]	51[f]	206–208	$C_{32}H_{35}FN_4O_8S_2$
21	$NHCONHCH_2C_6H_4SO_2F$-*p*	$C(NH_2)$=NH·TsOH	$O(CH_2)_3O$	E[p]	56[f]	179–181	$C_{31}H_{33}FN_4O_8S_2 \cdot H_2O$
22	$NHCONH(CH_2)_2C_6H_4SO_2F$-*p*	$C(NH_2)$=NH·TsOH	$O(CH_2)_3O$	E[q]	17[f]	202–205	$C_{32}H_{35}FN_4O_8S_2 \cdot H_2O$
23	$NHCONHC_6H_3$-2-Cl-5-SO_2F	$C(NH_2)$=NH·picrate	$O(CH_2)_2O$	E[n]	73[r]	212–215	$C_{28}H_{23}ClFN_7O_{12}S$
24	$NHCOC_6H_4$-4-Me-3-SO_2F	$C(NH_2)$=NH·picrate	$O(CH_2)_4O$	D[g]	19[f]	193–195	$C_{31}H_{29}FN_6O_{12}S$
25	$NHCONHC_6H_3$-2-Cl-5-SO_2F	$C(NH_2)$=NH·TsOH	$O(CH_2)_4O$	E[c]	33[f]	164–167	$C_{31}H_{32}ClFN_4O_8S_2$
26	$NHCONHC_6H_4SO_2F$-*p*	$C(NH_2)$=NH·picrate	$(CH_2)_4$	E[s]	34[k]	214–216	$C_{30}H_{28}FN_7O_{10}S$
27	$NHCONHC_6H_4SO_2F$-*m*	$C(NH_2)$=NH·picrate	$(CH_2)_4$	E[n]	55[r]	210–213	$C_{30}H_{28}FN_7O_{10}S$
28	*o*-NO_2	CN	$O(CH_2)_2O$	A	42[t]	145–147	$C_{15}H_{12}N_2O_4$
29	*o*-NO_2	CN	$O(CH_2)_4O$	A	62[u]	90–93	$C_{17}H_{16}N_2O_4$
30	*o*-NO_2	$C(NH_2)$=NH·HCl	$O(CH_2)_2O$	B	62[d]	154–157	$C_{15}H_{15}N_3O_4 \cdot HCl$
31	*o*-NO_2	$C(NH_2)$=NH·TsOH	$O(CH_2)_4O$	B	21[f]	112–114	$C_{24}H_{27}N_3O_7S$
32	*o*-NH_2	C(NH)=NH·2picrate	$O(CH_2)_2O$	C	12[v]	230–232	$C_{27}H_{23}N_9O_{16}$
33	*o*-NH_2	$C(NH_2)$=NH·2TsOH	$O(CH_2)_4O$	C	85[d]	149–153	$C_{31}H_{37}N_3O_8S_2 \cdot H_2O$
35	*o*-NH_2	C(NH)=NH·2picrate	$(CH_2)_4$	C, B	59[f,v]	181–183	$C_{29}H_{27}N_9O_{14}$

[a] Methods: A, alkylation of *m*-cyanophenol;[6] B, nitrile → imino ether → amidine;[7] C, $NO_2 \rightarrow NH_2$;[7] D, acylation of substituted aniline using acyl chloride;[3] E, acylation of substituted aniline using N-substituted *O*-*p*-nitrophenyl carbamate.[3] [b] Anal. C, H, N. [c] See ref 9 for starting acid. [d] Recrystd from H_2O. [e] Acid chloride, commercially available. [f] Recrystd from 50% aq EtOH. [g] See ref 2 for starting acid. [h] See ref 10 for starting acid. [i] See ref 11 for starting acid. [j] See ref 12 for starting acid. [k] Recrystd from 95% EtOH. [l] See ref 8 for procedure, mp 149–150°; K. D. Kopple *J. Amer. Chem. Soc.*, **79**, 6442 (1957). [m] Recrystd from 50% aqueous $MeOC_2H_4OH$. [n] See ref 8 for starting carbamate. [o] Recrystd from 50% aqueous Me_2CO. [p] See Experimental Section. [q] See ref 3 for starting carbamate. [r] Recrystd from EtOH. [s] See ref 13 for starting carbamate. [t] Recrystd from EtOAc. [u] Recrystd from C_6H_6. [v] Yield based upon the starting butadiene **34**.

dures[2,3,8–13] (see Table II). The only new intermediate was the carbamate for **21** which was prepared by fluorosulfonation of *N*-benzylacetamide to give **36**, acid hydrolysis of the Ac group to **37**, then reaction with *p*-nitrophenyl chloroformate to give **38**[3] (see Experimental Section).

Experimental Section

Melting points were detd in capillary tubes on a Mel-Temp block and are uncor. All anal. samples had ir spectra compatible with their assigned structures and moved as a single spot on tlc on Brinkmann silica gel GF or polyamide MN_{254}; each gave combustion values for C, H, and N within 0.4% of theory.

1-(*m*-Cyanophenyl)-4-(*o*-nitrophenyl)butadiene (34).—To 45.6 g (0.10 mole) of 3-cyanobenzyltriphenylphosphonium bromide[5] in 250 ml of dry DMF was added 12.4 g of DBN (0.10 mole) and 17.7 g (0.10 mole) of *o*-nitrocinnamaldehyde. The resulting dark soln was stirred at ambient temp for 16 hr, then poured into 250 ml of H_2O. The mixt was chilled, and the product was collected. Two recrystns from 2-methoxyethanol gave 19.2 g (70%) of yellow cryst, mp 169–171°. *Anal.* ($C_{17}H_{12}N_2O_2$) C, H, N.

***N*-(*p*-Fluorosulfonylbenzyl)acetamide (36)** was prepd in 29% yield by fluorosulfonation of *N*-benzylacetamide at −10° in FSO_3H.[3] Recrystn from C_6H_6 gave white cryst, mp 119–120°. The nmr spectrum was consistant with para substitution. *Anal.* ($C_9H_{10}FNO_3S$) C, H, N.

***p*-Fluorosulfonylbenzylamine·HCl (37)** was prepd in 53% yield by acid hydrolysis of **36**.[3] Recrystn from EtOH gave white cryst, mp 238–240°. *Anal.* ($C_7H_8FNO_2S \cdot HCl$) C, H, N.

***O*-(*p*-Nitrophenyl) *N*-(*p*-Fluorosulfonylbenzyl)carbamate (38)** was prepd[8] in 23% yield from **37** and *p*-nitrophenyl chloroformate. Recrystn from C_6H_6 gave white cryst, mp 171–173°. *Anal.* ($C_{14}H_{11}FN_2O_6S$) C, H, N.

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