Synthesis of 1,2,4-Triazole-Fused Heterocycles by Tandem Appel Dehydration/Thermal Rearrangement Methodology

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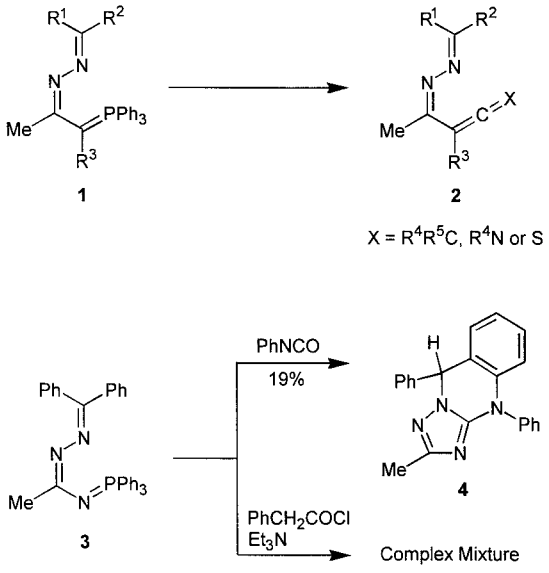
The reaction of α-substituted benzophenone 1-acetamidoethylidenehydrazones **6b,c** and **13a–d** with a mixture of triphenylphosphine, carbon tetrachloride, and triethylamine in dichloromethane (Appel's condition) provides a general route to a variety of 1,2,4-triazole-fused heterocycles such as compounds **9–11**, **16a–d**, **17b–d**, and **18** via the thermal rearrangement of the expected azino ketenimine intermediates.

The electrocyclic reaction of conjugated heterocumulenes as a synthetic route to heterocycles,[1] prompts us to report on our studies. We recently described a new route to 1,2,4-triazole-fused heterocycles such as 5,10-dihydro-[1,2,4]triazolo[5,1-*b*]quinazolines,[2] 4*H*-[1,2,4]triazolo[1,5-*c*][1,3,5]oxadiazines,[3,4] and 7*H*-imidazo[1,2-*b*][1,2,4]triazoles,[5,6] involving thermal rearrangement of azinocarbodiimides or *N*-aziridinyliminocarbodiimides obtained from the corresponding ureas using Appel's dehydration method.[7]

Also, Schweizer and co-workers reported that the reactions of azine ylides **1** with isocyanates, ketenes, and other species that contain carbonyl or thiocarbonyl moieties have provided excellent synthesis of a variety of pyrazolo-fused heterocyclic compounds via conjugated heterocumulenes **2**.[8]



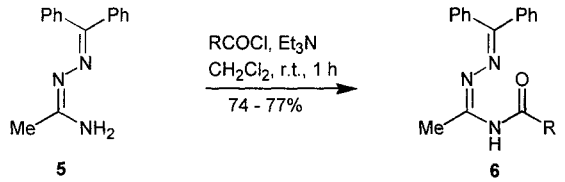
1 2 X = R^4R^5C, R^4N or S 3 4

However, aza-Wittig reaction of azino iminophosphorane **3** with phenyl isocyanate gave a poor yield (19%) of the 5,10-diphenyl-5,10-dihydro[1,2,4]triazolo[5,1-*b*]-quinazoline (**4**)[2] via carbodiimide intermediate. Reaction of **3** with phenylketene, generated in situ from phenylacetyl chloride and triethylamine, led to an extremely complex reaction mixture including benzophenone as indicated by thin layer chromatography; presumably **3** decomposed under the reaction conditions.

On the other hand, it is well known that ketenimines[9] are readily obtained from the dehydration of amides with triphenylphosphine dibromide,[10] phosphorus pentoxide[11] and dehydrochlorination of imino chlorides[12] produced from amides with phosphorus pentachloride. We now wish to report that ketenimines bearing azino moieties at the nitrogen atom, which are obtainable from the corresponding amides in the Appel's dehydration condition, give a variety of 1,2,4-triazole-fused heterocycles by thermal rearrangement.

The starting amides **6a–c** were obtained by the reaction of known benzophenone 1-aminoethylidenehydrazone (**5**)[2] with acid chlorides in the conventional way as shown in Scheme 1. Treatment of **6a** with triphenylphosphine, carbon tetrachloride, and triethylamine in dichloromethane at reflux temperature resulted only in the isolation of benzophenone (52%); presumably **6a** decomposed under the reaction conditions. Lack of acidity of the α-hydrogens is presumably responsible for this inertness. However, the reaction of aryl-substituted phenylacetamide **6b** led to the formation of three products which were separated by column chromatography. The first product was isolated as a white solid and assigned as one of the *cis*/*trans* stereoisomers of 2-methyl-5,10-diphenyl-5,10-dihydro[1,2,4]triazolo[1,5-*b*]isoquinoline (**9**, 9%) on the basis of the following spectral data.[13] A triazole ring was indicated by peaks at $\delta = 161.5$ (C2) and 154.0 (C10a) in the ^{13}C NMR spectrum. There was also a C2-methyl absorption at $\delta = 14.3$, as well as peaks at $\delta = 63.8$ (C5) and 44.8 (C10) for the dihydroisoquinoline ring. The second product was the other isomer of **9** (27%) and the ^{13}C NMR spectrum showed very similar absorptions. The third product was isolated as a white solid and was found to be the 2-methyl-5,5-diphenyl-5,10-dihydro[1,2,4]triazolo[1,5-*b*]isoquinoline (**10**, 10%). The ^{13}C NMR showed peaks at $\delta = 160.6$ (C2) and 152.8 (C10a) assignable to the triazole ring and at $\delta = 28.9$ (C5) and 44.3 (C10) for the dihydroisoquinoline ring, in addition to the aromatic and methyl peaks. In contrast, the diphenylacetamide **6c** yielded a single product, 2-methyl-5,5,10-triphenyl-5,10-dihydro[1,2,4]triazolo[1,5-*b*]isoquinoline (**11**) in a disappointing yield of 23%. Using excess Appel's dehydration reagent was also ineffective.[14]

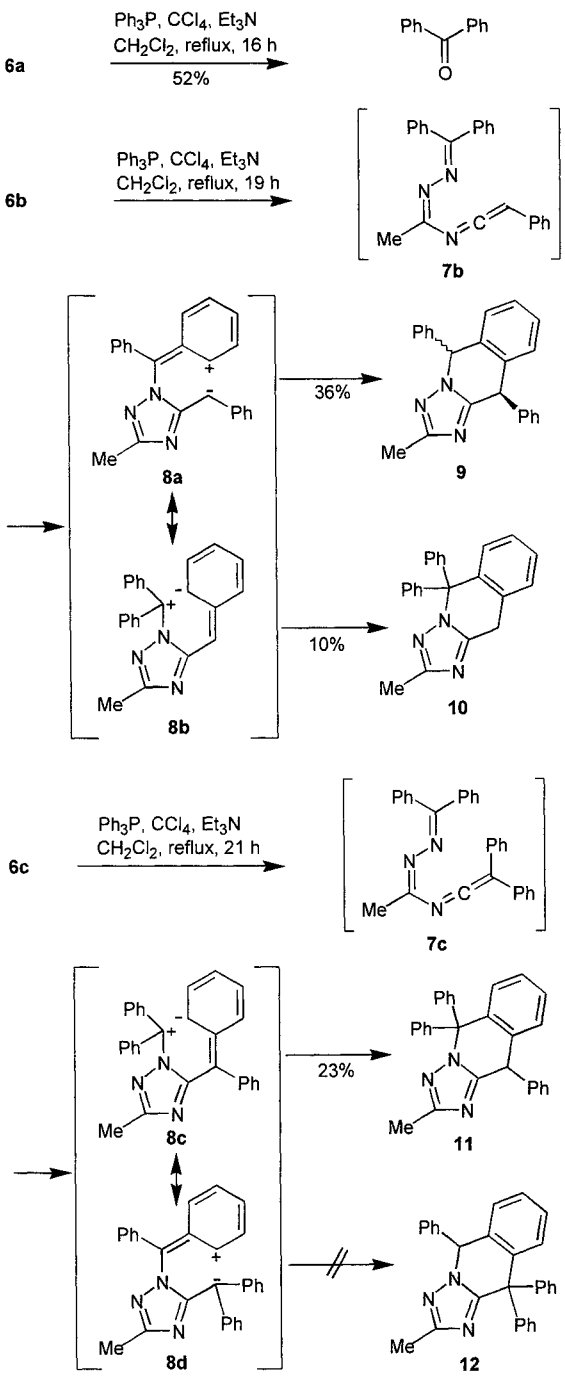
The proposed mechanism for formation of **9–11** is shown in Scheme 2. The presumed intermediate azino ketenimines **7** were too unstable to isolate, so the thermal reactions of **7** would give the resonance stabilized zwitterionic intermediates **8** followed by ring closure and rearomatization to give the products. In the case of **6c**, presumably unfavorable steric hindrance of tetrahedral triaryl-substituted carbanion in resonance form **8d** prohibited production of regioisomer **12**.



5 6

6	R
a	Me
b	$PhCH_2$
c	Ph_2CH

Scheme 1

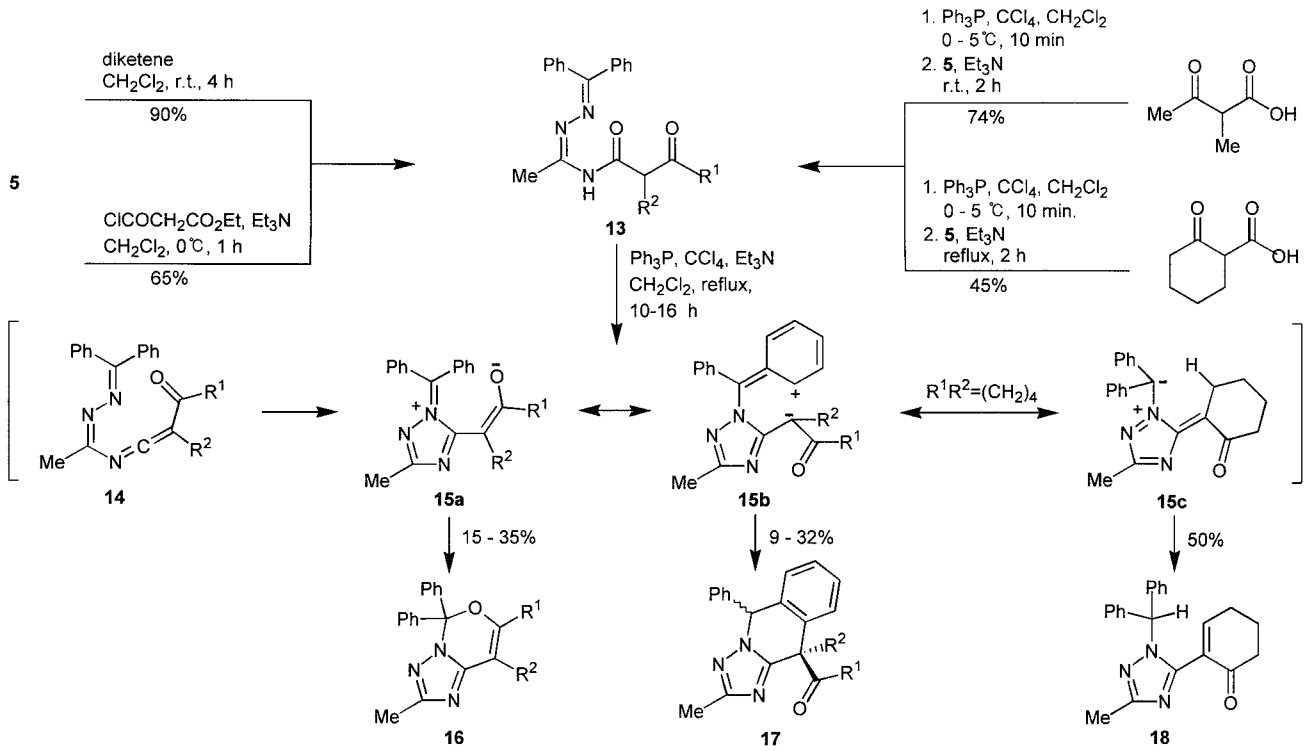


Scheme 2

Envisioning the synthesis of a variety of 1,2,4-triazole-fused heterocycles from azino ketenimines, we felt that the introduction of the electron-withdrawing group such as carbonyl group at the α-carbon atom of acetamide **6a** would promote dehydration and facilitate the formation of fused triazoles readily. In fact, treatment of acetoacetamide **13a**, which was readily obtainable by the reaction of **5** with diketene, under Appel's dehydration condition smoothly afforded *5H*-[1,2,4]triazolo[1,5-*c*][1,3]oxazine **16a** as the sole product in yield of 35%. The analog **13b**, which was produced by the reaction of **5** with 2-methylacetoacetic acid (generated in situ from hydrolysis of ethyl 2-methylacetoacetate)[15] under Appel's condition,[16] underwent similar reaction to furnish three isomeric heterocycles. One of the products was the expected *5H*-[1,2,4]triazolo[1,5-*c*][1,3]oxazine **16b** (21%). In addition, *cis*- and *trans*-isomeric 5,10-dihydro[1,2,4]triazolo[1,5-*b*]isoquinolines **17b** (23%, 6%) were isolable (Scheme 3).[13] As above, all structural assignments were based on spectral and analytical data. The characteristic absorptions of triazolooxazine **16a** in the ^{13}C NMR spectra appear as follows: $\delta = 14.3$ ($C2CH_3$), 20.2 ($C7CH_3$), 160.7 (C2), 96.1 (C5), 150.1 (C7), 94.1 (C8), and 157.8 (C8a). For **16b** found as follows: $\delta = 14.4$ ($C2CH_3$), 16.8 ($C7CH_3$), 10.9 ($C8CH_3$), 160.5 (C2), 95.3 (C5), 151.9 (C7), 101.1 (C8), and 151.7 (C8a). Interestingly, the ^1H- and ^{13}C NMR spectra of the *cis*- and *trans*-[1,2,4]triazolo[1,5-*b*]isoquinolines **17b** showed almost exactly same signals. The ^{13}C NMR exhibited peaks at $\delta = 162.0$ (C2) and 153.3 (C10a) assignable to the triazole ring and at $\delta = 63.4$ (C5) and 53.5 (C10) for the dihydroisoquinoline ring in addition to the aromatic, three methyl peaks ($\delta = 14.2$, 26.1 and 26.2) as well as a peak at $\delta = 202.2$ for the carbonyl carbon.

Although, the isolation of *N*-(azinoacyl)ketenimines **14** was unsuccessful under the reaction conditions, the thermal reactions of **14** would give the resonance stabilized zwitterionic intermediates **15a** or **15b**. Intramolecular alkylation of the enolate oxygen by the activated exocyclic Michael acceptor in **15a** would lead to the triazolooxazines **16a** or **16b**, while ring closure of the enolate carbon to one of the phenyl rings in **15b** would yield, after rearomatization of the phenyl ring, the *cis*- and *trans*-triazoloisoquinolines **17b** (Scheme 3). The reasons why the acetoacetamide **13a** only produces the triazolooxazine **16a** are uncertain.

The mode of reactivity of these acetyl stabilized azomethinimines (e.g., **15a** and **15b**) is dependent to a large extent on the nature of the substituents on the α-carbon atom. In order to probe the effect of perturbing the anionic portion of these zwitterionic intermediates, we have investigated the reaction of the enol form of 2-oxocyclohexanecarboxamide **13c**, which was produced by the reaction of **5** with 2-oxocyclohexanecarboxylic acid (generated in situ from hydrolysis of ethyl 2-oxocyclohexanecarboxylate)[17] under Appel's condition.[16] Two of the products were the expected spiro triazoloisoquinolinone **17c** (9%) and pentahydrotriazolobenzoxazine **16** (30%) by the *C*- and *O*-alkylation of the enolate **15b** and **15a**, respectively. In addition, significant amounts of the 5-(2-oxocyclohex-1(5)-enyl)triazole **18** (50%) was obtained.



13, 16, 17	R^1	R^2
a	Me	H
b	Me	Me
c	$-(CH_2)_4-$	
d	EtO	H

Scheme 3

Monocyclic triazole **18** can be derived from **15c** by a simple intramolecular proton transfer from the β-hydrogen of cyclohexenone to the anionic portion of the molecule (Scheme 3).[18]

Finally, to further probe the effect of substituents at the α-carbon atom on the course of these thermal reactions, we allowed ethyl malonamide **13d**, generated from the reaction of **5** with ethyl malonyl chloride, to react with a mixture of triphenylphosphine, carbon tetrachloride, and triethylamine. Thermal rearrangement of the resulting ethoxycarbonylketenimine **14** led to a complex reaction mixture from which we were able to identify three isomeric compounds. One of these was the triazolooxazine **16d** (15%) and the others were the *cis*- and *trans*-isomeric triazoloisoquinolines **17** (23%, 9%)[13] again. Triazolooxazine **16d** and triazoloisoquinolines **17** would result from *O*- and *C*-alkylation of the enolate portion of **15a** or **15b** as discussed above (Scheme 3). All structural assignments were based on, and are entirely consistent with, spectral and analytical data.

In conclusion, the above method demonstrates that the tandem Appel's dehydration/thermal rearrangement methodology, complementary to the tandem aza-Wittig/thermal rearrangement strategy, provides a new entry to the synthesis of a variety of 1,2,4-trazole-fused heterocycles. The advantage of the present method is the ready availability of the starting acid derivatives compared with the relatively unobtainable ketenes. There are some limitations as regards to the reactivity of simple aliphatic amides with Appel's dehydration reagent.

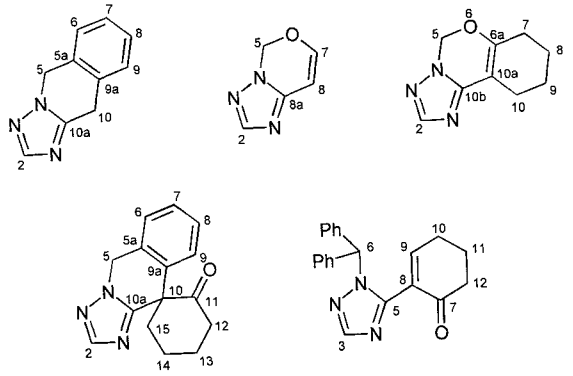
CCl_4 and CH_2Cl_2 were dried and distilled from P_2O_5. Et_3N was dried and distilled from sodium metal. Silica gel EM 7747 for column chromatography was used througout for product separation. Melting points were taken using an electrothermal melting point apparatus and are uncorrected. Microanalyses were obtained using a Perkin-Elmer 240 DS element analyzer. Compounds gave C, H, N analysis ±0.32%. IR spectra were recorded on a Nicolet Magna 550 FTIR spectrometer. ^1H and ^{13}C NMR spectra were measured on a Varian Gemini 300 spectrometer.

Benzophenone 1-aminoethylidenehydrazone (**5**) was prepared following the literature procedure.[2] In reporting NMR data, the numbering systems for a variety of heterocycles are as shown.

Benzophenone 1-Carboxamidoethylidenehydrazones 6a–c, 13a and 13d; General Procedure:

To a stirred solution of benzophenone 1-aminoethylidenehydrazone (**5**, 1.19 g, 5.0 mmol) in CH_2Cl_2 (20 mL) was added Et_3N (0.77 mL, 5.5 mmol) and RCOCl (5.5 mmol) in a dropwise manner at r.t. After stirring for 1 h at r.t., the reaction mixture was poured into H_2O (20 mL) and extracted with CH_2Cl_2 (2 × 20 mL). The combined extracts were dried ($MgSO_4$), concentrated to dryness, and crystallized from Et_2O/hexane to give **6a–c** as a pale yellow solid, while **13d** was obtained by column chromatography on silica gel eluting with hexane/EtOAc (3:1).

In the case of **13a**, diketene (0.57 mL, 7.5 mmol) was used and stirred at r.t. for 4 h. The resulting solution was concentrated to dryness, and chromatographed on silica gel column eluting with hexane/EtOAc (1:1) to give **13a** as a pale yellow solid (Table 1).



Benzophenone 1-(2-Methyl-3-oxobutanoylamino)ethylidenehydrazones; Typical Procedure for 13b and 13c:

To a solution of 85% KOH (2.18 g, 33 mmol) in H_2O (70 mL) was added ethyl 2-methylacetoacetate (4.32 g, 30 mmol). The mixture was stirred at r.t. for 16 h, then extracted with Et_2O (70 mL). The aqueous layer was treated with 1 N HCl (40 mL, 40 mmol) slowly at 0 °C and stirring was continued at 0 °C for 0.5 h. The mixture was extracted with Et_2O (2 × 100 mL), and the organic layer was separated, dried ($MgSO_4$), and concentrated in vacuo to give the crude 2-methylacetoacetic acid (1.69 g, 48%) as a pale yellow oil. Then a solution of Ph_3P (3.67 g, 14 mmol) and CCl_4 (8.7 mL, 90 mmol) in CH_2Cl_2 (50 mL) was heated at reflux temperature for 20 min. The reaction mixture was cooled to 0–5 °C, and crude 2-methylacetoacetic acid (1.69 g, 14.5 mmol) was added, then stirred

Table 1. Benzophenone 1-Carboxamidoethylidenehydrazones **6** and **13** Prepared

Product	Reaction Time (h)	Yield[a] (%)	mp (°C)[b] (solvent)	Molecular Formula[c]	^{1}H NMR ($CDCl_3$/TMS)[d] δ, J (Hz)
6a	1	72	88–90 (Et_2O)	$C_{17}H_{17}N_3O$ (279.3)	2.16 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 7.29–7.62 (m, 10H$_{arom}$), 9.39 (br s, 1H, NH)
6b	1	74	130–131 (Et_2O)	$C_{23}H_{21}N_3O$ (355.4)	2.42 (s, 3H, CH_3), 3.75 (s, 2H, CH_2), 7.19–7.46 (m, 15H$_{arom}$), 9.50 (br s, 1H, NH)
6c	1	73	114–115 (Et_2O)	$C_{29}H_{25}N_3O$ (431.5)	2.40 (s, 3H, CH_3), 5.00 (s, 1H, CH), 7.03–7.43 (m, 20H$_{arom}$), 9.56 (br s, 1H, NH)
13a	4	90	115–116 (EtOAc)	$C_{19}H_{19}N_3O_2$ (321.4)	2.33 (s, 3H, CH_3CO), 2.42 (s, 3H, CH_3), 3.57 (s, 2H, CH_2), 7.25–7.80 (m, 10H$_{arom}$), 10.67 (br s, 1H, NH)
13b	2[e]	74	83–84 (EtOAc)	$C_{20}H_{21}N_3O_2$ (335.4)	1.49 (d, 3H, J = 7.1, CH_3), 2.32 (s, 3H, CH_3CO), 2.42 (s, 3H, CH_3), 3.56 (q, 1H, J = 7.1, CH), 7.24–7.78 (m, 10H$_{arom}$), 10.25 (br s, 1H, NH)
13c	2[e]	45	142–143 (EtOAc)	$C_{22}H_{23}N_3O_2$ (361.4)	1.73 (t, 4H, J = 2.9, CH_2), 2.33 (m, 4H, CH_2), 2.49 (s, 3H, CH_3), 7.27–7.65 (m, 10H$_{arom}$), 9.88 (s, 1H, NH), 13.85 (s, 1H, OH)
13d	1	65	57–58 (Et_2O/pet.ether)	$C_{20}H_{21}N_3O_3$ (351.4)	1.28 (t, 3H, J = 7.1, CH_3), 2.44 (s, 3H, CH_3), 3.47 (s, 2H, CH_2), 4.24 (q, 2H, J = 7.1, CH_2), 7.30–7.78 (m, 10H$_{arom}$), 10.75 (br s, 1H, NH)

[a] Yield of isolated pure product.
[b] Uncorrected.
[c] Satisfactory microanalyses obtained: C ± 0.26, H ± 0.16, N ± 0.27.
[d] Recorded on a Varian Gemini 300 spectrometer.
[e] Reflux temperature.

Table 2. 1,2,4-Triazole-Fused Heterocycles **9–11**, **16a–d**, **17b–d**, and **18** Prepared under Appel's Conditions

Reactant	Reaction Time (h)	Product	Yield[a] (%)	mp (°C)[b] (solvent)	Molecular Formula[c]	IR (KBr)[d] ν (cm^{-1})	^{1}H NMR ($CDCl_3$/TMS)[e] δ, J (Hz)	^{13}C NMR ($CDCl_3$/TMS)[e,f] δ
6b	19	**9**	9	210–212 (Et_2O/hexane)	$C_{23}H_{19}N_3$ (337.4)	1512, 1459, 1346, 1293	2.32 (s, 3H, CH_3), 5.54 (d, 1H, J = 2.4, C10H), 6.59 (d, 1H, J = 2.4, C5H), 7.18–7.39 (m, 14H$_{arom}$)	14.3 (CH_3), 44.8 (C10), 63.8 (C5), 133.5 (C5a), 133.9 (C9a), 154.0 (C10a), 161.5 (C2)
			27	179–180 (Et_2O/hexane)	$C_{23}H_{19}N_3$ (337.4)	1512, 1453, 1346, 1288	2.37 (s, 3H, CH_3), 5.63 (d, 1H, J = 2.2, C10H), 6.54 (d, 1H, J = 2.2, C5H), 7.19–7.31 (m, 14H$_{arom}$)	14.3 (CH_3), 44.4 (C10), 63.6 (C5), 132.9 (C5a), 133.5 (C9a), 153.5 (C10a), 161.6 (C2)
		10	10	204–205 (Et_2O/hexane)	$C_{23}H_{19}N_3$ (337.4)	1507, 1448, 1411, 1314	2.40 (s, 3H, CH_3), 4.09 (s, 2H, CH_2), 6.87–7.36 (m, 14H$_{arom}$)	14.4 (CH_3), 28.9 (C5), 44.3 (C10), 131.4 (C5a), 133.5 (C9a), 152.8 (C10a), 160.1 (C2)
6c	21	**11**	23	181–183 (Et_2O/hexane)	$C_{29}H_{23}N_3$ (413.5)	1512, 1432, 1330	2.37 (s, 3H, CH_3), 5.46 (s, 1H, C10H), 6.94–7.32 (m, 19H$_{arom}$)	14.5 (CH_3), 45.0 and 45.1 (C10), 73.5 (C5), 134.9 (C5a), 139.2 (C9a), 155.0 (C10a), 160.6 (C2)
13a	10	**16a**	35	154–156 (EtOAc)	$C_{19}H_{17}N_3O$ (303.4)	1658, 1528, 1507, 1432	2.06 (s, 3H, C7CH_3), 2.39 (s, 3H, C2CH_3), 5.83 (s, 1H, CH), 7.21–7.40 (m, 10H$_{arom}$)	14.3 (C2CH_3), 20.2 (C7CH_3), 94.1 (C8), 96.1 (C5), 150.1 (C7), 157.8 (C8a), 160.7 (C2)

Table 2. (continued)

Reactant	Reaction Time (h)	Product	Yield[a] (%)	mp (°C)[b] (solvent)	Molecular Formula[c]	IR (KBr)[d] ν (cm^{-1})	^1H NMR ($CDCl_3$/TMS)[e] δ, J (Hz)	^{13}C NMR ($CDCl_3$/TMS)[e,f] δ
13b	15	**16b**	21	157–158 (EtOH)	$C_{20}H_{19}N_3O$ (317.4)	1657, 1528, 1507, 1432	1.97 (s, 3H, C8CH_3), 2.02 (s, 3H, C7CH_3), 2.40 (s, 3H, C2CH_3), 7.00–7.38 (m, 10 H_{arom})	10.9 (C8CH_3), 14.4 (C2CH_3), 16.8 (C7CH_3), 95.3 (C5), 101.1 (C8), 151.7 (C8a), 151.9 (C7), 160.5 (C2)
		17b	23	215–216 (Et_2O)	$C_{20}H_{19}N_3O$ (317.4)	1720, 1507, 1453, 1191	1.77 (s, 3H, C10CH_3), 1.93 (s, 3H, CH_3CO), 2.39 (s, 3H, C2CH_3), 6.58 (s, 1H, CH), 7.17–7.37 (m, 9 H_{arom})	14.2 (C2CH_3), 26.1 (C10CH_3 and CH_3CO), 53.5 (C10), 63.4 (C5), 132.9 (C5a), 133.0 (C9a), 153.3 (C10a), 162.0 (C2), 202.2 (CO)
			6	205–207 (Et_2O)	$C_{20}H_{19}N_3O$ (317.4)	1723, 1510, 1454, 1194	1.77 (s, 3H, C10CH_3), 1.93 (s, 3H, CH_3CO), 2.39 (s, 3H, C2CH_3), 6.58 (s, 1H, CH), 7.17–7.37 (m, 9 H_{arom})	14.2 (C2CH_3), 26.1 (C10CH_3), 26.2 (CH_3CO), 53.5 (C10), 63.4 (C5), 132.9 (C5a and C9a), 153.3 (C10a), 162.0 (C2), 202.2 (CO)
13c	15	**17c**	9	240–242 (EtOAc)	$C_{22}H_{21}N_3O$ (343.4)	1721, 1518, 1448	1.85 (m, 1H, CH), 2.00 (m, 2H, CH_2), 2.35 (s, 3H, CH_3), 2.45 (m, 2H, CH_2), 2.73 (m, 2H, CH_2), 3.68 (m, 1H, CH), 6.46 (s, 1H, C5H), 7.13–7.39 (m, 9 H_{arom})	14.2 (C2CH_3), 21.3 (C14), 25.9 (C13), 40.9 (C15), 43.7 (C12), 55.3 (C10), 63.3 (C5), 151.9 (C10a), 160.7 (C2), 207.9 (C11)
		16c	30	159–160 (EtOAc)	$C_{22}H_{21}N_3O$ (343.4)	1662, 1539, 1507, 1443	1.62 (m, 2H, CH_2), 1.73 (m, 2H, CH_2), 2.29 (m, 2H, CH_2), 2.40 (s, 3H, CH_3), 2.43 (m, 2H, CH_2), 7.21–7.40 (m, 10 H_{arom})	14.4 (C2CH_3), 21.5 (C8), 21.6 (C10), 22.2 (C9), 27.3 (C7), 95.6 (C5), 103.1 (C10a), 151.0 (C6a), 154.1 (C10b), 160.4 (C2)
		18	50	172–174 (EtOH)	$C_{22}H_{21}N_3O$ (343.4)	1683, 1507, 1421	2.05 (m, 2H, C11H_2), 2.35 (s, 3H, CH_3), 2.44 (dd, 2H, J = 10.2, J = 5.8, C10H_2), 2.56 (t, 2H, J = 7.1, C12H_2), 6.39 (s, 1H, C6H), 7.17–7.50 (m, 10 H_{arom}), 7.66 (dd, 1H, J = 11.9, J = 6.8, C9H)	14.2 (C3CH_3), 22.3 (C11), 26.4 (C10), 38.2 (C12), 65.8 (C6), 130.6 (C8), 151.6 (C5), 155.7 (C9), 160.2 (C3), 195.9 (C7)
13d	16	**17d**	23	144–146 (EtOH)	$C_{20}H_{19}N_3O_2$ (333.4)	1742, 1518, 1459	1.26 (t, 3H, J = 7.1, CH_3), 2.40 (s, 3H, C2CH_3), 4.22 (q, 2H, J = 7.1, CH_2), 5.34 (s, 1H, C10H), 6.47 (s, 1H, C5H), 7.23–7.63 (m, 9 H_{arom})	14.1 (CH_3), 14.2 (C2CH_3), 45.5 and 45.6 (C10), 62.5 (CH_2), 63.9 (C5), 148.2 (C10a), 161.6 (C2), 169.3 (CO)
			9	169–170 (EtOH)	$C_{20}H_{19}N_3O_2$ (333.4)	1740, 1520, 1459	1.25 (t, 3H, J = 7.1, CH_3), 2.40 (s,3H, C2CH_3), 4.22 (q, 2H, J = 7.1, CH_2), 5.33 (s, 1H, C10H), 6.46 (s, 1H, C5H), 7.22–7.62 (m, 9 H_{arom})	14.1 (CH_3), 14.2 (C2CH_3), 45.4 and 45.7 (C10), 62.5 (CH_2), 63.8 (C5), 148.3 (C10a), 161.6 (C2), 169.2 (CO)
		16d	15	179–180 (EtOAc)	$C_{20}H_{19}N_3O_2$ (333.4)	1630, 1507, 1432, 1223	1.37 (t, 3H, J = 7.0, CH_3), 2.36 (s, 3H, C2CH_3), 4.01 (q, 2H, J = 7.0, CH_2), 5.07 (s, 1H, C8H), 7.23–7.42 (m, 10 H_{arom})	14.0 (CH_3), 14.3 (C2CH_3), 65.5 (C8), 68.9 (CH_2), 97.1 (C5), 152.6 (C8a), 161.0 (C2), 162.6 (C7)

[a] Yield of isolated pure product in order of elution. *cis*- and *trans*-Stereoisomers **9**, **17b**, and **17d** were not determined.
[b] Uncorrected.
[c] Satisfactory microanalyses obtained: C ± 0.31, H ± 0.27, N ± 0.32.
[d] Recorded on a Nicolet Magna 550 FTIR spectrometer.
[e] Recorded on a Varian Gemini 300 spectrometer. Numberings shown in experimental.
[f] Only selected spectral data reported.

for 10 min, and again **5** (1.90 g, 8.0 mmol) and Et_3N (1.95 mL, 14 mmol) were added. The resulting solution was then stirred at r.t. for 2 h, and poured into H_2O (20 mL). The organic layer was separated, dried ($MgSO_4$), and concentrated to dryness in vacuo. The residue was chromatographed on a silica gel column eluting with hexane/EtOAc (2:1) to give **13b** (1.98 g, 74%) as a pale yellow solid. By the above method, compound **13c** has also been prepared by using ethyl 2-cyclohexanonecarboxylate (Table 1).

Preparation of 1,2,4-Triazole-Fused Heterocycles 9–11, 16a–d, 17b–d and 18 from the Amides 6b,c and 13a–d under Appel's Conditions; General Procedure:

To a stirred solution of the appropriate amide **6b,c** or **13a–d** (3.0 mmol) in CH_2Cl_2 (30 mL) were added Ph_3P (1.26 g, 4.8 mmol), CCl_4 (1.47 mL, 15 mmol), and Et_3N (0.66 mL, 4.8 mmol) at r.t. The mixture was heated at reflux temperature for the time indicated in Table 2, and the resulting solution was concentrated to dryness. The residue was chromatographed on silica gel column eluting with hexane/EtOAc (3:1) to give the products as white solids (Table 2).

In the case of **6a**, decomposition product, benzophenone (0.28 g, 52%) was obtained as a solid, mp 46–48 °C (petroleum ether) (Lit.[19] 47–48 °C).

^1H NMR ($CDCl_3$): δ = 7.42–7.81 (m, 10 H_{arom}).

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(1) Barluenga, J.; Palacios, F. *Org. Prep. Proced. Int.* **1991**, *23*, 1.
Gusar, N.I. *Russ. Chem. Rev.* **1991**, *60*, 146.
Gololobov, Y.G.; Kasukhin, L.F. *Tetrahedron* **1992**, *48*, 1353.
Eguchi, S.; Matsushita, Y.; Yamashita, K. *Org. Prep. Proced. Int.* **1992**, *24*, 209.
(2) Lee, K.-J.; Kim, S.H.; Kim, S.; Park, H.; Cho, Y.R.; Chung, B.Y.; Schweizer, E.E. *Synthesis* **1994**, 1057.
(3) Lee, K.-J.; Kim, S.; Kim, S.H.; Park, H.; Cho, Y.R.; Chung, B.Y. *Bull. Korean Chem. Soc.* **1995**, *16*, 73.
(4) Lee, K.-J.; Lee, Y.-S.; Song, D.-H. *Bull. Korean Chem. Soc.* **1995**, *16*, 1037.
(5) Lee, K.-J.; Kang, S.-U. *Tetrahedron Lett.* **1995**, *36*, 2815.
(6) Lee, K.-J.; Song, D.-H.; Kim, D.-J.; Park, S.-W. *J. Heterocycl. Chem.* **1996**, *33*, 1899.
(7) Appel, R.; Kleinstück, R.; Ziehn, K.-D. *Chem. Ber.* **1971**, *104*, 1335.
(8) Schweizer, E.E.; Cao, Z.; Rheingold, A.; Bruch, M. *J. Org. Chem.* **1990**, *55*, 6363, and references cited therein.
(9) For a review on synthesis and reactions of ketenimines, see: Krow, G.R. *Angew. Chem.* **1971**, *83*, 455; *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 435.
(10) Bestmann, H.J.; Lienert, J.; Mott, L. *Liebigs Ann. Chem.* **1968**, *718*, 24.
Aoyama, T.; Nakano, T.; Marumo, K.; Uno, Y.; Shioiri, T. *Synthesis* **1991**, 1163.
(11) Stevens, C.L.; Singhal, G.H. *J. Org. Chem.* **1964**, *29*, 34.
(12) Stevens, C.L.; French, J.C. *J. Am. Chem. Soc.* **1954**, *76*, 4398.
(13) *cis*- and *trans*-stereoisomers were not determined. The numbering systems are shown in the experimental section.
(14) The major product indicated by TLC was benzophenone.
(15) Reynolds, G.A.; Van Allan, J.A. *Org. Synth.* **1952**, *32*, 84.
(16) Barstow, L.E.; Hruby, V.J. *J. Org. Chem.* **1971**, *36*, 1305.
Yamada, S.; Takeuchi, Y. *Tetrahedron Lett.* **1971**, *39*, 3595.
Appel, R. *Angew. Chem.* **1975**, *87*, 863; *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 801.
(17) Benner, S.A.; Morton, T.H. *J. Am. Chem. Soc.* **1981**, *103*, 991.
(18) Schweizer, E.E.; Evans, S. *J. Org. Chem.* **1978**, *43*, 4328.
(19) Marvel, C.S.; Sperry, W.M. *Org. Synth. Coll. Vol. 1* **1941**, 95.