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A NEW ROUTE TO QUINAZOLINONES VIA INTRAMOLECULAR AZA-WITTIG REACTION

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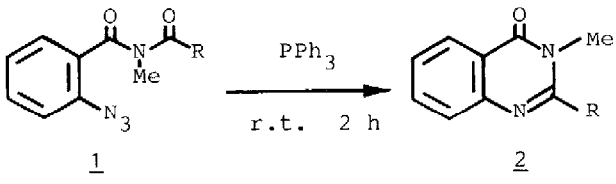
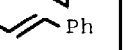
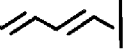
Summary: Treatment of the imide derivatives 1 and 3 readily obtainable from 2-azidobenzoyl chloride and the corresponding amide derivatives with triphenylphosphine or tributylphosphine in xylene at room temperature gave quinazolinones 2 and 4 in excellent yields via the Staudinger reaction, followed by the intramolecular aza-Wittig reaction.

The intramolecular aza-Wittig reactions have drawn considerable attention recently because of their high synthetic potential for nitrogen heterocycles.[1] The ready and clean generation of iminophosphoranes from azide, and their aza-Wittig type reaction with carbonyl group provides a regiospecific imine synthesis. Recently we reported the new synthesis of oxazole from β-(acyloxy)vinyl azide by intramolecular aza-Wittig reaction.[2] Ester carbonyls are unreactive generally in intermolecular aza-Wittig reactions but they react in intramolecular version. Therefore, we applied this reaction to imido carbonyl group and report here an efficient synthesis of quinazolinone derivatives 2 in milder conditions.

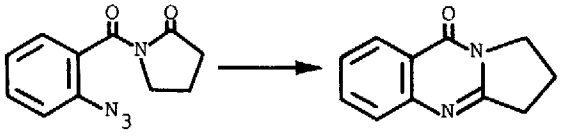


1 2

	R	Yield(%)	m.p.(°C)
a	Me	99	104-107
b		99	77-80
c		99	171
d		95	140-143

The starting imide derivatives 1 were readily obtained from 2-azidobenzoyl chloride and the corresponding amides. The reaction of 1 with an equimolar amount of triphenylphosphine (TPP) in xylene occurred spontaneously at room temperature. After stirring for 2 hr at room temperature, the quinazolinone derivatives 2 were obtained after preparative TLC or chromatography (silica gel, hexane-AcOEt system). The yields of 2 were higher than 95%. Usual synthetic method of quinazolinone derivatives requires strong acids as a catalyst or the heating at high temperature. In our method, the reaction

conditions were very mild (in neutral medium at room temperature). Thus, 2b-d were obtaind in high yields, although they have the substituents sensitive for acid and/or heating.



3 4

phosphorus reagent	temp(°C)	Yield(%)
PPh_3	140	99.5
PBu_3	r.t.	99

We applied this method to synthesis of deoxyvacisinone[3] 4. Azide 3 was treated with TPP in xylene for 5 h to afford compound 4, but in this case, the cyclization conditions required the heating conditions (140 °C). However, using tributylphosphine (TBP) instead of TPP could afford 4 at room temperature for 2 h. As the reacting carbonyl group is in the five membered ring of 3, it was expected to require a strained transition state in the four center reaction.[4] Therefore, TBP, which is more reactive and less hindered than TPP, afforded 4 in the milder conditions.

REFERENCES AND FOOTNOTES

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2. H. Takeuchi, S. Yanagida, T. Ozaki, S. Hagiwara, and S. Eguchi, J. Org. Chem., 1989, 54, 431.
3. M. F. Grundon, Natural Product Reports, 1988, 5, 293, and references cited therein.
4. An oxazaphosphetane intermediate was previously detected by NMR spectroscopy in the intramolecular aza-Wittig reaction of 7-endo-(azidomethyl)bicyclo[3.3.1]nonan-3-one: T. Sasaki, S. Eguchi, and T. Okano, J. Am. Chem. Soc., 1983, 105, 5912.

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