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NEW "GABRIEL" SYNTHESES OF AMINES[1a]

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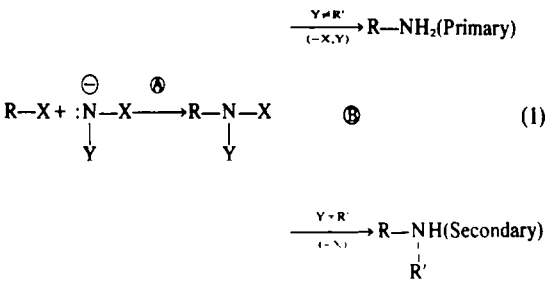
Abstract—The Gabriel synthesis is generalized as monoalkylation of an ammonia or primary amine derivative with subsequent removal of the derivatizing group(s) from nitrogen. Two new derivatives for this purpose are introduced: phenacylsulfonamides and triflamides, with discussion of their generality and effectiveness.

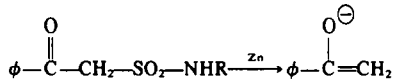
Primary, secondary and tertiary amines are synthesized most directly by alkylation of ammonia or lower amines. The major drawback consists of polyalkylation; in terms of net structural change this problem can be characterized as the substitution of more than one hydrogen on the substrate ammonia/amine by the alkyl group. The solution to the problem then lies in the prior replacement of extra hydrogens on nitrogen with other groups (X, Y), as in eqn (1), such that there remains but one hydrogen to substitute in alkylation (Ⓐ). This avoids polyalkylation but requires an additional removal step for the replacing groups X, Y (Ⓑ).



For primary amines the classical implementation lay in the Gabriel synthesis (X, Y = phthaloyl) with removal Ⓑ by hydrolysis or hydrazinolysis;[2] more recently the Carpino variant (X=Y=COOt-Bu) allows non-hydrolytic removal Ⓑ with acid.[3] The azide variant (X, Y = N_2^+) utilizes a reductive removal step Ⓑ.[4] For secondary amines (eqn (1), Y=R') prior acylation of the substrate primary amine acidifies the remaining hydrogen for monoalkylation of the amide anion. With carbon acylation (X=COR") removal is commonly by hydrolysis, while with sulfonation (X=SO_2R") the monoalkylation occurs more easily owing to the greater acidity of $-NHSO_2-$ but the sulfonamides are much more difficult to open for step Ⓑ.

This generalized solution to the polyalkylation problem (hereafter referred to as the general Gabriel synthesis) is essentially an example of the synthetic conception of protection-deprotection, to render unreactive certain groups when another is intended for reaction. In this case the extra N-H groups are rendered unreactive by replacement. As in all protection devices in synthesis the procedure introduces two extra steps: protection, which here is the creation of HNXY; and deprotection, here the removal step Ⓑ. After the main alkylation operation Ⓐ, however, the nitrogen remains protected and in synthesis can often profitably retain this protection during other reactions in the sequence before the final removal Ⓑ is carried out. This implies that the protecting groups X, Y should protect against as broad a range of reaction conditions as possible. Conversely, the removal step Ⓑ should be mild and specific so as to interfere as little as possible with other functionality in the molecule. Furthermore a choice of options in protecting groups is desirable to adapt to the particular other functionalities of particular synthetic problems, as exemplified in the Gabriel variants above. With nitrogen the major protection needed is a neutralization of the intrinsic nucleophilicity (and corresponding ease of oxidation) of amino nitrogen, and this suggests electron-withdrawing groups X, Y, as above. The sulfonamide group fills the need for broad-spectrum protection stability and mild monoalkylation conditions, is created from amines with facility, but is not easily removed. Hence we sought sulfonamide groups adapted for specialized removal.

Phenacylsulfonamides. The first sulfonamide examined was the phenacylsulfonamide, $\phi COCH_2SO_2NHR$, since we believed that mild zinc reduction could be used to effect specific removal.† Analogous to α-halo-ketone reduction with zinc,[6] this reduction should be facilitated by loss of the relatively stable sulfinate ion as in eqn (2).



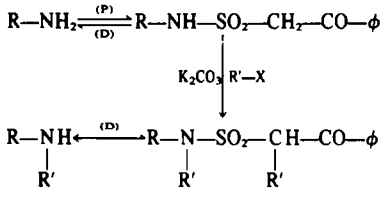
$$+:\overset{\ominus}{S}O_2NHR \xrightarrow{2H^+} \phi COCH_3 + SO_2 + H_2NR. \qquad (2)$$

The full protection (P), alkylation, and deprotection (D) scheme is embodied in eqn (3), and generally works well as written. Phenacylsulfonyl chloride[7]‡ behaves normally as an active, efficient sulfonating agent for the amines at ice temperature in methylene chloride with pyridine as base. Addition of the sulfonyl chloride to the amines is preferable, presumably because of intermediate generation of the sulfene ($\phi COCH{=}SO_2$) as the active agent.[8] The

†We also consider the t-butylsulfonyl group on the expectation that thermal removal of isobutylene and sulfur dioxide would constitute a particularly clean and specific deprotection, but it has been reported[5] that t-butylsulfonyl chloride itself so decomposes with amines. It seems likely that 1-cyclopropylethane or dicyclopropylmethane-sulfonyl chlorides might circumvent this and serve in the same role but initial attempts to prepare these were unsuccessful.

‡The solid chloride (m.p. 88°) appears indefinitely stable on the shelf and, contrary to this previous report, affords acceptable analyses.

phenacylsulfonamides were prepared in over 90% yield without optimization; they are high-melting and generally crystallize well. Their alkylation proceeded normally with dry potassium carbonate in acetone at room temperature (18–24 hr) using methyl iodide and benzyl bromide as model alkylating agents. Results are tabulated in Table 1.



(3)

(P): $\phi COCH_2SO_2Cl/C_5H_5N/0°$ (D): $Zn/CH_3COOH/H^+$

The deprotection (D) with zinc proceeds smoothly at room temperature in acetic acid with catalytic mineral acid added, the yields of six examples are collected in Table 1. Acetophenone was isolated and sulfur dioxide detected by smell. When larger amounts of hydrochloric acid were used, up to 10% of thioacetophenone was identified also, though with negligible effect on the yield of amine.

The procedure has two difficulties. Monoalkylation of methylene always occurred, concurrent with and apparently faster than N-alkylation, e.g. with R'=CH_3 in eqn (3), propiophenone was isolated following zinc reduction. With simple alkylating agents this offers no problem but with more complex alkylating agents the waste is serious. Presumably this may be corrected by the initial use of propiophenone-α-sulfonyl chloride, but our attempts to prepare this reagent by anology with phenacylsulfonyl chloride failed. The second difficulty lies in the instability of phenacylsulfonamides to aqueous alkali, presumably because of acyl cleavage to benzoic acid.

The phenacylsulfonamides are acceptable, with these qualifications, for preparation of secondary amines, but mono-N-alkylation of the parent phenacylsulfonamide, as a Gabriel synthesis of primary amines, could not be realized under a variety of conditions for benzylation or methylation. Mixtures of mono- and di-alkylated products were invariably obtained.

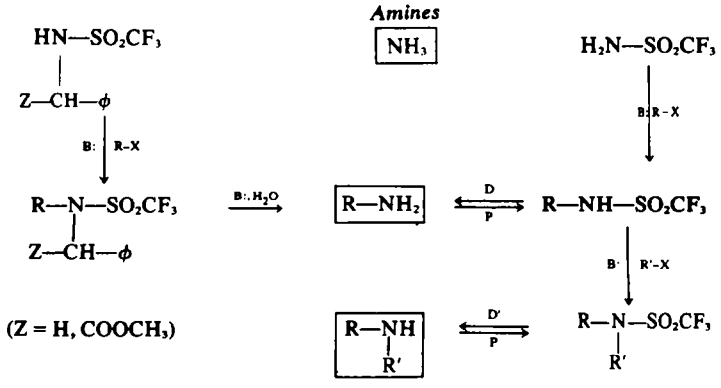
Triflamides. Our work with trifluoromethanesulfonamides ("triflamides")[9,10] suggested that this group might offer an alternative without the drawbacks of phenacylsulfonamides. The elimination of triflinate[9] also provides an alternative to Gabriel synthesis of primary amines and the general scheme for both is shown in Chart 1. The parallel with the phenacylsulfonamides is found at lower right, for creating secondary from primary amines. The triflation (P) is rapid and near quantitative with triflic anhydride, $(CF_3SO_2)_2O$, in methylene chloride with triethylamine at −78°. The stable, crystalline and less reactive triflating agent $\phi N(SO_2CF_3)_2$ (m.p. 93–4°), is more convenient for triflation of secondary aliphatic amines since the by-product phenyltriflamide ($\phi NHSO_2CF_3$) is readily removed by carbonate extraction. This reagent is unusually selective in that it does not react with aromatic secondary amines.[10] As with the phenacylsulfonamides, normal alkylation proceeds with potassium carbonate in acetone at room temperature overnight. The phenacylsulfonamide shortcomings of multiple alkylation and alkali-instability of the sulfonamide are not found with the triflamides, which are also stable to hydrogenation and borohydride, zinc or phosphine/phosphite reductions as well as acid and base and mild oxidants.

Thus the triflamide represents a broadly stable protecting group. Its removal, however, is smoothly effected by

Table 1. Phenacylsulfonamides as Gabriel reagents: eqn (3)

R-	(P) mp (yield)	(D) yield	R'-X alkylation mp (yield)	(D) yield[a]
C_6H_5	110-111° (94%)	72%	CH_3I: 101-102° (93%)	78%
			ϕCH_2Br: 151-153° (94%)	98%
C_6H_{11}- (cyclohexyl)	139-140° (91%)	67%	CH_3I: 106-107° (80%)	--
n-C_4H_9-	97-99° (92%)	66%	CH_3I: oil (78%)	75%

[a] Zinc removal of the alkylated derivative



D = Red Al[11]; D' = $LiAlH_4$; P = $(CF_3SO_2)_2O/Et_3N$

Chart 1. Triflamides in Gabriel synthesis

lithium aluminum hydride in boiling ether for secondary amines (D') and by Red-Al[11] for the primary triflamides (D), which only form stable salts with lithium aluminum hydride. The reduction of primary triflamides with Red-Al occurs in refluxing bezene with high efficiency, in contrast to the harsher conditions and poorer yields characteristic of simple sulfonamides.[12] Results are summarized in Table 2.

For Gabriel synthesis of primary amines the parent triflamide ($CF_3SO_2NH_2$) could not be cleanly monalkylated. When two hydrogens of ammonia are replaced as in benzyltriflamide ($\phi CH_2NHSO_2CF_3$) monoalkylation is facile as before and triflinate ion is then eliminated in base to form an imine, hydrolyzable to the free amine, as outlined in eqn (4).

$$R{-}X + HNSO_2CF_3 \xrightarrow{B:} R{-}N(CH_2\phi){-}SO_2CF_3 \xrightarrow[\Delta]{B:} R{-}N{=}CH\phi + {:}SO_2CF_3^- \xrightarrow{H_3O^+} R{-}NH_2 + \phi CHO. \quad (4)$$

The base required for the elimination was sodium hydride in dimethylformamide, three hours at 100°; potassium carbonate, even on long heating, caused no elimination. The resultant benzaldimines were not isolated but hydrolyzed directly by refluxing in 10% hydrochloric acid: tetrahydrofuran (1:2) for 3 hr. Benzaldehyde was isolated as a 2,4-dinitrophenylhydrazone (75% yield) in one case. Seeking more activation of the benzylic proton, we found the alkylated *p*-nitrobenzyltriflamides would eliminate with carbonate in boiling acetone but required up to 10 days time. Hence we added a carbomethoxy group to the benzylic position, creating the methyl ester of phenylglycine triflamide, $CH_3OCOCH\phi NHSO_2CF_3$ (Chart 1, upper left), as a potential Gabriel reagent. In this case the basic conditions used for alkylation were found to be sufficient to carry out the elimination as well (potassium carbonate in boiling acetonitrile for up to 80 hr) and the subsequent imine hydrolysis was facile enough to proceed during aqueous acid work-up. This then allows the free primary amine to be prepared in only one operation from the phenylglycine ester triflamide and alkyl halide. The results are quite satisfactory, as shown in Table 3. Our concern that the imine might tautomerize out of conjugation with the ester group, and so yield no amine R–NH_2, was realized only to an insignificant extent for benzyl bromide yielded only 10% of phenylglycine ester and cinnamyl bromide none.*

*Preliminary examination of the reagent, N-phenacyltriflamide ($\phi COCH_2NHSO_2CF_3$), showed that benzylation followed by hydrolysis led to significant quantities of benzaldehyde, thus implying considerable tautomerization to N-phenacylbenzaldimine ($\phi COCH_2N{=}CH\phi$) following triflinate elimination.

Secondary halides, however, are apparently too sterically hindered for alkylation.

As an alternate activation of the acidic benzylic proton we considered Z=ϕ in Chart 1 but tried instead the variant 9-fluorenyltriflamide to obtain greater benzylic acidity for the base-initiated elimination step. The reagent has the added advantage of dispensing with the more reactive carbomethoxyl group, and in fact also proceeded like the other in undergoing both alkylation and subsequent elimination under the same basic conditions (potassium carbonate in boiling acetonitrile). The results of two cases (Table 3) allow a favorable comparison with the glycine ester reagent. Overall the procedure represents a simple, efficient one-step Gabriel synthesis of primary amines from primary halides, and the reagents are readily made by triflation of the commercial phenyl glycine ester or 9-fluoreneneamine.

EXPERIMENTAL

Trifluoromethansulfonic acid was purchased from 3-M company. All m.ps were taken on a Fisher-Johns melting point apparatus. NMR spectra were recorded on a Varian Model A-60A spectrometer. Elemental analyses were taken of representative members of each series and were carried out by Galbraith Laboratories, Inc.

N-Phenyl phenacylsulfonamide. Phenacylsulfonyl chloride[7] (21·8 g, 0·1 mol) in 50 ml $CHCl_3$ was added dropwise to a stirred soln of aniline (9·30 g, 0·1 mol) and pyridine (8·2 g 0·1 mol) in $CHCl_3$ (250 ml) at 0°. The reaction was stirred for an additional 6 hr then washed with 2 × 40 ml distilled water, 2 × 30 ml 10% HCl, 2 × 40 ml distilled water, dried (Na_2SO_4) and evaporated *in vacuo* leaving a solid, 25·4 g (93%) which was recrystallized from hexane, m.p. 110–111° (lit.[13] 106–108°). NMR ($CDCl_3$) δ 7·17–7·50 (m, 10 H), 4·57 (s, 2H).

The following compounds were prepared using the same procedure as described for N-phenyl phenacylsulfonamide:

N-Cyclohexyl phenacylsulfonamide, yield: 91%; m.p. 139–140°; NMR ($CDCl_3$) δ 7·3–8·1 (m, 5 H), 4·63 (s, 2H), 1·0–2·2 (m, 11H). (Found: C, 59·88; H, 6·68. Calcd for $C_{14}H_{19}NO_3S$: C, 59·76; H, 6·80%).

N-Butyl phenacylsulfonamide, yield: 92%; m.p. 97–99; NMR ($CDCl_3$) δ 7·30–8·20 (m, 5H), 4·60 (s, 2H), 3·17 (t, 2H, J = 7 Hz), 0·7–1·8 (m, 9H). (Found: C, 56·62; H, 6·72. Calcd for $C_{12}H_{17}NO_3S$: C, 56·48; H, 6·71%).

N-Benzyl-N-phenyl-(α-benzylphenacyl)-sulfonamide. Benzyl bromide (3·40 g, 0·02 mol) was added to a suspension of N-phenyl phenacylsulfonamide (2·75 g, 0·01 mol) and K_2CO_3 (2·84 g, 0·02 mol) in acetone (30 ml). The reaction was stirred for 18–20 hr at room temp. The solvent was evaporated *in vacuo* and the residue extracted 5 × 30 ml $CHCl_3$. The combined $CHCl_3$ extracts were washed with 3 × 20 ml H_2O, dried (Na_2SO_4) and evaporated

Table 2. Triflamides as Gabriel reagents: Chart 1

R-	(P) mp (yield)	(D) yield	R^*-X alkylation mp (yield)	(D') yield
C_6H_5	66-67° (97%)	94%	CH_3I: liquid (94%)	90%
			C_3H_5I: liquid (93%)	90%
			ϕCH_2Br: 80-81° (97%)	89%
$C_6H_5CH_2$-	39-40° (96%)	95%	CH_3I: liquid (95%)	93%
			C_3H_5I: liquid (96%)	88%

Table 3. Primary amines via triflamides: Chart 1

Reagent	R-X alkylation	$R-\overset{+}{N}H_3\ Cl^-$
Ph-CH-NHSO$_2$CF$_3$ (Z)	product:yield/mp [a]	yield/mp
Z=H (mp 39-40°)	PhCH$_2$Br: 90%/mp 40-41°	84%/258° (lit. 255°) [b,c]
	n-C$_7$H$_{15}$Br: 97%/oil	80%/waxy solid [c]
Z=COOC$_2$H$_5$ (mp 71-73°)	PhCH$_2$Br	90%/258-9° (lit. 255°) [b,c]
	n-C$_7$H$_{15}$Br	78%/waxy solid [c]
	PhCH$_2$CH$_2$CH$_2$Br	65%/219° (lit. 218°) [b]
	PhCH$_2$CH$_2$Br	65%/216-8° (lit. 217°) [b]
	PhCH=CHCH$_2$Br	60%/232-4° (lit. 236°) [b]
	PhCHBr (CH$_3$)	53%/156-8° (lit. 158°) [b,c]
	EtOCOCHBr (CH$_3$) / Br — No reaction	
9-fluorenyl triflamide (mp 183-184°)	PhCH$_2$CH$_2$Br	80%/217-8° (lit. 217°) [b,c]
	PhCH$_2$CH$_2$CH$_2$Br	65%/217-8° (lit. 218°) [b]

[a] Intermediate isolated only for Z=H

[b] Dictionary of Organic Compounds, Fourth Edition, Oxford Univ. Press, 1965.

[c] Compared with authentic samples.

in vacuo. The residue was recrystallized from benzene/hexane affording 4·28 g (94%), m.p. 151–153°. NMR ($CDCl_3$) δ 7·10–7·90 (m, 20 H), 5·20–5·50 (m, 1H), 4·80 (s, 2H), 3·35–3·70 (m, 2H). (Found: C, 73·97; H, 5·50. Calcd for $C_{28}H_{25}NO_3S$: C, 73·82; H, 5·53%).

The following compounds were prepared by the same procedure as described for N - benzyl - N - phenyl(α - benzylphenacyl) - sulfonamide except the course of the reaction was monitored by TLC:

N - *Methyl* - N - *phenyl* - (α - *methylphenacyl*) - *sulfonamide*, yield: 93%; m.p. 101–102°; NMR ($CDCl_3$) δ 7·0–8·0 (m, 10 H), 5·15 (q, 1 H, J = 7 Hz), 3·30 (s, 3H), 1·62 (d, 3 H, J = 7 Hz).

N - *Cyclohexyl* - N - *methyl* - (α - *methylphenacyl*) - *sulfonamide*, yield: 80%; m.p. 106–107°; NMR ($CDCl_3$) δ 7·30–8·15 (m, 5 H), 5·10 (q, 1 H, J = 7 Hz) 2·75 (s, 3H), 0·97 (d, 2H, J = 7 Hz), 0·90–2·0 (m, 14 H).

N - *Butyl* - N - *methyl* - (α - *methylphenacyl*) - *sulfonamide*, yield: 78% (oil); NMR ($CDCl_3$) δ 7·30–8·20 (m, 5 H), 5·13 (q, 1H, J = 7 Hz), 3·15 (t, 2H, J = 7 Hz), 2·82 (s, 3H), 1·65 (d, J = 7 Hz), 0·8–1·8 (m, 12 H). (Found: C, 59·26; H, 7·57. Calcd for $C_{14}H_{21}NO_3S$: C, 59·34; H, 7·47%).

Aniline from N-*phenyl phenacylsulfonamide*. N-phenyl phenacylsulfonamide (2·75 g, 0·01 mol) was added to a stirred suspension of Zn dust (2·0 g) in glacial AcOH (25 ml) and concentrated HCl (5 λ). The mixture was warmed on a steam bath for 20 min and filtered. The filtrate was diluted with 30 ml H_2O, extracted with 5 × 30 ml ether and the combined ether extracts were washed with 10% $NaHCO_3$, dried (Na_2SO_4) and evaporated *in vacuo* leaving 0·94 g (78%) of acetophenone. The DNP derivative was made, m.p. 236–237° (lit. 237°).

The aqueous phase was covered with 60 ml ether and the pH was adjusted to 11·0 with 2N NaOH. The ether was separated and the aqueous phase extracted with 4 additional 30 ml portions of ether. The combined ether extracts were dried (Na_2SO_4), evaporated *in vacuo* to approx. 20 ml and saturated with dry HCl gas forming a white ppt. which was collected by vacuum filtration, yielding 0·93 g (72%) of aniline hydrochloride, m.p. 196–197° (lit. 198°).

The procedure for the Zn reduction of the other phenacylsulfonamides was the same. The yields and m.ps of the amine hydrochlorides are collected in Table 1.

N-*Benzyl triflamide*. Triflic anhydride[14] (14·1 g, 0·05 mol) in 50 ml of CH_2Cl_2 was added dropwise to stirred soln of benzylamine (10·7 g, 0·10 mol) in 150 ml CH_2Cl_2 at 0°. The mixture was allowed to warm to room temp and stirred for 1 hr. The mixture was then washed with 2 × 20 ml 10% HCl, 3 × 30 ml H_2O, dried (Na_2SO_4) and evaporated *in vacuo* leaving 1·0 g (93%) of a white solid which was recrystallized from $CHCl_3$/hexane; m.p. 39–40°; NMR ($CDCl_3$) δ 7·26 (s, 5H), 5·23 (s, 1H) 4·37 (s, 2H). (Found: C, 40·18; H, 3·40. Calcd for $C_8H_8F_3NO_2S$: C, 40·17; H, 3·37%).

N-*Phenyl triflamide*. The same procedure as for N-benzyl triflamide was followed. Yield: 97%; m.p. 66–67°; NMR ($CDCL_3$) δ 7·27 (s). (Found: C, 37·30; H, 2·67. Calcd for $C_7H_6F_3NO_2S$: C, 37·33; H, 2·68%).

N-*Benzyl-N-ethyl triflamide*. EtI (0·78 g, 0·005 mol) was added to a stirred soln of N-benzyl triflamide (1·18 g, 0·005 mol) and anhyd. K_2CO_3 (0·69 g, 0·005 mol) in acetone (50 ml). The reactants were stirred at room temp. for 14 hr. The acetone was evaporated *in vacuo* and the residue extracted with 3 × 25 ml $CHCl_3$. The combined $CHCl_3$ extracts were washed with 3 × 20 ml H_2O, dried (Na_2SO_4) and evaporated *in vacuo* leaving 1·21 g (91%) of a clear oil; NMR ($CDCl_3$) δ 7·35 (s, 5H), 4·50 (s, 2H), 3·36 (q, 2H, J = 6 Hz), 1·08 (t, 3H, J = 6 Hz). (Found: C, 44·92; H, 4·52. Calcd for $C_{10}H_{12}F_3NO_2S$: C, 44·94; H, 4·53%).

The following compounds were prepared by the same procedure as described for N-benzyl-N-ethyl triflamide:

N-*Benzyl*-N-*methyl triflamide*, yield: 95% (liq); NMR ($CDCl_3$) δ 7·35 (s, 5H), 4·38 (s, 2H), 2·75 (s, 3H).

N,N-*Dibenzyl triflamide*, yield: 90%; m.p. 40–41°; NMR ($CDCl_3$) δ 7·1–7·4 (m, 10H), 4·4 (s, 4H).

N-*Benzyl*-N-*heptyl triflamide*, yield: 97% (liq); NMR ($CDCl_3$) δ 7·34 (s, 5H), 4·50 (s, 2H), 3·25 (t, 2H, J = 7 Hz), 0·7–1·6 (m, 13H).

N-*Methyl*-N-*phenyl triflamide*, yield: 94% (liq); NMR ($CDCl_3$) δ 7·34 (s, 5H), 3·42 (s, 3H). (Found: C, 40·28; H, 3·42. Calcd for $C_8H_8F_3NO_2S$: C, 40·17; H, 3·37%).

E-*Ethyl*-N-*phenyl triflamide*, yield: 93% (liq); NMR ($CDCl_3$) δ 7·34 (s, 5H), 3·79 (q, 2H, J = 7 Hz), 1·12 (t, 3H, J = 7 Hz).

N-*Benzyl*-N-*phenyl triflamide*, yield: 97%; m.p. 80–81°; NMR ($CDCl_3$) δ 7·24 (s, 10H), 4·90 (s, 2H).

N-*Ethyl benzylamine from* N-*benzyl*-N-*ethyl triflamide*. N-benzyl-N-ethyl triflamide (2·67 g, 0·01 mol) in anhyd. ether (20 ml) was added dropwise to a stirred suspension of LAH (1·14 g, 0·03 mol) in anhyd. ether (75 ml). The mixture was refluxed for 3 hr and then cooled. The excess LAH was decomposed by dropwise addition of 3·5 ml water, 3·5 ml 15% NaOH and finally

10·5 ml H_2O. The mixture was then filtered, the ether layer separated, dried (Na_2SO_4) and evaporated *in vacuo* leaving 1·21 g (90%) of a liquid. The liquid was taken up in ether and saturated with dry HCl gas producing a white PPT which was collected by filtration, yielding 1·50 g (88%) of N-ethyl benzylamine hydrochloride; m.p. 183° (lit. 184°).

A general procedure for the reduction of primary triflamides to primary amines. The procedure of Gold and Babad[12] was followed using Red-Al[11] as the reducing agent. The reaction times were shorter and the course of the reaction was followed by TLC. The amines were characterized as hydrochloride salts.

Benzylamine from N-N-dibenzyl triflamide. N,N-dibenzyl triflamide (3·29 g, 0·01 mol) in DMF (8 ml) was added to a stirred suspension of NaH (0·24 g, 0·01 mol) in DMF (12 ml). The mixture was heated on a steam bath for 12 hr, allowed to cool, diluted with 200 ml ether and washed with 10 × 20 ml distilled H_2O. The ether phase was dried ($NaSO_4$) evaporated *in vacuo* leaving 1·76 g of an oil. The residue was taken in 10% HCl (30 ml) and THF (10 ml) and refluxed for 3 hr. The THF was evaporated *in vacuo* and the remaining aqueous phase was extracted with 5 × 30 ml ether. The combined ether extracts were dried (Na_2SO_4) and evaporated *in vacuo* leaving 0·8 g (75%) of benzaldehyde, identified as the DNP derivative, m.p. 237–238° (lit. 237°). The aqueous HCl was neutralized with 3 N KOH, extracted with 4 × 20 ml ether, the combined ether extracts dried (Na_2SO_4) and evaporated *in vacuo*, leaving 0·90 (84%) of benzylamine. A portion of the benzylamine was converted to the hydrochloride (by treating of an ether soln of the amine with HCl gas) and recrystallized from EtOH, m.p. 255–257° (lit. 255–258°).

N-heptylamine from N-benzyl-N-heptyl triflamide. The procedure was the same as that for benzylamine, yield: 80%; waxy solid compared with authentic sample.

DL-α-Phenyl-N-trifyl-glycine methyl ester. Triflic anhydride (14·1 g, 0·05 mol) in CH_2Cl_2 (30 ml) was added dropwise to a stirred suspension of DL-α-phenyl-glycine methyl ester hydrochloride[13] (10·05 g, 0·05 mol), and Et_3N (10·1 g, 0·1 mol) in CH_2Cl_2 (250 ml) at −78°. After the addition was completed (about 30 min), the mixture was allowed to warm to room temp and stirred overnight. The mixture was washed with 2 × 25 ml 10% HCl, 3 × 25 ml brine, dried (Na_2SO_4) and evaporated *in vacuo* to yield 12·86 g (87%). Recrystallization from CH_2Cl_2/hexane afforded 12·0 g (81%) white crystals; m.p. 71–73; NMR δ 7·45 (s, 5H), 6·50 (broad s, 1H), 5·37 (s, 1H), 3·80 (s, 3H). (Found: C, 40·52; H, 3·42; N, 4·90. Calcd for $C_{10}H_{10}F_3NO_4S$: C, 40·41; H, 3·39; N, 4·71%).

Cinnamyl amine from DL-α-phenyl-N-trifyl glycine methyl ester. DL-α-phenyl-N-trifyl glycine methyl ester (0·627 g, 2·1 mmol) and cinnamyl bromide (Aldrich; 0·394 g, 2·0 mmol) were dissolved in dry MeCN (10 ml). The soln was stirred at room temp. with anhyd. K_2CO_3 (0·567 g, 4·1 mmol) for 48 hr. The mixture was evaporated *in vacuo*, taken up in ether (30 ml) and 10% HCl (5 ml) and stirred at room temp for 1 hr. The 10% HCl was separated and the ether layer was extracted with two additional portions of 10% HCl. The combined aqueous fractions were evaporated *in vacuo*, dissolved in sat K_2CO_3aq and extracted with 5 × 25 ml ether. The combined ether extracts were dried ($MgSO_4$), saturated with dry HCl gas and evaporated *in vacuo* to yield 230 mg (70%). A sample recrystallized from MeCN/EtOH melted at 232–234° (lit. 236°).

The procedure for the other alkyl halides was essentially the same. With less reactive halides the reaction was carried out in refluxing CH_3CN (up to 80 hr for complete disappearance of the alkyl halide (TLC)) with the addition of the catalytic amount of KI. The yields and m.ps are collected in Table 3.

9-Fluorenyltriflamide. 9-Fluoreneamine hydrochloride (Aldrich 2·17 g, 10·0 mmol) was dissolved in a soln of Et_3N (2·02 g, 20·0 mmol) in 100 ml CH_2Cl_2. To this was added, dropwise at −78°, with stirring, a soln of triflic anhydride (2·82, 10·0 mmol) in 20 ml CH_2Cl_2. A ppt formed after about 2/3 of the anhydride has been added. After the addition was complete (about 30 min) the mixture was allowed to warm to room temp and stirred overnight. The mixture was filtered and the filtrate washed with 2 × 20 ml 10% HCl, 2X brine, dried (Na_2SO_4) and evaporated *in vacuo* to yield 2·2 g (70%). (The ppt was unreacted 9-fluoreneamine hydrochloride. The yield based on recovered starting material was 97%). The 9-fluorenyltriflamide was recrystallized from benzene; m.p. 183–184°; NMR (CD_3CN) δ 7·2–7·9 (m, 8H) 5·59 (s, 1H). (Found: C, 53·54; H. 3·13. Calcd for $C_{14}H_{10}F_3NO_2S$: C, 53·67; H, 3·22%).

1-Amino-3-phenylpropane from 9-fluorenyl triflamide and 1-bromo-3-phenylpropane. 9-Fluorenyl triflamide (313 mg, 1·0 mmol) and 1-bromo-3-phenylpropane (199 mg, 1·0 mmol) were dissolved in dry acetonitrile (10 ml). The resultant soln was stirred with anhyd. K_2CO_3 (276 mg, 2 mmol) at reflux for 16 hr. The mixture was filtered, evaporated *in vacuo*, taken up in THF (20 ml) and 10% HCl (5 ml) and stirred at room temp. 1 hr. The THF was evaporated *in vacuo* and the residue was extracted twice with ether. The ether was washed with two 5 ml portions of 10% HCl. The aqueous fractions were combined, evaporated *in vacuo* and the residue recrystallized from EtOH, yielding 110 mg (65%) of 1-amino-3-phenylpropane hydrochloride m.p. 217–218° (lit. 218°).

β-Phenethylamine. The procedure was the same as that for 1-amino-3-phenylpropane, yield of β-phenethylamine hydrochloride 80%; m.p. 217–218° (lit. 217°).

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