153. Structural Characteristics of the Carboxylic Amide Group

by **Pinakpani Chakrabarti** and **Jack D. Dunitz**

Laboratorium für Organische Chemie, ETH-Zentrum, CH-8092 Zürich

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Summary

Average bond distances and bond angles as well as conformational preferences in the φ and ψ torsion angles of carboxylic amides with different substitution patterns have been derived by analyzing data from many crystal structures retrieved from the *Cambridge Structural Database* (CSD).

As a continuation of our study of structural characteristics of the carboxylic ester group [1] we describe here results for the carboxylic amide group. As in the previous study [1], the experimental results were taken from the *Cambridge Structural Database* (CSD, version of January, 1981 with 30058 entries in the bibliographic file [2]). An initial search for the fragment C–CO–N yielded a subfile containing 2372 structures. This file was then searched for various classes of amides along the same lines as described [1], except that the criteria for accepting structures were slightly different (σ(C–C) $\leq$ 0.01 Å, $R \leq 0.09$).

Dimensions of carboxylic amide groups. – Average dimensions of primary, secondary and tertiary amide groups are given in the *Table.* The results do not differ significantly from those given by *Ramachandran et al.* [3] or, more recently, by *Benedetti* [4]. As with the esters, the variability in the geometry within each class is much larger than that expected from the standard deviations estimated in the individual analyses. In addition to differences among the substituents, differences in

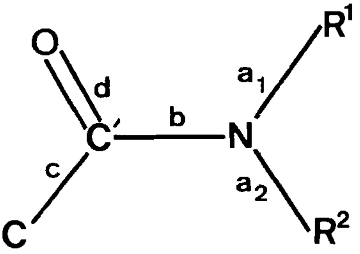

Fig. 1. *Explanation of symbols used in the* Table

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Table. *Standard dimensions* (distances in Å, angles in degrees) *of various types of carboxylic amide groups, based on structures with* σ *(C–C)* $\leq$ *0.010 Å* (See *Figure 1* for explanation of symbols. Distances and angles involving H-atoms are omitted because of their unreliability)

Amides	Distances					
	N	a_1	a_2	b	c	d
1) Primary; $R^1 = R^2 = H$	52	–	–	1.322(13)	1.520(18)	1.234(11)
2) Secondary						
a) trans(noncyclic); $R^1 = C(sp^3)$ $R^2 = H$	158	1.451(14)	-	1.331(11)	1.515(14)	1.231(11)
b) *cis*-δ-lactam; $R^2 = H$ $R^2 = C(sp^3)$	38	–	1.462(13)	1.332(11)	1.516(13)	1.234(11)
3) Tertiary; $R^1 = R^2 = C(sp^3)$						
a) noncyclic	16	1.472(7)	1.469(6)	1.346(10)	1.533(14)	1.228(9)
b) R^1–N–R^2 being part of a proline ring	24	1.471(11)	1.469(12)	1.335(9)	1.522(21)	1.234(11)

	Angles					
	a_1a_2	a_1b	a_2b	bc	bd	cd
1)	–	–	–	116.7(16)	123.0(12)	120.4(15)
2) a)	–	122.0(19)	-	116.1(13)	122.8(12)	121.1(13)
b)	–	–	124.8(33)	117.1(27)	122.7(11)	120.2(21)
3) a)	117.5(13)	117.7(14)	124.4(15)	118.7(12)	122.0(6)	119.2(12)
b)	111.8(13)	122.4(27)	125.5(33)	116.2(24)	122.4(19)	121.4(12)

H-bonding patterns may be responsible for this variability. The C′,O-distance in the carbonyl bond is significantly longer in a typical amide (~ 1.23 Å) than in a typical ester (~ 1.20 Å). The adjacent C,C′-bond also appears to be slightly longer (1.515–1.535 Å *vs.* 1.485–1.515 Å).

As pointed out in the ester study [1], interatomic distances derived from room-temperature crystal-structure data tend to be short and therefore are not directly comparable with results obtained by other methods for the isolated molecules. For amides in the solid state there is an additional complication: H-bonding. This leads to slight lengthening of the C′,O-carbonyl bond *d*, shortening of the C′,N-amide bond *b*, and compression of the N–C′–O bond angle *bd* [5]. Only when all these factors are taken into account is comparison possible between the dimensions listed in the *Table* for the various types of amide and results of gas-phase electron diffraction or *ab initio* calculations for isolated molecules [6].

Preferred conformations of substituents. – Histograms for C′–N–C–C or C′–N–C–H torsion angles in amides derived from primary, secondary and tertiary alkyl amines are shown in *Figure 2*. Compared with the corresponding esters, fewer examples are available and any conformational preferences that may be present are much less pronounced. Indeed, the only conclusion to emerge is that the C(α),C(β)-bond of an alkyl substituent avoids the synperiplanar orientation to the amide C′,N-bond. For the tertiary alkyl substituents, one of the three C(α),C(β)-bonds is always antiperiplanar to the C′,N-amide bond; but there are only five examples.

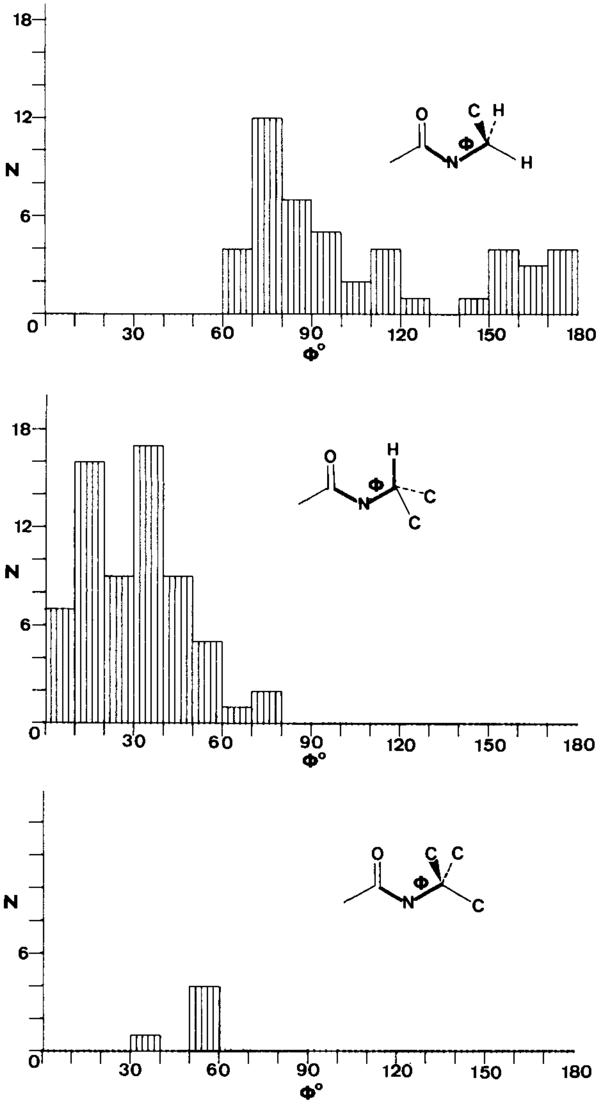

Fig. 2. *Histograms of C′–N–C–C (or C′–N–C–H) torsion angles φ* (absolute values) *in* N-*alkyl amides derived from primary, secondary, and tertiary amines* (of the three possible |φ| values for the tertiary case, only the one closet to 60° is counted)

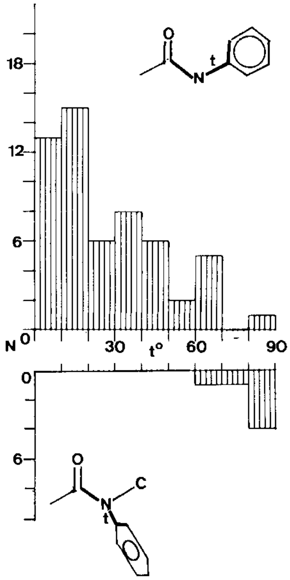

Fig. 3. *Histogram of C′–N–C–C torsion angles* (absolute values) *t for* N-*aryl amides*

Information for *N*-aryl amides is more abundant and is shown in *Figure 3.* While there is no very strong conformational preference for the secondary amides, the plane of the aromatic system does tend to lie closer to the plane of the amide group than perpendicular to it, in contrast to the corresponding esters [1]. In the few avail-

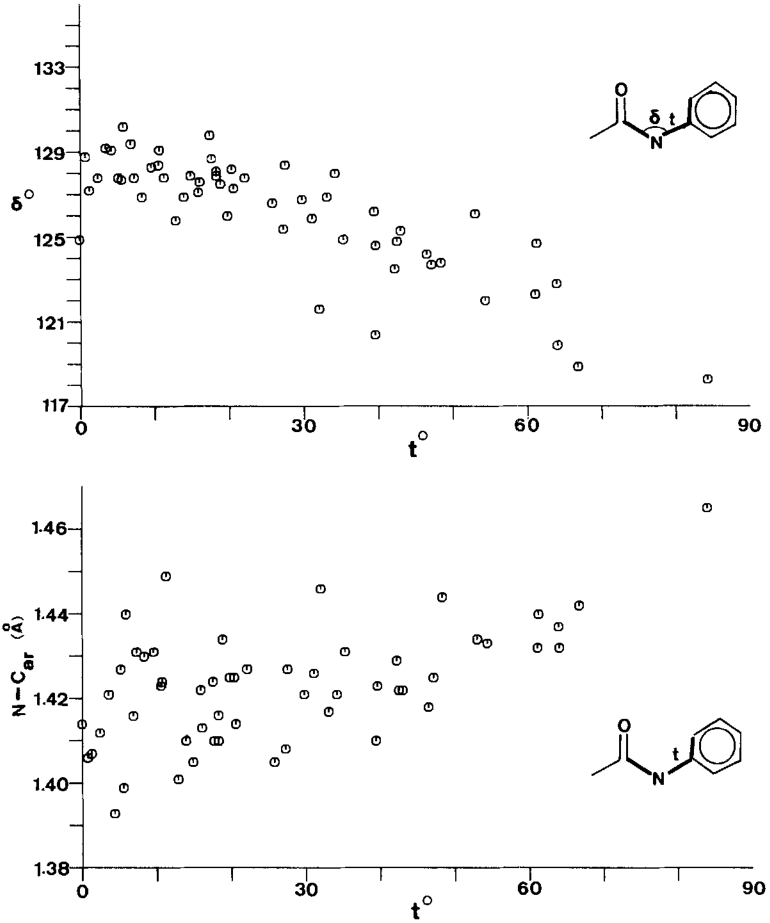

Fig. 4. *Scatter-plots of C–N–C–C torsion angle* t vs. *C′–N–C_{ar} angle δ and N,C_{ar} distance in* N*-aryl amides*

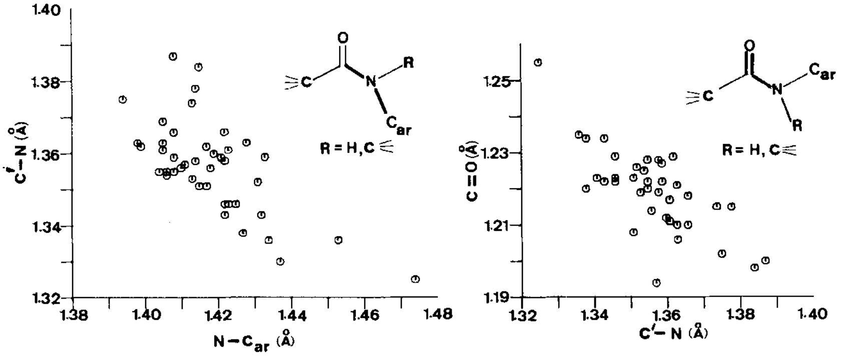

Fig. 5. *Scatter-plots of C′,N distance* vs. *N,C_{ar} and C′, O distances in* N*-aryl amides*

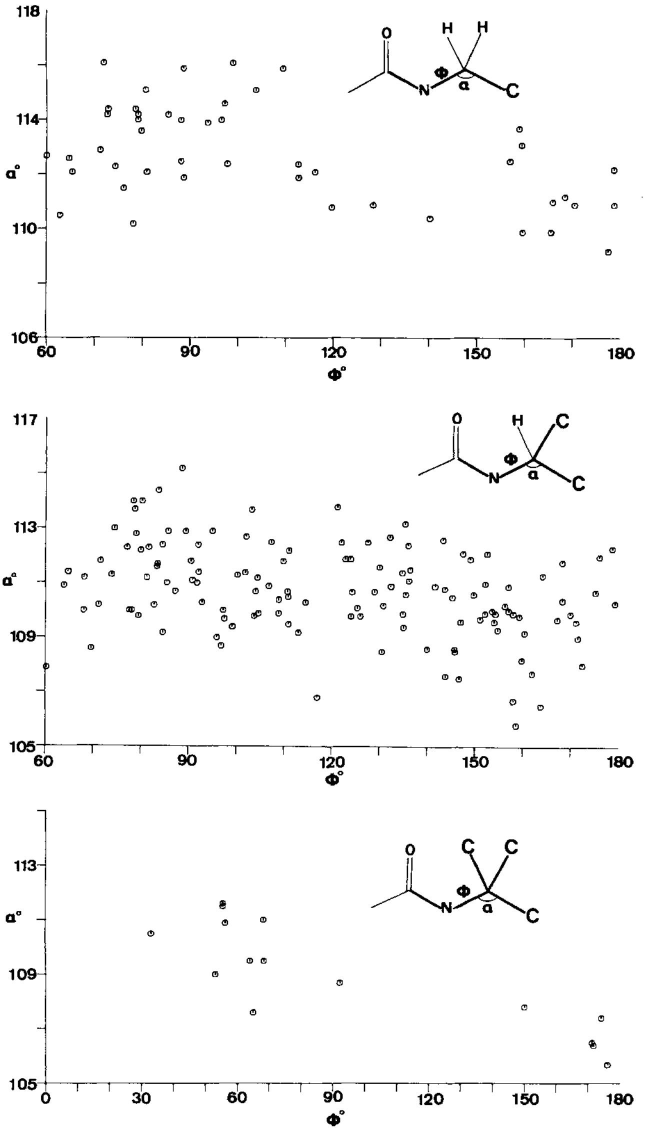

Fig. 6. *Scatter-plots of C'–N–C–C torsion angle φ vs. N–C–C bond angle α in the* N*-alkyl amides derived from primary, secondary, and tertiary amines*

able examples of *N*-alkyl anilides the aromatic substituent is always *anti* to the carbonyl bond and nearly perpendicular to the amide plane.

Figure 4 shows that as the dihedral angle *t* between the amide and aromatic planes decreases the C'–N–C_{ar} angle δ widens and the N,C_{ar}-bond distance contracts. The first correlation presumably has a steric origin, while the second is an expression of conjugation between the amide group and the aromatic system. The

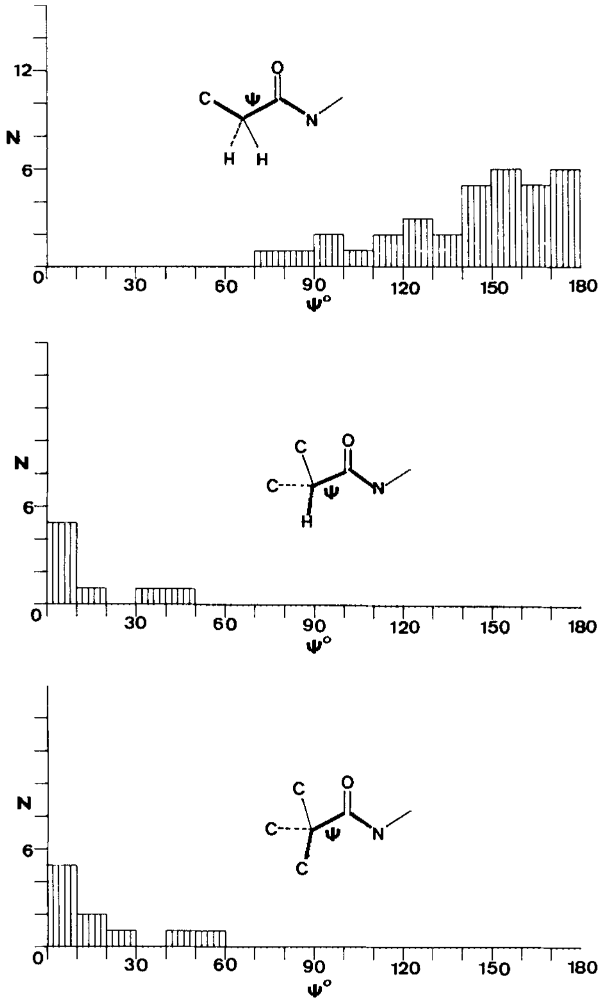

Fig. 7. *Histograms of C–C–C′–N (or H–C–C′–N) torsion angles* ψ (absolute values) *for alkyl substituents at the carbonyl end of primary and secondary amides* (of the three possible torsion angles for tertiary alkyl substituents only the one closest to zero is counted)

spread of the observed distribution at small *t* values is an indication that the N, C_{ar}-distance depends on other factors (such as the nature and position of substituents) as well. *Figure 5* shows that as the N, C_{ar}-distance shortens the C′, N-distance lengthens and the C′, O-distance shortens, *i.e.* conjugation between the amide and the aromatic substituent disturbs the normal amide conjugation. Only for large values of the dihedral angle *t* are the N, C_{ar}-, C′, N- and C′, O-distances the same as in alkyl amides *(Table)*.

In contrast to the corresponding parameters in esters, amides derived from primary and secondary amines do not show a strong dependence of the N–C–C

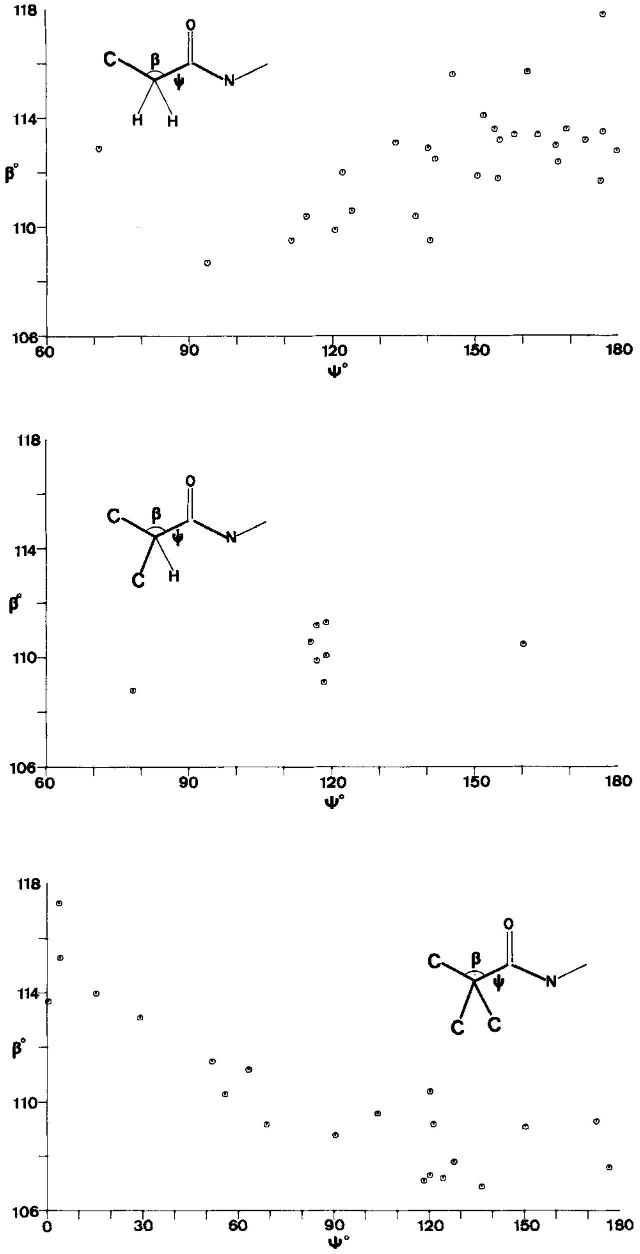

Fig. 8. *Scatter-plots of C–C–C′–N torsion angle ψ* vs. *C–C–C′ bond angle β for alkyl substituents at the carbonyl end of primary and secondary amides*

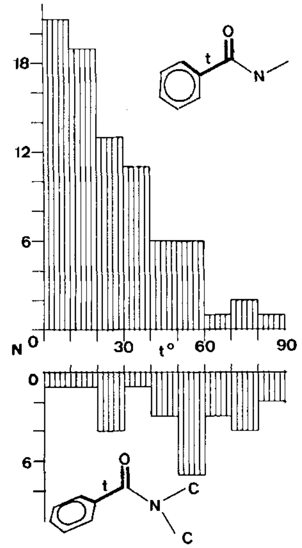

Fig. 9. *Histograms of C–C–C′–N torsion angles* (absolute values) *for aromatic substituents at the carbonyl end of primary and secondary amides*

bond angles on the C′–N–C–C torsion angle φ *(Fig. 6)*. If anything, the bond angles tend to be somewhat wider than the tetrahedral angle over the entire range of φ. The somewhat meagre information for amides derived from tertiary amines suggests that of the three N–C–C angles the smallest is always for the antiperiplanar C,C-bond ($\varphi \sim 180°$). This is the same pattern as found in the corresponding esters [1].

Figure 7 shows histograms for conformational preferences at the carbonyl end of the amide group. In amides derived from RCH_2–COOH type carboxylic acids, the tendency of the C(α),C(β)-bond to be synperiplanar to the carbonyl group is not as pronounced as in the corresponding esters. The C′–C(α)–C(β) angle tends to widen as the C(α),C(β)-bond approaches the synplanar orientation *(Fig. 8)*. The few examples of amides derived from R^1R^2CH–COOH and $R^1R^2R^3C$–COOH type carboxylic acids suggest that in these molecules there is a tendency for two C(α),C(β)-bonds to be ± synclinal of the carbonyl group rather than for one to be synplanar to it.

For amides with an aromatic substituent on the carbonyl group the data are more extensive *(Fig. 9)*. Primary and secondary amides of this type show a clear preference for the aromatic system to lie near the plane of the amide group; for tertiary amides the preference is often outweighed by steric factors.

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